Hypertension and Stroke Control in the Community

WORLD HEALTH ORGANIZATION
HYPERTENSION AND STROKE CONTROL IN THE COMMUNITY

Proceedings of a WHO meeting held in Tokyo
11–13 March 1974

Edited by
S. HATANO
I. SHIGEMATSU
T. STRASSER

WORLD HEALTH ORGANIZATION
GENEVA
1974
CONTENTS

Preface ............................................. 6
Acknowledgements .................................. 6
List of participants ................................. 7
Welcoming addresses: Mr K. Saito .................. 13
Mr M. Arai ........................................ 14
Dr Y. Mikamo ....................................... 15
Opening address: Dr T. Strasser ................... 16
Introduction: Dr S. Katsuki ....................... 17

I. HYPERTENSION AND STROKE AS WORLDWIDE PROBLEMS

The worldwide problem of hypertension and stroke: Dr S. Hatano 19
Epidemiology of hypertension and stroke in various regions:
  Africa: Dr O. O. Akinkugbe ....................... 28
  Americas: Dr O. Paul ............................ 43
  Asia: Dr N. Kimura ................................ 55
  Europe and Mediterranean: Dr J. Richard .......... 60
  Japan: Dr T. Kobayashi .......................... 80
  Oceania: Dr A. Kagan ............................ 97

II. THE CONTROL OF HYPERTENSION AND STROKE IN POPULATIONS

A. Approaches

  The community approach to cardiovascular diseases:
    Dr T. Strasser .................................. 108
  The uses of hypertension registers: Dr T. Strasser .... 113
  Experiences with community stroke registers: Dr S. Hatano .... 117
A combined hypertension and stroke control programme in a Japanese community: Dr Y. Hirota .......................... 130

Problems of stroke control in rural settings in Japan: Dr K. Isomura .................................................. 141

Practical aspects of hypertension and stroke control in a rural population: Dr S. Kojima .......................... 149

The participation of physicians and patients: Dr. Y. Komachi .......................................................... 163

B. Methods

Measurement of blood pressure in the population: Dr Y. Fukuda ......................................................... 175

Use of eyeground examination in populations: Dr H. Arai .................................................................. 184

Diagnosis of hypertension in the community: Dr T. Omae ................................................................. 200

Diagnosis of hypertension: recent advances and possible applications: Dr H. Ueda ........................................ 204

Frequency and diagnosis of cerebrovascular diseases in aged people: Dr M. Kameyama ................. 211

Experience of hospital care for stroke patients: Dr K. Ito ................................................................. 219

Management of stroke in populations: Dr J. F. Toole ......................................................................... 233

III. BORDERLINE PATHOLOGY

A. Mild hypertension

The dilemma of mild hypertension: Dr A. E. Doyle ........................................................................... 240

Prognosis and pathology of mild hypertension and systolic hypertension in the aged: Dr M. Ikeda .... 248

Nine therapeutic trials in mild hypertension: Dr R. Reader .......................................................... 258

B. Transient cerebral ischaemia

Transient cerebral ischaemia as a community problem: Dr J. Marquardsen .................................... 279

Natural history of transient cerebral ischaemia as observed among the Japanese: Dr T. Omae .......... 284
IV. GUIDELINES FOR ACTION

Perspectives of hypertension and stroke control: Dr E. D. Freis .................................. 296
Antihypertensive therapy for stroke patients: Dr S. W. Hoobler ................................. 304
Stroke as an emergency problem: Dr E. V. Shmidt ....... 308
Rehabilitation of stroke patients in the community: Dr M. Weiss .................................. 316
From pilot studies to nationwide control: Dr S. Kakurai ................................. 326
Hypertension and stroke control in a large occupational group: Dr Y. Chiba .................. 330

V. SUMMARY AND RECOMMENDATIONS ................ 341

Closing addresses ................................................. 345
Annex .......................................................... 347
PREFACE

A WHO Meeting on the Control of Hypertension and Stroke in the Community was held in Tokyo on 11–13 March 1974.

The purpose of the meeting was to make a critical review of current knowledge on the control of hypertension and stroke and to establish guidelines for application at the community level. Participants from all continents presented up-to-date information and exchanged views.

This volume contains the papers and discussions from the meeting, which the authors and WHO hope will give incentives to postgraduate students, investigators in epidemiology and clinical and preventive medicine, clinicians, and public health administrators, and will also be a source of reference concerning the practice of community control of hypertension and stroke.

ACKNOWLEDGEMENTS

The meeting was largely financed by the Life Insurance Association of Japan (President, Mr M. Arai) and supported by the Ministry of Health and Welfare of Japan (Minister, Mr K. Saito), the Japan Circulation Society (Chief Director, Dr M. Takayasu), and the Japan Heart Foundation (President, Mr G. Kusano). The Japanese Preparation Committee (President, Dr T. Soda; Secretary-General, Dr I. Shigematsu) gave an enormous amount of ‘behind-the-scenes’ assistance, without which the meeting would not have proceeded so smoothly. WHO greatly appreciates the work of all those who kindly contributed to the meeting.

The additional contribution of the Life Insurance Association of Japan for publication of this volume is equally appreciated.
LIST OF PARTICIPANTS

Dr O. O. AKINKUGBE  
Dean, Faculty of Medicine  
University of Ibadan  
Ibadan  
Nigeria

Dr H. ARAI  
Chiba University  
Training Institute for School Nurses  
1 Yayoi-cho  
Chiba City  
Japan

Dr Y. CHIBA  
Central Health Institute  
Japanese National Railways  
2-1 Yoyogi, Shibuya-ku  
Tokyo  
Japan

Dr A. E. DOYLE  
Department of Medicine  
University of Melbourne  
Austin Hospital  
Melbourne, Victoria 3084  
Australia

Dr E. FRIES  
Veterans Administration Hospital  
50 Irving Street NW  
Washington, DC 20422  
USA

Dr Y. FUKUDA  
Central Health Institute  
Japanese National Railways  
2-1 Yoyogi, Shibuya-ku  
Tokyo  
Japan

Dr F. GROSS  
Pharmakologisches Institut  
Hauptstrasse 47-51  
6900 Heidelberg  
Federal Republic of Germany

Dr Y. HIROT A  
Department of Internal Medicine  
Kyushu Dental College  
Fukuoka  
Japan

Dr M. IKEDA  
Third Department of Internal Medicine  
Faculty of Medicine  
Tokyo University  
Hongo, Bunkyo-ku  
Tokyo  
Japan

Dr K. ISOMURA  
Saku General Hospital  
Usuda Town  
Minami Saku-gun  
Nagano  
Japan

Dr K. ITO  
Akita Prefectural Cerebrovascular Research Centre  
6-10 Senshu-Kubota-Cho  
Akita City  
Japan

Dr A. KAGAN  
Honolulu Heart Study  
347 North Kuakini Street  
Honolulu, Hawaii 96817  
USA

Dr M. KAMEYAMA  
Vice-President  
Tokyo Metropolitan Geriatric Hospital  
35 Sakaemachi  
Itabashi-ku  
Tokyo  
Japan

Dr S. KATSUKI  
Director, Kyushu Central Hospital  
882 Shiobaru, Minami-ku  
Fukuoka City  
Japan

Dr N. KIMURA  
Chief, Third Department of Internal Medicine  
Research Institute for Cardiovascular Diseases  
Kurume University Medical School  
67 Asahimachi, Kurume-shi  
Kyushu  
Japan
Dr T. KOBAYASHI
Professor of Internal Medicine
Tokyo University Branch Hospital
3-28-6 Mejirodai, Bunkyo-ku
Tokyo
Japan

Dr S. KOJIMA
Akita Prefectural Institute of Hygiene
Senshu-Meitoku-cho
Akita City
Japan

Dr Y. KOMACHI
Osaka Centre for Adult Diseases
3 Nakamichi 1-chome
Higashinari-ku
Osaka
Japan

Dr J. MARQUARDSEN
Department of Neurology
Frederiksberg Hospital
2000 Copenhagen
Denmark

Dr T. OMAE
2nd Department of Internal Medicine
Faculty of Medicine
Kyushu University
Fukuoka City
Japan

Dr O. PAUL
Passavent Memorial Hospital
303 East Superior Street
Chicago, Illinois 60611
USA

Dr R. READER
Director, National Heart Foundation of Australia
PO Box 691
Canberra
Australia

Dr J. RICHARD
Chief, Cardiology Department
National Institute of Health and Medical Research
3 Rue Léon Bonnat
Paris 16
France

Dr I. SHIGEMATSU
Institute of Public Health
4-6-1 Shirokanedai
Minato-ku
Tokyo
Japan

Dr E. V. SHMIDT
Director, Institute of Neurology
Academy of Medical Sciences of the USSR
Volokolamskoe Shosse 80
Moscow D.367
USSR

Dr J. F. TOOLE
Chairman, Department of Neurology
Bowman Gray School of Medicine
Wake Forest University
Winston-Salem, North Carolina
USA

Dr H. UEDA
Heart Institute of Japan
Central Hospital
Japanese National railways
3-47-8 Ogikubo, Suginami-ku
Tokyo
Japan

Dr M. WEISS
Chief, Rehabilitation Centre
Warsaw School of Medicine
Konstancin, Wierzejewskiego 12
Warsaw
Poland

Dr L. WERKÖ
Sahlgrenska Sjukhuset
Department of Medicine I
Faculty of Medicine
University of Göteborg
S-413 45 Göteborg
Sweden
GUESTS

Dr M. ARAI
President, Life Insurance Association of Japan
3-4-1 Marunouchi
Chiyoda-ku
Tokyo
Japan

Dr Y. GOTO
Professor of Medicine
Keio University Hospital
35 Shinano-machi, Shinjuku-ku
Tokyo
Japan

Dr Y. ITO
Professor of Medicine
Tokyo University Branch Hospital
3-28-6 Mejirodai, Bunkyo-ku
Tokyo
Japan

Dr S. KAKURAI
Director, Bureau of Public Health
Ministry of Health and Welfare
1-2-2 Kasumigaseki
Chiyoda-ku
Tokyo
Japan

Dr Y. MIKAMO
Vice President, Japan Heart Foundation Inc.
603 Marubiru
2-4 Marunouchi
Chiyoda-ku
Tokyo
Japan

Dr M. MURAKAMI
President, Tokyo Metropolitan Geriatric Hospital
35-2 Sakae-cho, Itabashi-ku
Tokyo
Japan

Dr H. OKADA
Professor of Preventive Medicine
Nagoya University School of Medicine
65 Tsurumai-cho, Showa-ku
Nagoya City
Japan

Dr N. SASAKI
Professor of Hygiene
Hirosaki University School of Medicine
5 Zaifu-cho
Hirosaki City
Japan

Dr T. SODA
Director, Institute of Public Health
4-6-1 Shirokanedai
Minato-ku
Tokyo
Japan

Dr M. TAKAYASU
National Kyoto Hospital
1-1 Fukakusa-Mukaihata-cho
Fushimi-ku
Kyoto
Japan

Dr Y. TATENO
Yasuda Mutual Life Insurance Co.
1-9-1 Nichishinjuku
Shinjuku-ku
Tokyo
Japan

Dr S. TORII
Nihon Mutual Life Insurance Co.
4-7 Inahashi
Higashi-ku
Osaka
Japan

Dr S. WAKATSUKI
Director, Saku General Hospital
Usuda-machi
Minamisaku-gun
Nagano Prefecture
Japan

Dr M. YOSHIKAWA
Department of Geriatrics
Faculty of Medicine
University of Tokyo
Bunkyo-ku
Tokyo
Japan
OBSERVERS

Dr M. ASHIZAWA
Secretary, WHO CVD Project Team
in Japan
Department of Epidemiology
Institute of Public Health
6-1 Shirokanedai 4-chome
Minato-ku
Tokyo
Japan

Dr D. S. DOCK
Chief of Medicine
Atomic Bomb Casualty Commission
5-2 Hijiyama Park
Hiroshima 730
Japan

Dr S. W. HOOBLER
Department of Internal Medicine
University of Michigan Medical Center
University Hospital
Ann Arbor, Michigan 48108
USA

Dr H. HORIBE
Department of Preventive Medicine
Nagoya University School of Medicine
65 Tsutsumi-cho, Showa-ku
Nagoya City
Japan

Dr H. KATO
Department of Statistics
Atomic Bomb Casualty Commission
Hiroshima
Japan

Dr K. KONDO
Chief, Section for CVD Prevention
Central Health Institute
Japanese National Railways
2-1 Yoyogi, Shibuya-ku
Tokyo
Japan

Dr T. MATSUZAKI
Division of Epidemiology
Tokyo Metropolitan Institute of Geriatrics
35-2 Sakae-cho
Itabashi-ku
Tokyo
Japan

Dr T. MIHARA
Meiji Mutual Life Insurance Co.
2-1-1 Marunouchi
Chiyoda-ku
Tokyo
Japan

Dr M. MIYANISHI
2nd Department of Internal Medicine
Shiroshima University School of Medicine
1-2-3 Kasumi-cho
Hiroshima City
Japan

Dr Y. MORISAWA
Department of Hygiene
Faculty of Medicine
University of Tokyo
Bunkyo-ku
Tokyo
Japan

Dr Y. OTAKE
Asahi Mutual Life Insurance Co.
1-7-3 Nishishinjuku
Shinjuku-ku
Tokyo
Japan
Dr T. OZAWA  
Department of Geriatrics  
Faculty of Medicine  
University of Tokyo  
Bunkyo-ku  
Tokyo  
Japan

Dr T. L. ROBERTSON  
Internist, Atomic Bomb Casualty Commission  
5-2 Hijiyama Park  
Hiroshima 730  
Japan

WHO STAFF MEMBERS

Dr S. HATANO  
Cardiovascular Diseases  
World Health Organization  
1211 Geneva 27  
Switzerland

Dr T. STRASSER  
Cardiovascular Diseases  
World Health Organization  
1211 Geneva 27  
Switzerland
WELCOMING ADDRESSES

By Mr Kunikichi Saito

I should like to extend my greetings to the experts from all over the world who have come to Tokyo to attend this meeting on the control of hypertension and stroke in the community. Ever since its establishment in 1948, WHO has been making great efforts in the control of cardiovascular diseases. I should therefore like to take this opportunity, on behalf of the government of Japan, to express our deepest gratitude and respect to WHO for this work.

In recent years we have seen great advances in medical science and its skills have contributed much to the health of our people. However, the mortality rate for cerebrovascular diseases is nowhere higher than in Japan and that for heart diseases ranks third; this demonstrates the urgent need for a comprehensive control programme, ranging from the prevention of these diseases to the rehabilitation of the patients. I sincerely hope that the presentations and discussions at this meeting will make a significant contribution to the cardiovascular diseases control programmes in countries in all parts of the world.

I should like to thank the participants and hope they will also find time to become better acquainted with Japan. I end these words with an earnest prayer for their happiness and prosperity.

* Minister, Ministry of Health & Welfare, Japan. (His message was read by Dr Susumu Shimada, Head, Tuberculosis and Degenerative Diseases Division, Ministry of Health & Welfare, Japan).
By Mr Masaaki Arai

It is my very great pleasure, as representative of the Life Insurance Association of Japan, to be given this opportunity to express words of welcome at this WHO Meeting in Tokyo.

Cardiovascular diseases, especially cerebrovascular and hypertensive diseases, present the most serious health problems in Japan at present. Therefore, nothing could have been more appropriate than this meeting, which has brought together experts from all over the world to discuss the measures for controlling these diseases in the community. I am certain that this will result in a very fruitful contribution to the policies against cardiovascular diseases not only in Japan but also all over the world.

The Life Insurance Association is a body made up of 20 life insurance companies in Japan. Of our numerous important undertakings, one is a grant for the development of medicine and public health. It is therefore both a pleasure and an honour that we could have the opportunity to provide financial support for this meeting. The Association hopes to strengthen its field of international cooperation in the future and I should like to ask each delegate to assist us in this endeavour. Lastly, I sincerely hope that this meeting will accomplish its objectives.
By Dr Yoshio Mikamo

It is a great pleasure for me, representing the Japan Circulation Society and Japan Heart Foundation, to deliver this welcoming address. Needless to say, cardiovascular diseases are the greatest cause of impairment or death among middle-aged and elderly people. The resulting loss is not only personal but also social and even national. It is well known that cerebral stroke is a number one killer, especially in Japan. The pattern of mortality statistics of the Japanese population is different from that in the USA and in some European countries where most deaths are due to heart attacks. Accordingly, the stroke problem is of national concern in Japan, like heart attacks in the USA and European countries. However, in recent times, the pattern of the mortality of the Japanese population is changing, shifting slowly towards that of the USA and European countries, probably as a result of the industrialization of this country and the changes in dietary habits of the Japanese people. Against this background, it is not by chance that this conference on hypertension and stroke control at community level, under the auspices of WHO, should be held in Tokyo.

We look forward to listening to your reports on your investigations and wish the meeting every success.
OPENING ADDRESS

By Dr T. Strasser

The world has never been static, it has always been changing, but somehow in this latter half of our century it seems to be changing more rapidly than before. Never have so many countries been born in such a short time and, in the fields of culture and science, never has mankind made such great efforts to achieve international cooperation.

Our values are also changing. Health has always been among the foremost concerns of the individual, but the notion of health is shifting nowadays from the individual to the concept of the health of entire populations.

Against this very general background, I should like to define why we are here. Important changes have occurred in our knowledge of cardiovascular diseases concerning treatment, prevention, and epidemiology in all parts of the world, but only a fraction of the available knowledge seems to be implemented for the benefit of entire populations. Therefore, it is becoming increasingly urgent that the advances in clinical medicine should be utilized in the health care of whole population groups; hence our topic is community control. Since hypertension and stroke are among the leading health problems in many countries, we shall be discussing the community control of hypertension and stroke. This is not a new subject because much has been done and even much more has been said about this topic during the past years, but whenever there is some advance it is useful to pause from time to time in order to look back and examine critically. Therefore, the objective of our meeting is to make a critical review of the present situation all over the world, to identify trends, and to outline priority problems in the community control of hypertension and stroke; also, conforming with the World Health Organization's striving for international coverage, we should like to try and do this on a global level.

Just one more word about why we are here. Besides the fact that hypertension and stroke are such pressing problems in Japan, it is Japanese hospitality which has brought us here. Allow me to express therefore the deepest appreciation of the World Health Organization to all those who helped to make this meeting a reality.

On behalf of Dr Halfdan Mahler, Director-General of the World Health Organization, I have the pleasure and the honour to welcome you and to wish you three busy and successful days.
INTRODUCTION

By Dr Shibanosuke Katsuki

It is a great pleasure and honour for me to give this introduction to the meeting on the control of hypertension and stroke in the community. And it is not without significance that this meeting should be held in Japan, since cerebrovascular disease is the most important cause of death in the Japanese population.

As I have been involved in WHO's activities on stroke from the start, I should like to give a brief account of the historical background to this meeting. In February 1964, Dr Millikan and Dr Moosy from the USA, Dr Yates from the United Kingdom, Dr Shmidt from the USSR, and myself from Japan were asked by Dr Fejfar, the then Chief of Cardiovascular Diseases, WHO headquarters, to meet in Geneva in order to discuss cerebrovascular diseases and the methods towards their control. Epidemiological and clinicopathological studies in the community, and the classification and differential diagnosis of cerebrovascular disease were suggested as the main points of WHO's programme. At that time, we had already started the Hisayama study, a prospective population survey in Hisayama town, Fukuoka, Japan, and I insisted on having the reliability of our results checked by careful follow-up of the population and by autopsy verification of the diagnosis of the disease. Our second meeting was held in Riga, USSR, in 1966, two years after the first meeting, and the discussions were extended further to include the methodology of the epidemiological approach.

In 1967 at the third meeting held in Moscow, USSR, the protocols for a prospective study were re-examined and simplified, and prospective studies were instituted to determine the frequency of the main cerebrovascular lesions in different populations. A pilot study was begun in 1968 in Fukuoka and Tokyo (Japan); in Riga, Moscow, and Ryazan (USSR); and in Prague (Czechoslovakia). Preliminary communications of these studies have been reported in a WHO report.

In 1970, a meeting was held in Monaco with 41 participants. The importance of the international cooperative study on cerebrovascular disease was again confirmed and the discussions were focused on the epidemiology of stroke, on classification and differential diagnosis, the care of stroke patients, and on prevention and stroke control programmes. A condensed report of the meeting has been published.2

The protocols were revised again at the next meeting in Göteborg, Sweden, in order to avoid technical difficulties. Registration programmes were started in 1971 in 13 centres in Denmark, Finland, Ireland, 

Israel, Japan, Sweden, the USSR, and Yugoslavia. In Japan, five centres in Akita, Fukuoka, Osaka, Saku, and Tokyo were started to operate the WHO programme. Progress of the study in each centre has been critically reviewed at the annual meetings of investigators and the methodology is continually being improved.

In 1972, I attended a WHO meeting in Geneva and had the opportunity to discuss the possibility of holding a WHO meeting in Japan in the near future. Thanks to the kind financial support of the Life Insurance Association of Japan and the continuous enthusiasm and preparatory work of WHO and the Japan Preparation Committee, we are able to meet together today.

As I mentioned before, the control and prevention of cerebrovascular disease and hypertension are among the most important health problems in Japan, as well as in other countries, and many research workers are actively contributing to this field. They should be encouraged and stimulated by hearing the presentations and discussions of experts in this field. It will also be our pleasure to show you some of the activities in this field in our country.

I cordially wish that the present meeting will be enjoyable and fruitful.
I. HYPERTENSION AND STROKE AS WORLDWIDE PROBLEMS

THE WORLDWIDE PROBLEM OF HYPERTENSION AND STROKE

by

S. Hatano

Size of the problem

The size of the problem differs according to how hypertension is defined, since blood pressure is a continuous variable in populations. A slight variation of measurement owing to the type of machine used, the examiner, or the subject can introduce a significant difference, particularly at the steeper part of the bell-shaped distribution curve of blood pressure, and the utmost care to minimize bias is needed in making geographical or chronological comparisons. A standardized technique has been described in WHO documents and is widely followed by many centres.

Any dividing line between "normal" and "high" pressure is, by nature, arbitrary. An expert committee convened by WHO in 1961 recommended operational criteria which, in spite of some inherent limitations, has helped in the screening of populations in various areas of the world.

An exhaustive review of the literature on the epidemiology of hypertension is not the purpose of the present paper, and our experience is referred to just as an example. In a cross-sectional population study of men aged 50-64 years in some places in Czechoslovakia, Japan, Sweden, and the USSR, hypertension was commonly observed, although the prevalence of subjects with systolic blood pressure of 160 mmHg and above varied, e.g., from 10 to 33% in men aged 50-54 years. In other areas where blood pressure was measured in a population, hypertension is invariably present in about 10-20% of middle-aged people. The number of hypertensives in the population is enormous. In the USA, for example, 22 million people are estimated to have hypertension. However, in some areas of the world, in people who are either living in a primitive way or residing at high altitudes blood pressure does not rise with age. These populations are exceptions and their number is small, but the reasons for this and the possible therapeutic application deserve further study.

Cerebrovascular disease has been discussed together with hypertension at several WHO meetings, since stroke is one of the major consequences of hypertension and the control of hypertension is one of the best ways of
preventing stroke. Stroke is a disease with usually typical signs and symptoms of sudden onset, and the clinical diagnosis is reasonably accurate. Although large differences have been reported in the mortality rate from stroke, this condition usually ranks as the third commonest cause of death in many countries. This feature is different in ischaemic heart disease or rheumatic heart disease, both of which are distributed quite unevenly in the world. Worldwide collaboration is desirable and should help to promote the control of hypertension and stroke, since both are so prevalent everywhere.

What is the situation of stroke in the world? According to the available national mortality statistics, mortality from stroke is decreasing continuously in many countries (Fig. 1). A reason for this may be that potent modern treatment has been effectively given to a number of severe hypertensive patients with a high risk of stroke, preventing the stroke and contributing to the decline of mortality from stroke. Likewise, the relative frequency of the types of stroke may have changed, i.e., the percentage of intracerebral haemorrhage, which is highly fatal and is more closely associated with high blood pressure, may have decreased and the percentage of cerebral infarction, which is less closely associated with high blood pressure and is less fatal, may have increased. The decreasing mortality trend, however, started long before the introduction of new antihypertensive drugs, and it is unknown to what extent this trend is due to treatment.

Another possibility is that many severe stroke patients who would have died from the attack itself or from complications were able to survive because of improved general medical care and died later from other diseases. It is therefore unknown whether the decline of stroke mortality is coupled with that of stroke incidence. Reduced case fatality may in fact have increased the number of survivors from stroke who need the support of the community.

Decrease in mortality from stroke differs by country. Even the largest reductions observed in some countries should not be regarded as perfect. By the successful countrywide control of hypertension, an even larger fall in stroke mortality might be achieved.

Hypertension and cardiovascular disease

Should we attempt to treat a huge number of people? A report based on a large number of healthy applicants for life insurance gives us a clear answer about the increased mortality associated with a modest rise of blood pressure. Not only total mortality, but also the incidence of acute myocardial infarction, cerebral haemorrhage, and cerebral infarction increase with the level of blood pressure. Most epidemiological observations from different countries support this. Modern antihypertensive drug therapy can reduce high blood pressure effectively and can reduce the excess risk significantly. But we still do not know enough about the effects of treatment of mild hypertension.

When considering treatment, various other aspects of the patients should be taken into account, where possible. The risk of dying in a 10-year period is three to five times as high where one or two other risk factors (cigarette smoking and/or hypercholesterolaemia) exist.
The evolution of hypertensive disease can be differentiated into three stages: hypertension without organ damage, hypertension with changes in the heart and arteries only, and hypertension with other organ damage. From the point of view of prevention, the first two stages are the most important for taking action.
It is also important to identify hypertension resulting from known causes. When the cause of hypertension is understood, the possibility of rational and radical therapy increases. Antihypertensive drug therapy is, after all, a symptomatic treatment, and cannot treat the cause of the disease, thus necessitating continued therapy. In the majority of cases, the cause of hypertension is unknown and research is needed on its etiology and mechanisms in order to prevent or treat it without imposing on a patient drug-treatment for possibly his lifetime.

How we can distinguish secondary hypertension, which will benefit from treatment of the cause, from among the almost 10-20% of the total population who are hypertensive is an open question. The prognosis of glomerulonephritis is rather poor, and renal parenchymal hypertension does not account for a substantial part unless the population concerned is young, particularly in tropical areas. Chronic pyelonephritis is not rare but its actual implication is not yet clearly determined. The possible benefits should be weighed against the tremendous logistic problems of making detailed examinations of a large number of patients. Early detection using simple diagnostic methods needs to be developed.

A recent report by Brunner, Laragh and co-workers on high, normal, and low renin levels is another approach to differentiate hypertensive patients with different degrees of risk, which is awaiting further tests and confirmation. The progress of technology is very rapid and the measurement of renin and angiotensin may soon become a common practice once this hypothesis has been proved to be valid.

The same applies to the role of ophthalmoscopic examination. There is no doubt about the usefulness of ocular fundus examination in clinical medicine, but the quality and amount of additional information from fundus examination in mass screening has yet to be demonstrated.

Community problem

Because of the large number of people involved, the problem of controlling hypertension cannot be dealt with by a single institution, and requires the acceptance, willingness, and cooperation of the entire medical corps in each community. This creates a diversion of resources and perhaps a more rational use of medical resources and physicians' time, according to the needs of a community; and it may hopefully restore the former role of the physician in the community as a teacher of family health or a leader of public health.

Also required are the understanding and participation of the government at various levels, as well as of the general public. Patients with no symptoms who may experience uncomfortable side-effects from treatment may respond entirely differently from patients visiting a physician with various complaints and expecting drugs. The experiences obtained at a high-powered, advanced hospital centre cannot therefore be made generally applicable to a community before they have been tested at the community level.

Preventive medicine

Preventive medicine is taken for granted as the main stream in the control of communicable diseases, and this concept is also increasingly
accepted in non-communicable disease control, though still not nearly
enough. To know is one thing, to do another. Everybody agrees that
prevention is better than treatment, and is perhaps achieved at a much
lower cost. The successful saving of the lives of thousands of people may
not be as spectacular and appealing as one heart transplant, even if the
latter is a failure. Preventive cardiology needs more support.
Insufficient recognition of the possibility of prevention of many cardio­
vascular diseases is itself a highly prevalent community failing.

Lack of awareness of the risks and of disease, reluctance to consult
a physician, and inadequate treatment and follow-up are also common problems
in a community. Modern industry is in the process of rapid development in
the application of new laboratory discoveries to mass production at the
factory level, but still the progress of preventive medicine at the
community level is disappointingly slow. WHO hopes to promote a compre­
prehensive and well-balanced development in order to fill the gap between
knowledge about hypertension and stroke control and its implementation in
the community.

Community services

Are mass health examinations necessary for the community control of
hypertension and stroke? The answer should be "yes", but only under
certain conditions. All subjects, once their risks have been identified
by screening, must have adequate medical supervision. If the latter
cannot be provided owing to a shortage of physicians or the high cost of
drugs, for example, there is no point in screening in the community at
large; it may even be harmful just to warn them while depriving them of
effective treatment, and to give them cause for anxiety without relief.

The provision of a valid automatic sphygmomanometer in public places
and the encouragement of do-it-yourself measurement from time to time, with
advice on when to consult a doctor, or the measurement of blood pressure at
every medical consultation may be cheap, alternative approaches to mass
screening, but again good after-care must be readily available to all who
need it.

Periodic home visits by a nurse or social worker may be indispensable
to motivate hypertensive patients to continue their therapy; also, the
teaching of practical rehabilitation procedures to members of a stroke
patient's family should be most helpful. The training and use of other
kinds of assistants, such as the barefoot doctor or volunteers, may be more
practicable in some places. Information services to first-line physicians
about progress and about modern concepts of diagnosis and treatment of
various common diseases are also very necessary.

Stroke patients are, like all of us, ordinary members of the popula­
tion, and they need their own living space, recreation, participation, and
also money. Day hospitals and places for meeting may be useful. For the
increasing number of lonely patients, social services including meals-on­
wheels, washing of clothes, house-cleaning, and chiropody are perhaps more
important than medical rehabilitation. These do not require highly
professional skills, and depend mainly on the finances and the organization
of the goodwill of other members of the community, including the decision­
makers in the government.
The best method for one place at one time may not necessarily apply to another place at another time. Control measures should be adapted to local conditions, in order to use the existing services most effectively.

Comprehensive cardiovascular disease control

The prevention of stroke mortality can be set as one of our main goals for stroke control. However, is it desirable to reduce the mortality from stroke while the early mortality from myocardial infarction is increasing? And what about the following situations: a decrease in the relative share of stroke mortality to be soon replaced by an increase in cancer mortality? A decrease in the incidence of intracerebral haemorrhage to be compensated by an increase in cerebral infarction? And decreasing the fatality rate of stroke by increasing the number of vegetating patients? Comprehensive approaches are essential in any community action, and cardiovascular disease control is meaningful only when it can be integrated into a part of the general national health programme.

In one European town, seven cardiovascular disease projects were being carried out simultaneously by different parties. One resident may be invited many times for blood pressure measurement - which is not bad. However, venous blood may be drawn while fasting on one occasion, and post-prandial or casual on other occasions. A patient may be warned by one party to consult a physician, another party may invite him for a more detailed examination, and yet another may tell him that he is a borderline case and need not worry. The need for coordination is therefore apparent.

Obviously, individual programme operation is a necessary step to test the feasibility of a programme and improve its effectiveness. A variety of cardiovascular disease programmes have been initiated by WHO in cooperation with a number of national centres, particularly in Europe, with a view to later integration of these programmes. Single and multiple factor prevention trials for ischaemic heart disease, various cardiovascular disease registers, and a study of the early signs and symptoms of acute myocardial infarction are all being carried out. Except for primary prevention trials, the other studies were started as a logical development from the community register of acute myocardial infarction, according to the interests and facilities at the individual cooperating centres. Thus, no additional organizational effort was required in these centres and the programmes are well integrated in the comprehensive control of acute myocardial infarction. This pattern of the systematic development of research presents an excellent model for the planned and systematic building up of control programmes.

WHO is now giving more consideration to setting up comprehensive cardiovascular disease control programmes in the community. All the principles and experiences gained in an individual programme, including those on hypertension and stroke control, are precious resources and will, of course, be included to the greatest possible extent in the comprehensive cardiovascular disease control programmes.
REFERENCES


**DISCUSSION**

Dr Werkö: You showed that the decrease in stroke was more apparent in Sweden during the period you mentioned than in any other country. This certainly cannot be due to efficient treatment of hypertension because we have exactly the same experience as any other country, namely, that only a fraction, perhaps 20%, of those who are hypertensive are under adequate treatment. This means that we have to search for other factors of importance for stroke and for explaining why mortality has decreased during this period. I do not think it is due to better care either, during the acute phase of the stroke.

Dr Hatano: Dr Yates also showed that the decrease in mortality in intracerebral haemorrhage in the United Kingdom started a long time before the introduction of effective hypotensive drugs, i.e., approximately 1930.

Dr Strasser: This is certainly a very interesting fact, and I should like to ask what else has been changed? Are the risk factors associated with stroke changing? Have the risk factors decreased? Has salt intake changed, or obesity, or other factors that may be associated with such a trend?

Dr Werkö: During this period I don't think that any of the known risk factors in the population changed. The standard of living has improved. We find in some reports from Japan that there is some relation between low income and low social class and a high death rate from cardiovascular and cerebrovascular causes and that may give some hint as to how this is connected. This change in stroke incidence does not seem to be associated with any alteration in obesity, hyperlipidaemia, treatment of high blood pressure, or smoking.

Dr Hatano: There are several studies in Japan concerning the effect of nutrition on stroke and hypertension; for example, Dr Murakami suggested that a high protein or a high fat diet would be protective against intracerebral haemorrhage. Dr Ueda indicated that a high protein diet appeared to have a protective effect against hypertension in spontaneously hypertensive rats. I wish to stress another point, namely, that mortality from cerebrovascular disease in Japan started to decrease some years ago. It is possible that the recent spread of hypertension control in Japanese communities might have contributed to the decline of the death rate from stroke.
Dr Reader: I should like to express a contrary view to that of Dr Werktö and several other people about whether this trend is due to improved treatment, because I believe it could. I think it is easy to say that in your country and in our country hypertension is badly treated, and to a certain extent it is. But there are a lot of patients in your country and in my country who are well treated. Now I suggest that you look at the quantitative aspects of the problem. In Australia, the mortality rate from stroke in adults under 65 years has fallen from 82 to 60 per 100 000. That means that 1000 fewer people died in a year. In Australia the number of people with well-established hypertension, say, a diastolic pressure over 110 mmHg, would be of the order of 100 000 people. Our figures suggest that about one-third of those, 30 000, are on treatment. I believe that 1000 of those 30 000 could in fact be effectively treated and their lives saved over a period of a year.

Like Dr Werktö, I do not believe that a reduction of risk factors could be the explanation, and the other alternative is that there is a change in diagnostic habits. I have looked at the changing diagnostic habits of the doctors and I do not believe either that there is a significant change over the period we are looking at.

Dr Shigematsu: I think that the degree of decline in mortality from stroke could be related also to the changes in the type of stroke influenced by the treatment of hypertension.

Dr Freis: I wish to mention some new data. We examined the question of whether normalization of the blood pressure with treatment was necessary. We divided up the treated group in the Veterans Study; the one-third who had the poorest reduction of blood pressure all had a diastolic blood pressure during treatment of over 90 mmHg and their average reduction of diastolic blood pressure was only 7 mmHg. These results were compared with the one-third that had the greatest reduction of blood pressure; all of these had diastolic pressure below 80 mmHg and an average reduction of 17 mmHg. We compared the morbidity in these two groups with that in the control group who received no treatment. The group with the highest diastolic blood pressure during treatment showed a significant difference compared with the control group in that their morbidity was about half that of the untreated group. But it was not significantly different from the group that had the reduction of blood pressure down to completely normal levels. The group with the smaller reduction in pressure had a slightly better morbidity experience than the group with the bigger pressure reduction, but it was not significantly different, and it would suggest that perhaps normalization of blood pressure, although desirable, is not essential to achieve significant protection.

Dr Werktö: There is no controversy between Dr Reader and myself. The time period shown by Dr Hatano was from 1951 and there was a decrease in cerebrovascular mortality from 1951 onwards. The treatment of hypertension in the 1950s was so effective that you could account the decrease to that. I quite agree with Dr Reader that there are many cases which are now under treatment. It has been shown that with treatment there is a decrease in cerebrovascular mortality in patients with hypertension. This cannot be the only answer to the question why the decrease has occurred, and certainly not during the earlier time period. As to changes in diagnostic procedure, the autopsy rate in Sweden has been around 50% in the whole country from the 1950s; there has not been any marked change in diagnostic procedures which can account for this change in cerebrovascular mortality.
While we confine our efforts in the next three days to the problem of hypertension and stroke in various communities we must be mindful of certain drawbacks, the most fundamental of which is that the definition of hypertension itself begs many questions. It would in actual fact be more appropriate to examine the pattern of blood pressure (not hypertension) in the different populations, for few would deny that arterial pressure is a quantity that has a wide range of variation and that the dividing line between "normotension" and "hypertension" is no more than an artefact. This debate belongs to the sixties, and we must not be drawn into semantics.

Although my brief relates especially to the African setting, it is tempting even at this stage to allude to certain constraints in the interpretation of epidemiological data on arterial pressure in any population. Random within-subject variation, systematic bias in observer variation, circumstances of measurement, seasonal changes, fat arms and short cuffs all conspire to vitiate meaningful comparison. Randomized sampling of different communities, although legitimate, is far from ideal, and it is in the application of this procedure that early studies on arterial pressure in the African continent appear most vulnerable.

The student of cardiovascular disease in Africa soon identifies four categories of study in the area of arterial pressure, stroke and hypertension:

A. Pattern of blood pressure in African communities
B. Prevalence of "hypertension" in whole populations or selected samples
C. Morbidity: clinical aspects of "hypertensive disease", including stroke
D. Mortality: data based on the causes of mortality obtained from autopsy, vital statistics, or death certificates derived from government reports.

In reviewing African studies in this field I have deliberately drawn on sets of data that fulfill the criteria of being reasonably complete, readily comparable, and prospective. These data, taken from studies in East, West, Central, and South Africa, are summarized in Table 1.
## Table 1
### ARTERIAL PRESSURE STUDIES IN AFRICA

<table>
<thead>
<tr>
<th></th>
<th>East</th>
<th>West</th>
<th>Central</th>
<th>South</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>POPULATION:</strong></td>
<td>Rural (R), Urban (U)</td>
<td>Selection Random</td>
<td>R Selected</td>
<td>R &amp; U Selected</td>
</tr>
<tr>
<td><strong>Age-bracket</strong></td>
<td>10-65 Home</td>
<td>20-80 Open</td>
<td>20-60 Courtyard</td>
<td>Open</td>
</tr>
<tr>
<td><strong>Locale</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>OBSERVERS:</strong></td>
<td>No. 4</td>
<td>1</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td><strong>Cuff size</strong></td>
<td>CM</td>
<td>12.5 cm CM</td>
<td>12 cm CM</td>
<td>13 cm CM</td>
</tr>
<tr>
<td><strong>Diastolic level</strong></td>
<td>160</td>
<td>95</td>
<td>150</td>
<td>140</td>
</tr>
<tr>
<td><strong>DEFINITION OF HYPERTENSION:</strong></td>
<td>160</td>
<td>95</td>
<td>150</td>
<td>140</td>
</tr>
</tbody>
</table>

\[a\] Indicated by CM (cuff muffle) or CD (cuff disappearance)
Shaper & Saxton (1969) measured arterial pressures and body build in a rural community in the Kasangati area of Uganda; 900 subjects were examined and the community was stratified into the baganda group (about 2/3rd) and the other ethnic group (Bantu, Nilotic, Sudanese, Nilo-Hamitic) collectively called the non-Baganda immigrant group (1/3rd). They observed that in both male and female Baganda, arterial pressures rose with age and that the prevalence of hypertension (as defined by 160/95 mmHg and above) was strikingly similar to that in white Americans. This was not the case with the non-Baganda immigrant group.

In another East African study, Williams (1969) examined two rural communities in northern Kenya, the settled agro-based Kikuyu just north of Nairobi and the nomadic Samburu much farther north. At virtually all age levels and in both sexes the blood pressures in the Kikuyu were higher than in the Samburu (Fig. 1). Average systolic pressures rose appreciably with advancing age only in the Kikuyu.

FIG. 1 THE RURAL COMMUNITIES IN KENYA

<table>
<thead>
<tr>
<th>KIKUYU</th>
<th>SAMBURU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eastern Bantu</td>
<td>Nilo - Hamitic</td>
</tr>
<tr>
<td>Agriculturists</td>
<td>Nomadic - herdsmen</td>
</tr>
<tr>
<td>2° south of equator</td>
<td>2° North of equator</td>
</tr>
<tr>
<td>5000ft above sea level</td>
<td>4,500ft above sea level</td>
</tr>
<tr>
<td>Men short, rise in ponderal index</td>
<td>Men tall, ponderal index constant</td>
</tr>
<tr>
<td>Carbohydrate staple (cereal)</td>
<td>Protein staple (milk &amp; meat)</td>
</tr>
</tbody>
</table>
Much has been made of this observation that in some communities the arterial pressure does not appear to rise with age, and Shaper and his colleagues (1969) have extended Williams' findings by comparing pressures, body build, blood chemistry in the Samburu with those of their number serving in the Kenyan Army. They found that when Samburu warriors enter the Army they undergo considerable change in their dietary habits, physical activity, and way of life. Significant changes occur in body build and skinfold thickness and subsequently the systolic blood pressure goes up (Fig. 2). Preliminary impressions from a recent study of nomadic herdsmen in northern Nigeria also show that in that group the blood pressure does not normally rise with age (personal communication). Other "pockets of populations" have been identified outside Africa, notably in Oceania (Maddocks & Rovin, 1965; Maddocks & Vines, 1966; Lovell, 1967). Speculation is rife concerning the reasons for this - diet, salt intake, physical activity, absence of stress, concomitant chronic infection - but no durable answer has emerged. Yet the rapidly changing social and economic status of these communities demands urgent studies if a distinct opportunity is not to be missed.

**FIG. 2** MEAN ARTERIAL PRESSURES (WITH S.D.) IN SAMBURU WARRIORS

![Graph showing mean arterial pressures in Samburu warriors](image-url)
West Africa

Abrahams, Alele & Barnard (1966) chose the small town of Ilora (pop. 26,000) some 30 miles north of Ibadan, Nigeria, and showed that the blood pressure rose with age in both sexes. No clear relationship existed between the arterial pressure and weight, diet, or climate. These observations have been taken further by my colleagues and me in studies of rural and urban communities in the same locality. We surmised that casual systolic and diastolic pressures differed in no important respects from those in negro populations in the Caribbean but that systolic and diastolic values are marginally higher in the US negroes than in West Indian or West African negroes (Fig. 3).

Central Africa

Here Kaminer and Lutz (1960) measured arterial pressures in small restricted groups of nomadic and pastoral subjects in the Kalahari Desert and observed that in women the systolic and diastolic pressures were higher than in men, and that arterial pressures showed no tendency to rise with age.

Fig. 3
The studies of Scotch, Gampel, Abramson & Slome (1961) were confined to urban Zulu adults in an African housing scheme and showed that in both sexes the levels of mean arterial pressure and the prevalence of hypertension (as defined by pressures of 140/90 mmHg and above) rose with age, this "disease" being more marked after the age of 35 years in women and 45 in men.

Certain considerations point to the need for interpreting the foregoing data with caution, for the seeming geographical unity of Africa hides an astonishing range of environmental, cultural, and dietary diversity. For instance, it seems appropriate to ask how rural is rural in an African setting. The changing rural population often characterized in studies of arterial pressure in Africa commonly lives in villages situated on or near main roads and is more accessible to external influences that the unchanged traditional society in which the people are essentially nomadic and are closely bound to one another in habits and social custom. Moreover, settled indigenous tribes may differ from immigrant people even when they live in the same environment, and so rural studies of blood pressure must take account of tribal origins.

In the African milieu, the urban society is equally hard to define. For instance, Ibadan, which is often described as the largest indigenous African city, is but a city-village in the Western sense. Its core is peopled by farmers, small traders, and artisans living in large compounds organized on principles of common descent. Those who are full-time farmers live for much of the year in one of several hundred hamlets on the outskirts of the city and commute regularly between compound and farm. Truly urban societies must therefore be distinguished from this migrant group, and again from those in the young adult age group who through seeking job opportunities leave the villages to settle in the cities.

The main burden of illness associated with high blood pressure arises not from the relatively small number of severe cases but from the very large number of people with pressures, which are in the mild hypertensive range (while remaining symptomless) or though above average are still within the range conventionally regarded as normal. This then is the essence of the present WHO multicentre effort at community control of hypertension and stroke. Three such centres already exist in the African region (Ibadan/Epe and Ibarapa in Nigeria, and Accra, Ghana). A fourth is just beginning in Nairobi, Kenya. A uniform protocol ensures comparability of data, but certain basic differences exist in the approach to data collection. In the blood pressure studies the programme population varies from total survey (Epe) to random sample (Igbo-Ora). The Accra survey is restricted to an occupational group (civil servants). Largely because all three centres joined the programme at different times, the number of subjects found at the initial screening who were later subjected to further evaluation, as contained in the protocol, has varied from centre to centre (Table 2). It is early days yet to draw any firm conclusions from the studies being undertaken in the African centres, for the returns are still too small to be statistically significant. Nevertheless, this multicentre cooperative approach will no doubt provide for the first time a valid basis for comparing data from one part of Africa with another, and more importantly, in comparing the results from Africa with those from other areas of the world.
Table 2
WHO COMMUNITY CONTROL OF HYPERTENSION
STATUS IN THE AFRICAN REGION BY DEC. 1973

<table>
<thead>
<tr>
<th>Location</th>
<th>Size of population</th>
<th>Start</th>
<th>Programme population</th>
<th>Reference population</th>
<th>No. examined by Nov. 1973</th>
<th>No. found hypertensive</th>
<th>Drug intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPE (Nigeria)</td>
<td>8 000</td>
<td>1972</td>
<td>Total rural</td>
<td>Nearby village 10 000</td>
<td>3 943 (2 403 †) (1 540 ‡)</td>
<td>37 Clinic started Aug. 1973</td>
<td>Yes</td>
</tr>
<tr>
<td>IGBO-ORA (Nigeria)</td>
<td>30 000</td>
<td>1971</td>
<td>Sample rural</td>
<td>Eruwa 22 000</td>
<td>3 000</td>
<td>150 Clinic started 1972</td>
<td>Yes</td>
</tr>
<tr>
<td>ACCRA (Ghana)</td>
<td>800 000</td>
<td>1973</td>
<td>Occupational group (civil servants aged 15-55)</td>
<td>Same class of civil servants</td>
<td>6 900</td>
<td>Joined existing HT clinic</td>
<td>Yes</td>
</tr>
</tbody>
</table>
STROKE AND HYPERTENSION

Global statistics show that cerebrovascular disease ranks among the three leading causes of death in 40 countries. In 1966, cerebrovascular disease accounted for 12.5% of the total deaths in Europe, North America, and Oceania and 8.2% in Africa, Asia, and Latin America.

Most of the early work on cerebrovascular disease in subjects of African descent have been retrospective and based on hospital or autopsy studies. Although it is less than 15 years ago that cerebrovascular disease was reported, like coronary artery disease, to be uncommon in the African (Humphries, 1957), subsequent studies have shown that this is in fact not so (Laurie & Woods, 1958; Strong, Wainswright & McGill, 1959; Walker, 1963; Collomb, Dumas & Lemercier, 1966; Osuntokun, Odoku & Adeloye, 1969; Billinghurst, 1970). Williams & Resch (1969) have shown, however, that atherosclerosis of the cerebral vessels is less severe and prevalent in Nigerians than in American negroes and caucasians. Being retrospective, their studies did not attempt to correlate the prevalence of cerebral atherosclerosis with that of hypertension and diabetes mellitus, two diseases that are known to predispose to atherosclerosis and occur commonly in the Nigerian (Kinnear, 1963; Osuntokun et al., 1969; Akinkugbe, 1972).

It is usual to confine our definition of cerebrovascular disease to cerebral infarction, cerebral haemorrhage and hypertensive encephalopathy (three syndromes that are recognized to be causally related to elevated blood pressure). Spontaneous subarachnoid haemorrhage, a not uncommon form of cerebrovascular accident, is less clearly causally related to hypertension, except in association with coarctation of the aorta, although hypertension was present in one-fifth of Nigerians who suffered from spontaneous subarachnoid haemorrhage (Osuntokun et al., 1969). The next series of data show the result of comprehensive clinicopathological studies on cerebrovascular disease in Nigerians as seen in the University College Hospital, Ibadan, during the sixteen years (1957-73). In the period under consideration over 300,000 patients were admitted into the hospital or seen in the outpatients' clinic.

Table 3 shows the relative frequency of the various types of cerebrovascular disease in African and US negroes. The Nigerian and Ugandan data were compiled from retrospective hospital records and the Baltimore ones are weighted and drawn from retrospective population-based data.

It is seen that cerebral infarction is far and away the commonest type of cerebrovascular accident in the African group but intracerebral haemorrhage is more important in the case of the US negro. It is possible that the African figures are a gross underestimate of the situation in the community, and this is where the conclusions from the WHO Expert Study of Cerebrovascular Disease (WHO Technical Report Series No. 469, 1971) become highly relevant. The report states inter alia:

"Information on the size of the cerebrovascular disease problem could be improved by international agreement on terminology, classification and diagnostic criteria, and by uniform procedures for collecting data on the extent and nature of morbidity from cerebrovascular disease."

A Stroke Registry established in an urban centre (Ibadan) and a rural centre (Epe) as part of a WHO multicentre programme is already yielding
<table>
<thead>
<tr>
<th>Author</th>
<th>Date of study</th>
<th>Age group</th>
<th>Cerebral infarction</th>
<th>Cerebral haemorrhage</th>
<th>Subarach. haemorrhage</th>
<th>Cerebral embolism</th>
<th>Other categories</th>
<th>Total No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBADAN (Nigeria)</td>
<td>Osuntokun</td>
<td>1957-1973</td>
<td>All ages</td>
<td>55.6</td>
<td>17.0</td>
<td>8.7</td>
<td>3.2</td>
<td>15.5</td>
</tr>
<tr>
<td>LAGOS (Nigeria)</td>
<td>Dada et al.</td>
<td>1962-1967</td>
<td>11+</td>
<td>57.6</td>
<td>22.3</td>
<td>13.6</td>
<td>4.9</td>
<td>1.6</td>
</tr>
<tr>
<td>KAMPALA (Uganda)</td>
<td>Billinghurst</td>
<td>1968-1970</td>
<td>All ages</td>
<td>57.0</td>
<td>9.3</td>
<td>14.9</td>
<td>6.8</td>
<td>12.0</td>
</tr>
<tr>
<td>BALTIMORE* (USA)</td>
<td>Kuller</td>
<td>1964-1965</td>
<td>40-64</td>
<td>31.9</td>
<td>45.5</td>
<td>44.7</td>
<td>9.7</td>
<td>0.1</td>
</tr>
</tbody>
</table>

* Retrospective population-based data - figures under Cerebral Infarction include embolism.
some interesting results. The urban exercise covers hospitals in the Ibadan area, and in the first eight months a total of 130 patients with cardiovascular disease have been registered, and hypertension was present in 70% of these patients. Although it may be premature to extrapolate, it seems significant that a total of only 472 cases of cerebrovascular accidents was reported from the University College Hospital, Ibadan, during the period 1957-68 (Osuntokun et al., 1969).

In most studies of various racial groups, a number of factors or conditions have been associated with the presence of cerebrovascular disease (Table 4). These include arterial hypertension, ischaemic heart disease, atrial fibrillation, diabetes mellitus, abnormalities of blood lipids, smoking, and obesity. Of these, arterial hypertension is much the most important and this is followed in the African context by diabetes mellitus. There is strong evidence that adequate treatment of hypertension reduces the frequency of cerebrovascular accidents in all communities, although it does not appear to diminish the prevalence of myocardial infarction among caucasians (Veterans' Administration Cooperative Study Group on Antihypertensive Agents, 1967; Carter, 1971).

Whilst our experience in Ibadan does show that serum cholesterol and phospholipids may not play a significant role in the pathogenesis of cerebral atherosclerosis (although they appear to reflect socioeconomic status in Nigerians), the mean serum triglyceride is significantly higher in Nigerian patients who suffer from cerebral infarction than in normal Nigerians from upper, middle, and lower socioeconomic groups (P<0.001) but lower than the mean level in Europeans living in Ibadan (Table 5).

Diabetes mellitus is not uncommon in Nigerians, the incidence in the teaching hospital population in Ibadan being 0.43% (Osuntokun, 1971). Diabetic patients have a special tendency to develop atherosclerosis and its complications and European figures show that cerebrovascular disease is twice as common in diabetics as in non-diabetics (Bryfogle & Bradley, 1957). It has been suggested that deficient insulin activity may either directly or indirectly induce an impairment of the metabolism of vascular tissue, and that on this initial lesion the atherosclerotic plaque develops. The clinical features of transient ischaemic attacks (TIA) in the African are similar to those described in the caucasian but its prognosis is worse in the former, for of the 15 patients in the Ibadan series who suffered from intermittent ischaemia in the internal carotid territory and who were followed up for six months to 10 years, 11 developed major strokes and one died.

INTRIGUING FEATURES OF HYPERTENSIVE VASCULAR DISEASE IN THE AFRICAN

It is tempting in a discourse of this nature to mention also, however briefly, some of the peculiar and challenging features of hypertensive disease as seen in clinicopathological studies in the African.

(a) Retinopathy

The first relates to the rarity of severe retinal changes in the presence of marked hypertension (Akinkugbe, 1968). Our studies have shown that retinopathy among Nigerians does not depend on the height of the blood pressure. If we accept the view that marked vascular changes and papilloedema are unusual features of severe hypertension in the African, the importance of retinal changes in this condition as a criterion of prog-
Table 4
CEREBROVASCULAR DISEASES:
ASSOCIATED CONDITIONS
(RETROSPECTIVE HOSPITAL STUDIES)*

<table>
<thead>
<tr>
<th>Condition</th>
<th>Cerebral infarction</th>
<th>Cerebral haemorrhage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>44.8</td>
<td>81.5</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>5.6</td>
<td>-</td>
</tr>
<tr>
<td>Hypertension &amp; diabetes mellitus</td>
<td>4.8</td>
<td>9.6</td>
</tr>
<tr>
<td>Obesity</td>
<td>1.2</td>
<td>-</td>
</tr>
<tr>
<td>Hypertension &amp; obesity</td>
<td>1.8</td>
<td>-</td>
</tr>
<tr>
<td>Sickle-cell disease</td>
<td>1.2</td>
<td>-</td>
</tr>
<tr>
<td>Malignant trophoblastic disease</td>
<td>-</td>
<td>4.1</td>
</tr>
<tr>
<td>Malignant lymphomas and leukaemias</td>
<td>-</td>
<td>4.1</td>
</tr>
<tr>
<td>Presumed old-age arteriosclerosis</td>
<td>17.9</td>
<td>-</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>22.7</td>
<td>0.7</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

* after Osuntokun, 1974.

Table 5
SERUM LIPIDS AND NON-EMBOLIC ISCHAEMIC CEREBROVASCULAR DISEASE (NEICVD) IN NIGERIANS AND EUROPEANS IN NIGERIA*

<table>
<thead>
<tr>
<th></th>
<th>Serum cholesterol (mg/100 ml)</th>
<th>Serum triglycerides (mg/100 ml)</th>
<th>Serum phospholipids (mg/100 ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nigerians with NEICVD &amp; without</td>
<td>196</td>
<td>88.7</td>
<td>194.2</td>
</tr>
<tr>
<td>diabetes mellitus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal Nigerians: upper &amp;</td>
<td>200</td>
<td>65.5</td>
<td>216.0</td>
</tr>
<tr>
<td>middle socioeconomic group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal Nigerians: low income</td>
<td>153</td>
<td>55.2</td>
<td>172.0</td>
</tr>
<tr>
<td>group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Europeans in Ibadan</td>
<td>219</td>
<td>102.0</td>
<td>222.0</td>
</tr>
</tbody>
</table>

* after Osuntokun, 1974.
nosis must be open to some doubt. To await the appearance of severe retinopathy in the African before making a diagnosis of malignant hypertension and instituting prompt treatment would be to wait too long.

(b) Hypertension and the heart

It is common knowledge that Africans are relatively immune to myocardial infarction from coronary artery disease, though they may develop a mild degree of coronary atherosclerosis of the non-fatty type, especially if they are hypertensive (Scott et al., 1961). They may also develop electrocardiographic signs of left ventricular hypertrophy and strain, but no myocardial infarction or ischaemia (Smith, 1966). Treatment of the hypertension often causes all signs of heart disease to disappear. Bantus are exceptional in having less cerebral than coronary atherosclerosis (Reef & Isaacson, 1962). In Nigeria, heart muscle disease seems particularly common (Edington & Jackson, 1963). It has been suggested that hypertension may be the cause of some of the cardiomyopathies and that, as cardiomyopathy develops, the patient may become normotensive or hypertensive (Foster, 1965). It has even been suggested that the myocardium of the African is unduly susceptible to digitalis, even in the presence of a normal serum potassium, and that potassium deficiency does not develop with prolonged thiazide therapy without potassium supplements.

(c) "Resilient" hypertension

A small but important group of patients is often encountered in Africa who carry the effects of a marked sustained rise in blood pressure lightly for a number of years. They are generally free of symptoms and show no evidence of retinopathy or cardiac or renal failure and their blood pressure is exceptionally difficulty to control with conventional antihypertensive agents.

(d) Hypertension, renal failure and schistosomiasis

Whilst it is recognized that essential hypertension is generally the most common type of hypertension, many studies in Africa have shown that in young people it often results from renal disease and that young severely hypertensive males are peculiarly liable to die of malignant hypertension and uraemia (Smith, 1966). Vesical schistosomiasis constitutes a major epidemiological problem in adolescents living in both rural and urban areas of the more humid parts of Africa and it seems logical to relate its prevalence to that of secondary hypertension in these areas. Many young patients develop a combination of hypertension, proteinuria, oliguria, and azotaemia and eventually die, and autopsy studies often reveal ova of S. haematobium in their bladder imprint. A cause-effect relationship between urinary schistosomiasis and hypertension in the African context has not been demonstrated (Soyannwo, 1974).

CONCLUSION

We have come a long way from the initial observations of Donnison (1929) who in a two-year period failed to find any evidence of "raised blood pressure" in the African indigène. Nearly 20 years ago Humphries (1957) made a similar type of observation with respect to cerebral infarction and haemorrhage. It is not for us to challenge the basis on which these observations were made, but we now know that these early impressions
Hypertension is easily the most common cardiovascular condition in most African countries today (Fig. 4). The present WHO-inspired multicentre study of the community control of stroke and hypertension will no doubt bring us nearer to a meaningful comparison of the various studies and, hopefully, through these geographical clinicopathological data provide durable answers to some of the perplexing problems that have bedevilled this worldwide problem over many decades.

FIG. 4 CARDIAC MORBIDITY IN IBADAN 1968-69
(CARDIAC REGISTRY U.C.H. IBADAN)
(AFTER CARLISLE)
REFERENCES

DISCUSSION

Dr Ueda: Dr Akinkugbe, you mentioned that the cardiomyopathy of your country may be related to hypertension. On what data do you base the suspected relationship between cardiomyopathy and hypertension?

Dr Akinkugbe: Work on this has been carried out largely in East Africa by Shaper and his colleagues and in West Africa by us and we have noticed that some cases of so-called heart muscle disease are in fact hypertensive. The interesting thing about their hypertension is that when these patients are treated for hypertension, and they are brought out of cardiac failure, they remain normotensive in spite of the fact that you stop specific antihypertension treatment. This is rather intriguing, because it is a very unusual type of hypertension, which tends to subside with the management of the cardiac failure, but the cardiomyopathy often remains.
In 1964, the Chicago Heart Association sponsored a symposium on the epidemiology of hypertension which resulted in the publication of the proceedings in 1967. I believe it may be advantageous to look at the topics discussed in 1964 and then review briefly the important studies, particularly relating to North America, which have appeared since that time.

The sections of the 1964 symposium were devoted to heredity; age, sex and body build; race; diet, salt, tobacco, and alcohol; environmental and socioeconomic aspects including occupation, physical activity, and education; psychological factors; and to the natural history, prognosis, and mortality. It is instructive to realize that certain topics which appear today of great interest such as atherosclerosis, renin, paediatric hypertension, and epidemiologic aspects of control received minimal or no mention. The Pickering-Platt controversy is today uncommonly mentioned, but then was at the front and centre. We were much less knowledgeable than we are today of the impact of hypertension and its dimensions as an international health problem.

I should mention that the progress of investigations having epidemiologic importance has indeed been so great in the last 10 years that the Chicago Heart Association is holding a second symposium in Chicago on the same topic, 18-20 September 1974.

In discussing the epidemiology of hypertension in the last 10 years, I am planning to refer briefly to certain areas quite different from those of 1964, namely: mortality trends, local differences in mortality, the renin-aldosterone issue, diabetes, toxaemia, paediatric aspects, atherosclerosis and hypertension, treatment, and the role of government programmes.

Since 1964, there has been considerable new information relating to mortality trends and the factors involved in mortality. One striking find has been the downward trend of mortality rates in the USA, beginning in 1940 and apparently extending till 1972 (Tables 1-3). This trend has involved all age groups, both sexes, and both white and non-white persons. However, the downward trend in non-whites has been distinctly less than in...
Table 1. Death rates for hypertension in the United States of America (approximate rates per 100,000 population)* for three different age groups

<table>
<thead>
<tr>
<th>Year</th>
<th>White (male)</th>
<th></th>
<th></th>
<th></th>
<th>White (female)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>45-54</td>
<td>55-64</td>
<td>65-74</td>
<td></td>
<td>45-54</td>
<td>55-64</td>
<td>65-74</td>
<td></td>
</tr>
<tr>
<td>1940</td>
<td>49</td>
<td>160</td>
<td>475</td>
<td></td>
<td>50</td>
<td>160</td>
<td>405</td>
<td></td>
</tr>
<tr>
<td>1950</td>
<td>41</td>
<td>140</td>
<td>320</td>
<td></td>
<td>38</td>
<td>105</td>
<td>310</td>
<td></td>
</tr>
<tr>
<td>1960</td>
<td>19</td>
<td>58</td>
<td>150</td>
<td></td>
<td>13</td>
<td>40</td>
<td>150</td>
<td></td>
</tr>
<tr>
<td>1967</td>
<td>12</td>
<td>40</td>
<td>100</td>
<td></td>
<td>7</td>
<td>25</td>
<td>90</td>
<td></td>
</tr>
</tbody>
</table>


Table 2. Death rates for hypertension in the United States of America (approximate rates per 100,000 population)* for three different age groups

<table>
<thead>
<tr>
<th>Year</th>
<th>Non-white (male)</th>
<th></th>
<th></th>
<th></th>
<th>Non-white (female)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>45-54</td>
<td>55-64</td>
<td>65-74</td>
<td></td>
<td>45-54</td>
<td>55-64</td>
<td>65-74</td>
<td></td>
</tr>
<tr>
<td>1940</td>
<td>250</td>
<td>425</td>
<td>700</td>
<td></td>
<td>260</td>
<td>440</td>
<td>700</td>
<td></td>
</tr>
<tr>
<td>1950</td>
<td>200</td>
<td>425</td>
<td>720</td>
<td></td>
<td>250</td>
<td>425</td>
<td>780</td>
<td></td>
</tr>
<tr>
<td>1960</td>
<td>150</td>
<td>270</td>
<td>500</td>
<td></td>
<td>130</td>
<td>250</td>
<td>460</td>
<td></td>
</tr>
<tr>
<td>1967</td>
<td>115</td>
<td>200</td>
<td>440</td>
<td></td>
<td>90</td>
<td>185</td>
<td>400</td>
<td></td>
</tr>
</tbody>
</table>


Table 3. Mortality rates for hypertensive disease (ICDA 400 - 404) per 100,000 in the United States of America

<table>
<thead>
<tr>
<th>Year</th>
<th>Mortality Rate</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1968</td>
<td>13.4</td>
<td></td>
</tr>
<tr>
<td>1969</td>
<td>12.3</td>
<td></td>
</tr>
<tr>
<td>1970</td>
<td>11.0 (provisional)</td>
<td></td>
</tr>
<tr>
<td>1971</td>
<td>10.3 (provisional)</td>
<td></td>
</tr>
<tr>
<td>1972</td>
<td>10.0 (provisional)</td>
<td></td>
</tr>
</tbody>
</table>
whites. The reasons for this favourable change have not been clear. It does not appear that changes in fashion or in reporting the causes of death can explain the phenomenon. The possibility that better treatment of hypertension has brought a reduction in mortality is attractive, but it seems highly unlikely that all the reduction is explicable on this basis. The downward trend commenced before the modern era of drug therapy. Further, there is ample evidence that drug therapy has been used effectively in only a minority of hypertensive individuals. A lessened incidence of renal inflammatory disease has taken place during and indeed prior to the same period, and could be one significant factor. The true explanation is at present not known.

Comparable data from other portions of the Americas are not as easily obtained. I am grateful to Mr Tavia Gordon of the National Heart and Lung Institute of the United States who has kindly provided me with some helpful statistics relating to Canada and Colombia (Table 4). In the period 1955 to 1966, the age-adjusted death rates for hypertensive diseases (ICD 440-447) showed for males a 44% decrease in the USA, a 58% decrease in Canada, and a 26% decrease in Colombia. For females, the decrease in this same period was 49% in the USA, 62% in Canada, and 28% in Colombia. It is apparent that there has been a decline in mortality from hypertensive disease in both North and South America and that this has affected both sexes; and it would appear to involve all age categories, if the US experience has been duplicated in these other areas, which seems most likely.

Table 4. Decrease (%) in age-adjusted death rates for hypertensive diseases (ICD 440 - 447) between 1955 and 1966*

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>United States of America</td>
<td>44</td>
<td>49</td>
</tr>
<tr>
<td>Canada</td>
<td>58</td>
<td>62</td>
</tr>
<tr>
<td>Colombia</td>
<td>26</td>
<td>28</td>
</tr>
</tbody>
</table>

* Data from the National Heart and Lung Institute.

The racial differences in mortality in the USA have been emphasized by the vital statistics extending through the 1960s. The age-adjusted death rates from cerebrovascular diseases in non-whites were nearly twice that of whites in both sexes. Recent data have indicated that the whites, both males and females, with only rudimentary education had higher mortality rates from hypertensive disease than did those with high school or college training.

A report from a pooling of long-term studies of middle-aged males disclosed in 1971 more fully the risks of mild hypertension. Among the 6640 men followed up for 10 years, it was evident that diastolic blood pressures of 85 to 105 mmHg were associated with highly significant increases in mortality as compared with diastolic pressures below 85 mmHg.
and that the highest rates were observed among men who were also cigarette smokers and/or who had elevated serum cholesterol levels. There was a clear association between overweight and hypertension. This report and one from Framingham also underscored the importance of elevated blood pressures (encountered in routine screening) as a precursor of strokes (Table 5). The Framingham study has also demonstrated that over a 16-year period six times more congestive heart failure developed in hypertensive (systolic pressures of 160 mmHg or more, diastolic of 95 mmHg or more) than in normotensive individuals (Table 6).

Additional material has become available since 1964 reporting the long-term fate of hypertensive individuals. Data from a 20-year follow-up of 631 individuals studied at the Mayo Clinic showed an unfavourable outlook for men with hypertension as compared with women, and especially of persons with retinal haemorrhages, proteinuria, and electrocardiographic abnormalities. Coronary heart disease was the dominant cause of death followed by cerebrovascular disease; these findings are consistent with previous reports.

Table 5. Fourteen-year follow-up study of men aged 30-62 years at entry (Framingham)

<table>
<thead>
<tr>
<th>Hypertension* at initial exam.</th>
<th>Morbidity** ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemorrhagic stroke</td>
<td></td>
</tr>
<tr>
<td>absent</td>
<td>70</td>
</tr>
<tr>
<td>present</td>
<td>206</td>
</tr>
<tr>
<td>Non-haemorrhagic stroke</td>
<td></td>
</tr>
<tr>
<td>absent</td>
<td>76</td>
</tr>
<tr>
<td>present</td>
<td>183</td>
</tr>
</tbody>
</table>

* Hypertension = ≥160 and/or 95 mmHg.

** Ratio = cases observed x 100
cases expected

Table 6. Incidence of congestive heart failure (Framingham study) (average annual rate per 10,000)

<table>
<thead>
<tr>
<th>Age at exam</th>
<th>Sex</th>
<th>Hypertension (≥160 and/or 95 mmHg) at first exam.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Absent</td>
</tr>
<tr>
<td>45 - 54</td>
<td>M</td>
<td>5</td>
</tr>
<tr>
<td>45 - 54</td>
<td>F</td>
<td>5</td>
</tr>
<tr>
<td>55 - 64</td>
<td>M</td>
<td>19</td>
</tr>
<tr>
<td>55 - 64</td>
<td>F</td>
<td>10</td>
</tr>
<tr>
<td>65 - 74</td>
<td>M</td>
<td>18</td>
</tr>
<tr>
<td>65 - 74</td>
<td>F</td>
<td>11</td>
</tr>
</tbody>
</table>
Certain local differences in mortality from cardiovascular, including hypertensive, disease have been reported from Canada, which are in part confirmatory of earlier studies elsewhere, including Japan and the United Kingdom. Fodor et al.\(^9\) reported from Newfoundland that there was an exceptionally high mortality from cardiovascular disease, including hypertensive disease and cerebrovascular disease, in St John's, a city with a soft water supply. "Soft" water was defined as having a low calcium carbonate content. Thus, the cardiovascular-renal death rate per 100 000 residents aged 36 to 69 years for males was 793 in St John's and 412 in two towns having hard water. The respective figures for females were 286 and 201. The authors did not relate these differences to differences in the prevalence of risk factors.

The same authors also reported\(^10\) that the mean age- and sex-adjusted blood pressures were higher in three coastal fishing villages in Newfoundland, Canada, than in an inland logging and mining community.

In an interesting report from LaOroya, Peru, Marticorena et al.\(^11\) observed that men born at sea level but residing at LaOroya (where the altitude is 3759 m) appeared to show an actual decline in both systemic systolic and diastolic pressures on acquiring residence at high altitude. This is of course in contrast to the pulmonary vascular bed, which may develop an increase in pressure under such circumstances.

Since 1964, there has been a brisk discussion and considerable controversy in the USA especially relating to the "typing" of hypertensive patients. Laragh\(^12\) has promoted the concept that among those with essential hypertension it is possible to identify subgroups on the basis of high, normal, or low renin and aldosterone levels (Table 7). He has also indicated that low renin hypertension may be more common among blacks, and further that low renin hypertension may be accompanied by few cardiovascular complications (heart attacks and strokes). Such a concept has important epidemiological and therapeutic implications, if true, but it would appear to require confirmation in a much larger population. As stated by Kirkendall & Overturf,\(^13\) until much more is known "it would not seem prudent to modify drug treatment on the basis of renin activity levels".

<table>
<thead>
<tr>
<th>Renin</th>
<th>Aldosterone</th>
</tr>
</thead>
</table>
| Low     | 27% Low 5 - 8%  
|         | 27% Normal 13 - 21% |
|         | 27% High 1 - 2%   |
| Normal  | 57% Low 2 - 6%   |
|         | 57% Normal 36 - 54% |
|         | 57% High 3 - 6%   |
| High    | 31% Low -------  |
|         | 31% Normal 8 - 12% |
|         | 31% High 6 - 9%   |
It is interesting to look in the index of the 462-page proceedings of the 1964 symposium and see that the word diabetes is not to be found. Today, it is recognized that there is a significant association between diabetes and hypertension, and several studies\(^1\) have demonstrated not only more high blood pressure but also more hypertensive heart disease among persons with diabetes. The explanation for this association has not appeared.

Over the years, there have been many studies relating to hypertension in pregnancy, but only a modest literature regarding epidemiology. The community study\(^1\) in Tecumseh, Michigan, looked at the relation between toxaemia of pregnancy and essential hypertension in 1967. In this population of over 9000 persons, the women with a history of hypertension with toxaemia tended to have only first-order female relatives with hypertension, as compared with women with essential hypertension whose male as well as female relatives tended to be hypertensive. Their findings suggested significant differences between the causation of essential hypertension as compared with hypertension related to toxaemia. Another publication from Jersey City, New Jersey, surveyed 20 years of experience involving nearly 160,000 deliveries, and involved a re-examination of women with eclampsia six or seven years after the event.\(^1\) It was concluded that hypertension was no more frequent among these women at the time of re-examination than among the female population at large. However, there was a conspicuous association between the development of late diabetes and the history of eclampsia. These and other investigations emphasize one facet of hypertension which justifies continued inquiry - a facet having certain distinctive characteristics.

The last 10 years have finally produced an interest in and some investigation of high blood pressure and its possible precursors among children and adolescents. The 1964 symposium essentially neglected the topic. Recent surveys of the overall issues of hypertension have called for an awakening of studies by paediatricians and epidemiologists in this potentially important area. In North America, we are on the threshold of collecting useful data, including a better definition of optimum levels of blood pressure among the young. An example of the type of study now being undertaken is the epidemiological project in Evans County, Georgia.\(^1\) The workers in this investigation followed a group of adolescents with elevated blood pressures over a seven-year period and documented in 1969 a close association between overweight and subsequent weight gain with later sustained hypertension. They also observed an incidence of vascular complications of hypertension which was most disturbing. We surely need to know much more about this whole issue.

Since 1964, there has been a steady increase in our knowledge of the important role of hypertension in contributing to the appearance of premature as well as what may be called more mature atherosclerosis. The unfavourable influence of high blood pressure in accelerating cerebral atherosclerosis has been described by Baker et al.,\(^1\) documenting the arterial changes with careful pathological and clinical observations on 3824 persons. Much more attention has been paid, however, in North America to coronary circulation than to the cerebral circulation. Epidemiological studies have repeatedly stressed over the past decade that hypertension is one of the big three risk factors for heart attacks, and for sudden death. A recent summary of the evidence by Hollander\(^1\) stated: "The results of a number of epidemiological studies indicate that the risk of every manifestation of coronary heart disease, including angina, coronary insuf-
ficiency, myocardial infarction, and sudden death is significantly related to the antecedent level of both systolic and diastolic blood pressure." Hollander also stated that "it is not clear that hypertension per se, in the absence of other atherogenic factors, can cause atherosclerosis", and he concluded that the vascular effects of hypertension might not be reversed by treatment of the high blood pressure. In the USA particularly, the knowledge that hypertension was a critical factor in atherosclerosis had become widely dispersed by 1970 and was having important consequences in clinical practice and in public health programmes.

Thus, community programmes to detect, follow up, and treat high blood pressure were undertaken in various forms in the Americas. Such a programme was initiated in Atlanta, Georgia, in 1970 in seven areas with a population of about 23,000 adults, most of whom were black. Hypertension was diagnosed in 23%, of whom 19% did not know they were hypertensive. Among those known previously to be hypertensive, 71% were under treatment with adequate control in 63%. Thus, among all the hypertensive persons, 64% were undiagnosed, not on treatment, or not under control (Table 8).

Table 8. Results of a community screening programme to detect hypertension in Atlanta, Georgia, in 1970

<table>
<thead>
<tr>
<th>Screened (6012)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension or on treatment (1358) (100%)</td>
</tr>
<tr>
<td>Known (1095) (80.6%)</td>
</tr>
<tr>
<td>On treatment (778) (57.3%)</td>
</tr>
<tr>
<td>Controlled (489) (36%)</td>
</tr>
</tbody>
</table>

Crucial to an active programme to attack this vast problem has been the need to document the benefits and limitations and hazards of treatment. Freis,21,22 who is present at this meeting, must receive the plaudits of the scientific world for his demonstration of the favourable effects of anti-hypertensive management upon morbidity in males with mild and moderate
hypertension. He will doubtless wish to discuss his findings himself. However, I wish to emphasize that these cooperative investigations from the Veterans' Administration illustrate very beautifully how under the stimulus of epidemiological data from Framingham and elsewhere, this type of study became critically important and was accomplished. Questions about what persons with high blood pressure should be treated were not fully answered adequately, since there was as yet minimal data on the results in females, and in young people. The exact blood pressure levels justifying intervention were also not clearly established.

The persuasiveness of all these bits and pieces of scientific evidence was not without its impact on government bodies. Thus, in 1971 in the USA the Task Force on Arteriosclerosis, appointed by the Department of Health, Education and Welfare, made seven recommendations on hypertension, including the collection of further data regarding "the frequency, magnitude, distribution and natural history of elevated blood pressure in the population at all ages". The National Heart and Lung Institute, with these and other recommendations in mind, also initiated a broad study for the detection and follow-up of high blood pressure, as well as a large multicentre multiple risk factor intervention trial, which included the treatment of hypertension (Tables 9 and 10). Voluntary health agencies, notably the American Heart Association, undertook professional and lay educational efforts, as did many local official health bodies.

It may fairly be said that in the last 10 years, the Americans have gone from a stage of a limited collection of epidemiological data, small clinical trials, and a large reservoir of experimental work, to a greatly expanded total effort to define, treat, and prevent the problem of hypertension. If the epidemiologist still has an important role to play, it would appear to be particularly in the collection of information leading to a true primary prevention. The available knowledge regarding obesity and salt do not at present permit effective community preventive programmes. We await further leads from population as well as laboratory studies which may allow simple public health prophylactic measures to replace our current pharmacological therapy.

<table>
<thead>
<tr>
<th>Table 9. Hypertension detection and follow-up programme of the National Heart and Lung Institute United States of America</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aim:</strong> Assess the effect of the stepped-up care programme on total mortality, cardiovascular complications, and to judge complications of therapy</td>
</tr>
<tr>
<td><strong>Population:</strong> About 10 500 hypertensive persons</td>
</tr>
<tr>
<td><strong>Age:</strong> 30 to 69</td>
</tr>
<tr>
<td><strong>Sex:</strong> Male and Female</td>
</tr>
<tr>
<td><strong>Randomization:</strong> To regular care and stepped-up care</td>
</tr>
<tr>
<td><strong>Definition of hypertension:</strong> Diastolic ( \geq 95 ) mmHg</td>
</tr>
<tr>
<td><strong>Duration:</strong> 5 years</td>
</tr>
</tbody>
</table>
Table 10. Multiple risk factor intervention trial of the National Heart and Lung Institute United States of America

| Aim: | Assess the effect of an Intervention Programme against hypertension, hypercholesterolaemia and cigarette smoking on total mortality in a high risk population. |
| Population: | 12 000 in 20 centres selected as top 15% risk by Framingham criteria |
| Age: | 35 to 57 |
| Sex: | Male |
| Randomization: | To Regular Care and Intervention Programme |
| Duration: | 6 years |

REFERENCES


DISCUSSION

Dr Werko: Dr Paul, you cited the Framingham data on the relationship between hypertension observed at the first investigation and the later incidence of congestive failure and stroke. Is it known to what extent these patients have been under treatment? It is conceivable that they ought to be under treatment since the results of the survey had been given to the physician, but I have not seen in any report how much and what kind of treatment they received and what effect the treatment had. Another comment I should like to make is that you stressed that diabetes and obesity may have some relation to hypertension. It has been discussed whether physical activity may not also play some role. In future studies, attention should be paid to the amount of physical activity since this may be of help in regulating the body weight and perhaps in this way to regulate the blood pressure. Finally, in the studies you have shown, what is regular care as compared with stepped-up care?

Dr Paul: As regards the first question, the data from Framingham does include the role of the physician who has in some of these cases intervened and managed a patient. Framingham, Massachusetts, is a fairly high-income community, and in general the level of medical care there is better than one sees in the typical community of the United States. I would say, therefore, that this is indicative of a relatively favourable response rather than one that might be less favourable in certain other communities. Regarding exercise and its role in weight control, and its relation to obesity and diabetes, I would agree with the general tenor of your comment that exercise programmes may indeed be helpful in weight control, although by themselves I believe they are quite inadequate. I think the success will be gained only with a combination of the discipline of diet plus exercise. I think that the studies on exercise in its specific relation to hypertension would indicate that the blood pressure is often low at the end of an exercise period than it is at the beginning, although during actual moments of physical stress it may be higher. I think the last question was in relation to stepped-up care. The usual care for both the high blood pressure detection follow-up programme and the multiple risk-factor intervention trial refers to that care given by the participant's own physician. That is, the physician is notified of the findings of the study and no specific management is given by the investigative group. We would not say that this was an ideal kind of contrast between treatment and nontreatment, but we believe that this will represent, nevertheless, a meaningful contrast between intensive intervention and the level of intervention provided by the community physicians.
Dr Gross: Dr Paul, you have mentioned the study of Laragh and colleagues, indicating that renin may be an additional risk factor for cardiovascular complications; I should like to say a word of warning. In my opinion, this hypothesis, attractive as it seems, was in various ways oversimplified and, as you mentioned, needs careful checking. So far, most investigators who tried to repeat Laragh's work or undertook similar studies could not confirm his findings and conclusions. One may say that, in view of Laragh's work, determinations of plasma renin activity should be included in all large-scale epidemiological studies of hypertension, but I think it is far too early for such a generalization and we have to be very careful in accepting Laragh's hypothesis, and even more so, his conclusions.

Dr Paul: I value Professor Gross's comments with which I would agree. The reason for including this item in my review is because I believe that it has epidemiological implications, were it true, and in the United States at this time (and this may not be true for other countries) we see a great many physicians who obtain renin levels on patients with hypertension with the notion that this will allow them to classify an individual in terms of eventual risk. Dr Walter Kirkendall, whom I quote in here, has been concerned because the measurements of renin have often been poorly done by laboratories where the control is not adequate. However, this is currently a topic of considerable discussion and application in the United States and perhaps elsewhere. Whether we feel this item is a significant one or not, it has certain current implications which are worthy of mention.
The mortality rate from cerebrovascular disease, which according to national health statistics has been the leading cause of death in Japan since 1951, was 176 per 100,000 in 1965 and 170 per 100,000 in 1971 and appears to show very little variation. This is higher than the rate for the USA, Australia, New Zealand, and Israel but almost the same as that for France, Hungary, and England. However, while in these countries cerebral infarction accounts for the majority of cases, in Japan the frequency of cerebral haemorrhage is higher than that of cerebral infarction. Recently, however, along with the rapidly changing living and eating habits in Japan, cerebral infarction has been increasing gradually, and at the same time cerebral haemorrhage has been decreasing year by year.

Data on the epidemiology of hypertension and stroke are scarce in the Orient and even national health statistics are insufficient. Therefore it is not possible to make an international comparison of the occurrence of cardiovascular diseases in Asian countries. A real epidemiological study of hypertension and stroke, therefore, needs to be carried out on an international level in Asia by establishing standardized criteria and methods.

A comparison of the life expectancy at birth of males in the Asian area shows that in Japan it was 42.5 years in 1946 but by 1972 had risen rapidly to 70.5 years. Such data for some other countries - e.g., India, 41.9 (in 1951-60); Thailand, 53.6 (in 1960); Sri Lanka, 63.8 (in 1968); and Taiwan (Province of China), 65.8 (in 1965) - show that there are still substantial differences between countries.

The influence of mortality from infectious diseases on the average life expectancy in Asian countries is considerable, but since 1951 in Japan cerebrovascular disease has become the most frequent cause of death, replacing infectious diseases such as pneumonia, bronchitis, and tuberculosis. A high frequency of deaths from infectious diseases still continues in the Philippines and Thailand, and a relatively high frequency is found in Sri Lanka, Taiwan (Province of China), and Singapore (Tables 1 and 2). Therefore, variations in the frequency of deaths from infectious diseases could probably explain the differences in life expectancy in the Asian area. Accordingly, the trend of infectious diseases would influence not only the life expectancy but also the prevalence of cerebrovascular disease and of hypertension.
Comparative epidemiological studies of cerebrovascular disease and hypertension conducted in Japan indicate that cerebral stroke occurs more frequently in farmers than in fishermen or those in specialized professions in the cities. There is also a substantial difference between farmers and non-farmers in terms of food intake (1971) - animal protein 30.3 g as against 36.4 g and fat 41.4 g as against 51.4 g - despite the improvement in the average nutritional level in Japan from year to year. The low dietary intake of protein and fat is regarded as a possible factor in the more frequent occurrence of cerebrovascular disease among farmers in Japan.

Table 1. Death rates per 100 000 population for 1970\textsuperscript{a} listed according to the ICD, 8th Revision (1965)\textsuperscript{b}.

<table>
<thead>
<tr>
<th></th>
<th>All infective and parasitic diseases (B1-B18)</th>
<th>Ischaemic heart disease (B28)</th>
<th>Cerebrovascular disease (B30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>America</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>USA</td>
<td>8.9</td>
<td>105.8</td>
<td></td>
</tr>
<tr>
<td>Asia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hong Kong</td>
<td>41.4</td>
<td>25.3</td>
<td>45.8</td>
</tr>
<tr>
<td>Israel (Jewish population)</td>
<td>10.4</td>
<td>201.7</td>
<td>95.7</td>
</tr>
<tr>
<td>Japan</td>
<td>23.3</td>
<td>37.6</td>
<td>174.9</td>
</tr>
<tr>
<td>Singapore</td>
<td>35.1</td>
<td>39.7</td>
<td>50.2</td>
</tr>
<tr>
<td>Oceania</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Australia</td>
<td>7.5</td>
<td>270.4</td>
<td>125.0</td>
</tr>
<tr>
<td>New Zealand</td>
<td>240.6</td>
<td></td>
<td>110.3</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Except for USA (in 1968) and New Zealand (in 1969).

Table 2. Death rates per 100,000 population for 1968[^a] listed according to the ICD, 7th Revision (1955)[^b].

<table>
<thead>
<tr>
<th>Country</th>
<th>All infective and parasitic diseases (B1-B17)</th>
<th>Vascular lesions affecting central nervous system (B22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>China (Province of Taiwan)</td>
<td>39.6</td>
<td>66.6</td>
</tr>
<tr>
<td>Hong Kong</td>
<td>44.4</td>
<td>45.9</td>
</tr>
<tr>
<td>Israel (Jewish population)</td>
<td>8.5</td>
<td>99.5</td>
</tr>
<tr>
<td>Philippines</td>
<td>123.3</td>
<td>19.1</td>
</tr>
<tr>
<td>Ryukyu Islands</td>
<td>19.2</td>
<td>94.7</td>
</tr>
<tr>
<td>Singapore</td>
<td>33.7</td>
<td>30.6</td>
</tr>
<tr>
<td>Sri Lanka</td>
<td>52.2</td>
<td>14.2</td>
</tr>
<tr>
<td>Thailand</td>
<td>50.6</td>
<td>6.4</td>
</tr>
</tbody>
</table>

[^a]: Except for China (Province of Taiwan), Israel, and Thailand (all in 1969) and Ryukyu Islands (in 1970).


REFERENCES

DISCUSSION

Dr Doyle: Dr Kimura, there did not seem to me to be that much difference in blood pressure between the two populations, i.e., the one with a very high incidence of cerebrovascular accidents and the other one with a lower rate. The same thing seemed to me to be true in relation to the comparison between the Koreans and the Japanese, that there are differences in the incidence of cerebrovascular disease but no very marked differences in blood pressure. Do you think that it is possible that there is a totally unknown and unidentified risk factor that causes the high incidence of cerebrovascular disease, which may have nothing to do with cigarette-smoking, fats, body weight, or blood pressure?

Dr Kimura: We have data on nutrition. Serum cholesterol and protein are very low in the Japanese and particularly in farmers. I should like to say that protein and fat malnutrition is one of the risk factors of cerebrovascular diseases.

Dr Shigematsu: The question is also related to the big differences between the Japanese and the Koreans. I think there is also some nutritional difference.

Dr Reader: This question of the strikingly different experience in Japan compared with many other countries is terribly important, and it would be a great help to me to know the basis of the national statistics? Are they based on medically qualified death certification? Are they based on registration of all deaths in Japan, or on a sample of deaths? I wonder if you could give us some information about the figure of death certification. Death certification in all countries is subject to a great deal of variability and inaccuracy, and it is important that we do not draw conclusions without examining this aspect very carefully.

Dr Shigematsu: So far as Japan is concerned, death certification is made by physicians and, of course, it covers all the deaths.

Dr Kobayashi: I should like to mention a difference between Japan and Korea. The system of protection against the cold climate is quite different. In rural Japan a wooden, draughty house with only a small fireplace is common and the room is very cold, at 2-4°C in winter. In Korea they have a famous ondolu system and inside the home it is warm. I think this might be related to the difference in stroke mortality.

Dr Doyle: Surely, Dr Kobayashi, if that was the case, the English would have the highest incidence of cerebrovascular accidents in the world. England is notoriously inadequately heated, and I believe Scotland would be at least as cold as Northern Japan.

Dr Ueda: May I say that some hereditary component concerning the cerebral arteries is important. Japanese people frequently produce microaneurysm in arteries. I think that is the chief reason why cerebral haemorrhage is very frequent.

Dr Strasser: Are data available on the seasonal differences in stroke mortality in northern Japan?
Dr Kimura: In winter, the frequency of cerebrovascular disease is high in northern Japan.

Dr Hatano: We are collecting data from Japan in several places. In December the incidence of stroke was low, but it was high in January and April. However, the number is still small to draw a conclusion.
INTRODUCTION

In Europe, as among white populations in all the industrialized countries, cardiovascular diseases constitute a major public health problem. In almost every country cardiovascular diseases are the most important cause of death and affect not only old people but middle-aged people too. It is very probable that their incidence has been increasing in both sexes since the end of the Second World War, particularly in males between 40 and 70 years old(47).

There are, however, geographical or national differences. Very roughly, it can be said that there is quite a strong correlation between the degree of industrialization or standard of living and the overall incidence of these diseases in the second half of life(12). The people from 40 years of age onwards in northern and western Europe are the most affected by these diseases. The Mediterranean countries are relatively spared.

The consequences of this situation are quite obvious: cardiovascular pathology is an important obstacle to increased longevity and an essential cause of premature death, particularly in men. A large number of individuals are also prevented from maintaining a state of physical and mental well-being. Economic, social, and human consequences are therefore conspicuous.

Cardiovascular pathology takes many varied clinical forms and has a complex etiology. However, apart from a few countries around the Mediterranean where the death rate from rheumatic heart disease is still high in children and young adults, two pathological mechanisms play an essential part in the etiology of these diseases: atherosclerosis and arterial hypertension. The two conditions are, moreover, very closely interconnected.

Thus, ischaemic heart disease, hypertensive heart disease, cerebrovascular disease, and atherosclerosis in other locations, particularly in the arteries of the lower limbs, are the most frequent cardiovascular diseases encountered among the European peoples. The situation seems quite different in the countries on the southern shore of the Mediterranean where such diseases remain rare in most cases, or even altogether exceptional.
Mortality and morbidity from cardiovascular diseases

Fig. 1 to 3 illustrate for certain European and Mediterranean countries, whose health statistics have been published by WHO, the proportion of deaths (out of the total number from all causes) ascribed in 1969 to cardiovascular diseases as a whole (A80-A88), a to ischaemic heart disease (A83), and to cerebrovascular disease (A85). On the left of each figure the percentages recorded in Japan and the USA are given for comparison. The other countries concerned are classified by an increasing percentage of deaths among males(48).

Fig. 4 to 6 show the variation in the proportion of deaths from these same diseases, according to age groups in a few selected countries in various parts of Europe or the Mediterranean. The mortality statistics reveal appreciable differences between the countries, particularly in the case of ischaemic heart disease. These differences may to a certain extent be due to variations in the way the causes of death are certified. In France a critical analysis has shown that the real death rates from ischaemic heart disease are probably two-and-a-half times as high in men and twice as high in women as the rates recorded in the official mortality statistics. This would make them of the same order of magnitude as those recorded in neighbouring countries, such as Switzerland or Italy(39).

FIG. 4
DEATHS FROM CARDIOVASCULAR DISEASES (ABIHB)
PERCENTAGE OF ALL CAUSES ACCORDING TO AGE GROUPS IN YEARS IN 1969

FIG. 5
DEATHS FROM ISCHAEMIC HEART DISEASES (ABIH)
PERCENTAGE OF ALL CAUSES ACCORDING TO AGE GROUPS IN YEARS IN 1969
Cardiovascular diseases taken all together (A80, A88) are responsible in all countries (except Egypt) for a very high proportion of the overall mortality, the range being from 30% to over 50%. The geographical differences are quite obvious: except for Israel, the highest proportions of cardiovascular deaths are found in the countries of the north and west of Europe. Considering the age groups, the relative importance of cardiovascular diseases as the cause of death is very low until about 40 years of age, except in Egypt where there is a high mortality from rheumatic heart disease in young persons. From 40 years of age onwards, cardiovascular diseases become responsible for an increasing percentage of deaths, but the proportions in different countries vary over quite a wide range, particularly in men.

Fig. 2 and 5 suggest that the variations in the death rate from cardiovascular diseases as a whole are largely a reflection of the quite appreciable variations in the death rate from ischaemic heart disease. The proportion of ischaemic heart disease from among all causes of death seems very high in a large number of European countries and in Israel and very low in Japan and Egypt; clearly the situation in several European countries in this regard is very similar to that in the USA.

On the other hand, the proportion of deaths ascribed to cerebrovascular diseases in Europe is smaller and varies but little from country to country. Its relative importance does not become very high until an advanced age. This situation is entirely different from that found in Japan.
Fig. 7 and 8 give the age-related prevalence of cardiovascular diseases as a whole and of ischaemic heart disease in three occupational groups in Paris (39). These show clearly (a) the rapid increase of prevalence with age, particularly after the age of 40 years, (b) the high rates of prevalence among the highest age groups, and (c) the important proportion of ischaemic heart conditions, which from 45 years of age onwards represent roughly half of all cardiovascular diseases. The high prevalence indicates the importance of these diseases as a public health problem.

The prevalence rates reported in various European surveys differ, higher rates having been recorded in the countries in the north or west of Europe and markedly lower rates among the rural populations in the south (26, 28, 41). These variations in the prevalence rates agree well with the differences in death rates.

The data available on the incidence of acute cerebrovascular diseases in Europe are scanty. Table 1 shows the annual incidence recorded in two population surveys (2, 33). The incidence of these diseases is only appreciable from 50 years of age, thereafter increasing regularly with age. At least until 70 years of age the incidence of cerebrovascular diseases is markedly lower than the probable incidence of ischaemic heart disease in countries where the latter is frequent (12, 39).

Table 1. Annual incidence rates for cerebrovascular disease in European population surveys

(annual incidence per 100 000)

<table>
<thead>
<tr>
<th>Age</th>
<th>Carlisle (9) Rates (both sexes)</th>
<th>England and Wales (33) Rates Males</th>
<th>England and Wales (33) Rates Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 19</td>
<td>0</td>
<td>0 - 14</td>
<td>0</td>
</tr>
<tr>
<td>20 - 29</td>
<td>11.8</td>
<td>15 - 44</td>
<td>40</td>
</tr>
<tr>
<td>30 - 39</td>
<td>5.7</td>
<td></td>
<td>30</td>
</tr>
<tr>
<td>40 - 49</td>
<td>39.8</td>
<td>45 - 64</td>
<td>430</td>
</tr>
<tr>
<td>50 - 59</td>
<td>188.9</td>
<td>65 +</td>
<td>3040</td>
</tr>
<tr>
<td>60 - 69</td>
<td>429.9</td>
<td></td>
<td>2850</td>
</tr>
<tr>
<td>70 - 79</td>
<td>825.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>80 +</td>
<td>1206.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The first results of the stroke register instituted at Göteborg suggest that in that city the annual incidence of strokes may be roughly 150 cases per 100,000 inhabitants. It has been estimated that in Europe one million persons are affected every year. Comparison of the data on incidence and death rates suggests that in roughly half the cases acute cerebrovascular accidents proved rapidly fatal.

The role of arterial pressure in cardiovascular pathology

Arterial hypertension is one of the main factors associated with the onset of a cardiovascular disease and its etiological or predisposing role has been demonstrated or very strongly suggested.

Fig. 9 illustrates the prevalence and relative risk of cardiovascular disease in relation to arterial pressure in a male group in Paris. At every age group, prevalence increases with increased blood pressure. The relative risk is between two and six times as high, according to age, in persons with high blood pressure. Between the ages of 50 and 59 years, one person with hypertension out of four is already certainly suffering from a cardiovascular disease.

Fig. 10 shows, on the basis of prevalence data, the increase with increased blood pressure of the relative risk of arterial disease in the lower limbs and of major electrocardiographic abnormalities in a middle-aged male population in Paris, thus presenting the wide repercussions of hypertension.

Fig. 11 shows the preliminary results of the Paris Prospective Study among 8,000 middle-aged men and confirms the well-known increase in the risk of the onset of ischaemic heart disease with increased systolic or diastolic arterial pressures. The data available from this study do not yet allow a rigorous analysis of the risk of cerebrovascular accidents in relation to arterial blood pressure, but the first results suggest that the risk is very marked.

These data confirm the results in numerous surveys in white populations (of European origin) in the USA and in Europe, as well as in black or yellow populations.

The very high frequency of ischaemic heart disease in white populations makes the nature of the relationship between arterial pressure and coronary atherosclerosis or its complications a subject of special interest. It is still uncertain whether there is a causal relationship. The results of controlled therapeutic trials, the first of which has been carried out in Europe, show clearly a considerable reduction in heart failures and cerebrovascular accidents in persons treated for hypertension. The results are confirmed by clinical studies which demonstrate a lower frequency of myocardial infarction in treated cases of hypertension. An answer to the question about the possible reduction in the incidence of ischaemic heart disease by treating arterial hypertension would have considerable practical implications, but it seems difficult to obtain this answer because it would require a single-factor therapeutic trial on very large numbers of people.
Figure 7

PREVALENCE OF ALL CARDIOVASCULAR DISEASES IN TWO PROFESSIONAL GROUPS

- CIVIL SERVANTS
- DRIVERS

PARIS PROSPECTIVE STUDY

DEFINITE + POSSIBLE

DEFINITE
FIGURE 8
PREVALENCE OF ISCHEMIC HEART DISEASE IN TWO PROFESSIONAL GROUPS

FIGURE 9
RELATIVE RISK OF CARDIOVASCULAR DISEASE BY AGE ACCORDING TO BLOOD PRESSURE
(2988 MEN 22 - 59 YEARS OLD)

THE HORIZONTAL LINE GIVES THE PREVALENCE IN THE WHOLE POPULATION
**Figure 10**

Relative risk of some cardiovascular disease

<table>
<thead>
<tr>
<th>PREVALENCE</th>
<th>PERIPHERAL VASCULAR DISEASE</th>
<th>E.C.G. MAJOR ABNORMALITIES</th>
</tr>
</thead>
<tbody>
<tr>
<td>%</td>
<td>2.3</td>
<td>2.3</td>
</tr>
<tr>
<td>1.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Blood Pressure

<table>
<thead>
<tr>
<th>&lt;140/80</th>
<th>140-154</th>
<th>155-174</th>
<th>&gt;175/105</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.3</td>
<td>2.3</td>
<td>1.2</td>
</tr>
</tbody>
</table>

The horizontal line gives the prevalence in the whole population.

**Figure 11**

Risk of coronary disease according to blood pressure (incidence)

<table>
<thead>
<tr>
<th>INCIDENCE</th>
<th>SYSTOLIC</th>
<th>3.9</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.3</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>5.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.9</td>
<td></td>
</tr>
</tbody>
</table>

Blood Pressure

<table>
<thead>
<tr>
<th>&lt;140</th>
<th>140-154</th>
<th>155-174</th>
<th>&gt;175</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.3</td>
<td>2.3</td>
<td>1.2</td>
</tr>
</tbody>
</table>

The horizontal line gives the annual incidence in the whole population.
The prevalence and treatment of arterial hypertension

Table 2 shows the prevalence of hypertension recorded in a few European studies (6,13,15,30). The rates are very close to those recorded in other surveys and those found in the white population in the USA (36). However, various well-known conditions may cause these prevalence rates to vary quite appreciably; they are markedly higher, for instance, in case-finding surveys which only entail single measurements and in which no particular precautions are taken (7,30). These differences are due in part to the instability of blood pressure in many people (32) but they also reflect real variations in prevalence among different population groups in Europe (26).

Despite these reservations, an approximate, probably reasonable estimate of the prevalence of arterial hypertension according to age in Europe has been put forward (38): 4-10% of the population as a whole and 15-30% of persons aged 45 to 74 years are suffering from permanent arterial hypertension. These estimates are compatible with the results of epidemiological surveys in Europe (2,43,50).

There has been little study of the incidence of hypertension. In an Israeli survey it was estimated as slightly above 1% per annum in men of European origin between 40 and 59 years of age (24).

Moreover, it is very probable that arterial hypertension is infrequently treated and that the effects of any treatment are often inadequate (30,32). Fig. 12 illustrates the conditions under which arterial hypertension is treated in an occupational group in Paris; it shows that only 10% of persons with hypertension were treated in 1967-70 and that the treatment was really effective in only less than half of them. It has been shown that systematic case finding of hypertension even in European countries with highly developed health services would lead to the discovery of a high proportion of untreated cases (18).

Factors associated with arterial hypertension in European populations

Epidemiological studies have suggested the possible etiological role of numerous factors in arterial hypertension. Two factors are closely associated with the condition among European populations.

The relationship with weight has often been studied (10, 14). Fig. 13 shows the variations in systolic pressure in relation to the "fat body mass" estimated on the basis of various morphological measurements in 4,200 men aged 50 years old. The relationship is obvious, since the percentage of persons with pressure of 170 mmHg or above shows a regular increase from 30% to over 50% when the "fat body mass" rises from 8 to 30 kg (40). It has been shown that this relationship explains to a large extent that observed between arterial pressure and age (Table 3 and reference 31).

The relationship with heart rate also seems close, as shown by Fig. 14, which is similar to Fig. 13.
<table>
<thead>
<tr>
<th>Study Criteria</th>
<th>Lyon (13) (France)</th>
<th>Paris (38)</th>
<th>London (15)</th>
<th>Bergen (6) (Norway)</th>
<th>London (15)</th>
<th>Bergen (6) (Norway)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ages</td>
<td>160/95</td>
<td>160/95</td>
<td>160</td>
<td>95</td>
<td>160</td>
<td>95</td>
</tr>
<tr>
<td>10 - 14</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>15 - 19</td>
<td>-</td>
<td>-</td>
<td>2.2</td>
<td>3.4, 1.4</td>
<td>-</td>
<td>0.6, 0.5</td>
</tr>
<tr>
<td>20 - 24</td>
<td>1</td>
<td>8.5</td>
<td>3.2</td>
<td>-</td>
<td>-</td>
<td>1.4, 0.8</td>
</tr>
<tr>
<td>25 - 29</td>
<td>2.3</td>
<td>8.6</td>
<td>4.1</td>
<td>-</td>
<td>3.5</td>
<td>2.1, 1.1</td>
</tr>
<tr>
<td>30 - 34</td>
<td>6.3</td>
<td>10.9</td>
<td>6.2</td>
<td>1.3</td>
<td>7.9</td>
<td>8.7, 5.7</td>
</tr>
<tr>
<td>35 - 39</td>
<td>4.0</td>
<td>11.9</td>
<td>8.7</td>
<td>7.9</td>
<td>8.7</td>
<td>8.7</td>
</tr>
<tr>
<td>40 - 44</td>
<td>10.0</td>
<td>16.1</td>
<td>11.5</td>
<td>9.7</td>
<td>12.7</td>
<td>14.2, 8.3</td>
</tr>
<tr>
<td>45 - 49</td>
<td>16.1</td>
<td>20.6</td>
<td>15.3</td>
<td>26.3, 14.4</td>
<td>26.3</td>
<td>14.4</td>
</tr>
<tr>
<td>50 - 54</td>
<td>20.4</td>
<td>30.7</td>
<td>21.0</td>
<td>41.5, 23.2</td>
<td>41.5</td>
<td>23.2</td>
</tr>
<tr>
<td>55 - 59</td>
<td>23.8</td>
<td>38.8</td>
<td>23.4</td>
<td>33.5, 29.7</td>
<td>54.1</td>
<td>27.2</td>
</tr>
<tr>
<td>60 - 64</td>
<td>38.8</td>
<td>54.2</td>
<td>26.8</td>
<td>65.5, 32.4</td>
<td>65.5</td>
<td>32.4</td>
</tr>
<tr>
<td>65 - 69</td>
<td>35.5</td>
<td>58.4</td>
<td>29.0</td>
<td>57.8, 44.7</td>
<td>74.6</td>
<td>36.7</td>
</tr>
<tr>
<td>70 - 74</td>
<td>45.2</td>
<td>62.2</td>
<td>28.2</td>
<td>79.1, 46.5</td>
<td>79.1</td>
<td>46.5</td>
</tr>
<tr>
<td>75 - 79</td>
<td>54.2</td>
<td>69.5</td>
<td>26.3</td>
<td>84.6, 35.5</td>
<td>84.6</td>
<td>35.5</td>
</tr>
<tr>
<td>80 - 84</td>
<td>58.4</td>
<td>74.6</td>
<td>36.7</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
The dotted curve gives the percentage of subjects with systolic blood pressure equal or greater than 170 mm Hg.
FIGURE 14

SYSSTOLIC BLOOD PRESSURE ACCORDING TO HEART RATE

The dotted curve gives the percentage of subjects with systolic blood pressure equal or greater than 170 mm Hg.

Table 4 shows the percentage of persons with a systolic pressure of 170 mm Hg or over in relation to "fat body mass" and heart rate; the proportion is 2% in thin persons with a slow heart rate and it rises regularly for different combinations of these two factors to as high as 60% in very obese persons with a rapid heart rate.

It would be interesting to know whether such relationships are found in other populations, since they should be reflected in therapy, prevention, and cure.

Studies in progress

The importance of the public health problem posed in Europe by arterial hypertension and cerebrovascular accidents has led to numerous studies being undertaken. An exhaustive list of these is not possible. Roughly, three main types of study are in progress:
(1) Studies for information purposes, such as the registers instituted under WHO auspices in various European towns, which are intended primarily to determine the incidence of acute cerebrovascular accidents (19).

(2) Preventive therapeutic trials:

(a) Trials may be intended to determine the effects of the treatment of hypertension. Trials of this nature are in progress with a view to evaluating the effects derived from treatment in old persons (2) or in cases of moderate hypertension (2). Such a trial aims to reduce the incidence of ischaemic heart disease, but would be difficult to carry out for it requires a very large number of subjects.

(b) Trials may aim at evaluating the effect of multi-faceted preventive measures in regard to the main risk factors in ischaemic heart disease, including arterial hypertension. Such trials are in progress in Europe, but will not provide information on the particular problem of the effect of treating hypertension on the onset of ischaemic heart disease; they will nevertheless be of value in determining the possible effectiveness of reasonable preventive measures and could be valuable (2, 21).

(3) Public health studies at community level designed to evaluate the overall effects of systematic case finding and treatment for hypertension, such as the programme for community control of hypertension launched on the initiative of WHO (2).

Table 3. Correlations of blood pressure (B.P.) with age and weight or with age and fat body mass (F.B.M.)

(1769 men, 22-55 years old)

<table>
<thead>
<tr>
<th></th>
<th>Correlations</th>
<th>Partial correlations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age</td>
<td>Weight</td>
</tr>
<tr>
<td>Systolic B.P.</td>
<td>.24</td>
<td>.39</td>
</tr>
<tr>
<td>Diastolic B.P.</td>
<td>.25</td>
<td>.41</td>
</tr>
</tbody>
</table>

Table 4. Percentage of subjects with mean systolic blood pressure equal or greater than 170 mmHg according to fat body mass and heart rate

<table>
<thead>
<tr>
<th>Fat body mass (kg)</th>
<th>Heart rate (/min)</th>
<th>&lt;14</th>
<th>14 - 22</th>
<th>&gt;22</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;60</td>
<td>2</td>
<td>8</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>60 - 79</td>
<td>6</td>
<td>14</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>&gt;80</td>
<td>31</td>
<td>42</td>
<td>63</td>
<td></td>
</tr>
</tbody>
</table>
REFERENCES


**DISCUSSION**

**Dr Doyle:** Is there any relationship between fat body mass and heart rate? I have the impression that fat people usually have higher heart rates. Was this controlled in this relationship with blood pressure?

**Dr Richard:** I cannot answer because we are just looking at it.

**Dr Akinkugbe:** One of Dr Richard's earlier figures shows that deaths from ischaemic heart disease and cerebrovascular disease were lowest in Egypt. I just wonder to what extent this is due to the fact that Egypt is largely a Moslem country and autopsy reports might not be as easy to obtain in such countries as in other populations. The other point is the incidence of ischaemic heart disease which I see is highest in Sweden and also that cerebrovascular disease is highest in Bulgaria. I wonder to what extent these are clinical or mortality figures and if there is any correlation between this and the actual distribution of cerebral atherosclerosis in the Bulgarian group, or coronary atherosclerosis in the Swedish group?
Dr Richard: The information is based on statistics published by WHO. The percentage of unknown causes is very high in Egypt and this is in accordance with your opinion, but ischaemic heart disease is rare in Egypt according to Egyptian doctors.

Dr Werktl: The figures that Sweden has the highest mortality rate from coronary heart disease is due to this being calculated for all ages. If you break it down to different age groups, Sweden differs markedly from Finland, Scotland, and the USA. In the age group below 40, Sweden has one-fifth of the mortality rates in ischaemic heart disease and between the ages of 50 and 60 mortality from ischaemic heart disease in Sweden is about one-third of that in the United Kingdom and the USA. It is thus not very illuminating to compare the figures for all ages, because they only show that people have to die from something. Autopsy rates are high in Sweden and in some of the Scandinavian countries. The accuracy of the death certificates is fairly good, and is still improving. Some changes of diagnosis during the last 10-20 years are due to an increase in the autopsy rate, except for the big cities.

Dr Gross: I think we have to be very careful in interpreting these figures of mortality rates because the causes of death are judged on different bases in various countries. The mortality figures which are sent to WHO are not comparable, and the figures for the German Federal Republic are also not comparable to those of the other countries mentioned here.

Dr Richard: Yes, I agree perfectly with Dr Werktl and Dr Gross. My aim in presenting such figures was only to give some very gross information, not to do a sophisticated analysis. These figures must be considered prudently.

Dr Strasser: May I say just a word concerning mortality statistics and their reliability. I think I need to say a word because WHO has been mentioned several times. Death rates from myocardial infarction in a series of countries, as given by the general mortality statistics reported in the WHO Statistical Annual, showed an excellent correlation with the incidence rates of myocardial infarction as computed for those countries from the special myocardial infarction registration studies which were population based and in which practically all cases of infarction in the community were registered. My point is that this correlation is very good, which means that death statistics - general mortality statistics - are not at all as unreliable as we are usually inclined to think.

Dr Paul: To come back to the matter of heart rate again, I wonder if Dr Richard has any information regarding slow heart rates. We have data indicating that both rapid and slow heart rates were associated with an increased ischaemic heart disease mortality. Of course, with blood pressure we have the problem of the length of the diastolic period which has its own physiological effect, I just call this to your attention.

Dr Richard: Yes, we have observed the same relationship between the risk of coronary disease and heart rate - the risk is higher for slow and fast heart rates, and is lower for heart rates of about 70 per minute. This risk is linked with heart rate and seems to be independent of blood pressure.
Epidemiological study of cerebral apoplexy and ischaemic heart disease in Japan

The significant characteristics of cardiovascular disease in Japan are the high incidence and high mortality rate of cerebral apoplexy caused by hypertension, which are in contrast to the high rates of ischaemic heart disease in other nations. It is, therefore, of more than general interest to try and find out why in Japan the death rate from cerebral apoplexy is so high compared with that from heart disease.

In order to investigate the causes and to establish preventive measures, an epidemiological study is being carried out by the Japanese Association for Cerebro-cardiovascular Disease Control. The Association was established in 1967 with the cooperation of the community, employment agencies, and the members of the Japanese Society of Public Health and the Japanese Circulation Society.

Diagnostic techniques for the examination of blood pressure, fundus of the eyes, and electrocardiogram were standardized by the Association with the support of the Ministry of Health and Welfare in 1967. A study on the prediction of cerebral and cardiac attacks was carried out using these techniques for three years (1965-67).

The cerebral accidents totalled 676. According to the criteria of the National Institute of Neurological Diseases and Stroke (NINDS) ad hoc Committee on Cerebrovascular Diseases, USA, 273 of these were caused by


See Neurology, May 1958 issue.
haemorrhage and 252 by infarction (109 by thrombosis, 18 by embolism, and the remainder not clearly defined). The number of cardiac accidents (myocardial infarction and acute cardiac death) totalled 126.

Twice as many healthy (sex and age matched) subjects were chosen as controls.

Fig. 1, on the left, shows the relative risk depending on the systolic blood pressure as divided into four grades, namely those under 140, 140-160, 160-200, and above 200 mmHg. The risk of a cerebral haemorrhage for a hypertensive patient with a systolic blood pressure of over 200 mmHg is 13 times that for subjects with a blood pressure under 140 mmHg. The risk for subjects with a blood pressure of 160-200 mmHg is 8 to 9 times that for subjects with a blood pressure of 140-160 mmHg and 4 to 5 times that for subjects with a blood pressure under 140 mmHg. The risk of a cerebral thrombosis is greater by 11 times for subjects with a blood pressure over 200 mmHg, 9.5 times for those with a blood pressure of 160-200 mmHg, and less than 3 times for subjects with a blood pressure between 140-160 mmHg compared with subjects with a blood pressure under 140.

Similar patterns were observed based on levels of diastolic blood pressure (Fig. 1); a small difference is that the relative risks from high diastolic blood pressures are greater in cerebral haemorrhage than in cerebral thrombosis.

The relative risk of a cerebral haemorrhage for subjects with a past history of hypertension is five times that for control subjects; the risk of a cerebral thrombosis and of heart attack is doubled for hypertensive compared with control subjects (Fig. 1).

The influence of nutrition was also studied and showed no relationship between the prevalence of stroke and cholesterol values. Farmers, especially in the north-eastern district (for example in Akita), consume nearly twice as much rice daily as the national average. Salt intake is high in areas with a high rice intake, i.e., over 20 g in Akita and 13 g in Osaka (results from Dr Komachi and Dr Kojima).

As for the role of different occupations, Fig. 2 demonstrates that for workers with a heavy work load the incidence rate of stroke is high, which is an opposite relationship to that on the incidence rate of cardiac attacks (results from Dr Chiba and Dr Fukuda).

Fig. 3 illustrates the relationship between the age-adjusted cerebrovascular death rate and average temperature in January for various districts in Japan. The negative correlation is clear, except in Hokkaido.

In Fig. 4 the extent of the availability of domestic heating (gas or oil stoves) in the winter is related to the cerebrovascular mortality rate. Large cities are located in the upper section. Warm prefectures are shown in two pentagons in the lower section; the only exception is Hokkaido where coal stoves are more commonly used. All of these areas are located on the left of the figure, i.e., where the cerebrovascular mortality is low. The north-eastern prefectures are mostly located on the right, lower down, indicating the poor protection against the cold climate in the areas with high stroke mortality.
Fig. 1

**FIG. 2 OCCUPATIONAL CLASSIFICATION AND INCIDENCE OF STROKES (40-54 YEARS OF AGE)**

![Bar chart showing incidence ratio of strokes per year for different occupations.](image)

- **Day Shift**
- **Overnight Shift**
- **M Mild**
- **MH Moderate**
- **H Heavy**

<table>
<thead>
<tr>
<th>Occupation</th>
<th>Incidence Ratio (Person Year Per 10,000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motorman</td>
<td>2.7</td>
</tr>
<tr>
<td>Clerk</td>
<td>7.5</td>
</tr>
<tr>
<td>Conductor</td>
<td>8.3</td>
</tr>
<tr>
<td>Lineman</td>
<td>10.4</td>
</tr>
<tr>
<td>Technician</td>
<td>11.4</td>
</tr>
<tr>
<td>Passenger</td>
<td>13.9</td>
</tr>
<tr>
<td>Engineer</td>
<td>14.0</td>
</tr>
<tr>
<td>Crossing Watchman</td>
<td>17.1</td>
</tr>
<tr>
<td>Baggage Man</td>
<td>20.1</td>
</tr>
<tr>
<td>Water Tender</td>
<td>29.3</td>
</tr>
<tr>
<td>Shunter</td>
<td>29.9</td>
</tr>
</tbody>
</table>
Fig. 3 Ambient temperature and cerebrovascular (CVD) mortality rates in males

Fig. 4 Domestic heating in winter and cerebrovascular (CVD) mortality rates in males
<table>
<thead>
<tr>
<th>Disease</th>
<th>Japan</th>
<th>USA</th>
<th>France</th>
<th>Federal Republic of Germany</th>
<th>Sweden</th>
<th>Denmark</th>
<th>Australia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic rheumatic heart disease</td>
<td>4.0</td>
<td>7.5</td>
<td>4.0</td>
<td>7.0</td>
<td>12.3</td>
<td>8.0</td>
<td>7.7</td>
</tr>
<tr>
<td>Hypertensive heart disease</td>
<td>17.6</td>
<td>12.2</td>
<td>11.9</td>
<td>20.4</td>
<td>10.4</td>
<td>7.8</td>
<td>13.9</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>37.7</td>
<td>331.7</td>
<td>80.9</td>
<td>172.5</td>
<td>333.9</td>
<td>297.1</td>
<td>270.4</td>
</tr>
<tr>
<td>Other forms of heart disease</td>
<td>44.5</td>
<td>18.7</td>
<td>111.9</td>
<td>116.4</td>
<td>21.1</td>
<td>27.3</td>
<td>38.2</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>174.8</td>
<td>102.6</td>
<td>147.4</td>
<td>174.4</td>
<td>105.5</td>
<td>107.1</td>
<td>125.0</td>
</tr>
</tbody>
</table>
The mortality rates for different types of cerebrovascular disease in Japan have been changing from 1950 to 1970. Fig. 5 shows the changing pattern of cerebrovascular death rates. The gradual increase in the cardiovascular death rate is probably due to prolongation of the life span. Deaths from cerebral haemorrhage have been tending to decrease since 1960, probably as a result of a general improvement in medical care (especially with the common use of antihypertensive treatment) and different systems of reporting. A rapid increase in deaths from cerebral infarction may also be explained by the latter reason (Fig. 5).

FIG. 5 MORTALITY RATE OF CEREBROVASCULAR DISEASE IN JAPAN (1950-1970)
The age-adjusted mortality rate for cerebrovascular disease in the north-eastern part of Japan is higher than that in the south-western part (Fig. 6). The exception is Hokkaido, which is located in the extreme north, but the rate there is about the same as the average over the whole of Japan (Fig. 6).

A nationwide survey on cardiovascular diseases was conducted in Japan in 1971 under the auspices of the Ministry of Health and Welfare. Two hundred census areas were selected on an area-sampling basis over the whole country. The number of persons, aged 30 years and over, examined was 13,882 with a response rate of 72.6%. The examinations included taking the past medical history and blood pressure; carrying out funduscopy and an electrocardiogram; measuring height, weight, and skin fold thickness; testing the urine; and making a general physical examination.

Fig. 7 shows the prevalence of essential hypertension by sex and age. Stage 3 hypertension (with organ damage) is indicated by a dotted column. From the fourth decade onwards, the frequency of hypertensives increases with age up to over 50% at the age of 70 years and over.

Fig. 8 shows the frequency of abnormal ECG findings by sex and age, classified by the Minnesota code. (Abnormal comprises 1-1, 4-1, 5-1, 6-1 or 2, 7-1, 2 or 4, 8-0 or 5.) The abnormal ECG findings increase with age and are slightly more frequent in hypertensives in each age group. Fig. 9 shows the frequency of abnormal ECG findings by blood pressure, which indicates an influence of high blood pressure on the heart. Ocular fundus abnormalities also increase with the subject’s age and blood pressure (Figs. 10 and 11).

Fig. 12 shows the distribution curves of blood pressure taken in the national surveys on cardiovascular diseases in 1961 and 1971. The median values are 120-129 mmHg for systolic and 80-89 mmHg for diastolic blood pressures.
FIG. 7  THE FREQUENCY OF ESSENTIAL HYPERTENSION
BY SEX AND BY AGE

- Hypertension (Stage 1 and Stage 2)
- Hypertension (Stage 3)

Stage 1; Only high blood pressure was observed.
Stage 2; Hypertensive findings were observed.
Stage 3; Hypertensive findings were observed in brain, heart, and kidney.
FIG. 8  THE FREQUENCY OF ABNORMAL ECG FINDINGS BY SEX AND BY AGE

Mild abnormality

Abnormal

<table>
<thead>
<tr>
<th>Age in Years</th>
<th>30s</th>
<th>40s</th>
<th>50s</th>
<th>60s</th>
<th>70s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>29.9</td>
<td>33.0</td>
<td>44.3</td>
<td>51.9</td>
<td>61.4</td>
</tr>
<tr>
<td>Female</td>
<td>8.1</td>
<td>12.2</td>
<td>21.7</td>
<td>26.5</td>
<td>38.5</td>
</tr>
</tbody>
</table>

%  

PER CENT

40  

30  

20  

10  

0

All | Males | Female

39.6 | 44.7 | 38.7

17.4 | 13.6 | 20.2

...
FIG. 9  THE FREQUENCY OF ABNORMAL ECG FINDINGS BY BLOOD PRESSURE

- Mild abnormality
- Abnormal

<table>
<thead>
<tr>
<th>Systolic B.P.</th>
<th>Diastolic B.P.</th>
</tr>
</thead>
<tbody>
<tr>
<td>140-160</td>
<td>90-96</td>
</tr>
<tr>
<td>138</td>
<td>88</td>
</tr>
<tr>
<td>158</td>
<td>94</td>
</tr>
</tbody>
</table>

- Mild abnormality: 30.1%, 19.9%, 13.6%
- Abnormal: 43.8%, 33.9%, 26.5%

- Mild abnormality: 64.1%, 60.1%
FIG. 10  THE FREQUENCY OF ABNORMAL FUNDUS FINDINGS BY SEX AND BY AGE

- Mild abnormality
- Abnormal

FIG. 11  THE FREQUENCY OF ABNORMAL FUNDUS FINDINGS BY BLOOD PRESSURE

- Mild abnormality
- Abnormal

90
Fig. 12 gives the prevalence of cerebrovascular diseases by sex and age and shows that it is highest in males over 60 years of age. These data were also analysed in the following five districts with climatic and other environmental differences:

(A) Hokkaido and the north-eastern district of the mainland
(B) Tokyo and its surroundings
(C) Kinki district
(D) Japanese coastline and the mountainous district of the mainland
(E) Kyushu, Shikoku, and the southern part of Chugoku.

The age-adjusted prevalence rate of cerebrovascular disease is high in the districts of D and A, where the climate is cold in winter; the prevalence of angina of effort is highest in D district and that of myocardial infarction is highest in A district.

In relation to ecological factors, the prevalence rate of cerebrovascular disease is high in the following groups (Fig. 14):

(1) those living and working in farm villages or fishing villages;
(2) those working outdoors with heavy labour;
(3) those with obesity more than 20% over the standard;
(4) those with low living standards.
Fig. 13 The frequency of cerebrovascular diseases by sex and age.

CEREBRAL HEMORRHAGE

CEREBRAL THROMBOSIS

SUBARACHNOIDAL HEMORRHAGE

CEREBRAL EMBOLISM

OTHER TYPES OF STROKE

ALL CEREBRO- VASCULAR DISEASES

ALL

AGE IN YEARS

30 40 50 60 70

39 49 59 69
Regarding the ECG abnormalities, the Japanese subjects showed fewer Q-QS and more high R and ST-T changes compared with the age-adjusted samples of railroad employees in the USA (Fig. 15).

To sum up, stroke is still the commonest cause of death in Japan. Hypertension is a problem requiring immediate action. Intensive preventive measures and a rehabilitation programme for stroke should be provided.
Fig. 14 Cerebrovascular disease and ecological factors
(all Japan = 100)

The consciousness of those with long urban residency

Hardness of labour

Obesity

Living standard

City
Farm or fishing village
Not specified

Pattern I
II
III

Obese, danger
Obese, warning
Safe
Thin, danger

High
Middle
Low

Fig. 15 ECG abnormality by Minnesota code
National survey in Japan and railroad employees in USA
Rate per 1000 men, 40-59 yrs

Japan
USA
REFERENCES


DISCUSSION

Dr Reader: Dr Kobayashi, the crude mortality rates for cerebrovascular accidents in Japan is about 200 per 100 000 population. Could you give us the total mortality rate and the death rate for ischaemic heart disease in Japan?

Dr Kobayashi: 25% of all deaths are due to cerebrovascular disease and 7-8% to ischaemic heart disease.

Dr Hoobler: We have heard a great deal about the relationship between salt intake and stroke in Akita prefecture, which it has been assumed, is the result of a greater prevalence of hypertension in Akita compared with other parts of Japan. I do not believe you commented on this in your talk; for example, there is a twofold increase in prevalence of stroke in Akita compared with other parts of Japan. Is there a corresponding increase in hypertension in Akita compared with Hokkaido or other parts of the country?

Dr Kobayashi: Hypertension is frequent in Hokkaido but it is more frequent in the Akita area and particularly in the young age groups. The death rate from stroke is highest in the north-eastern district and is lower in Hokkaido.

Dr Freis: The prevalence of hypertension that you list here is very high - 23%, I believe - but the age groups that you list are 30-70 years. What is the lowest limit of age? In the National Health Survey in the USA the lower level of age was, I think, 15 years, and this would have quite an influence on what the average blood pressure would be in the survey. What was the youngest age which you included in your survey?

Dr Kobayashi: We studied all subjects aged 30 years and over.

Dr Freis: That is a very important point because, if that is the case, then the difference that you observed may only be because of the age structure. If we had taken in the National Health Survey only subjects aged 30 years and over, the overall prevalence of hypertension in the USA would be much higher than the 13% that we quote.

Dr Soda: I will answer the question raised by Dr Freis for Dr Kobayashi: The Japanese Government carries out a national nutrition survey every year. This includes the population aged 18 years and over on a sample area basis. Information comparable to that from the USA is therefore available. The survey reported by Dr Kobayashi is another national survey on adult health.
Dr Werkö: It is very important to try to really get the figures for the prevalence of hypertension in Japan. Fig. 7 of Professor Kobayashi's paper shows that in the age group 50-59 years there is 29% hypertension, and if you compare this with Table 2 of Dr Richard's paper, the Bergen survey in Norway showed that in the same age group the blood pressure was elevated above 160 mmHg in 30%. So there may not be such a large difference between Japan and other countries after all.

There is also a question that I would like to ask: You said that in the mountainous district of the mainland the prevalence rate for cerebrovascular disease is high. There are studies conducted by WHO showing that high blood pressure is less prevalent at high altitudes. Have you studied the influence of altitude in the mainland on the prevalence of cerebrovascular disease or high blood pressure? Is there any difference between this part of the world and South America, for example?

Dr Kobayashi: I will answer the second point first. In Japan the mountains are not so high, many are approximately 1000 m high and the highest about 3000 metres. In the mountains the way of life is similar to that in the north-eastern districts. As regards the first point, I do not know why there is a high prevalence of hypertension in Bergen.

Dr Akinkugbe: It is my impression from the literature that diabetes in Japan is less common in the north-east than in the south-west or in the Tokyo area. I should like some explanation for this, because we know that diabetes and hypertension tend to be associated. Is there any epidemiological study on the lipid profile in these populations?

Dr Kobayashi: As I showed, the average cholesterol level is not so high and the analysis of lipoprotein has just been started. The geographical distribution of diabetes is not so different. Diabetes is more related, in my opinion, to atherosclerosis than to hypertension.
There is no precise, agreed definition of Oceania. One generally accepted designation includes all of the islands of the Pacific Ocean bordered by, but not including, Australia, Indonesia, the Philippines, Taiwan, and Japan. In Oceania, we are dealing in the main with isolated small land areas, scattered across a vast ocean of 70 million square miles.

To the southwest, there is Melanesia; the major land area is New Guinea with its isolated highland communities and its coastal Melanesians similar ethnically to the residents of the archipelagos of the Solomons, New Hebrides, New Caledonia, and Fiji. Although New Guinea is a large land mass, the individual highland villages are isolated by rugged terrain; there may be little or no contact with neighboring villages a few miles away; and, indeed, they may speak different languages.

In Micronesia to the northwest, there are no large land masses; and in this region of the Pacific, with an area comparable to that of the mainland of the USA, there are more than 2,000 islands with a total land area of a little more than 1,000 square miles and a population of about 200,000.

To the east is the Polynesian Triangle. Only New Zealand at its southwestern angle and Hawaii at its northern angle have substantial land areas.

These geographic facts lead to both strengths and weaknesses for the study of hypertension and stroke epidemiology. Since there is such a scattering of small populations, often with comparatively isolated gene pools, it is hazardous to extrapolate the findings. Blood pressure distributions can be studied, and it is possible to compare the rates of hypertension, while taking note of the effect of variability of blood pressure distributions on the estimation of such rates\(^1\). Furthermore, because of isolation and different degrees of Westernization, it is possible to study the effects of diet, acculturation, and migration on blood pressure and on other "risk factors" for coronary heart disease and stroke.

In many of the studies involving these island populations the size and age structure of the population is such as to preclude an estimate of stroke prevalence and incidence. In fact, most of the studies do not even mention stroke, specifically. However, in a recent publication\(^2\) describing a New Guinea highland population, a community of 1,489 people, Sinnett & Whyte state, "... no subject showed evidence ... of previous cerebrovascular accident."
MELANESIA

In New Guinea cardiovascular disease is uncommon. In an analysis of 2 000 admissions to the Port Moresby General Hospital(1), only 0.9% were admissions for any form of cardiovascular disease. To complement this hospital observation, a general population of 1 000 persons living near Port Moresby was followed up for a year(4). None of the illnesses recorded in this population was associated with hypertension or coronary heart disease.

In the previously mentioned study by Sinnett & Whyte, of the total population of Tukisenta, 95% of the population were examined(2); 780 of them were over the age of 15 years. The economy of this village is entirely one of subsistence farming based primarily on the sweet potato. It is a young population with only 21% over the age of 40 compared with 35% in Australia. The diet in this village is mainly the sweet potato, with carbohydrate providing 94% of the calories. Despite the low protein intake, there was no frank evidence of malnutrition, and serum albumin and globulin levels were normal. The salt intake was also very low, sodium excretion averaging only 10 mEq per day.

Almost all of the individuals were near 100% of the ideal weight in the age group 20-29 years; then the weight diminished with increasing age. There was little tendency noted for blood pressures to increase with age and hypertension was quite uncommon with only a 3% prevalence in males over the age of 40 years (Table 1).

Table 1. Percentage prevalence of hypertension (≥ 160/95 mmHg) in the population aged 40 years and over

<table>
<thead>
<tr>
<th>Melanesia (New Guinea)</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tukisenta&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3</td>
<td>8.8</td>
</tr>
<tr>
<td>Highlanders</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Polynesia (Small Islands)</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atiu-Mitiaro&lt;sup&gt;b&lt;/sup&gt;</td>
<td>10</td>
<td>21</td>
</tr>
<tr>
<td>Rarotonga&lt;sup&gt;b&lt;/sup&gt;</td>
<td>25</td>
<td>26</td>
</tr>
<tr>
<td>Cook Islands</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rarotonga&lt;sup&gt;c&lt;/sup&gt;</td>
<td>28</td>
<td>46.5</td>
</tr>
<tr>
<td>Pukapuka&lt;sup&gt;c&lt;/sup&gt;</td>
<td>3</td>
<td>6.7</td>
</tr>
<tr>
<td>Tokelaus</td>
<td>10</td>
<td>14.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>New Zealand&lt;sup&gt;c&lt;/sup&gt;</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ruatuhuna</td>
<td>11.4</td>
<td>25</td>
</tr>
<tr>
<td>Maoris</td>
<td>21</td>
<td>39</td>
</tr>
<tr>
<td>Rotorua</td>
<td>25</td>
<td>37</td>
</tr>
<tr>
<td>Europeans</td>
<td>27.5</td>
<td>33</td>
</tr>
</tbody>
</table>

<sup>a</sup> Sinnett & Whyte<sup>(2)</sup>.  
<sup>b</sup> Hunter<sup>(11)</sup>.  
<sup>c</sup> Frior et al. (12,13)
Maddocks \(^{(4)}\) studied a number of Melanesian populations. He found little hypertension in rural Fijians or among New Guineans, either highlanders or lowlanders, although the blood pressures were a little higher in coastal communities. In some of these New Guinea populations, there was a tendency for blood pressures to fall in the older age groups. He found salt intake to be low in many of these groups, especially in the highlands.

Lovell et al. \(^{(5)}\) compared blood pressures in Fijians and in Indians living in Fiji with Londoners studied by Hamilton et al.; the latter were taken to be representative of American and European findings. They found little difference in mean blood pressures up to the age of 45 years. Then, in the sixth decade, there was a divergence of blood pressures with the Londoners showing steeper slopes of rise with age. These earlier findings of Lovell among primarily urban Fijians differed from Maddocks' finding in rural Fijians and other Melanesians.

Lovell \(^{(6)}\) summarized the findings in seven studies in Melanesia. In five of the studies the mean blood pressures did not change with age. In two of the studies, the blood pressures actually declined with age.

Page et al. \(^{(7)}\) reported on six societies in the Solomon Islands. There were 1,267 males and females over the age of 15 years. Acculturation was paralleled by differences in diet, in the levels of serum cholesterol and uric acid, and in intrapopulation trends of blood pressure with age. In the three most acculturated societies systolic blood pressure rose with age in the females only (there was no change in diastolic pressure). In the four least acculturated societies diastolic blood pressure declined with age in the males only (there was no change in systolic pressure). Cardiovascular disease was absent in all six societies.

MICRONESIA

Lovell \(^{(6)}\) reviewed blood pressure findings in Micronesia - in the Gilberts, the Marianas, the Carolines, and the Marshalls. Blood pressures tended to be similar to those in Melanesia except for a slight increase in blood pressure with age. In several of the Micronesian islands, the blood pressures of women remained below those of men in later years, unlike the findings in most other studies. Labarthe and his colleagues \(^{(8)}\) studied three populations in various parts of Palau in the Carolines, southwest of Guam. The residents of Koror, the administrative centre of Palau, were more modern. They were found to be taller, heavier, and had higher blood pressures than individuals living in the more isolated and more traditional communities. Even in Koror, however, the blood pressures were low compared with most Caucasian populations.

The same group of investigators examined the effects of migration on Chamorros \(^{(2)}\), the natives of the Marianas Islands, and living in Rota, Guam, and California. Guam has undergone considerable westernization since the Second World War, but Rota, only 32 miles north of Guam, remains relatively unchanged and traditional. Blood pressure distributions were similar for all three areas. Systolic blood pressures increased with age, particularly among the females. High prevalence rates of hypertension and of stroke were found in all three Chamorro groups, and in this study no effects of westernization or migration could be shown with regard to blood pressure levels, blood pressure slopes with age, or the prevalence of hypertension (Table 2).
POLYNESIA

Murphy \(^{(10)}\) described blood pressures in Pukapuka, an isolated atoll in the northern Cook Islands near the equator. Hunter \(^{(11)}\) studied groups in the southern Cook Islands, in Atiu-Mitiaro (which, like Pukapuka, shows a traditional planting and fishing subsistence economy and a large dietary intake of coconut) and in Rarotonga, the Europeanized administrative, cultural, and commercial centre where the people adopt a more sedentary urban life-style and have a larger intake of calories and of animal fat. Prior and his colleagues also studied groups in Pukapuka and Rarotonga \(^{(11)}\), in the Tokelaus \(^{(12)}\), 300 miles to the west of Pukapuka, as well as three New Zealand Maori populations \(^{(13,14)}\), one isolated rural group living in Ruatahuna, a less isolated group living in Tikitiki, and a third group living in a major population centre, Rotorua.

Both Murphy and Prior found blood pressures in Pukapuka to be as low as anywhere in the world. In the Tokelaus and in Atiu-Mitiaro, equally isolated and traditional islands, and among the isolated rural New Zealand Maoris, intermediate levels of blood pressure and intermediate prevalence rates of hypertension were found. In the relatively urbanized and westernized Rarotongans in the southern Cook Islands and in Rotorua in New Zealand, there were high levels of blood pressure and a high prevalence of hypertension (Table 1).

The New Zealand Maoris were found to be at high risk for cardiovascular disease with regard to many factors: in blood pressure levels, in saturated fat content in the diet, in metabolic abnormalities such as diabetes, gout, and obesity, and in their serum cholesterol levels. The relatively urbanized Rarotongans in the southern Cook Islands were similar, although they had less exposure to westernization. Pukapukans were the healthiest of these Polynesian populations, leanest, with little hypertension, and a low rate of diabetes mellitus. Salt intake was very low in Pukapuka. In the Tokelaus salt intake was also low, but they showed more of an increase of blood pressure with age and more cases of hypertension. The Tokelaus also had much higher cholesterol levels (more

---

Table 2. Percentage prevalence of hypertension and stroke in male and female Chamorros, aged 20 years and over

<table>
<thead>
<tr>
<th>Place</th>
<th>Hypertension</th>
<th>Cerebrovascular accident</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Interview</td>
<td>Neurologist's diagnosis</td>
</tr>
<tr>
<td></td>
<td>history</td>
<td>diagnosis</td>
</tr>
<tr>
<td>---------</td>
<td>--------------</td>
<td>--------------------------</td>
</tr>
<tr>
<td>Rota</td>
<td>M 31 0 1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>F 30 1 2</td>
<td></td>
</tr>
<tr>
<td>Guam</td>
<td>M 34 2 0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>F 35 1 3</td>
<td></td>
</tr>
<tr>
<td>California</td>
<td>M 34 1 1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>F 32 2 3</td>
<td></td>
</tr>
</tbody>
</table>

---

100
than 200 mg%) owing, at least in part, to a much higher fat intake - 56% of calories in the Tokelaus compared with 35% in Pukapuka, with approximately 80% of the fat coming from coconut in both populations. Genetic factors may be important. A tsunami that devastated Pukapuka 300 years ago, leaving only 30 survivors, may have left a surviving gene pool low in susceptibility to hypertension.

Prior and Evans (11) studied sodium intake in relation to hypertension in Pukapuka, the Tokelaus, Rarotonga, and among New Zealand Caucasians living in Carterton. Despite the marked discrepancies between the low sodium intake among the Pukapukans and the Tokelauans on the one hand, and the high sodium intake among the Rarotongans and the Cartertons on the other, no association was found between blood pressure levels and the levels of 24-hour urine sodium output in any of these populations.

Cruz-Coke et al. (16) studied the effects of migration on the Easter Islanders. Among the islanders who remained he found a mean age of 32.8 years, mean diastolic pressure of 84.2 mmHg, and a slight increase of blood pressure with age. Among those who had migrated to mainland Chile, the mean age and blood pressure were similar at 34.4 years and 86.8 mmHg respectively, but the slope of blood pressure with age was significantly steeper among those living on the continent. These investigators gave no precise figures; however, they indicated that hypertensives were found in the continental population, but none among the islanders. Their criterion for hypertension was quite severe, requiring a diastolic pressure greater than 105 mmHg.

Data about stroke are available only for New Zealand (17) and for Hawaii (18). Data for the years 1954 to 1968 show that mortality from stroke was higher among the Maoris than among Europeans up to the age of 64 years; over this age, the European stroke mortality rate was higher. In the age ranges 25-44, 45-64, and 65 years and over, the respective Maori/European mortality ratios were, for males, 1.5, 1.5, and 0.7; for females the ratios were 1.6, 2.1, and 0.9, respectively.

HAWAII

Stokes et al. (19) examined 1 167 male employees of the City and County of Honolulu and of the Hawaiian Telephone Company. Of these, 1 131 were between the ages of 35 and 64 years. The prevalence of hypertension was greatest in the pure Polynesian group (27.9%), followed by the part-Polynesians (20.5%), the Filipinos (14.8%), the Japanese (14.5%), the Caucasians (13.1%), and the Chinese (lowest of all at only 5.8%) (Table 3). The finding of a high prevalence of hypertension among the Hawaiian-Polynesians is in accord with the findings among the more westernized Polynesians in New Zealand and Rarotonga.

From a study of a number of indices of cardiovascular disease among the various ethnic groups in Hawaii, it is clear that the Polynesians rank highest in every index, both among men and among women. The prevalence of hypertension in men is highest in the Polynesians, followed by the Filipinos, Japanese, and Caucasians with very similar prevalence rates, and then the Chinese with quite low rates. This last may represent a sampling variation since the Chinese are not low in other indices of cardiovascular disease associated with hypertension.
Table 3. Percentage prevalence of hypertension and mortality rates from hypertension and stroke by ethnic groups, Hawaii

| Ethnic groups | Prevalence (%) of hypertension \(^a\) (ages 35-64 years) | Age-adjusted death rates \(^b\) per 100 000 (ages 35-74 years) | | 
|---------------|-------------------------------------------------|-------------------------------------------------|---|---|
|               | Hypertension \(^c\)                            | Cerebrovascular lesions \(^c\)                  | 440-447 | 330-334 |
| Males:        |                                                 |                                                 | --- | --- |
| Polynesian    | 27.9                                           | 274                                             | 233 | --- |
|              | 20.5                                           | 204                                             | 179 | --- |
| Chinese       | 5.8                                            | 131                                             | 121 | --- |
| Caucasian     | 13.1                                           | 109                                             | 183 | --- |
| Filipino      | 14.8                                           | 94                                              | 165 | --- |
| Japanese      | 14.5                                           |                                                  | --- | --- |
| Females:      |                                                 |                                                 | --- | --- |
| Polynesian    |                                                 |                                                  | --- | --- |
| Chinese       |                                                 |                                                  | --- | --- |
| Caucasian     |                                                 |                                                  | --- | --- |
| Filipino      |                                                 |                                                  | --- | --- |
| Japanese      |                                                 |                                                  | --- | --- |

\(^a\) Stokes et al. \(^{19}\).
\(^b\) Bennett et al. \(^{18}\).
\(^c\) ICD, Seventh Revision.

Stroke incidence and mortality \(^{18}\) are highest among the Polynesians; the Caucasians are lowest, and the other three ethnic groups are intermediate.

Coronary heart disease mortality is lowest among the Japanese and Filipinos of both sexes with the Chinese and Caucasians in intermediate positions, and again the Polynesians at the top.

The rank order for total cardiovascular-renal disease mortality reflects the position of coronary heart disease mortality among men and it more closely parallels stroke mortality among women.

THE NI-HON-SAN STUDY

Some 12 000 Japanese men were studied \(^{20}\). They were aged 45-69 years at the time of their initial examination, and were living in Japan, Hawaii, and California. The age-adjusted prevalence rates for hypertension were respectively 22%, 19%, and 32%. The Hawaiian-Japanese rate of 19% appears consistent with the findings of Stokes et al., given the older age of our subjects. The prevalence rate of stroke was 39.0, 14.8, and 10.8 per thousand respectively (Table 4).
Table 4. Prevalence of hypertension and stroke and mortality rates from stroke (Ni-Hon-San study on Japanese males, aged 45-69 years)

<table>
<thead>
<tr>
<th>Study site</th>
<th>Prevalence of hypertension (%)</th>
<th>Prevalence of stroke (per thousand)</th>
<th>Average annual mortality from stroke (age 55-64 years) per 1000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Japan</td>
<td>22</td>
<td>39.0</td>
<td>3.6</td>
</tr>
<tr>
<td>Hawaii</td>
<td>19</td>
<td>14.8</td>
<td>1.3</td>
</tr>
<tr>
<td>California</td>
<td>32</td>
<td>10.8</td>
<td>0.9</td>
</tr>
</tbody>
</table>

a  Marmot et al. (21).

b  Worth et al. (22).

The three cohorts were followed by death certificate and other surveillance for the period between 1965 and 1971. Only in the older age range was the number of deaths from stroke large enough for analysis (22). The average annual mortality rate for men aged 55-64 years at the time of entry into the study was for Japan 3.6 per thousand, for Hawaii 1.3 per thousand, and for California 0.9 per thousand. The mortality from stroke among the California and Hawaii Japanese was similar to that among U.S. whites, while the stroke mortality in the same age cohort in Japan was nearly three times as high.

DISCUSSION

Lovell (6) suggested that, in young men, race is linked with blood pressure levels through the determinants of body build, with a strong correlation between systolic blood pressure and the weight/height ratios. Any such relation in older age is overwhelmed by potent environmental factors independent of race. His studies in Fiji suggested that some at least of these environmental factors are associated with westernization. This hypothesis gained some support from Labarthe's study of the Palauans where the Koror subjects, residents of an administrative centre, are taller, heavier, and have higher blood pressures than the more traditional atoll dwellers. It was also confirmed in Hunter's and Prior's studies of the Polynesian Cook Islanders where the more modern group, the Rarotongans, also showed greater height, weight, and blood pressure levels than the more traditional Cook Islanders living in Pukapuka and Atiu-Mitiaro. Cruz-Coke found more hypertension among those Easter Islanders who had migrated to Chile.

The suggestion from these studies of the Melanesians, Micronesians, and Polynesians, is that westernization, with its environmental, dietary, and behavioural influences, leads to higher cholesterol levels, greater weight and obesity, and higher blood pressure levels. The Ni-Hon-San data display the expected effects with regard to weight and cholesterol levels, but there is an inconsistent effect on blood pressure levels and on the complications of hypertension. The findings among the Chamorros in Rota, Guam, and California also show no effect of westernization on the prevalence
of hypertension. Moreover, the possibility of genetic selection owing to the isolation of islands cannot be ruled out.

In summary, marked differences have been found in the epidemiology of hypertension in Oceania. The data are contradictory with regard to the relative importance of genetic and environmental factors.

REFERENCES


DISCUSSION

Dr Doyle: Dr Kagan, in your Hawaiian studies, it appeared as though the Japanese had a significantly lower incidence of coronary artery disease than the other two groups. This was striking. Do you suppose that the comparatively high incidence of stroke could in fact be related to a peculiarly low incidence of ischaemic heart disease? As Dr Werkle said this morning, they have got to die of something.

Dr Kagan: If you look at those data, you will find that the stroke mortality is also low for the Japanese, at least when you compare it with that for the Polynesians, and not very much higher than that for the Caucasians.
Dr Doyle: A bit higher than the Caucasians.

Dr Kagan: But if you take total cardiovascular and renal mortality, it does not make up for it.

Dr Werky: Is the diagnosis of stroke in Japan in the Ni-Hon-San study an autopsy diagnosis? Is the diagnostic procedure comparable between Japan, Hawaii, and the USA?

Dr Kagan: The Ni-Hon-San study is a long prospective study. The data that we have here are strictly based on prevalence estimation. They are not based on mortality or incidence figures at all.

Dr Akinkugbe: Is there any intermarriage or cross-migration between the Polynesians and Micronesians? There is such a distinct contrast in these findings.

Dr Kagan: I do not have any specific data on that. The first slide shows primarily the patterns of migration perhaps 1000 or 2000 years ago from the Asian mainland and then within Oceania. You will notice that the distances we are talking about are really quite enormous and I would estimate that the chances of any of the Polynesians being in the Micronesian area are rather small. We are talking from West to East of probably 6000 miles or more, and these arrows show old-time patterns of migration. We know that there is some migration now from the Tokelaus to New Zealand, to Samoa, and to Hawaii; and there is migration from Samoa to Hawaii. I am not familiar with current patterns of migration in other parts of Polynesia.

Dr Sasaki: I should like to comment on Dr Kagan's paper. I reported, in 1966, on epidemiological clues to hypertension from a global viewpoint. I made a comparison of the daily salt intake and the blood pressure of populations according to the literature from various parts of the world, and I showed that there is some correlation between the two. Dr Dahl at Brookhaven National Laboratory in New York, I think in 1960, reported on the correlation between average habitual salt intake and the prevalence of hypertension, but I preferred the level of mean blood pressure and its distribution. I believe that these are more meaningful than the prevalence of hypertension.

The accompanying figure shows the kind of relationship we obtained and this would be an epidemiological clue to the problem of hypertension. Dr Akinkugbe mentioned that in Africa there are regional variations and there are also regional differences within Japan and they are related to salt intake. I think a long-term follow-up study of blood pressure and salt intake from childhood onwards is necessary.
**Global epidemiological studies on high blood pressure in the population and its relationship to the sodium chloride intake**

![Graph showing relationship between blood pressure and sodium chloride intake](image)

**Dr Kagan:** I would agree with Dr Sasaki that it would be very useful to gather as much information as is possible about dietary sodium. Any of us who are involved in epidemiological studies of large populations know how difficult it is to obtain reliable data on salt intake. Perhaps the most reliable would be to try to determine the 24-hour urine sodium output, which is not terribly practical when dealing with several thousands of people. If you are trying to do it on the basis of dietary interviews, particularly in Japan, I think you will have great difficulties: people eating salted pickles, people eating foods that are prepared with soy sauce and people using sauce as a dip. If a housewife buys a gallon of soy sauce and uses it all in a month, how much of that is ingested and how much is discarded after the food is prepared? The determination of salt in the diet is difficult and measuring salt output is time-consuming and difficult in large-scale population studies.

**Dr Shigematsu:** If you agree, I should like to close this session with a brief summary. First, how can we obtain useful data in developing countries? Concerning this point, Dr Kimura has mentioned the idea of conducting a survey by an international team. There may be several other methods to obtain the data. For example, a so-called tuberculosis surveillance study in developing countries is being planned with tuberculin testing in some selected areas. WHO has established world serum banks, one in Czechoslovakia, one in the USA, and one in Tokyo, collecting serum in various parts of the world, particularly in the developing countries. We can at least know the cholesterol level or some other biochemical markers. The most useful method is naturally to conduct a survey of a sample in developing countries. The second topic I wish to propose to you is what risk factors are the most important and amenable for intervention. I should like your opinion or suggestions concerning this matter but unfortunately there is not time left and I now declare this session closed.
II. THE CONTROL OF HYPERTENSION AND STROKE IN POPULATIONS

A. APPROACHES

THE COMMUNITY APPROACH TO CARDIOVASCULAR DISEASES

by

T. Strasser

Cardiovascular diseases - a public health problem

Cardiovascular diseases have evolved into a public health problem for two reasons. Firstly, their rate of occurrence in technically developed societies is so high that practically nobody is untouched by cardiovascular diseases. Even clinically healthy people may have a high prevalence of atherosclerotic changes of various degrees of severity\(^1\). The epidemiology of coronary risk factors would show that, in "western-type" societies, few middle-aged persons are free of at least one of the risk factors; and those individuals who would be found healthy from the clinical, anatomical and preclinical point of view would still be socially affected by some of the major cardiovascular diseases, because there are probably very few people whose relatives or friends remain spared from this epidemic.

The second reason why cardiovascular diseases are a public health problem, and more specifically, in the community health category is that the services needed for their control are, in many instances, so complex that they have to be based on the joint resources of entire communities. Naturally, efforts for the control of cardiovascular diseases ought to be made on a nationwide level, but facilities, such as emergency services, outpatient clinics, hospitals, rehabilitation services, patient home-care, and geriatric institutions are community categories almost by definition. Finally, the indispensable information system for the planning, functioning and evaluation of such a complex set-up of services is, by preference, organized on a community basis.

Community and disease control

After such assertive statements it may sound discouraging to say that it is rather difficult to define the term "community". In general, a "community" is a group of people, living in a locality or an area, having some common characteristics. The important point is that there are common
interests among the members of a community, making common action possible and desirable. The concept of community is changing, emphasis is shifting from topographical boundaries to considerations of the interaction in the common activities of life\(^{(2)}\). Communities themselves are nowadays changing rather rapidly, having, like the amoeba, changing shapes and surfaces, and incorporating and digesting parts of other, often foreign, populations. The mobility of populations is sometimes quite considerable, and the extent of inflow may differ widely from that of outflow. This living, dynamic, rather fluid social category differs considerably from the stable, well-established, traditional communities. From the point of view of health care and disease control, the important point is the level of general community organization. There is an interdependence between the level of health services and the general level of organization of a community\(^{(1)}\), and this interdependence fully applies to the control of cardiovascular diseases.

The term "control of disease" is used in its widest sense, referring to all aspects of prevention of disease or its complications, early diagnosis, appropriate treatment, rehabilitation, health education, and includes also endeavours to acquire more knowledge of diseases\(^{(4)}\). Several elements of disease control may, of course, be substantiated within the classical, traditional, individual doctor-patient context, but only at an exceedingly high cost of energy, time and money. It does not seem possible to reach the majority, even less all the members of a community, unless a designed, organized approach is taken within the context of the whole community, i.e., a control programme is established. A control programme of a disease or a group of diseases is viable only if it is not an isolated undertaking but an organic part of overall health activities, a subsystem of a more comprehensive system. To make it efficient, it has also to be tailored to the situation in the community, it ought to suit the needs and resources of a particular community, and should take into account the epidemiological and health-care specificities of the given community.

The information basis of control programmes

The epidemiology of disease and of health care has some common characteristics on a worldwide level, but important features may differ even between adjacent communities. In order to establish a control programme with the right design, the "community history" of a disease should be known in general. It is also essential to become acquainted with the specific epidemiological and health-care situation in the particular community: a "community diagnosis" of a disease or group of diseases should be established prior to organizing a control programme.

Let us take some examples. The natural history of ischaemic heart disease has been studied for many years and a great amount of data were accumulated on the evaluation and the course of the disease, such as the prognostic significance of various ECG abnormalities, of the site and size of infarction, and of enzyme levels. This information was based on hospital observations. More recently, however, when investigators started collecting data based on whole communities, it became apparent that hospital observations cover only part of the problem, because a great number of patients die early, and do not reach the hospital at all. From various studies\(^{(2-10)}\) a new picture of the natural history of acute ischaemic heart disease has emerged, as seen in whole communities, where most of the fatalities occurred during the first hour after the onset of symptoms. This information has led to the well-known reconsiderations and reorgani-
zation of services for acute ischaemic heart disease, with an emphasis on the earliest stages of health care, such as coronary ambulances (mobile coronary care units).

When the reasons for the delays in admission to hospital were analysed, it became evident that several factors were involved. Patients or their family members were hesitant in calling a physician when the attack started. It took some time for the physician to respond to a call. It also took time to get an ambulance and to transport the patient to the hospital, and even after arrival at the hospital valuable time was often lost before a patient was admitted to a coronary care unit. Thus a three-hour lag between the onset of symptoms and admission to the coronary care unit may be due in one community, typically, to prolonged hesitation on the part of the patient, but once he has called for an ambulance he may find himself, within a few minutes, in a coronary care unit. In another community, it may be that very frequently the patients summon their physicians as soon as they feel violent chest pain, but it may take almost an hour for him to arrive, after which the physician may hesitate between home care and hospital; finally, he will call an ambulance, but owing to heavy traffic there may be further delays and it may even have to proceed to several hospitals before a vacant coronary care bed is found. The delay in both cases may be the same, but the "community diagnosis" is different, and different action should be undertaken. In the first case, emphasis should be on information and education of the public, perhaps with special attention paid to high-risk people in the community. In the second case, the emergency services themselves should be reorganized, and made more efficient at the community level.

These examples have been simplified intentionally. In real life situations a greater number of factors may be involved, but the effect and even the viability of a control programme in a community depend on exact knowledge of the actual situation. Planned action to overcome general as well as specific difficulties must be founded on comprehensive community based information.

In many parts of the world, a community approach to hypertension will probably show that there are a considerably greater number of hypertensives in the general population than anticipated on the basis of current statistical data. Many people may not be aware of their elevated blood pressure; those who are aware of it may still be untreated or inadequately treated. It may also happen that current morbidity figures show a large number of visits to physicians for hypertension; closer scrutiny of the situation in the particular community may reveal that this is in fact due to overutilization of health services by a certain group of patients, say, elderly rather obese female patients with slight elevations of blood pressure. At the same time, the bulk of those younger patients to whom treatment would be of much greater benefit may remain undetected. Yet another possibility would be that few hypertensives in the community are undetected, but most of those under treatment still have high blood pressure values, far higher than the optimum that could be reached by up-to-date therapy in spite of their being under medical care. In all three cases, different control actions should be undertaken. In the first case, the solution may be large-scale screening for hypertension in the whole population. In the second case, it would be more practical to search for hypertension in occupational groups, perhaps in cooperation with occupational health services. The third case may call for an emphasis on physicians' education, to achieve better treatment of the already detected hypertensives. In
practice, all three and even many other elements may be combined. However, by knowing more about the community, the control programme can be adjusted to the actual situation, and thus better results may be obtained in less time and with less investment.

Similarly, the "community diagnosis" of stroke may reveal, besides reliable figures on the incidence in the general population, important details on health care in the acute stage, attitudes towards hospitalization as against home care, inadequacies in rehabilitation, and also information on missed opportunities to prevent stroke. Further examples could be quoted for pulmonary heart disease and rheumatic heart disease, to which also a community approach should be taken.

**Action**

Several measures are available for action at the community level. Disease registers are an important means for acquiring information on the community, the disease, and its care. Usually, control programmes are built up around registers, registration being the backbone of many community control programmes. Registers are not only passive instruments for collation of data, they should also play an active role in the community health services, particularly in securing systematic follow-up of registered patients.

Screening is another important element of community control programmes. Screening (for example, in rheumatic heart disease) can be done from house to house, or in occupational groups at the place of work or in schools. Screening may also be carried out as an additional activity in the course of normal health care; thus, measuring the blood pressure of any person who goes to his physician for any cause (common cold, dermatitis, back pain, etc.) may reveal any previously undiagnosed cases of hypertension. The introduction of new systems to the health services, such as the reorganization of emergency services, establishment of outpatient polyclinics, introduction of domiciliary nurses or social workers, and starting "meals on wheels" or "meals by mail" services are important aspects of community control programmes.

Education is a rewarding component of community control programmes, both the education of physicians and that of the general public. Such activities may yield an important return for relatively modest investments, and the results may be self-multiplying. Considerable experience is needed in order to make educational activities effective. Lip-service is of no use. The framework of a community may be the best setting for both physicians' education and lay education on selected cardiovascular topics.

We are still just beginning to understand the community approaches to cardiovascular diseases. There is no doubt that mass phenomena need mass approaches. In many respects, the behaviour of both the lay public and the medical profession is of crucial significance; much more should be known in this field. We are still far from mastering any of the methods of community intervention, and of being able to measure and evaluate the effects of community control programmes. The programmes that are under way are still experimental, pilot undertakings. Eventually, they will result in more knowledge on how cardiovascular diseases can be brought under control in entire population groups. In the meantime, more research is needed. WHO is therefore fully engaged in investigating the various pathways of community approaches to cardiovascular diseases.
REFERENCES

1. Data from WHO collaborative study of atherosclerosis in populations. (to be published)


THE USES OF HYPERTENSION REGISTERS

by

T. Strasser

Registers are often used in epidemiological studies of cardiovascular diseases and these registers are of various types: hospital, health service, community, and nationwide registers. Concerning their objectives, one may distinguish registers that serve only for collation of information, and those that are actively being used for intervention work in the control of cardiovascular diseases. As far as the subjects are concerned, there are single-disease registers and comprehensive registers, covering all the major cardiovascular diseases, such as hypertension, stroke, myocardial infarction, and chronic cor pulmonale.

Truly comprehensive registers are still to be devised and WHO hopes to tackle this important task very soon. Experience has accumulated, however, on the other types of register.

For example, a simple hospital-based cardiovascular register has been operating for several years at the Department of Medicine, University Teaching Hospital in Ibadan, Nigeria. Data were recorded on manually operated peripheral punch cards. The structure of hospital morbidity indicated that hypertensive heart disease is the leading cardiovascular cause of hospital admission, far ahead of the second cause, rheumatic heart disease.

From the epidemiological point of view, population-based registers are far more important than hospital registers. According to the basic requirement, they cover a whole, defined population group. An entirely different pattern of a disease, or of disease groups, may thus be gained, as in the experience with the myocardial infarction registers: only when all the cases in entire populations were studied did it become evident that most deaths occur during the first hour after the onset of symptoms.

Community-based registers are the backbone of community control programmes of cardiovascular diseases. This definitely applies to hypertension control programmes. In the cooperative WHO Hypertension Control Project the register is conceived as an operant control instrument, or a tool of intervention. The purpose of the hypertension register in the context of the community control programme is to identify the community problem, to monitor the operation of the control programme, to provide feedback information for improving the intervention, and to yield the data for a final evaluation of its effectiveness.
Fig. 1 shows the functions of the hypertension register in the WHO project. Its first function is to assess the extent of the hypertension problem in the community at the initial stage, i.e., to yield information on the number of hypertensive persons, on the load hypertension imposes on the community, and on the health care situation before intervention is started. In other words, the first purpose of the register is to make an initial "community diagnosis" of hypertension.

Based on the initial information, the next step is to start intervention. The main components of intervention in the community are promotion of early diagnosis and of consistent, continuous treatment. The principal pathways are the search for undetected cases, the education of physicians, and education of the public. Intervention will alter the hypertension situation in the community. The register monitors these alterations by community surveillance of hypertension. Data are obtained by annual follow-up examinations of all registered hypertensives. This information is analysed by the register and fed back to the intervention programme. Possible deficiencies of the programme can be corrected in this way. Accordingly, the control programme continues its corrected operation. By the end of a study period the hypertension situation is reassessed and, based on the final assessment, the overall effectiveness of the control programme is evaluated.

The register thus really plays a leading role in the community control programme of hypertension. The whole operation is viable only if there is a smooth and steady flow of information between the community and the register. The vehicles for all this information are the record forms (initial and follow-up records) containing relatively simple data. A detailed protocol is available with instructions on data collection so that standardized comparable information from the various centres cooperating with WHO will be obtained.

Information flows within the programme as presented in Fig. 2 and 3. The flow-charts show two main circuits consisting of the initial stage and follow-up. Two smaller circuits show how a search is carried out if follow-up information is missing, or how a registered hypertensive person may be removed from the register.
FIG. 2
FLOW-CHART OF PROGRAMME OPERATION I
(Medical activities and data collection)

Programme Centre

Conclusions
Evaluation
Feed-back to
programming
Feed-back to WHO

Data Analysis

Individual Physicians

Screening

Patient’s initiative

Physician joining

Hypertension Clinic

Referral from hospital or physician

Initial examination

Inpatient examination

Special work-up (if necessary)

Complete initial record

Complete initial record

Regular follow-up

Regular follow-up

Annual follow-up

Annual follow-up

Cure: 5-year follow-up

Death

Permanent absence

Reiterated refusal

Cure

FIG. 3
FLOW-CHART OF PROGRAMME OPERATION II
(Search for medical information)

Record expected by Registry

Received

Not received

Inquiry with clinic or physician

Patient brought to doctor

Data Analysis

Record received

Record not received

Removal point reached

Removal point not reached

Send out field worker

Information not obtainable

Information obtained

Removal point reached

Removal point not reached

Remove from Register

Remove from Register
All information flows towards the register, which is indeed at the centre of the whole community programme. The register is thus the "memory" of the community control programme, in a certain sense its "brain".

Very much like the computer itself, the register does only what it has been programmed to do. It is of use only if the information processed by the register is evaluated, i.e., absorbed and digested, and if the results of this process are resynthesized into new knowledge. This is exactly what the pilot projects, coordinated by WHO, are designed to achieve.
EXPERIENCES WITH COMMUNITY

STROKE REGISTERS*

by

S. Hatano

The possibility of preventing premature stroke, particularly intracerebral haemorrhage, by controlling hypertension has been well documented. The principles of rehabilitation of stroke patients have also been developed to such an extent that many of them are able to look forward to reintegration in society. The application of all this knowledge for the best benefit of the maximum number of people calls for a systematic approach. Accurate information on the current situation is also a prerequisite for planning, promoting, and evaluating control measures for any disease, including stroke.

National mortality statistics

Mortality statistics are available for many parts of the world and should be used more widely and wisely. Even with the use of the international classification of diseases, however, the mortality statistics from many countries cannot be accepted without reservation. The cause of death is frequently given on the basis of poor evidence - or no evidence at all - or is, in some places, decided by a district officer with no medical training. It is known that strong bias is introduced by the diagnostic methods of physicians; for example, a tremendously rapid fall in the ratio of cerebral haemorrhage to infarction from 41 to 0.6 over 22 years in Japan cannot yet be explained.

Hospital and community case study

Selection bias is inevitable in the study of hospitalized patients. The frequency or severity of a disease among hospitalized patients depends upon the admission policy of individual hospitals, and also on social or medical factors. A higher fatality rate is experienced in the more specialized hospitals, owing to the fact that they admit the more severe cases. In order to investigate the magnitude of the problem and the quality of medical services in a community, the whole community must be covered by the study.

* This is an account of a collaborative study coordinated by WHO. The centres and principal investigators are as follows: G\text{"oteborg (P. Harmsen); Copenhagen (J. Marquardsen); Dublin (A. Radic); Espoo (K. Aho); North Karelia (P. Puska and K. Salmi); Moscow (E. V. Shmidt, T. A. Makinskij and V. E. Smirnov); Zagreb (Z. Poljakovic); Zerifin (L. Getner); Ibadan (O. O. Akinkugbe and B. Osuntokun); Akita (S. Kojima); Saku (K. Isomura); Fukuoka (T. Omae); Osaka (Y. Komachi); Japan National Railways (K. Kondo); Ulan Bator (N. Dondog); WHO (S. Hatano and K. Uemura).
Stroke is the commonest cause, after heart disease, of death and disability in the elderly. Thus, mentally or physically handicapped old people present a serious family and social problem in many countries and the study of all age groups is necessary to assess the weight of the problem in the community. How can a country or community provide better services and make more efficient use of the existing medical services? And how can the present conditions of health care be improved? Studies on the current situation of stroke patients in the community are awaited. For this purpose, a WHO group has worked out the essential items and methods for the collection of relevant data.

Multicentre approach

The experiences in one community cannot be generalized for application in different countries, or even in different communities in the same country. However, a comparison between different communities enables us to identify the common features that can be applied to other communities as well, such as the possibility of preventing stroke by the control of arterial hypertension, and the ineffectiveness of current medical services for this purpose unless specifically reinforced. On the other hand, when differences are recognized, we should seek an explanation. This offers an opportunity to gain fresh ideas on etiology, to observe different approaches to care and rehabilitation, and to evaluate the effect of prevention and the effectiveness of the available medical services.

In order to compare the results from several centres, the definitions, terminology, data to be collected, and procedures should be standardized and strictly followed in all the collaborating centres.

Adequate size

When the number of patients is small, the reliability of data is limited because age, sex, accompanying disease, and other factors concerning individual patients have an influence on morbidity, case fatality, and recovery potential. Sufficiently large numbers of patients are therefore required to draw reasonable conclusions.

WHO stroke registers

Considering all these points, a WHO stroke register was initiated in 1971 in order to improve the situation in prevention and in the treatment and rehabilitation of stroke patients of all ages in a well-defined community. Until its feasibility and usefulness has been evaluated, this approach cannot be recommended for application to a whole country, or on a worldwide scale. Thus, the present study is, of necessity, a pilot one. To test the feasibility of the programme, it is desirable to organize the study in communities already providing a variety of medical services. Our ultimate goal is to build up gradually, in each centre according to local conditions, a comprehensive cardiovascular disease control programme as an integral part of the general health services.

Such a model already exists in the WHO cooperative study, for example, on a large scale in North Karelia, Finland, and on a smaller scale in a few Japanese centres (Akita, Fukuoka, Osaka, Saku, and an occupational group of the Japanese National Railways). At present, 15 centres (seven in Asia
of which five are in Japan, one in Africa, and seven in Europe) are cooperating in the study. The smallest area, Frederiksberg County of Copenhagen, has a population of about 100,000 living in 8.7 km$^2$. The largest area, North Karelia, Finland, covers a population of 180,000 living in a forest area of 21,000 km$^2$. The study comprises cities, towns, villages, plains, and mountain areas, as well as centres in temperate, subtropical, and tropical zones (see Table 1).

In all study areas, a stroke register centre has been established under a permanent physician with secretarial staff and visiting nurses. In these areas, the standard of medical services may be higher than in other parts of the country, since the centres are particularly interested in the stroke problem, and thus naturally provide a higher quality of service than elsewhere. Therefore, the study areas cannot be representative of a whole country, but the register certainly offers the most accurate information from a particular area, and the information collected is expected to form a useful basis for research as well as for planning national and local health action.

Data collection

The following list shows the major items on which information is collected:

**Identification and registration**
- Registration number; centre
- Date of completion of record form
- Date of birth; sex
- State of patient at time of notification (alive or dead)
- Preliminary diagnosis

**Personal conditions**
- Civil status
- Living conditions
- Working conditions
- Occupation
- Type of help for personal care

**Previous medical history**
- Stroke
- Acute myocardial infarction
- Other heart diseases
- Arterial hypertension
- Treatment of hypertension immediately prior to stroke
- Diabetes mellitus
- Patient's capability of self-care before stroke
- Control of bladder before stroke

**Early stages of present attack**
- Date of onset or detection of stroke
- Admission to hospital
- Date of admission
Table 1. Centres collaborating in the WHO stroke register

<table>
<thead>
<tr>
<th>Country</th>
<th>Study area</th>
<th>Characteristics of the study area and population</th>
<th>Area (km²)</th>
<th>Total pop. (x 1000)</th>
<th>% pop. aged over 65</th>
<th>Other WHO studiesa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Denmark</td>
<td>Frederiksberg Copenhagen</td>
<td>Urban residential area, with commerce and light industry</td>
<td>9</td>
<td>100.0</td>
<td>21.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Espoo and Kauniainen</td>
<td>Developing neighbour towns to Helsinki. Rapid population growth, commerce, services and industry</td>
<td>315</td>
<td>103.5</td>
<td>5.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>North Karelia</td>
<td>Sparsely populated. Agriculture. Large emigration rate</td>
<td>21 000</td>
<td>180.0</td>
<td>8.6</td>
<td>Comprehensive CVD prevention, AMI register, HT control</td>
</tr>
<tr>
<td>Ireland</td>
<td>Southern Dublin</td>
<td>Urban, residential area. Some industry</td>
<td>19</td>
<td>133.7</td>
<td>8.4</td>
<td>AMI register</td>
</tr>
<tr>
<td>Israel</td>
<td>Ramle and Rehovot</td>
<td>Urban and rural</td>
<td>1 610</td>
<td>218.0</td>
<td>6.8</td>
<td></td>
</tr>
<tr>
<td>Japan</td>
<td>Akita</td>
<td>Agriculture. Northern part known to have very high incidence of stroke</td>
<td>896</td>
<td>36.1</td>
<td>5.9</td>
<td></td>
</tr>
</tbody>
</table>

a AMI: acute myocardial infarction; CVD: cardiovascular diseases; HT: hypertension; RHD: rheumatic fever and rheumatic heart disease.
Table 1. Centres collaborating in the WHO stroke register (continued)

<table>
<thead>
<tr>
<th>Country</th>
<th>Study area</th>
<th>Characteristics of the study area and population</th>
<th>Area (km²)</th>
<th>Total pop. (x 1000)</th>
<th>% pop. aged over 65</th>
<th>Other WHO studies¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Japan (contd)</td>
<td>Saku</td>
<td>Agriculture, and light industry. Central part hilly</td>
<td>1 044</td>
<td>105.2</td>
<td>10.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fukuoka</td>
<td>Rural towns plus a part of Fukuoka city. Age up to 65</td>
<td>79</td>
<td>36.8</td>
<td>7.2</td>
<td>HT control</td>
</tr>
<tr>
<td></td>
<td>Osaka</td>
<td>Developing neighbour town to Osaka. Agriculture and commuter area. Rapid population growth</td>
<td>106</td>
<td>40.4</td>
<td>4.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Japan National Railways</td>
<td>Male employees in Tokyo region. Age up to 60</td>
<td>14 752</td>
<td>74.7</td>
<td>0.0</td>
<td></td>
</tr>
<tr>
<td>Mongolia</td>
<td>Ulan Bator</td>
<td>Urban</td>
<td>261.3</td>
<td>4.4</td>
<td></td>
<td>RHD control</td>
</tr>
<tr>
<td>Nigeria</td>
<td>Ibadan</td>
<td>Urban</td>
<td>64</td>
<td>750.0</td>
<td>?</td>
<td>HT control</td>
</tr>
</tbody>
</table>

¹ AMI: acute myocardial infarction; CVD: cardiovascular diseases; HT: hypertension; RHD: rheumatic fever and rheumatic heart disease.
Table 1. Centres collaborating in the WHO stroke register (continued)

<table>
<thead>
<tr>
<th>Country</th>
<th>Study area</th>
<th>Characteristics of the study area and population</th>
<th>Area (km²)</th>
<th>Total pop. (x 1000)</th>
<th>% pop. aged over 65</th>
<th>Other WHO studies³</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sweden</td>
<td>Göteborg</td>
<td>Urban with industry, commerce and services. Age up to 65</td>
<td>451</td>
<td>450.9</td>
<td>9.6</td>
<td>AMI register, multifactor prev. of AMI, rehabilitation of AMI</td>
</tr>
<tr>
<td>USSR</td>
<td>Tusino rayon Moscow</td>
<td>Urban</td>
<td>30</td>
<td>209.0</td>
<td>?</td>
<td>HT control</td>
</tr>
<tr>
<td>Yugoslavia</td>
<td>Zagreb, part</td>
<td>Urban</td>
<td>14</td>
<td>85.5</td>
<td>13.2</td>
<td></td>
</tr>
</tbody>
</table>

³ AMI: acute myocardial infarction; CVD: cardiovascular diseases; HT: hypertension; RHD: rheumatic fever and rheumatic heart disease.
Clinical state at time of maximum impairment on date of attack

Level of consciousness
Motor defects of limbs
Speech disturbance
Blood pressure
Bed or pressure sores
Joint contracture

Diagnosis at three weeks after onset and examinations performed

Final clinical diagnosis
Examination by physician
Examination by neurologist
Lumbar puncture
Angiography
EEG
Brain scan
Echoencephalography
ECG
Blood pressure at three weeks after onset

Transfer of patient since previous interview

Type of institution where the patient was at previous interview
Type of institution and data of each transfer

Medical history between regular follow-up interviews

Recurrent stroke
Acute myocardial infarction
Antihypertensive treatment
Rehabilitation

Activity of daily living

Bed- or chair-ridden and must be carried
Control of bladder
Self-care
Walking

Death

Date of death
Place of death
Autopsy, brain autopsy
Clinical causes of death
Autopsy findings

The utmost care has been taken to achieve as complete coverage as possible, in order to obtain accurate information on the magnitude and nature of the stroke problem in each study area. Continued effort has been made to maintain regular contact with the hospitals and general practitioners in and around the study area, periodic checks of death certificates, and contact with a medico-legal department to ensure complete case finding.
Incidence rate of stroke

An annual incidence rate was calculated from the data collected during the initial one-year period. A striking contrast between the European and Israeli centres on the one hand, and the Japanese centres on the other was apparent. Differences were also observed within the European centres and within the Japanese centres. The age/sex-specific incidence rate was very high in Akita and the Japanese National Railways. No explanation for the different morbidity can be made at the present time. The incidence rates were relatively high in the two centres in Finland, where the highest mortality from cerebrovascular disease among European countries has been reported.

The study areas are not representative of the country as a whole. National mortality statistics reported to and published by WHO are strongly influenced by death certificates signed by general practitioners without reference to standardized diagnostic criteria. However, more accurate incidence rates from this register appeared to correspond to mortality rates in some countries, thus supporting the careful use of mortality statistics as a rough measure of the magnitude of the stroke problem.

Another interesting general feature, which emerged from the study, was the lower incidence rate in women, even in the age group of 65 years and over in both the European and Japanese study areas. The incidence rates in women exceeded those in men only in the top age group—over 75 years—but this, too, can be explained by a high frequency of very old female patients in this inhomogeneous age group. This is in accordance with recent reports from the USA, where the incidence of stroke in men exceeded that in women, even after 65 years of age in whites. This is contrary to the expectation that women have a higher incidence of stroke, since hypertension is more frequent in women after the menopause. It would be worthwhile to study blood pressure distribution in these populations in both sexes in the WHO programmes in the study area. Such combined hypertension and stroke control in the same area has been advocated for research and as a concerted public health activity.

Control of hypertension

Concerning the control of hypertension, which is the most effective means of preventing stroke according to present knowledge, two related questions are contained in the WHO stroke register: (1) Did the patient know that he had hypertension prior to the stroke? (2) Was the patient under treatment for hypertension by a physician prior to the stroke? Treatment in this instance means any kind of instructions, including drugs, given by a physician and is therefore rather loosely defined.

Nevertheless the data are interesting. About one half of the patients reported that they had hypertension. In the European and Israeli centres, the frequency of known hypertension was a little higher in women, whereas in the Japanese centres the reverse trend was observed. The frequency of known hypertension was slightly less in older than in younger patients. These data may indicate the section of the population to which more attention has been paid, or those who paid more attention to their health conditions, if the prevalence of actual (not only known) hypertension prior to the stroke is assumed to have been equal between these groups.
The frequency of known hypertensives was much higher in Japanese than in European centres (76% and 44% respectively). This is due to the awareness of the population in Japan about blood pressure and stroke, and to repeated earlier campaigns against hypertension and stroke. It is also possible that hypertension is more often associated with stroke, as shown by the high frequency of intracerebral haemorrhage in Japan. When antihypertensive treatment prior to stroke was studied, the results were rather disappointing. About 30% of the total number of stroke patients were on treatment. About half of these may have been treated inadequately according to experiences obtained from American, European, and Australian communities.12,13,14

Women generally received more frequent treatment than men, but no difference was observed between two age groups: under 65, and 65 years and over.

As regards treatment, the treatment of Japanese patients was no more frequent than European and Israeli patients, indicating that to keep hypertensive patients on effective antihypertensive treatment is a greater problem than case finding.

**Type of medical services used**

A great difference was apparent in the use of hospital services for stroke victims. Hospitalization is determined by the admission policy of individual hospitals or departments. Various other factors, such as the severity of stroke, the attitude of the family and general practitioner, and transportation facilities, are also implicated. As there is no doubt about the better quality of care in hospital, this should be made available to all patients with acute stroke.

In the western European centres, over 85% of patients were hospitalized, the remainder being those who died very early or who were found dead, and those whose symptoms were minor ones. In Japan, except for one occupational population, less than half the patients, an average of 43%, were hospitalized. This was true also for rehabilitation. More than two-thirds of stroke patients received rehabilitation treatment within three weeks after onset in the European centres, whereas fewer (31% on average) did so in the Japanese study areas.

**Diagnostic procedures carried out**

Home care has drawbacks, not only for rehabilitation but also for carrying out diagnostic procedures and therefore for rational therapy. It has been said that intracerebral haemorrhage is more frequent in Japan, but this has not been firmly established. The low reliability of the clinical diagnosis of the type of stroke is well known,15 but the Hisayama study with a high autopsy rate at the community level in Japan was unable to support this.16

In the WHO stroke register, the relative frequency of intracerebral haemorrhage was also extraordinarily high in the Japanese communities compared with the other communities (32% against 12% of the total numbers with stroke).
In three out of the five Japanese study areas, lumbar puncture was not performed in a single case diagnosed as intracerebral haemorrhage. In the other two centres, it was done at the same frequency as in other study areas, i.e., on average, for all the collaborating centres in only 16% of patients with diagnosed intracerebral haemorrhage. However, considering the high early fatality rate of intracerebral haemorrhage, when only those who had survived up to three weeks after onset (which allowed sufficient time for examination) were studied, the frequency of patients who underwent lumbar puncture increased to 57% on average, and nearly 90% in the two Scandinavian centres.

Autopsy is the only way of confirming the clinical diagnosis, and was performed in about 25% of all the registered stroke patients who died. In North Karelia, Zagreb, Ramle, Rehovot, and all the Japanese study areas, the autopsy rate was low (10% on average). In the two Scandinavian cities, it was 75%.

The frequency of the following examinations: lumbar puncture, angiography, or brain autopsy, was taken as an indicator of the objective evidence for diagnosing the type of stroke. The Japanese centres that reported a higher frequency of intracerebral haemorrhage were using these examinations less than the European centres (70% against 90%), and these circumstances cast suspicion on the reliability of the frequent diagnosis of intracerebral haemorrhage in Japan.

It should be emphasized that the intention of this study was to ascertain the frequency of these examinations as applied to patients in the community at large, because indiscriminate lumbar puncture, or other clinical investigation, is not recommended. These examinations should be carried out in any place with only a view to the best benefit of the patient.

Case fatality

A sharp contrast is apparent between the European and the Japanese communities in case fatality rate. In the Japanese communities a large number of patients - almost a quarter - died on the first day, after which the fatality rate dropped. In the European centres, case fatality on the first day was about half, or even a quarter, of the Japanese figure, but thereafter the fatality rate decreased more gradually, reaching almost the same value as in Japan at two or three weeks.

There are three possible explanations:

(a) The fatality curve of Japanese patients is closer to that of young patients and that of European patients than to that of older patients, the difference being in the age composition of patients.

(b) The second possible explanation reflects the severity of the common types of stroke in the study areas. In the one case, about one-third of the patients with intracerebral haemorrhage died on the first day, and the fatality rate then decreased during the next 10 to 14 days. In the other case, only 5% died on the first day and this initially low fatality rate then continued in patients with ischaemic cerebral necrosis.

(c) Another possible explanation is that there is insufficient care for the patients treated at home who form the majority in the Japanese communities.
Explanation (a) is unlikely, because the age composition does not differ greatly between the European and Japanese centres; (b) and (c) are possible, but (b) has not been well confirmed so that (c) - lack of adequate care at home - seems to be the most likely cause of the initial very high fatality rate in Japan. This extremely high fatality rate in turn leads to a fatalistic attitude on the part of physicians, families, and administrators, thus making a vicious circle in any attempts to improve the quality of care.

The role of WHO and future study

Only a few results which appear to be relevant to the control of stroke in Japan are briefly introduced here. The available information from the stroke register suggests various ways of tackling the control of stroke at a community level - locally, nationally, and internationally - and also of assessing them.

WHO has been actively involved, from the start of the study, in planning and standardizing the methods; testing the uniformity of procedures; checking the data collected, data storage, and central analysis; organizing meetings of investigators; promoting exchange visits between investigators; and maintaining communication on the progress and problems between the collaborating centres.

WHO also provides token financial support, which is aimed at encouraging government and other voluntary contributions to the programme.

Starting from the stroke register in the community, various other related individual or joint studies are foreseen. A clinical study, too, will be strengthened by the avoidance of selection bias and other bias in the conclusions. Improving the criteria for the clinical diagnosis of the types of stroke, more sophisticated evaluation of various types of care, and the study of transient cerebral ischaemia at an international level are possible examples of substudies. Another important direction of community-oriented action is to develop a more comprehensive cardiovascular disease control programme, using the experience obtained in this collaborative study. These developments require fresh ideas and suggestions, discussion of which is the main purpose of the present meeting.

REFERENCES


**DISCUSSION**

**Dr Ito:** The registration system of stroke was introduced in Akita prefecture last year. It seems that the registration rate is very low, only 20-30%; therefore we cannot make any conclusions. Out of 19 patients who were referred to us our diagnosis differed in seven cases, after detailed examinations including cerebral angiography: two cases with the referral diagnosis of cerebral haemorrhage turned out to be subarachnoid haemorrhage and two others, referred as cerebral haemorrhage, had infarction; in three further cases, the initial diagnoses were incorrect.
Dr Komachi: In the areas in Akita prefecture where we are registering stroke patients, we explained the criteria for the diagnosis of stroke to the local doctors. Our clinical diagnosis agreed with the autopsy diagnosis in over 80% of the autopsied cases. The autopsy rate in a central hospital is around 85%.

Dr Hatano: A low registration rate may lead to erroneous conclusions in Dr Ito's register. In the WHO stroke registers we take great care to cover completely all stroke patients who appear in the registration area.

Dr Schmidt: I believe that Dr Hatano's proposal to register transient ischaemic attacks is very correct. Our experience showed that 6% of all calls related to patients with stroke were in reality not stroke cases, but patients with a transient ischaemic attack and we registered them.

Dr Toole: In North Carolina we have a stroke registry which encompasses 22 of its 100 counties divided among the mountains, the Piedmont, and the coastal areas so that we have a variety of altitudes and climatic conditions, which was mentioned earlier as a possible differentiating point in the frequency of stroke. We have registered over 2200 patients with various forms of stroke and selected from this large number 480 who had an evolving cerebral infarction. In this group we were able clearly to differentiate between those patients who had a good prognosis and those who did not. The most important prognostic factor was the level of consciousness at the time of admission to hospital. We found that hypertension did not influence the course of cerebral infarction, and we found further that early rehabilitation, instituted within 48 hours of the onset of the stroke, was definitely associated with better survival.

Dr Weiss: I heard that not very many of Japanese stroke patients get early rehabilitation. Do you have any late follow-up statistics to show how many patients are dependent and what kind of home rehabilitation is ensured for them?

Dr Hatano: We are at present collecting information at three weeks, three months, and one year to see how dependent the patients are and how many of them are working; but it is premature to report the results. In the Japanese centres, there is a slightly higher rate of complications, such as bedsores and joint contracture. The rate of dependency does not seem to differ very much between stroke patients who received early rehabilitation and later rehabilitation.

Dr Isomura: It has been mentioned that lumbar puncture was performed in a few cases in Japan. Of the total annual incidence of 286 cases in my area, 100 were admitted to my hospital and almost all of them were subjected to lumbar puncture. It was seldom performed on the patients treated at home by general practitioners.
A COMBINED HYPERTENSION AND STROKE CONTROL PROGRAMME IN A JAPANESE COMMUNITY

by

Yasuo Hirota

Since 1951, cerebrovascular disease has been the leading cause of death in Japan and has attracted much attention from specialists all over the world, especially because of a high incidence of cerebral haemorrhage in contrast to a low incidence of cerebral infarction, according to the mortality statistics in Japan. There has, however, been some criticism of the diagnostic level of stroke in this country.

For this reason, and with the purpose of elucidating the natural history of stroke, particularly the incidence of the three major types of cerebrovascular disease in Japan, the Hisayama Study was initiated in 1961, by Emeritus Professor S. Katsuki, the then Director of the Second Department of Internal Medicine, Faculty of Medicine, Kyushu University.

One of the remarkable features of this study has been the autopsy verification of the cause of death among almost all the deceased in the community for many years. As a result, it is expected that the most reliable incidence of each type of cerebrovascular disease will be obtained. In addition, the people's attention is drawn to their own health status by inviting them to undergo a medical examination every year, and by informing the families or relatives of the deceased of the autopsy-verified cause of death.

The Hisayama Study is still in progress; therefore the object of this paper is to present the 10-year follow-up results and to examine recent trends in the incidence of cerebral haemorrhage in the Japanese community of Hisayama.

Initial examination in 1961

The location, population, age/sex distribution, and other demographic characteristics of Hisayama have been described in detail elsewhere(1).

A mass examination to determine the cardiovascular status of the population was carried out in Hisayama from April to October 1961. All of the residents aged 40 years and over in the community were chosen for the initial examination. The name and age of the subjects were obtained from the Name List of Resident Registration in the Town Office.

The population of Hisayama was 8 521 according to the National Census in 1960.
The items of examination were as follows: body weight, height, blood pressure, serum total cholesterol, urinalysis, electrocardiogram, ophthalmoscopy, and neurological examination. Information on subjective complaints, past history, family history, and drinking and smoking habits were also obtained by means of questionnaires.

Out of 1,841 subjects, 1,658 or 90.1% were initially examined. These cross-sectional data have also been reported(1).

There were several findings, as follows: (1) Twenty-five (11 males and 14 females) out of the 1,658 persons examined showed signs of hemiplegia resulting from stroke; (2) Nearly 25.8% of the 1,658 persons were classified as hypertensives according to the WHO criteria and another 21.3% as borderline hypertensives; (3) 56.4% of the 1,658 persons showed abnormal ECG findings according to the Minnesota Code; (4) 22.5% of the 1,658 showed retinopathy classified as KW II, III and IV; (5) Proteinuria was found in 6.5% and glycosuria in 4.9%; (6) Hypercholesterolaemia (over 250 mg/dl) was found in about 2% of those examined.

Follow-up study

Since 25 of those examined had already developed stroke and another 12 had died or moved out from Hisayama after the initial examination, the remaining 1,621 out of the 1,658 examined have been followed up from November 1961 to the present time.

The main aims of the follow-up study are as follows: (1) To obtain the incidence rate of each type of cerebrovascular disease; (2) To examine the characteristics of a person prone to develop stroke; (3) To identify methods for the prevention of stroke.

Information on the incidence of stroke in the population is obtained during visits to the medical practitioners in the community once or twice a week. Moreover, the practitioner is requested to inform us about new cases as soon as possible by telephone, and we immediately visit the patient's home with the practitioner. We also advise the family or the practitioner on diagnosis, therapy, and prognosis if necessary. If the illness is severe, the patient is transported to the University Hospital. When a patient dies, we make a maximum effort to obtain the family's agreement for post-mortem examination. Persistent efforts had to be made to obtain such consent, particularly at the beginning of the study.

Despite our efforts, no autopsy was performed during November and December in 1961. In 1962 however, the cause of death was verified by autopsy in 6 (18%) of 33 deceased. Thereafter, the rate of autopsy in the Hisayama Study steadily went up to 100% in 1965 and has remained at a high level of over 90% since then.

Influential men in the area have shown their cooperation by organizing a "Health Promoting Club", members of which express their agreement for post-mortem examination. The "Health Promoting Club" was established in 1963. In addition, a priest used to preach to the supporters of his temple that autopsy is not against the principles of Buddhism.

These efforts continued for over 12 years; at present there are only a few residents who are reluctant to undergo a medical examination or to consent to post-mortem examination.
In October 1972, 10-year follow-up data were collected from the subjects by sending out questionnaires. If the subject died after he moved away from Hisayama, his family were requested to inform us of the name of the terminal illness and the attending physician who signed the death certificate. Thereafter, we asked the attending physician directly whether or not the subject died from stroke.

In this way, data on the health status or cause of death, particularly stroke, were collected from all of the subjects with the exception of 5 cases. For these 5, the registrar of their domiciles of origin informed us that they had not died, but that their present address was unknown. As a result, the follow-up rate was 99.7% (Fig. 1).

FIG. 1
TEN YEAR FOLLOW-UP IN HISAYAMA, KYUSHU ISLAND, JAPAN

Of the 1,621 persons, 333 (20.5%) died in the 10-year follow-up period. The cause of death was verified by autopsy on 271 (85.2%) of the 318 persons who died in Hisayama.

Cerebrovascular disease as an underlying cause of death was found among 81 (24.3%) of the 333 deceased cases. Their types were as follows: cerebral haemorrhage in 29, cerebral thrombosis in 37, cerebral embolism in 1, subarachnoid haemorrhage in 11, and ill-defined stroke in 3 cases in whom autopsy was not performed.

In addition, malignant neoplasm as an underlying cause of death was found in 72 (21.6%), heart disease in 46 (13.8%), and pneumonia or miscellaneous illnesses in the remaining 134 (40.2%).
The average annual incidence rate of stroke in the 10-year period in men over 40 years was 3.0 for cerebral haemorrhage, 8.1 for cerebral infarction, and 0.7 for subarachnoid haemorrhage. In women aged 40 years and over, it was 0.4, 4.8, and 0.8 respectively.

To study the efficacy of antihypertensive therapy in preventing stroke, a retrospective analysis was attempted in the Hisayama study. At the initial cross-sectional examination, 410 subjects were classified as hypertensive according to the WHO criteria. Out of these, 222 were diastolic hypertensives(2) of whom 55 were receiving antihypertensive drugs for six months or more, during the period from November 1961 to October 1966.

As a matched control, another 55 diastolic hypertensives were selected at random from the remainder. The matching was based on sex, 5-year age groups, initial blood pressure level, severity of retinopathy, ECG findings based on the Minnesota Code, and abnormal findings in urinalysis. Information on whether or not they had been treated with antihypertensive drugs was obtained principally by means of our survey of the medical practitioners' claims to the National Health Insurance Office in Hisayama for payment.

A comparison of the two groups showed that 24 deaths (5-year death rate, 14%) occurred in the control group and 5 deaths (9%) in the treated group during the same period of time(1). The difference between the mortality rates of these two groups is highly significant (p <0.01).

As a next step, both groups were combined and then divided into subgroups according to the number of months during which they received antihypertensive drugs. The incidence of cerebrovascular disease differed significantly according to the duration of therapy. Twenty-one or 34.4% of 61 hypertensives, who had no therapy or had received drugs for less than 7 months during the 5 years, developed stroke; on the other hand, only 3 or 6.1% developed stroke out of 49 hypertensives who received treatment for 7 to 60 months during the same period.

For a more detailed analysis, matched pairs from the same 2 groups were selected by a stratified random sampling method. This time, family history of stroke and drinking habits were added to the matched items because they were considered as risk factors of cerebrovascular disease. Stroke developed among 11 or 41% of the 27 hypertensives in the untreated or poorly treated group and in only 1 or 4% of the 27 treated hypertensives. The difference was statistically significant (p <0.01). Regarding the type of stroke, 6 cases of cerebral haemorrhage and 5 cases of cerebral thrombosis occurred in the untreated group; the one case in the treated group was due to subarachnoid haemorrhage.

This analysis has some shortcomings because it is retrospective, but the result is in agreement with a recent report confirming the preventive effect of antihypertensive therapy, even in relatively mild diastolic hypertensives(2,5).

Comparison of the incidence of stroke during the first 5 years with that in the second 5 years of the Hisayama study

As mentioned above, the effect of antihypertensive drug therapy in preventing complications has recently been assessed by a prospective and controlled study. An analysis to delineate the effect of a control programme in the community has also been designed by us.
The follow-up period was divided into two parts, i.e., two 5-year periods.

The subjects were assigned to two age groups: a middle-age group comprising subjects from 50 to 69 years; and an old-age group comprising those aged 70 years and over at the time of the initial examination in 1961.

The death rate from cerebral haemorrhage during the first 5-year period (November 1961 to October 1966) was 23.3 per 1 000 subjects and during the second period (November 1966 to October 1972) it decreased to 5.1 per 1 000 subjects, less than a quarter of that in the first period. The difference was statistically significant (P < 0.05) (Fig. 2). In women the death rate was less than that among the men and no marked change was found between the two periods.

FIG. 2
COMPARISON OF DEATH RATES FROM SEVERAL DISEASES IN FIRST AND SECOND HALF FOLLOW-UP PERIODS

The death rate from cerebral thrombosis became lower in the second period than that in the first period, in both sexes, but the difference was not significant.

No marked change in the death rate from such diseases as subarachnoid haemorrhage, malignant neoplasm, and myocardial infarction was found between these two follow-up periods.
The overlapping of subjects in both periods might cause some difficulty in this comparison; however, it seems noteworthy to point out that during the second period a marked decrease occurred in cerebral haemorrhage compared with no changes in the other diseases.

At the next step, age-adjusted death rates from the three types of cerebrovascular disease were calculated in each subgroup, based on their blood pressure level at the time of the initial examination in 1961. The 10-year age-adjusted death rate for cerebral haemorrhage was 7.3% (Fig. 3)

### FIG. 3
MORTALITY FROM C.V.D. ACCORDING TO INITIAL BLOOD PRESSURE LEVELS IN HISAYAMA

<table>
<thead>
<tr>
<th></th>
<th>0%</th>
<th>2%</th>
<th>4%</th>
<th>8%</th>
</tr>
</thead>
<tbody>
<tr>
<td>DIASTOLIC H.T.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(N=214)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SYSTOLIC H.T.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(N=183)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BORDERLINE H.T.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(N=340)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NORMOTENSIVES</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(N=855)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

among the diastolic hypertensives, 1.8% in the systolic hypertensives, 1.7% in the borderline hypertensives, and 0.4% in the normotensives. The difference in the death rate between the diastolic hypertensives and the other three subgroups was statistically significant (P < 0.05).

Although it might be expected that changes might have occurred in the blood pressure levels among the residents in the community or in the frequency of hypertensives during the 10-year follow-up period, no marked change was found in the mean of the middle-aged residents' blood pressure levels at the mass examination (Fig. 4).
Expansion of the programme for preventing stroke to Sasaguri and Naka, two neighbouring districts of Hisayama(7)

In January 1971, the Association for Preventing Stroke in Fukuoka Prefecture (Chairman: Emeritus Professor S. Katsuki) was established by the medical practitioners in Hisayama Town and Sasaguri Town in Kasuya County and Naka Koku in Fukuoka City, and by ourselves. The purpose of this association is to study in the field the harmful effects of hypertension on the cardiovascular status, to search for available procedures for preventing complications such as stroke or heart attack, and to reduce deaths from these illnesses among the general population.

The populations in 1971 were 7 289 in Hisayama, 15 178 in Sasaguri, and 13 099 in Naka, giving a total of 35 566. Initial examinations were performed in Sasaguri and Naka from January to April 1971.

Out of 4 252 subjects aged 40 to 69 years in Sasaguri, 3 816 (89.7%) underwent the initial examination; and 2 780 (81.5%) of 3 409 subjects aged 40 to 69 years in Naka were also examined.

Three hundred and fifty-six of those examined in Sasaguri and 208 in Naka were immediately treated with antihypertensive drugs because of their high blood pressure, i.e., over 180 mmHg systolic and/or over 110 mmHg diastolic pressure.
Those examined who had received some antihypertensive drugs at the time of the initial examination and those who had shown pressures from 160 mmHg to 179 mmHg in systolic and/or from 95 mmHg to 109 mmHg in diastolic were re-examined at the second examination from January 1972 in Sasaguri and Naka.

Of the subjects for the second examination, there were 433 with high blood pressure and 244 were receiving antihypertensive drugs in Sasaguri; there were likewise in Naka 304 and 119, respectively. Out of the remaining subjects, the borderline hypertensives (according to the WHO criteria) were followed up and their blood pressure was measured occasionally, and, if necessary, they underwent detailed re-examination.

Five hundred and eight subjects in Sasaguri and 658 in Naka were under observation for borderline hypertension. The remaining 2,275 in Sasaguri and 1,491 in Naka were normotensive.

Those who showed a high blood pressure level at the second examination of 160 mmHg and over in systolic and/or 95 mmHg and over in diastolic and those who received antihypertensive agents at the time of the second examination in 1972 were registered as hypertensives for the WHO Hypertension Control Study and were followed up; the number of cases is 601 in Sasaguri and 174 in Naka. There is mounting evidence that the early detection of hypertension and an appropriate therapeutic regimen for such patients will reduce the development of stroke, as shown in Hisayama.

These preventive procedures are gradually being popularized among the general population at the present time. The methods for cardiovascular mass examination have been improved and modern techniques have been developed year by year. Financial support for their practical application to the general population is insufficient. Technically qualified persons are needed in each district. It is also hard for practitioners who spend much time in their daily curative practices to find the time for preventive medicine.

Therefore, all facilities should be utilized and preventive procedures should be adapted to the local situation. As shown in the mass examination by medical practitioners - for instance, in the activity of the Association for Preventing Stroke in Fukuoka Prefecture - by means of coordination with local government and local medical associations, including public health centres or public hospitals, it is expected that mass examination of a high standard can be provided for everyone who wants it.

With regard to unification of the programme, it is desirable that (1) local governments should provide financial support; (2) local associations of medical practitioners should cooperate in treating hypertensives routinely; and (3) the university hospital or other public hospitals should provide a high standard of examination or hospitalization. It is planned to establish a centre for preventing stroke in the community which will also act as a medical data bank for the residents.

The organization should, in future, represent all the residents in the community, because it will deal with problems concerning their own health status.
Moreover, it cannot be overemphasized that re-examination of the current medical care insurance programme, particularly of financing not only curative but also preventive services, is inevitable for the development of control programmes for hypertension and stroke in Japan.

REFERENCES


7. The Association for Preventing Stroke in Fukuoka Prefecture: The procedure for preventing stroke, Series No. 1 (October 1971), No. 2 (October 1972), No. 3 (October 1973) (In Japanese).
DISCUSSION

Dr Toole: Dr Hirota for the first time introduces the idea of a very great effort of prevention in his discussion of the health promoting club and I would like to know a little about the details of what the club attempts to do; how do you educate the public, and what do you tell them? Do you tell them that they should go and see a doctor if they get early warning signs of stroke? Do you give them health promoting advice like weight reduction and exercise? What is the content of your health club message?

Dr Hirota: There were many things which we taught them. First of all, I think it is very important to inform them about the risk of cerebrovascular disease. People were given clear evidence that cerebrovascular disease is the most frequent killer. Their motivation for preventing cerebrovascular disease was thus strengthened. They also recognized that hypertensives, particularly diastolic hypertensives, were candidates for stroke.

A report of the annual examination was sent to each member of the health promoting club. When abnormal findings were reported, they were persuaded to see their home doctor who gave them advice - including advice on a change in life pattern, which may be etiologically important - and also prescribed antihypertensive drugs, if necessary.

Dr Toole: You showed a statistically significant difference in your intervention trial. Do you attribute that to treatment of hypertension by physicians or do you attribute it to the health club and the preventive activities which the patients, the population itself, undertook? If it is due to what the population did, I would like to know what it was that they changed so that we could have some idea as to why the incidence of stroke declined.

Dr Hirota: At present, I cannot attribute the change in death rate from cerebral haemorrhage to either one of these two components separately. Although this question should be answered in future, I believe that not only antihypertensive drug therapy but also public health education is very valuable for the prevention of cerebrovascular disease.

Dr Paul: I would just like to introduce in this discussion the role of non-professional personnel in the management of this particular problem. We have been stressing the ability of nurses to take blood pressure in the home as well as in the clinic or hospital setting, and the ability of these individuals to follow up patients guiding them not only in advice regarding general health but also, under a physician's supervision, guiding them in terms of information as to drug reactions, dosage, fidelity of taking medication, and changes in medication. Our problem and yours is of such a magnitude that we have appreciated that physicians alone are not necessarily the only, or indeed the best ones, to do this. In this discussion today, and I think the next two days, it is well for us to bear in mind that the nurses' ability to work in a hypertension and a stroke control programme makes them really indispensable. I would like to indicate also that, in some respects, they are better than physicians because with a particular interest and motivation in this area, they can carry on programmes sometimes more adequately than physicians who are faced with many other obligations and responsibilities.
Dr Kagan: Stress has been laid here on the desirability of autopsy in the precise diagnosis of the types of stroke. Our pathologist tells us that he sometimes has trouble distinguishing between haemorrhagic infarction and cerebral haemorrhage. Would you comment on that, Dr Hirota, and do you have some better technique than we have for distinguishing these two conditions?

Dr Hirota: We had only 2 or 3 cases of haemorrhagic infarction; however, I am not a pathologist and I think Dr Kameyama may provide an answer.

Dr Kameyama: It is occasionally difficult to differentiate cerebral haemorrhage from haemorrhagic infarction at autopsy, especially in the old lesions. However, there are some clues for this problem, as pointed out by Scholz and co-workers of the German school. There are differences in the site and extent of the lesions, the mode of destruction of the cerebral tissue, and vascular changes. In many cases of cerebral haemorrhagic infarctions, a more or less dense capillary network is found in the softening area; however, this is not common in cerebral haemorrhage.
PROBLEMS OF STROKE CONTROL IN RURAL SETTINGS IN JAPAN

by

Koji Isomura

The cerebrovascular accident (CVA) mortality rate in the Saku district of Nagano prefecture was high, 241.6 per 100,000 population in 1965 and 183.5 in 1970.

Mortality statistics are an insufficient indication of the real situation of CVA and we embarked upon a CVA incidence survey on the 105,185 inhabitants of the area participating in the WHO cooperative cardiovascular study.

Survey area and local characteristics

The Saku district is a rural area, 692 to 1,182 m above sea level. The maximum temperature was 36°C and the minimum temperature -21°C in 1965. Inadequate insulation in houses compels the inhabitants to suffer the stress of cold weather.

According to the National Census, the population of the Saku district was 105,185 in 1970, registering a decrease of 7.4% since 1960. Depopulation of rural communities in the mountains is accelerated by most of the young people leaving for urban areas.

There are 110 physicians practising in the Saku district, and the ratio of physicians is 1 to 956 of the population. However, they are concentrated in Saku City and its adjacent community, Usuda Town. The further a rural community is situated in the mountains, the fewer the number of physicians available to them. There are two villages in this district with no doctor at all. Hospitals are available only in Saku City and in the nearby towns. The Saku district has 1,078 beds, or one bed per 1,003 population. The Saku Central Hospital, which is the stroke registration centre, has 761 beds. One public health nurse is available in this district per 4,207 population.

Survey methods

With the Saku Central Hospital serving as the centre, a CVA incidence survey is under way in collaboration with the Department of Geriatrics of the University of Tokyo, the Saku Medical Association, the Saku Public Health Nurses' Association, and the Saku Public Health Centre.

The physician who takes care of the initial diagnosis of CVA is usually a general practitioner. The preparatory phase to secure the understanding and cooperation of physicians took one year.
Since this survey began, information on the incidence of CVA has been compiled by the registration centre in the form of a monthly bulletin for distribution to the members of the Saku Medical Association and the physicians assigned to each medical service with a view to arousing their interest in this survey. An annual tabulation was also distributed.

The public health nurse in a rural village is normally well known to her CVA patients and she knows their living conditions, because the inhabitants in an area with few medical services normally consult the public health nurse who regularly visits the community. A regular meeting of these nurses is held at the Saku Central Hospital every month concerning the CVA study and measures for taking care of the CVA patients.

For diagnosing the type of CVA, the criteria (1) of the U.S. ad hoc committee (Chairman, C. H. Millikan) and the cerebrovascular disease index (2) based on the Hisayama study were used. Reference was also made to the autopsy findings, where available. Subjects who had not consulted a physician before death were excluded from the registration.

**Results of the survey**

During the one-year period from April 1972 to March 1973, 286 cases of CVA occurred in the Saku district. The incidence rate was 276 per 100,000 population. These included 88 cases of cerebral haemorrhage (31%), 172 cases of cerebral infarction (60%), and 26 cases of subarachnoid haemorrhage (9%).

The incidence rate in Saku City was 239 per 100,000 population and that in South Saku County was higher at 308. The incidence of all types of stroke is higher in the mountain areas than in the plateaus (Table 1). The incidence of CVA was higher in males than in females, i.e., 1.4 times higher for cerebral haemorrhage and 1.2 times for cerebral infarction.

By season, the incidence of cerebral haemorrhage was high in spring, particularly in April, whereas cerebral infarction registered a high incidence in the winter, particularly in January. No seasonal variations were observed in the incidence of subarachnoid haemorrhage.

With regard to prognosis by types, the case fatality rate of cerebral haemorrhage was 78%; of these deaths, 99% died in less than three weeks. Deaths from cerebral infarction, which took place in less than three weeks, accounted for only 20%; or 29% for deaths within three months (Table 2).

**Rehabilitation programme at a rural hospital**

Of the CVA patients registered in the one-year period from April 1972, 35% were admitted to the Saku Central Hospital. The frequency of hospitalization in patients with cerebral haemorrhage was small, because of death within a short period and because of difficulties in carrying a patient in a critical condition to hospital from rural communities.

Right hemiplegia was more frequent than left hemiplegia in 20 cases of cerebral haemorrhage and 70 cases of cerebral infarction. The death rate was higher in right hemiplegia. Rehabilitation was often less effective for left hemiplegia, presumably because of the existence of agnosia and organic mental syndromes in some patients (Table 3).
Table 1. CVA incidence in different communities of Saku district from 1 April 1972 to 31 March 1973

<table>
<thead>
<tr>
<th>Community</th>
<th>Cerebral haemorrhage</th>
<th>Cerebral infarction</th>
<th>Subarachnoid haemorrhage</th>
<th>All CVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kawakami Village</td>
<td>8</td>
<td>7</td>
<td>4</td>
<td>19</td>
</tr>
<tr>
<td>Minamimaki Village</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Minamiaiki Village</td>
<td>1</td>
<td>8</td>
<td>-</td>
<td>9</td>
</tr>
<tr>
<td>Kitaaiki Village</td>
<td>2</td>
<td>1</td>
<td>-</td>
<td>3</td>
</tr>
<tr>
<td>Yachiho Village</td>
<td>6</td>
<td>9</td>
<td>1</td>
<td>16</td>
</tr>
<tr>
<td>Koumi Town</td>
<td>14</td>
<td>12</td>
<td>3</td>
<td>29</td>
</tr>
<tr>
<td>Saku Town</td>
<td>6</td>
<td>23</td>
<td>3</td>
<td>32</td>
</tr>
<tr>
<td>Usuda Town</td>
<td>12</td>
<td>23</td>
<td>3</td>
<td>27</td>
</tr>
<tr>
<td>South Saku County a</td>
<td>52(104) b</td>
<td>86(172)</td>
<td>15(30)</td>
<td>153(306)</td>
</tr>
<tr>
<td>Saku City a</td>
<td>36(65)</td>
<td>86(156)</td>
<td>11(20)</td>
<td>133(241)</td>
</tr>
<tr>
<td>Total</td>
<td>88(84)</td>
<td>172(164)</td>
<td>26(25)</td>
<td>286(272)</td>
</tr>
</tbody>
</table>

a Population (1970 National Census) of South Saku County was 49,971 and Saku City 55,214.
b Incidence rates per 100,000 population are given within parentheses.

Table 2. Case fatality a within 3 weeks and 3 months of CVA by types

<table>
<thead>
<tr>
<th></th>
<th>Cerebral haemorrhage</th>
<th>Cerebral infarction</th>
<th>Subarachnoid haemorrhage</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death in less than 3 weeks</td>
<td>68 (77)</td>
<td>35 (20)</td>
<td>11 (42)</td>
<td>114 (40)</td>
</tr>
<tr>
<td>Death between 3 weeks and 3 months</td>
<td>1 (1)</td>
<td>15 (9)</td>
<td>8  (31)</td>
<td>24 (8)</td>
</tr>
<tr>
<td>Death in less than 3 months</td>
<td>69 (78)</td>
<td>50 (29)</td>
<td>19  (73)</td>
<td>138 (48)</td>
</tr>
</tbody>
</table>

a Number of persons and percentages within each group (in parentheses).
<table>
<thead>
<tr>
<th>Type of CVA</th>
<th>Effect of Rehabilitation</th>
<th>Death</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Significantly high</td>
<td>High</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemorrhage (20 cases)</td>
<td>R-hemiplegia</td>
<td>1 (5)</td>
<td>3 (15)</td>
</tr>
<tr>
<td></td>
<td>L-hemiplegia</td>
<td>1 (5)</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Infarction (70 cases)</td>
<td>R-hemiplegia</td>
<td>14 (20)</td>
<td>10 (14)</td>
</tr>
<tr>
<td></td>
<td>L-hemiplegia</td>
<td>12 (17)</td>
<td>13 (19)</td>
</tr>
<tr>
<td>Total (90 cases)</td>
<td>R-hemiplegia</td>
<td>15 (17)</td>
<td>13 (14)</td>
</tr>
<tr>
<td></td>
<td>L-hemiplegia</td>
<td>13 (14)</td>
<td>14 (16)</td>
</tr>
</tbody>
</table>

*Number of patients and percentages within each group (in parentheses).*
Difficulties are encountered in the attempt to get patients back to their previous mode of life. The depopulation of rural areas, for instance, often means that, even if the patient could return to the family, there would be virtually no person in the family available to look after him. Another problem is the lack of nursing homes for the elderly. Even when a patient has recovered, it is difficult for him to resume heavy physical labour, such as farm work, and there are almost no possibilities for other employment. A general hospital in a rural area is often expected to function as a nursing home for the aged, too.

Hypertension control programme in a rural community

In the village of Yachiho (pop. 5,449, National Census in 1970) in the Saku district, a village health control programme including hypertension control was instituted in 1959 for all the inhabitants over 15 years of age.

At present, the population of not only Yachiho village but also other rural areas of Japan finds it difficult to exist on only an agricultural income. Many of the young and middle-aged people have side-employment in other industries, or they work as day-labourers, with the inevitable consequence that the elderly are compelled to take care of the bulk of the farm work. It is for this reason that the control of hypertension, the prevalence of which is high in the elderly, constitutes one of the most important questions in the rural community.

A total village health control programme for the village of Yachiho has been instituted with the participation of physicians, nurses, and laboratory technicians from the Saku Central Hospital, of public health officials from the village authorities, and representatives of the local Women's Association. In any health control programme, the education of the inhabitants on disease prevention is no less important than the mass health examination.

The mass health examination is conducted once a year by a team from the Saku Central Hospital, the members of which have to carry out routine hospital work too. The execution of this programme has placed a heavy burden on the hospital management. When the first mass health examination was held, 80% of the inhabitants participated. Of those over 40 years of age, 85% of males and 92% of females were included.

When a mass health examination is carried out in a rural setting, many diseases are detected. Many of the farmers have what is called "latent disease" (2), which comprises the "unawareness" type (in which the patient is not aware of his ailment), the "patience" type (in which the patient tries to put up with the disease without consulting a doctor), and the "discontinuance" type (in which patients give up further medical treatment). The prevalence rate of "latent disease" in the village of Yachiho was as high as 79% at the first mass health examination.

One factor responsible for the high prevalence of latent diseases in a rural setting is the lack of medical services and transport, and also the general poverty of the rural population. Another factor is the lack of time to visit a hospital during a busy farming season. Furthermore, farmers tend to pay less attention to illness.
For the inhabitants aged 40-69 years, 46% of males and 48% of females were normotensive, 29% of males and 24% of females were borderline, and 26% of males and 28% of females were hypertensive, according to the WHO Criteria\(^3,4\).

Hypertension was quite common in the initial period, but the prevalence of "latent disease" has been decreasing as a result of the long-term mass health control programmes.

A survey in 1969 revealed 303 hypertensives who required medical treatment in this district. Of these, 155 persons (51%) received continuous medical treatment, 36 persons (12%) underwent occasional treatment, and 11 persons (36%) received no treatment.

As hypertension control has been carried out in the village of Yachiho for the last 14 years, a comparison is made between the first seven years (1959-65) and the second (1966-72). The incidence of CVA in the earlier period averaged 23.7 persons a year; it averaged 16.4 persons a year in the later period or 31% less than the earlier. The decrease in the incidence of cerebral haemorrhage was conspicuous: 12.3 and 6.4 persons a year for the earlier and later periods respectively. The decrease in the incidence of cerebral infarction was not significant: from 10.6 persons a year in the earlier to 9.7 persons in the later period (Table 4).

When a comparison is made between the mountain and plateau areas of Yachiho village, the decrease in incidence in the mountain area was conspicuous; this may be due to the fact that the incidence of cerebral haemorrhage has decreased conspicuously in these areas under the hypertension control programme.

### Table 4. Incidence of CVA and coronary heart disease in Yachiho village\(^a\)

<table>
<thead>
<tr>
<th>Average annual incidence (number of persons)</th>
<th>Percentage drop</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1959 - 1965</strong></td>
<td><strong>1966 - 1972</strong></td>
</tr>
<tr>
<td>Cerebral haemorrhage</td>
<td>12.3</td>
</tr>
<tr>
<td>Cerebral infarction</td>
<td>10.6</td>
</tr>
<tr>
<td>Subarachnoid haemorrhage</td>
<td>0.9</td>
</tr>
<tr>
<td>CVA (total)</td>
<td>23.7</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1.3</td>
</tr>
<tr>
<td>Angina pectoris</td>
<td>1.1</td>
</tr>
<tr>
<td>Sudden death</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) Population (National Census) in 1960 was 6,227 and in 1970 was 5,449.

\(^b\) Increase (%).
The incidence of myocardial infarction and angina pectoris averaged 1.3 persons a year in the earlier and 1.7 persons a year in the later period. The ratio of CVA to these two diseases was 18:1 and 10:1 in the earlier and later periods, respectively.

Summary

(a) The annual incidence of CVA in the Saku district was 276 per 100,000 population. The relative frequency of cerebral haemorrhage, cerebral infarction, and subarachnoid haemorrhage was 3:6:1.

(b) The incidence of cerebral haemorrhage and subarachnoid haemorrhage was high in rural communities in the mountains.

(c) CVA occurred more frequently in males than in females: 1.4 times higher in cerebral haemorrhage and 1.2 times in cerebral infarction.

(d) With regard to the prognosis of CVA, deaths which occur within three months accounted for 78% of cerebral haemorrhage, 29% of cerebral infarction, and 73% of subarachnoid haemorrhage.

(e) The rate of hospitalization was low in the rural areas.

(f) In rural areas many difficulties were encountered by patients on their return to family life and society. The reasons for this have been discussed.

(g) Hypertension control was effective in the prevention of cerebral haemorrhage.

(h) The hospital in charge of a hypertension control programme is often forced to conduct it with a limited number of medical personnel and to overcome economic difficulties.

REFERENCES


147
DISCUSSION

Dr Toole: For me, the most surprising aspect of what has been said today is the very low frequency of hospitalization of patients in Japan after they have had a stroke. You mentioned, at least in your district, about 50% or possibly less. That leads me to the question: Do the patients who have cerebral infarction have treatment with anticoagulants or are they just left to lie and recover on their own?

Dr Isomura: We rarely use anticoagulants and then only when the diagnosis of a transient ischaemic attack is confirmed.

With regard to the reasons for a low hospitalization rate in Japan, patients with cerebral haemorrhage die in many instances before their hospitalization. Another factor is that difficulties are encountered in moving serious patients to hospital from remote hamlets in the mountains.

Dr Freis: It is very striking in your report that the incidence of stroke was reduced from 24% to 16.5% during the second 7-year period. I wondered how effective your treatment programme was; how many hypertensives were actually under good treatment during those second seven years? What percentage of patients were actually receiving good treatment?

Dr Isomura: The incidence of stroke has decreased in a pilot study area of Yachiho, where a long range hypertension control programme for inhabitants aged 15 years and over has been under way since 1959. The incidence of cerebral haemorrhage has decreased by half, whereas there has been no significant drop in the incidence of cerebral infarction. The incidence rate of stroke has decreased for those under 69, but has changed little for those over 70 years of age.
This report is an attempt to describe the measures in hypertension and stroke control in Akita prefecture in Japan, which is known for its high incidence of cerebrovascular accidents (CVA) and prevalence of hypertension.

Any hypertension and CVA control programme should encompass as many persons as possible. Without a systematic programme for hypertension control, it is difficult to provide treatment to all the inhabitants with hypertension.

Occurrence of CVA in the rural communities in Akita prefecture

The persons included in this report as having cerebral stroke are those whose focal signs lasted for more than 24 hours, or those who were diagnosed as having subarachnoid haemorrhage with severe headache not associated with focal signs. Cases of transient ischaemic attack and hypertensive encephalopathy are not included.

Table 1 shows a comparison of the incidence of CVA in three rural communities of Akita prefecture and in two urban districts of Osaka, where the rate was relatively lower in comparison with other parts of Japan. The incidence both in males and females was higher in Akita than Osaka for all age groups under 80 years of age. The difference between Osaka and Akita was relatively more significant in the younger age groups than in the older age groups. The incidence was 1.3 times higher for males and 1.9 times higher for females in Akita than in Osaka in the age group of 60 years and over. In the age group 30-59 years, the rate was 4.7 times higher in males and 4.5 times higher in females.

The incidence rate of cerebral haemorrhage and cerebral infarction was higher both in males and females in Akita than in Osaka. The difference between Akita and Osaka was more conspicuous in the younger age groups.

In order to clarify the factors responsible for the occurrence of CVA in Akita, we compared the findings prior to the onset of stroke in Akita with those in Osaka. Table 2 shows the number of patients for whom the findings on blood pressure, fundus examination, and ECG are all available. The findings are classified into 4 groups. Group 'A' includes hypertensive patients with hypertensive fundus and ECG changes. Group 'B' shows hypertensive patients with less significant or no hypertensive changes in the
Table 1. Incidence rates (per year per 1,000 population) of CVA, cerebral haemorrhage, and cerebral infarction in Akita and Osaka.

<table>
<thead>
<tr>
<th>District</th>
<th>Akita</th>
<th>Osaka</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>30 - 39</td>
<td>1,548</td>
</tr>
<tr>
<td></td>
<td>40 - 49</td>
<td>1,095</td>
</tr>
<tr>
<td></td>
<td>50 - 59</td>
<td>896</td>
</tr>
<tr>
<td></td>
<td>60 - 69</td>
<td>590</td>
</tr>
<tr>
<td></td>
<td>70 - 79</td>
<td>221</td>
</tr>
<tr>
<td></td>
<td>80 +</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>all ages</td>
<td>9,541</td>
</tr>
<tr>
<td>female</td>
<td>30 - 39</td>
<td>1,600</td>
</tr>
<tr>
<td></td>
<td>40 - 49</td>
<td>1,258</td>
</tr>
<tr>
<td></td>
<td>50 - 59</td>
<td>937</td>
</tr>
<tr>
<td></td>
<td>60 - 69</td>
<td>668</td>
</tr>
<tr>
<td></td>
<td>70 - 79</td>
<td>283</td>
</tr>
<tr>
<td></td>
<td>80 +</td>
<td>57</td>
</tr>
<tr>
<td></td>
<td>all ages</td>
<td>9,940</td>
</tr>
</tbody>
</table>


Pop. = population  Haem. = cerebral haemorrhage  Inf. = cerebral infarction.
Table 2. Findings of mass examinations of persons (30-69 years old) who subsequently had a CVA in Akita and Osaka

<table>
<thead>
<tr>
<th>Type of CVA</th>
<th>Haemorrhage</th>
<th>Infarction</th>
<th>All CVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>total A</td>
<td>B</td>
<td>C</td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Akita</td>
<td>19</td>
<td>16</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>(100.0)</td>
<td>(84.2)</td>
<td>(5.3)</td>
</tr>
<tr>
<td>Osaka</td>
<td>7</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>(100.0)</td>
<td>(57.1)</td>
<td>(28.6)</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Akita</td>
<td>12</td>
<td>11</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>(100.0)</td>
<td>(91.7)</td>
<td>(-)</td>
</tr>
<tr>
<td>Osaka</td>
<td>6</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>(100.0)</td>
<td>(83.3)</td>
<td>(-)</td>
</tr>
</tbody>
</table>

Persons were grouped as follows:

A: Persons who had hypertension (systolic 160 mmHg or more, and/or diastolic 95 mmHg or more) and showed ECG and fundal hypertensive changes (grade II or more).
B: Persons with hypertension but without such hypertensive changes.
C: Persons who showed ECG and fundal hypertensive changes without hypertension.
D: Persons without hypertension or hypertensive changes.

Persons who revealed ischaemic changes in the ECG are indicated within square brackets.

Percentages are within parentheses.

Persons were grouped as follows:

A: Persons who had hypertension (systolic 160 mmHg or more, and/or diastolic 95 mmHg or more) and showed ECG and fundal hypertensive changes (grade II or more).
B: Persons with hypertension but without such hypertensive changes.
C: Persons who showed ECG and fundal hypertensive changes without hypertension.
D: Persons without hypertension or hypertensive changes.

Persons who revealed ischaemic changes in the ECG are indicated within square brackets.

Percentages are within parentheses.
ocular fundi and ECG; group 'C' patients showed hypertensive changes in the fundi and ECG without having hypertension. And group 'D' represents the persons with no high blood pressure or hypertensive changes.

Among the CVA cases, the prevalence rate of 'A' is high both in Akita and Osaka; the prevalence rate of cases with hypertension before the stroke occurred ('A'+ 'B'+ 'C') was over 90%. The rate of group 'A' was higher among patients with cerebral haemorrhage than cerebral infarction and higher in Akita than in Osaka.

In summary, one of the features of stroke in Akita prefecture was that both cerebral haemorrhage and cerebral infarction occurred frequently in the younger age groups. Another feature is the high frequency of hypertension in patients with cerebral infarction and cerebral haemorrhage.

Relative ratio of risks for CVA

At present, more than 40% of the inhabitants over 40 years of age are hypertensive; but owing to limited resources of medical care it is difficult to provide guidance and treatment to all of them. Therefore, our primary objective was to detect those hypertensives who were most likely to develop stroke later. The relative risk ratio for stroke from various combinations of normal and abnormal findings in blood pressure, ECG, and fundus examinations is presented in Table 3. Data on the inhabitants and workers in business offices and industrial plants in Osaka are also included. The incidence of CVA was high among the inhabitants with an elevated blood pressure, abnormal ECG, and an abnormal fundus. The hypertensive subjects in Akita showed a higher CVA incidence rate than those in Osaka.

Table 3. Relative risk ratio\textsuperscript{a} of abnormal findings likely to give rise to CVA

<table>
<thead>
<tr>
<th>Blood pressure</th>
<th>Normotension</th>
<th>Hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(N) (A)</td>
<td>(N) (A)</td>
</tr>
<tr>
<td>Fundus oculi</td>
<td>(N) (A)</td>
<td>(N) (A)</td>
</tr>
</tbody>
</table>

\(\begin{array}{cccccc}
\text{Residents in Akita} & 1 & 5.0 & 3.8 & 6.9 & 18.0 & 21.8 & 45.7 \\
\text{Residents in Osaka} & 1 & 5.3 & 4.9 & 4.4 & 4.5 & 7.3 & 26.4 \\
\text{Industrial workers in Osaka} & 1 & 15.0 & - & 8.6 & 6.2 & 6.1 & 16.5 \\
\end{array}\)

\textsuperscript{a} The relative risk ratio is the relative incidence rate in each of the 6 groups shown above according to blood pressure, ECG, and fundus findings, assuming that the incidence rate for the group whose blood pressure, ECG, and fundus findings are normal is 1.0.

\textsuperscript{b} \(N\) = normal. \(A\) = abnormal.
Effectiveness of predicting CVA from the results of the initial examination

In our five years of activities, we studied the degree of abnormalities prior to the occurrence of CVA.

The frequency of abnormal findings in a mass examination of patients who later developed stroke is shown in Table 4. In the inhabitants and workers in Osaka, the rate of identifying possible stroke patients in advance based on only the blood pressure measurement was low (50-62%); in Akita this rate was 84%, but when based on both blood pressure measurement and past history the rate increased to 89%. By adding abnormal ECG and fundus findings, we were able to detect 82% of possible stroke patients from the inhabitants of Osaka, 70% from workers in Osaka, and 92% from the inhabitants of Akita. There was no additional increase in the detection rate of possible stroke patients when obesity and hypercholesterolaemia were added.

Prevention of CVA

To prevent the high incidence of CVA which occurs in the relatively young age group (30-69 years), there is the need (1) to control hypertensives and (2) to identify the persons in whom stroke is most likely to occur. It has been found that this screening is feasible through a mass examination.

(1) The methods and result of examination

The method employed is mass examination for risk factors, as shown in Table 5. All the inhabitants over 40 years in two rural communities - Ikawa and Ishizawa - in Akita prefecture underwent a mass examination for all the items listed. Out of 1,278 males and 1,463 females, 1,086 males and 1,339 females actually participated. Of the subjects aged 40-69 years engaged in farm work, the participation rate was 85% for males and 91.5% for females. The high participation rate in these two areas is presumably due to the fact that the mass examination and control system was established with the cooperation of the local inhabitants, and that effective orientation programmes were given by the local public health nurses. The organizational chart of this hypertension control system is given in Fig. 1.

The positive participation of local inhabitants was the result of community welfare workers, members of the local hygiene committee, and executives of the local women's association joining with public health nurses in encouraging the local inhabitants to undergo a mass health examination and serving as an intermediary between the officers in charge of the mass health examination and the local population in transmitting information about the examinations. The local population also helped by acting as receptionists, thus exhibiting their willingness to participate in this programme. The fact that such services were offered by the local inhabitants helped the general population to realize that this mass examination programme was conducted not just by medical specialists but that the community was actually involved.

It was technically difficult for the Akita Prefectural Institute of Public Health alone to complete the examination of a large number of people in a limited space of time, and the Institute called for technical assistance from a local university and from other prefectures. In our mass examination and control programme, two rural communities were selected.
Table 4. Study on the detectability of possible stroke occurrence in subjects (40-69 years old) based on abnormal findings at examination.

<table>
<thead>
<tr>
<th>Subjects</th>
<th>No. of stroke patients</th>
<th>Hypertension</th>
<th>History of hypertension</th>
<th>Overweight</th>
<th>ECG</th>
<th>F.O.</th>
<th>Ch</th>
</tr>
</thead>
<tbody>
<tr>
<td>Residents in Akita</td>
<td>109</td>
<td>92(84.4)</td>
<td>97(89.0)</td>
<td>97(89.0)</td>
<td>99(90.8)</td>
<td>100(91.7)</td>
<td>100(91.7)</td>
</tr>
<tr>
<td>Residents in Osaka</td>
<td>39</td>
<td>24(61.5)</td>
<td>27(69.2)</td>
<td>28(71.8)</td>
<td>30(76.9)</td>
<td>32(82.1)</td>
<td>32(82.1)</td>
</tr>
<tr>
<td>Industrial workers in Osaka</td>
<td>20</td>
<td>10(50.0)</td>
<td>11(55.0)</td>
<td>12(60.0)</td>
<td>14(70.0)</td>
<td>14(70.0)</td>
<td>14(70.0)</td>
</tr>
</tbody>
</table>

Note the following:

1. The figures show an increase in the detectable numbers of stroke patients from left to right in the table by the addition of abnormal findings.
2. Observation period: residents in Akita and Osaka, 5 years; and industrial workers in Osaka, 4 years.
3. Hypertension = 160 mmHg or over (systolic) and/or 95 mmHg or over (diastolic).
4. History of hypertension = previous history of hypertension.
5. Overweight = more than 120% of the relative normal weight.
6. ECG = abnormal ECG findings (Minnesota code 1-1, 2, 4-1-4, 5-1-3).
7. F.O. = abnormal ocular fundus findings (Scheie's classification II and/or S grade II or over).
8. Ch = hypercholesterolaemia (serum total cholesterol level 220 mg/dl or over).
| 1. Interview by physicians or public health nurses: | demographic information (age, occupation) |
|                                               | medical history                           |
|                                               | family history                            |
|                                               | symptoms                                  |

| 2. Urine tests: albumin and sugar              |

| 3. Height and body weight                      |

| 4. Blood pressure: sitting position, blood pressures were taken after at least 15 minutes' rest |

| 5. ECG: Minnesota code                         |

| 6. Fundus photograph: classification by Scheie |

| 7. Physical examination by physicians          |

| 8. Serum total cholesterol: modified Zak-Henly's method |
as the pilot communities and all our efforts were concentrated on the mass examination and control of their inhabitants in order to fulfil the aims of this programme. So that all the inhabitants of this prefecture may benefit from this programme, some reorganization on the part of the medical institutions in charge is needed. While striving to overcome all these difficulties, we have instituted a mass examination and hypertension programme for the two rural communities in the last ten years.

The results of the examination so far conducted on the whole population over 40 years old in the two communities may be summarized as follows:

Blood pressure taken in the mass examination was classified into normotensive, borderline, and hypertensive ranges, according to the WHO criteria. The results are shown in Table 6. The prevalence of hypertensives was noticeably higher in all age groups in Akita than in Osaka. There were no differences between the sexes in Osaka, whereas the prevalence was higher among males in Akita. The difference in ratio between Osaka and Akita was conspicuously large in the relatively young males.

Table 7 contains the results on the prevalence of hypertension, as classified by stages, in Ikawa village. In the age group 40-69 years, stage 1 hypertension (according to WHO criteria) accounted for 33.5%, stage 2 for 52.3%, and stage 3 for 14.2%.

The foregoing corroborates the high incidence of hypertension among the relatively young persons in Akita. Out of all the hypertensives, the percentage of those who require medical treatment (stages 2 and 3) was extremely high.
Table 6. Prevalence rates of normotension, borderline hypertension, and hypertension in Akita and Osaka

<table>
<thead>
<tr>
<th>District</th>
<th>Akita</th>
<th>Osaka</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NT</td>
<td>BHT</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td></td>
</tr>
<tr>
<td>40 - 49</td>
<td>221(47.5)</td>
<td>121(26.0)</td>
</tr>
<tr>
<td>50 - 59</td>
<td>126(36.1)</td>
<td>86(24.6)</td>
</tr>
<tr>
<td>60 - 69</td>
<td>53(19.5)</td>
<td>64(23.4)</td>
</tr>
<tr>
<td>total</td>
<td>400(36.8)</td>
<td>271(24.9)</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td></td>
</tr>
<tr>
<td>40 - 49</td>
<td>408(64.2)</td>
<td>141(22.2)</td>
</tr>
<tr>
<td>50 - 59</td>
<td>181(47.0)</td>
<td>90(23.4)</td>
</tr>
<tr>
<td>60 - 69</td>
<td>89(28.0)</td>
<td>80(25.2)</td>
</tr>
<tr>
<td>total</td>
<td>678(50.6)</td>
<td>311(23.2)</td>
</tr>
</tbody>
</table>

* NT = Normotension; BHT = borderline hypertension; HT = hypertension.

Figures within parentheses are percentages.
Table 7. Classification of hypertensive subjects according to the stage of hypertension in Ikawa village, Akita

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age group</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>30 - 39</td>
<td>40 - 49</td>
<td>50 - 59</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>34 (70.8)</td>
<td>35 (42.2)</td>
<td>33 (28.9)</td>
</tr>
<tr>
<td>Male</td>
<td>30 - 39</td>
<td>11 (22.9)</td>
<td>44 (53.0)</td>
<td>60 (52.6)</td>
<td>45 (48.4)</td>
</tr>
<tr>
<td></td>
<td>40 - 49</td>
<td>3 (6.3)</td>
<td>4 (4.8)</td>
<td>21 (18.4)</td>
<td>22 (23.6)</td>
</tr>
<tr>
<td></td>
<td>50 - 59</td>
<td></td>
<td></td>
<td>83 (100.0)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>60 - 69</td>
<td></td>
<td></td>
<td></td>
<td>93 (100.0)</td>
</tr>
<tr>
<td>Female</td>
<td>30 - 39</td>
<td>22 (68.8)</td>
<td>10 (31.2)</td>
<td>0 ( - )</td>
<td>32 (100.0)</td>
</tr>
<tr>
<td></td>
<td>40 - 49</td>
<td>19 (39.6)</td>
<td>4 (8.3)</td>
<td>48 (100.0)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>50 - 59</td>
<td>30 (31.6)</td>
<td>55 (57.9)</td>
<td>10 (10.5)</td>
<td>95 (100.0)</td>
</tr>
<tr>
<td></td>
<td>60 - 69</td>
<td>20 (27.8)</td>
<td>41 (56.9)</td>
<td>11 (15.3)</td>
<td>72 (100.0)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>40 - 69</td>
<td>male</td>
<td>94 (32.4)</td>
<td>149 (51.4)</td>
<td>47 (16.2)</td>
</tr>
<tr>
<td></td>
<td>female</td>
<td>75 (34.9)</td>
<td>115 (53.5)</td>
<td>25 (11.6)</td>
<td>215 (100.0)</td>
</tr>
<tr>
<td></td>
<td>both</td>
<td>169 (33.5)</td>
<td>264 (52.3)</td>
<td>72 (14.2)</td>
<td>505 (100.0)</td>
</tr>
</tbody>
</table>


- Figures within parentheses are percentages.
(2) Hypertension control

In hypertension control in Akita, we placed emphasis on the persons with a higher likelihood of having CVA in the future. The hypertension control programme was thus applied to the hypertensives in stages 2 and 3, and to those who were in stage 1 but whose systolic or diastolic blood pressure was at least 180 or 110 mmHg respectively, at the time of examination. For these subjects, the local general practitioners took charge of treatment and guidance, whereas the public health nurses and midwives gave advice and guidance on the way of living, encouraged them to continue with medical treatment, and took blood pressure measurements. Their guidance and encouragement were given according to a specific formula, and contacts with the local inhabitants were encouraged at every opportunity. The subjects were also invited to a group guidance meeting; those who had difficulty in attending were visited by public health nurses or midwives.

Effects of hypertension control

We assessed the effects of the activities launched for hypertension control. The extent of compliance with antihypertensive treatment is shown in Table 8. It was found that many patients discontinued medical treatment and that the frequency of persons taking medicaments every day was low. In the last half of the control programme, however, the frequency of these two groups rose and the number of persons continuously taking medicaments increased.

The incidence of CVA during the 3-year period is shown in Table 9, in relation to the compliance to therapy. The incidence rate of CVA in the group that continued treatment was 7.4 per 1,000 population a year, which is about half that in the other two groups, thus suggesting that continuous treatment is fairly effective for the prevention of CVA.

The incidence rates of CVA in the Ikawa and Ishizawa communities in the first and second halves of the control period are compared in Table 10. The incidence of CVA decreased in the latter half, that of cerebral haemorrhage decreasing conspicuously. Thus, the implementation of a hypertension control programme is instrumental in reducing the incidence of CVA, notably that of cerebral haemorrhage. Nevertheless, the incidence of CVA is still high in Akita. To clarify the reasons for this, 32 patients with CVA, aged 30-69 years, who had been registered between 1 January 1971 and 31 December 1972 were analysed. The 32 patients included 9 with cerebral haemorrhage, 15 with cerebral infarction, and 8 with subarachnoid haemorrhage, and it turned out that all the patients with cerebral haemorrhage had abandoned medical treatment. Three of the 15 patients with cerebral infarction received uninterrupted treatment, another 3 only intermittent treatment, and 9 received no medical treatment at all. This fact indicates that even with hypertension control, CVA still occurs among the inhabitants who are reluctant to take part in the programme.

Summary

1. Mass screening with the emphasis on hypertension control was conducted on the population in Akita. Guidance and medical treatment were provided for those who were considered likely to develop CVA. A method of
Table 8. Extent of medical care for persons requiring treatment during two control periods (Residents in Akita, 30 - 69 years)

<table>
<thead>
<tr>
<th>Phase of control period</th>
<th>Continuous</th>
<th>Occasional</th>
<th>Temporary or untreated</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1964 - 1967</td>
<td>103 (13.8)%</td>
<td>327 (44.0)</td>
<td>314 (42.2)</td>
<td>744 (100.0)</td>
</tr>
<tr>
<td>1968 - 1971</td>
<td>338 (44.9)</td>
<td>208 (27.6)</td>
<td>207 (27.5)</td>
<td>753 (100.0)</td>
</tr>
</tbody>
</table>

Continuous: patients received medication for more than 20 days a month, on average, and never stopped medication for more than a month.

Occasional: patients received medication for more than 20 days a month, on average, but had sometimes stopped medication for more than a month; or they received medication for 10 - 20 days a month, on average, but never stopped medication for more than half a year.

Temporary or untreated: all other patients.

b Figures within parentheses are percentages.

Table 9. CVA incidence rates among hypertensive patients, aged 30 - 69 years, based on their compliance to treatment in Ikawa Village, Akita, during 1968-70

<table>
<thead>
<tr>
<th>Extent of treatment</th>
<th>Hypertensive subjects (no.)</th>
<th>CVA</th>
<th>Incidence rate of CVA&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>continuous</td>
<td>occasional</td>
<td>temporary or untreated</td>
</tr>
<tr>
<td>Hypertensive subjects (no.)</td>
<td>180</td>
<td>359</td>
<td>227</td>
</tr>
<tr>
<td>Number of CVA</td>
<td>4</td>
<td>15</td>
<td>12</td>
</tr>
<tr>
<td>Incidence rate of CVA&lt;sup&gt;a&lt;/sup&gt;</td>
<td>7.4</td>
<td>13.9</td>
<td>17.6</td>
</tr>
</tbody>
</table>

<sup>a</sup> Incidence rate / year / 1 000 population.
Table 10. Changes in CVA incidence rates during two control periods in Akita (Ikawa and Ishizawa) among patients aged 30 - 69 years

<table>
<thead>
<tr>
<th>Phase of control period</th>
<th>Pop.</th>
<th>CVA incidence</th>
<th>Total CVA</th>
<th>Type of CVA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>Incidence rate</td>
<td></td>
<td>Haemorrhage</td>
</tr>
<tr>
<td>1964 - 1967</td>
<td>4368</td>
<td>102</td>
<td>44</td>
<td>39</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.84</td>
<td>2.52</td>
<td>2.23</td>
</tr>
<tr>
<td>1968 - 1971</td>
<td>4439</td>
<td>73</td>
<td>17</td>
<td>45</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4.11</td>
<td>0.96</td>
<td>2.53</td>
</tr>
</tbody>
</table>

² Incidence rate / year / 1 000 population.
examination, which would effectively identify the persons who are highly likely to develop CVA, has been described.

2. In view of the present situation of increasing demands on physicians, the application of a hypertension control programme to a wider segment of local inhabitants is difficult. An approach using public health nurses and other paramedical personnel should be made. The participation of the local inhabitants in the programme for health examination and control is desirable.

3. The examination for hypertension does not require to be carried out only in a general hospital with advanced equipment and facilities. As long as there is a systematically organized examination team, it is feasible to carry out such examinations - even outdoors.

4. The organization of a well-equipped examination team is essential for standardizing the control measures against hypertension.

DISCUSSION

Dr Akinkugbe: I am intrigued by these last two presentations, because in areas where there is an obvious shortage of medical manpower it is extremely important to be able to detect these cases early and when you have done so, to be clear as to how to manage them. The first thing I would like to find out from the last presentation is whether there was any difference in the response to management when qualified physicians dealt with these cases as opposed to public health nurses. That is, in an area where there are more public health nurses than physicians, is there any difference because a physician is obviously better able, by training, to reach a more definitive decision in respect of diagnosis than a public health nurse. This becomes important in the setting of a rural area where medical manpower may be a real problem. I would like to know whether you will find a distinct difference if you group these Tables in such a way that you can identify the populations in which physicians are responsible as distinct from public health nurses.

Dr Kojima: The diagnosis and treatment are always given by doctors and public health nurses give guidance on the basis of the advice of doctors, and not independently.

Dr Akinkugbe: Well, let us look at Table 5 - method of examination, the one that says 'interview by physician or public health nurse'. What does this mean? Is this last reply to indicate that the public health nurse has been specially trained by the physician, or is this done independently?

Dr Kojima: The doctors do educate the public health nurses who interview patients.
A hypertension control programme was organized for the local inhabitants of Yao City, a commuter area of Osaka. The organization of this programme was similar to that in Akita (see Fig. 1 in the previous paper, page 156). The programme was initiated primarily by the Yao Municipal Government. Also taking part in the programme was the Osaka Prefectural Government's Department of Public Health for administrative guidance, technical assistance, and financial support.

Because the general practitioners, public and private hospitals, and health centres in the district are so busy with routine medical care, they alone were unable to ensure effective implementation of the control programme. So the Centre for Adult Diseases, Osaka Prefecture, and the Institute of Public Health, Akita Prefecture, had to take over some of the responsibilities for the programme.

An essential factor is the participation of the population. In Yao City, voluntary bodies such as women's associations and clubs for the aged, as well as townsfolks' associations, took an active part in the programme. Representatives of these associations were members of a Hypertension and Stroke Control Committee and each member received a written commission from the mayor of Yao City.

Contact between the medical care workers and the inhabitants began with members of the Committee serving as intermediaries. An orientation programme on hypertensive diseases was started for the members of the Committee in 1963. Lectures were also given not only at conferences held in the district but also in clubs for the aged and in women's associations, with the primary purpose of orienting the local leaders first.

Whenever members of this Committee held a conference for the local inhabitants, we attended to give a lecture explaining how hypertension occurs and develops, what type of examinations are required, and why all people have to undergo a physical examination. Such a lecture was supplemented by brochures and visual aids, such as slides and motion pictures. These activities were attended not only by physicians but also by the public health nurses who visit families for consultation and guidance. The public health nurse, on her part, encouraged local inhabitants to attend the lectures, maintained liaison between physicians and members of the Committee, and supported the activities of members of the Committee. In these activities we realized how influential the public health nurses are in their contacts with the local inhabitants.
Meetings of medical care workers

The medical care workers also held meetings to discuss the details. The participants in these meetings concentrated on the mass health examination to be conducted in collaboration with local medical care institutions and on the criteria for assessing the examination results and for arriving at a comprehensive diagnosis. The participants also discussed the types of medical care and the guidance on the pattern of living which were to be recommended.

Implementation of mass health examinations for hypertension

Table 1 shows the roles of the medical care institutions and personnel in the examination. One unique feature is that not only members of the medical services but also representatives of the general population had their own roles in assuring a smooth implementation of the programme.

Three years were required to complete the examination in the pilot areas of Osaka and Akita. The response rate was high with Osaka at 89% and Akita at 88.6%. Abnormal findings were discovered in 23.5% in Osaka and 42% in Akita. Only 12.8% of hypertensive subjects in Osaka and 14.9% in Akita were under treatment (Fig. 1).

FIG. 1
PROPORTIONS OF HYPERTENSIVE SUBJECTS RECEIVING MEDICAL CARE AT THE TIME OF THE FIRST EXAMINATION (1964-1966), IN OSAKA (YAO) AND AKITA (IKAWA)

OSAKA

<table>
<thead>
<tr>
<th></th>
<th>III 12.8%</th>
<th>II 37.7%</th>
<th>I 49.5%</th>
</tr>
</thead>
</table>

AKITA

|    | III 14.9% | II 43.0% | I 42.1% |

I : Unknown hypertensives
II : Known but untreated hypertensives
III : Known and treated hypertensives
Table 1. Roles of the different participating organizations in the mass examination programme in Yao City

<table>
<thead>
<tr>
<th>Kind of work</th>
<th>City Government Authority PHN</th>
<th>City Government Authority Clerk</th>
<th>Local Residents Associations Dr. PHN</th>
<th>Local Residents Associations Technician</th>
<th>City Government Authority Dr.</th>
<th>Local Residents Associations Nurse</th>
<th>Local Residents Associations Technician</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Information</td>
<td>3</td>
<td>1</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>Chest X-ray</td>
<td></td>
<td></td>
<td>1</td>
<td>1</td>
<td></td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Urine test</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Height and weight</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Questionnaire</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Blood pressure</td>
<td></td>
<td></td>
<td></td>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>ECG</td>
<td>2</td>
<td></td>
<td></td>
<td>1</td>
<td>2</td>
<td>1</td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Serum cholesterol and triglyceride</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Fundus oculi</td>
<td>2</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Physical examination and diagnosis</td>
<td>1</td>
<td>3</td>
<td>1</td>
<td>5</td>
<td>1</td>
<td>5</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>5</strong></td>
<td><strong>1</strong></td>
<td><strong>10</strong></td>
<td><strong>1</strong></td>
<td><strong>5</strong></td>
<td><strong>1</strong></td>
<td><strong>2</strong></td>
<td><strong>42</strong></td>
</tr>
</tbody>
</table>

1 The figures show the number of persons engaged in each kind of work.

PHN = public health nurse; Dr. = physician.
The subjects with abnormalities were placed under the control of their own physicians, depending on the comprehensive diagnosis (i.e., whether care had to be exercised or treatment given). The representatives of medical care institutions discussed who should be given guidance and treatment, in addition to assessment of the findings and comprehensive diagnosis; it was decided, in principle, that local medical facilities should serve as the core for providing treatment. In Osaka, local general practitioners would take charge of guidance and treatment first of all, and when more elaborate treatment and check-ups were needed, the case would be referred to the Municipal Hospital. When a patient had a myocardial infarction, he was referred to the Centre for Adult Diseases. In Akita, national health insurance clinics were called upon to take charge of treatment first of all, and hospitals affiliated to the local Medical Association or Agricultural Coop would undertake more detailed examination and hospitalization.

Initiation of health guidance in home visits by public health nurses

In addition to the care provided by the medical services, the local public health nurses gave guidance to patients requiring hypertension control.

The population in the pilot area of Yao City, in which the hypertension control programme was instituted, numbered 3911 inhabitants over 40 years of age, of whom 819 persons were placed under the hypertension control programme. In accordance with the schedule shown in Table 2, 2 public health nurses of the Yao Health Centre and 5 public health nurses of the Yao Municipal Government provided guidance on work and other matters associated with daily living and they also encouraged the patients to consult the medical services.

The guidance given covered not only medical matters in the narrow sense, such as the findings of the physical examination, past history, subjective symptoms, and medical treatment received, but also included detailed descriptions on type of work, family planning, type of dwelling, availability of a heating system, and on dietary and living habits. Any doubtful points were brought to the attention of the attending physician and his instructions were noted. If the nurse discovered any point in the mode of living which still had to be improved, she would advise the patient accordingly. This advice was entered into a guidance card. On her next visit, emphasis was placed on checking whether the points previously advised upon had been improved.

Problems encountered in home visits

In the early stages of the hypertension control programme, only about 15% of the persons who had been diagnosed as needing medical treatment actually continued it in Osaka and Akita, and there were many who only temporarily or intermittently received treatment. When these patients were asked why they had stopped or resumed medical treatment, there were many who replied, "I have decided to stop receiving treatment because my symptoms have been cured" or "I have resumed treatment because my symptoms have returned". As public health nurses frequently called on the patients, it was known that their decision to discontinue or resume medical treatment did not necessarily stem from a lack of understanding about the disease on the part of the patients. For example, there were cases in which the husband was more inclined to receive treatment than the wife, or in which the frequency of receiving treatment was not sufficient among the older women who could not afford to pay for it. Whether a patient can afford to pay for medical treatment has a great impact on his or her willingness to continue it.
Table 2. Frequency of guidance given to hypertensive patients

<table>
<thead>
<tr>
<th>District and year</th>
<th>No. of PHN</th>
<th>No. of patients (A)</th>
<th>Standard frequency of guidance</th>
<th>Total no. of patients who took guidance (B)</th>
<th>Actual frequency of guidance B/A</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>II</td>
<td>III</td>
<td>II</td>
<td>III</td>
</tr>
<tr>
<td>Osaka 1964</td>
<td>10</td>
<td>408</td>
<td>411</td>
<td>2-3/year</td>
<td>3-4/year</td>
</tr>
<tr>
<td>Osaka 1969</td>
<td>7</td>
<td>434</td>
<td>468</td>
<td>1-2/year</td>
<td>2-3/year</td>
</tr>
<tr>
<td>Akita 1964</td>
<td>7</td>
<td>391</td>
<td>519</td>
<td>2/year</td>
<td>12/year</td>
</tr>
<tr>
<td>Akita 1969</td>
<td>6</td>
<td>345</td>
<td>534</td>
<td>2/year</td>
<td>6/year</td>
</tr>
</tbody>
</table>

Notes: (1) Persons in group II had high blood pressure (160-179/95-109) without evidence of organ damage or were normotensive with organ damage. Those in group III had very high blood pressure (180/110 or over) or high blood pressure (160-179/95-109) with evidence of organ damage.

(2) Guidance was given during the PHN's home interviews in Osaka, and during mostly group guidance sessions in Akita. Figures in parentheses in Akita show the number given guidance at home interviews.
Attention must be paid to the fact, therefore, that some of the statements made by a patient do not necessarily reflect the true reason for the discontinuance or resumption of medical treatment. Concerning the status of the housewife in Japan, there still remain a wide variety of feudal elements that have yet to be dispelled, and this holds true particularly in the rural areas. In the early stages of the hypertension control programme, there were many housewives, even though married for more than 20 years, who said "I don't want to consult a physician, because my mother-in-law will criticize me for paying too many visits to the physician." In such cases, the public health nurse contacted the attending physician and also held frequent consultations not only with these housewives, but with their husbands and mothers-in-law.

Our model area for hypertension control is relatively small, so we were able to keep in close contact with the local public health nurses and general practitioners, thus enabling us to have access to information about patients who were under the hypertension programme. For example, the public health nurse could secure a wide variety of information about a patient, when she happened to meet the attending physician in the patient's home, even though she had not yet called at his clinic.

Changes in the frequency of medical treatment and improvements in the living environment

The frequency of medical treatment is shown in Table 3 for two separate periods in the programme. As mentioned earlier, only 15% of the hypertensives received continuous medical treatment in the early stages of the hypertension control programme both in Osaka and Akita. In Osaka, however, the rate of continuous treatment rose to 45% since home visits had frequently been made by the public health nurses. Particularly in the areas where there was strong community awareness, the rate was as high as 60%.

Even in the second half of the programme, these high percentages were maintained. In Akita, however, the improvement in the rate of maintaining medical treatment was not so high in the early stages as in Osaka. The rate was lower in the first half than in Osaka, but the rate came close to 60% in the second half.

Improvements in the living environment were made first in matters not requiring a large financial outlay. For example, the use of hot water in cooking in winter was encouraged and the elderly were encouraged not to go out early in the morning and late at night, particularly in the winter. However, improvements in the heating systems, such as the use of oil stoves and electric blankets, could not be made because of the expense. However, in the late 1960s oil stoves were made available and even in Akita, where the temperature is low in the winter and where adequate heating facilities were not in use, improvements were made fairly rapidly so that it was possible for the local inhabitants to keep their homes warm in the winter.

Future developments

The measures for hypertension control have steadily become worth while since not only the local medical services and administration but also the local inhabitants have joined in ensuring a smooth implementation of this programme.
Table 3. Numbers of hypertensive patients, 40-69 years old, receiving treatment during two control periods in Osaka and Akita

<table>
<thead>
<tr>
<th>Phase of control period</th>
<th>Medical care</th>
<th>Treated</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>District</td>
<td>Continuously&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Occasionally&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
<td>Total</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Untreated&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osaka</td>
<td>1964 - 1967</td>
<td>178 (45.1)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>12 (3.0)</td>
<td>205 (51.9)</td>
<td>395</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1968 - 1971</td>
<td>185 (44.0)</td>
<td>101 (24.0)</td>
<td>134 (32.0)</td>
<td>420</td>
<td></td>
</tr>
<tr>
<td>Akita</td>
<td>1964 - 1967</td>
<td>208 (33.9)</td>
<td>140 (22.8)</td>
<td>266 (43.3)</td>
<td>614</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1968 - 1971</td>
<td>379 (58.1)</td>
<td>84 (12.9)</td>
<td>189 (29.0)</td>
<td>652</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> Duration of treatment: over 7 months a year.

<sup>b</sup> Duration of treatment: 1-6 months a year.

<sup>c</sup> Duration of treatment: under 1 month a year.

<sup>d</sup> Figures within parentheses are percentages.
The pilot area covered under the present programme is small, but enlargement of the programme area is expected. To meet this, mass health examinations have been conducted not only in the pilot area but also elsewhere in Yao City; however, it is not enough to carry out mass health examinations only once a year. Some of those who belonged to the local Medical Association, Municipal Hospital and Public Health Centre, and the Centre for Adult Diseases organized a cerebrovascular and cardiovascular disease control study group last year, and regular meetings have been held to work out measures for the future. In this group, physicians from different organizations present various topics for discussion, such as examination methods, diagnostic questions, and therapeutics, and at the same time they keep in close contact with the medical care institutions in the city so that the referral of patients from general practitioners to the Municipal Hospital may be implemented smoothly.

Parallel with these measures, a multiphasic mass examination division capable of conducting elaborate check-ups on as many as 15,000 people a year was established in the Centre for Adult Diseases, Osaka Prefecture, in September 1974 to ensure the implementation of more powerful and systematic hypertension control measures.

In the meantime, there are plans in Yao City to establish a subcentre for the systematic and continuous execution of mass health examinations, in collaboration with the Centre for Adult Diseases, and to place emphasis on the need for the population to undergo mass health examinations. With the participation of the community and the support of local medical associations and other medical care institutions, Yao City is scheduled to carry out mass examinations on the circulatory system not only for cases referred by general practitioners, but also for anyone in the general population who desires to have such an examination. If all these measures are implemented to the fullest extent, it will become possible for the hypertension and cardiovascular disease control programme to cover not only the population of the pilot area but also other citizens of Yao City.

DISCUSSION

Dr Hatano: Thank you very much for your presentation of the painstaking efforts made in the community control of stroke and hypertension. Multiphasic examination is expensive and you have examined 80 subjects per day and each subject for 3 hours. How many examiners work in the programme and how much does it cost? Secondly, how do you approach general practitioners and how do you influence them? Thirdly, in order to develop your programme to a much wider area than Yao, let us say the whole of Osaka prefecture, what kind of approach are you planning?

Dr Komachi: Let me try to explain the first point about the number of staff. The present report does not necessarily mean that multiphasic examination was conducted in the centre. We went out into the field with 10-15 staff per day, including 2 or 3 physicians, 3 nurses, public health nurses, and a few technicians, and this staff would handle around 100 people per day. In future, we would like to use automatic machines and to examine 15,000 people a year, handling 80 people a day. This would mean employing a permanent staff of 30. We are thinking of this expansion in order to attract enough physicians to the public health field. Cerebral infarction may be induced by other factors than hypertension and we have to introduce more refined methods of examination in order to examine more complex factors than blood pressure.
Since it is financed by the prefectural government, we can provide the examination at a low price of 2000 to 4000 yen (7-13 US$) per subject and, of course, we are running at a deficit which is borne by the government. Also, without the cooperation of the Citizens' Association and the Medical Society we cannot hope to achieve good results.

Concerning the possible enlargement of the programme to cover the whole of Osaka prefecture (there are seven counties in Osaka, each of which has about one million population), we are planning to establish one unit in each county and shall try to investigate the units in the various counties from our centre.

Dr Strasser: I very much appreciate Dr Komachi's paper and his discussion because he has introduced a new element, the participation of the general public. I think this is an extremely important issue. Mankind is getting more and more healthy and yet we need evermore doctors and medical services, for many reasons. If we try to extrapolate into the future and if health care is to be left entirely to the health services and health professionals, very soon, perhaps in a few decades, we might reach the hopeless situation of one half of mankind taking care of the other half. I think the solution, especially for the control of hypertension and some other chronic diseases, is to have increasing participation of the public itself, and this is why I think that what Dr Komachi said about participation or active involvement of the public in our struggle against hypertension is a very important issue, one that should also be tried out in other places. I have one question in this connexion: do you, Dr Komachi, have any experience with self-measurement of blood pressure and do you think this is applicable in Japan? I know it very much depends on the local culture and on local concepts; it may be very different in a European country compared with in Japan. According to a small study, self-measurement of blood pressure was not only completely acceptable but very much appreciated by the general public on whom it was tested. I must say that this 'general public' were employees of the World Health Organization. Among the participants we had two categories: professionals (physicians and secretaries) and lay people. It was better accepted by the lay people than by the physicians. How do you look upon this in Japan?

Dr Komachi: Concerning the self-measurement of blood pressure, I should say that the treatment itself must be delegated to the local physicians because in this way we can establish the relationship of trust between ourselves and the local physicians. If we should tell people that they can measure their blood pressure themselves, I think the physicians would see the number of patients coming to them decreasing and this might interfere with the physicians' trust in us. Therefore, at the present time, we are not considering the introduction of self-measurement in our field activities. Dr Hatano and Dr Strasser expressed their opinions which are not exactly the same as mine, and I think my opinion reflects the special conditions of the Japanese community. Doctors are against self-measurement or automated measurement by lay people.

Dr Reader: I would like to know, concerning the guidance given by the public health nurses in respect of such matters as an hour's sleep in the afternoon, not going out at night, having the dining-room warmed, and so on, whether the people cooperate in this kind of instruction. Could you tell us a little about how it is received.
Dr Komachi: Well, I think the people are most receptive when no cost is involved. If we recommend them to renovate the kitchen or heating system, people are reluctant to follow such instructions, but if we tell them not to stay up too late or not to get up too early in the morning, they are fairly receptive to such advice. It seems that people do bear this kind of advice in mind and that they refrain from some of the things which they would do unless they were told not to. We know this because the public health nurses visit people's homes and get information. Men are less receptive than women to instructions and the decreasing trend in the incidence of stroke is more clearly seen in women than in men. For example, drinking is a habit which is difficult to stop. We put more effort into persuading men to stop drinking than into persuading women.

Dr Sasaki: Earlier, Dr Komachi made a comment on self-measurement of blood pressure and I think he gave a Japanese point of view. I would like to say that I agree with the thoughts expressed by Dr Strasser. For the past twenty years, I have been thinking of ways and means to measure people's blood pressure in the community. I can say that it is important for the people to have the correct understanding of their own blood pressure by measurement. In the past, only the physicians knew how to measure blood pressure and this made blood pressure something of a mystical and esoteric phenomenon. I think we have to open up the field of blood pressure to the general public. We have advanced electronic gadgets and so I think the doors are already open for lay people. They should acquire a correct understanding of blood pressure and of the concept of health.

Dr Akinkugbe: I should just like to reinforce that last point by drawing your attention to Table 1. This table is interesting to me for a number of reasons. It shows the division of labour clearly in terms of the world where there are medical manpower constraints and where you do not expect physicians to be handling a number of these investigations. Looking quickly through this Table, we find that of a total personnel of 42 there are 3 physicians measuring blood pressures. I think this is interesting because it does show that in a screening population you might need an optimum number of physicians in handling a defined size of population. The other point is that a number of investigations, like ECGs and funduscopy, are in fact not done by physicians. I imagine a fundus photograph is taken by a technician and that the physician does not have to use the ophthalmoscope. I think that these routine chores, earlier handled by physicians, can gradually be shed to allow the physicians to concentrate more on the actual measurement of the blood pressure which seems to me the most crucial of all the measurements that we are doing in this context. The screening process might thus be considerably quickened. A meeting like this should be able to find a cheap, effective, and optimum way of constructing this type of chart so that it applies with equal force to Japan as it will to Europe or Africa.

Dr Komachi: The ECG can be taken by nurses or technicians or other auxiliaries but the diagnosis itself or the physical examination is conducted by 3 physicians from the centre. The fundus examination is done by a fundus camera and so the answers are not given on the day of the examination. The films have to be brought back to the centre and processed. The diagnosis has to be done by physicians but the physicians do not have to be present at the field examination. The blood pressure measurement and the interpretation of the ECG are also done by physicians, and all the other tasks can be handled by auxiliary personnel.
Dr Paul: I would just like to ask why the blood pressure has to be taken by the physician. In our high blood pressure detection and follow-up trial, and the multiple risk factor trial, this is done by nurses who receive special training. This is particularly important for subsequent examination. I wonder why the physician has to be put down for this particular task.

Dr Komachi: Blood pressure measurement is easy but we believe it has to be done in an accurate manner. The stethoscope has been used only by physicians and was considered to be one of the sacred tools that only the physicians are entitled to touch. Thanks to mechanization, it can now be done by auxiliaries. When we can trust the equipment, we might unofficially allow the auxiliary personnel to do the measurements but usually in these cases the physicians must be there supervising what is being done. I think in most cases the physicians will review the results and request a second measurement anyway. This is applicable only to the screening measurement. When treatment or guidance comes in, we can say that self-measurement is considered to be out of the question. I think what Dr Sasaki said was sound theoretically, but in reality the theory does not always work.

Dr Strasser: Of course, I am not criticizing Dr Komachi's programme because I think it is excellent. I just want to say that all investigators who have been involved in field studies where a great number of electrocardiograms have been recorded and coded, know that electrocardiograms are more reliably coded and interpreted by specially trained technicians than by physicians and the more competent a cardiologist is, the worse his readings are. This has been shown several times, including a quite recent WHO study in which 250 ECGs were read in 25 centres. Though some of the ECGs were quite difficult tracings, it has been shown again that technicians did a better job than cardiologists.

Dr Freis: Just a brief comment to follow up what Dr Strasser said about cardiologists. This is with respect to the measurements of blood pressure. A study was done in the USA by Dr Irving Wright, in which the comparability of blood pressure measurements by physicians and nurses was examined. The physicians did very poorly. Some of the poorest measurements were made by cardiologists.

Dr Katsuki: Now I want to call Dr Goto who has some remarks on prevention.

Dr Goto: I would like to talk about the primary prevention of ischaemic heart and cerebral diseases by using a serum lipid lowering drug or an anabolic steroid. In 1969 we screened people over 40 years of age in three communities, a mountain village, a farming village, and a fishermen's village, located in the northern and the middle part of this country. Out of 568 persons examined, a total of 280 subjects had several risk factors for ischaemic vascular disease. They were divided into two groups with nearly equal prevalence of risk factors, except for mean blood cholesterol concentrations. To the first group with higher cholesterol level, we administered daily 3 capsules, containing a blood lipid lowering drug, or an anabolic ethylandrol-steroid, or 100 mg of linoleic acid as a placebo. The mean cholesterol and triglyceride concentrations of the treated group in the three communities decreased by 9 - 17% and 19 - 64%, respectively, after six months. This decrease remained unchanged thereafter. Because of the small number of the total accidents, the difference in incidence of vascular disease between the groups was not statistically significant.
However, it is striking that we have not seen any fatal accident in the treated group during the last two years. Moreover, those who had minor accidents in the treated group were taking the medicine irregularly. Subjects who died from cerebral thrombosis were all over 66 years of age and most frequently had high systolic blood pressure as well as high serum cholesterol concentration, and those who died from cerebral haemorrhage were also over 66 years of age and their systolic and diastolic blood pressure and serum cholesterol concentrations were high. These results indicate that the three major risk factors for ischaemic brain and heart disease are age, high serum lipids, and high blood pressure. It seems important therefore to control blood pressure, as well as serum lipids, for the prevention of ischaemic vascular diseases.

Dr Arai: Concerning the competence of trained technicians versus doctors and cardiologists, the same applies to ophthalmology. The ophthalmologists of course are well aware of the technique involved but they are often too concerned about their diagnosis and have their own ways of looking at things.

Dr Katsuki: I hope that these studies, using standardized methods, will be continued for several years to come. The success of a cooperative study depends upon the available budget, and it would be very helpful if more moral support from WHO could be given to such studies in order to ensure better financial support from the respective granting agencies.
B. METHODS

MEASUREMENT OF BLOOD PRESSURE IN THE POPULATION

by

Y. Fukuda

The indirect measurement of blood pressure by auscultation of Korotkoff sounds has been studied in great detail. Recommendations have been made on the length and width of the cuffs, the speed of deflation, temperature of the examination room, the posture of the subject, etc. in order to minimize systematic errors. However, besides these technically controllable factors there remain other problems in epidemiological studies of blood pressure, such as inter-observer error and fluctuation of blood pressure. The purpose of this presentation is to assess the magnitude of these problems.

Since blood pressure may vary beat by beat, the inter-observer error must be studied by simultaneous reading. Two physicians and two well-trained nurses with normal hearing acuity measured the blood pressure simultaneously using a quadrifurcated rubber tube. The measurements were repeated three times on 20 healthy subjects. The frequency distribution of the differences between individual readings and the mean values are shown in Fig. 1. The standard deviation of the differences was 1.36 mmHg in systolic and 1.71 mmHg in diastolic.

However, this is a model experiment and much less agreement should be expected in field conditions. We measured the blood pressure of 12 male workers six times during two days. On each occasion, repeat measurements were made. The mean of the first systolic reading on each of the six occasions tended to be 2-3 mmHg higher than the second reading. In the afternoon, systolic blood pressure was higher on the average by about 10 mmHg. The tendency was the same for diastolic blood pressure.

The daily fluctuation of blood pressure was studied in 9 healthy subjects with serial measurements at 10 a.m., 1 p.m., and 4 p.m. from Monday to Friday. At each time, the measurements were made thrice and then repeated after 5 and 10 minutes - again three times on each occasion. Systolic blood pressures tended to be higher in the first two of each three measurements. The average reading after 5 minutes was 3-4 mmHg lower and increased again slightly after 10 minutes. The diastolic blood pressure did not show such a tendency. There were no systematic variations between the days of the week. The mean and standard deviations are summarized in Table 1. The 95% confidence range of variation was 12 mmHg.
FIG. 1 INDIVIDUAL ERROR OF BLOOD PRESSURE MEASUREMENTS

Systolic blood pressure

Diastolic blood pressure

\[ \sigma \approx 1.36 \]

\[ \sigma \approx 1.71 \]
Table 1. Daily fluctuations

<table>
<thead>
<tr>
<th></th>
<th>Systolic</th>
<th>Diastolic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monday</td>
<td>111.0</td>
<td>66.1</td>
</tr>
<tr>
<td>Tuesday</td>
<td>108.0</td>
<td>65.1</td>
</tr>
<tr>
<td>Wednesday</td>
<td>108.6</td>
<td>67.7</td>
</tr>
<tr>
<td>Thursday</td>
<td>107.2</td>
<td>65.2</td>
</tr>
<tr>
<td>Friday</td>
<td>111.1</td>
<td>66.8</td>
</tr>
</tbody>
</table>

Each value is the mean of blood pressure measurements taken on 9 persons with 18 measurements on each person.

for both systolic and diastolic pressures (Fig. 2). The standard deviation of daily fluctuation was proportional to the mean level of the subjects' blood pressure: 6% for systolic and 7% for diastolic blood pressure.

Individual fluctuations of blood pressure in time are relatively great; therefore single measurements may be far from the central value. For the purpose of individual health guidance, repeated measurements are therefore required.

Table 2 illustrates the incidence of stroke and ischaemic heart attacks among over 130,000 Japanese National Railway employees aged 40-59 years during three years. The incidence rates are shown according to the systolic blood pressure in the first year. The incidence of stroke (especially of cerebral haemorrhage) rose remarkably with the increase in blood pressure (both systolic and diastolic). The incidence rate was approximately doubled at every 20 mmHg increase in the systolic blood pressure. The incidence rate in subjects with the systolic blood pressure at 190 mmHg and over was almost 50 times higher than the incidence rate in subjects with normal blood pressure (120-139 mmHg).

A correlation was also observed between the blood pressure and the incidence rate of ischaemic heart attacks, though this was not so marked as for the incidence rate of stroke.

Fig. 3 shows the correlation of fatality from stroke and blood pressure at previous measurements. Fatality in the high blood pressure group was almost 3 times that of the lower blood pressure group.

**Automatic sphygmomanometer**

Automated measurement was introduced in sports physiology and in space medicine for the continuous monitoring of blood pressure. A handy instrument using transistors has appeared for general use. Such instruments provide the possibility of:
<table>
<thead>
<tr>
<th>Systolic blood pressure in annual examination (mmHg)</th>
<th>0-89</th>
<th>90-109</th>
<th>110-129</th>
<th>130-149</th>
<th>150-169</th>
<th>170-189</th>
<th>190-</th>
<th>Total</th>
<th>Not examined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral haemorrhage</td>
<td>0.3</td>
<td>0.8</td>
<td>2.9</td>
<td>15.0</td>
<td>34.5</td>
<td>83.3</td>
<td>84.3</td>
<td>29.3</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>(8.0)</td>
<td>(17.3)</td>
<td>(24.6)</td>
<td>(43.3)</td>
<td>(49.3)</td>
<td>(67.4)</td>
<td>(74.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(16.0)</td>
<td>(22.7)</td>
<td>(23.6)</td>
<td>(18.4)</td>
<td>(16.7)</td>
<td>(8.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebral infarction (a)</td>
<td>1.4</td>
<td>9.1</td>
<td>1.1</td>
<td>25</td>
<td>6.1</td>
<td>37</td>
<td>11.7</td>
<td>25</td>
<td>10.4</td>
</tr>
<tr>
<td></td>
<td>(4.0)</td>
<td>(10.0)</td>
<td>(13.6)</td>
<td>(9.5)</td>
<td>(6.0)</td>
<td>(3.2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subarachnoid haemorrhage (b)</td>
<td>0.2</td>
<td>1</td>
<td>0.5</td>
<td>11</td>
<td>3.1</td>
<td>19</td>
<td>4.2</td>
<td>9</td>
<td>3.9</td>
</tr>
<tr>
<td></td>
<td>(4.0)</td>
<td>(6.4)</td>
<td>(5.5)</td>
<td>(8.5)</td>
<td>(11.3)</td>
<td>(8.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Undifferentiated cerebral stroke (c)</td>
<td>0.2</td>
<td>1</td>
<td>0.3</td>
<td>7</td>
<td>0.7</td>
<td>11</td>
<td>2.8</td>
<td>17</td>
<td>7.9</td>
</tr>
<tr>
<td></td>
<td>(4.0)</td>
<td>(6.4)</td>
<td>(10.0)</td>
<td>(13.6)</td>
<td>(16.7)</td>
<td>(19.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(a) + (b) + (c)</td>
<td>1.8</td>
<td>11</td>
<td>1.9</td>
<td>43</td>
<td>5.0</td>
<td>85</td>
<td>12.0</td>
<td>73</td>
<td>23.8</td>
</tr>
<tr>
<td></td>
<td>(44.0)</td>
<td>(39.1)</td>
<td>(36.3)</td>
<td>(36.3)</td>
<td>(34.0)</td>
<td>(20.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebral stroke (Total) (A)</td>
<td>2.1</td>
<td>13</td>
<td>2.7</td>
<td>62</td>
<td>8.0</td>
<td>134</td>
<td>27.0</td>
<td>164</td>
<td>58.3</td>
</tr>
<tr>
<td></td>
<td>(52.0)</td>
<td>(56.6)</td>
<td>(67.3)</td>
<td>(81.6)</td>
<td>(83.3)</td>
<td>(87.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(B)</td>
<td>(48.0)</td>
<td>(43.6)</td>
<td>(32.7)</td>
<td>(18.0)</td>
<td>(16.7)</td>
<td>(12.6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coronary heart attack</td>
<td>1.9</td>
<td>12</td>
<td>2.1</td>
<td>48</td>
<td>3.9</td>
<td>65</td>
<td>6.1</td>
<td>37</td>
<td>11.7</td>
</tr>
<tr>
<td></td>
<td>(100%)</td>
<td>(100%)</td>
<td>(100%)</td>
<td>(100%)</td>
<td>(100%)</td>
<td>(100%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(A) + (B)</td>
<td>4.0</td>
<td>25</td>
<td>4.8</td>
<td>110</td>
<td>11.8</td>
<td>199</td>
<td>33.1</td>
<td>201</td>
<td>69.9</td>
</tr>
<tr>
<td></td>
<td>(100%)</td>
<td>(100%)</td>
<td>(100%)</td>
<td>(100%)</td>
<td>(100%)</td>
<td>(100%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>The total number examined</td>
<td>967</td>
<td>10,000</td>
<td>62,356</td>
<td>10,000</td>
<td>277,705</td>
<td>10,000</td>
<td>168,453</td>
<td>10,000</td>
<td>60,751</td>
</tr>
</tbody>
</table>

Notes: 1. Incidence and number of episodes are based on a study of annually health-checked employees of JNR in 1961. Such surveys were repeated on the 1962, 1963 and 1964 examinees.
2. Incidence rate is defined as the rate of episodes/cases, occurring during a year after the record of blood pressure, per 10,000 persons examined.
3. Figures within parentheses are percentages.
4. Inc. = incidence rate; No. = number of cases or episodes.
FIG. 2 DAILY VARIATIONS OF BLOOD PRESSURE

1. Increasing the number of examinations in a given period and economizing on doctors' and nurses' time. Non-medical personnel can take over blood pressure measurement.

2. Self-measurement by the patient.

3. Standardization of measurement and reducing measurement errors.

The choice of instrument depends on the aim of the survey and the cost. We have tested several types of instruments now on the market. A high correlation between the machine and conventional readings was obtained with two instruments (Fig. 4). Automatic sphygmomanometers can therefore be recommended for use in hypertension control programmes in populations.
Fig. 3 Stroke fatality according to systolic blood pressure before stroke (40-54 years)

Systolic blood pressure in annual examination (during one year before episodes)

Note: There were 855 cerebral and coronary episodes in patients from 40 to 54 years of age during the period 1961 to 1964. The study comprised 780 of them with the blood pressure record one year prior to the episodes.
Fig. 4 Comparison of Blood Pressure Reading between automatic and conventional sphygmomanometers

Machine A
systolic b.p.
$r=0.98$
diastolic b.p.
$r=0.97$

Machine B
systolic b.p.
$r=0.96$
diastolic b.p.
$r=0.94$
DISCUSSION

Dr Strasser: Dr Fukuda, when you compared blood pressure values between automatic and conventional sphygmomanometers, was the human element a single observer or several observers?

Dr Fukuda: We compared blood pressures measured with the conventional method by a single observer.

Dr Gross: How long does it take to make a measurement with the automatic machine, and do you make only one measurement at one time or do you repeat the measurement?

Dr Fukuda: The number of measurements differs. Generally speaking, in mass screening we measure only once. If we obtain high values, we designate that person as requiring detailed examination.

Dr Kagan: Dr Fukuda, I should like to enquire whether you did multiple blood pressure readings with the automatic apparatus in order to see whether the amount of blood pressure variation is the same with the automatic apparatus as when measured by conventional methods.

Dr Fukuda: We analyzed the variation of the auscultatory method, but we have not used automatic machines in our hypertension control project.

Dr Toole: In view of the fact that there is a diurnal variation in blood pressure and that people who work different shifts during the day or the night might have different blood pressures, is there any importance in standardizing the time of blood pressure determination in relationship to that person's life pattern?

Dr Fukuda: We usually measure during the day time, for practical reasons.

Dr Akinkugbe: I see that the least variation occurs at 4 o'clock in the afternoon in systolic and diastolic pressures. I just wonder if you have a similar figure for nocturnal variation, to find out whether one can correlate blood pressure change with the times when the strokes occur during the day.

Dr Fukuda: We have lower values at night. In the morning the blood pressure becomes a little higher and around mid-day it tends to decrease and in the afternoon rises again. I think this is the general pattern. Concerning the onset of stroke we have studied several hundred cases. The result of this investigation was that a peak appeared at about 7.30 in the morning, then it tended to decline a little at mid-day, and tended to increase again in the afternoon. How should we then interpret the concentration of attacks in the morning? People get out of a warm bed suddenly to cold air. The body wakes up from sleep and has to switch to active life and we can say that there are some internal changes within the body resulting from this shift. Concerning the relatively high peak in the afternoon, this may be due to exertion and fatigue.

Dr Toole: With regard to the two peaks in stroke which you mentioned, we have been under the impression that cerebral infarction occurs more in the morning, not because the body is beginning to move and blood pressure is rising but because during the night in sleep blood pressure falls and the
person develops his infarction, but it is only when he wakes in the morning
that he realizes he is paralyzed. With regard to the peak in the afternoon,
we have been led to believe that this is the time of cerebral haemorrhage.
Have you any information on this and would you disagree with this point of
view?

Dr Fukuda: We have no data to explain this mechanism and we would like to
continue our analysis further.

Dr Okada: On this same point I would like to add the following. Six
years ago, in Nagoya City, we sent questionnaires to physicians of
internal medicine and collected the data on the circumstances when stroke
occurred, and we gathered detailed data covering a hundred cases. We
found out that cerebral haemorrhage was seen more during the day and that
cerebral infarction was seen mostly during the night, in sleep, or when
the person was talking with the family, relaxing, and doing nothing. On
the other hand, cerebral haemorrhage would occur during actions, as when
people are walking, working, or getting up.

Dr Fukuda: Dr Okada made a point, which I think is a very good one.
Cerebral haemorrhage is often seen when the person is in action. As Dr
Kobayashi reported yesterday, there were more strokes among subjects with
strenuous physical labour.

Dr Paul: It is reassuring to know from you that the single blood pressure
measurement is obviously an important one and that those who say that a
single casual blood pressure is meaningless are really not informed about
the studies that have already been done.
USE OF EYEGROUND EXAMINATION
IN POPULATIONS

by

Hirotomo Arai

Much work, mostly carried out on hospital patients, has been published on retinal changes in diseases, such as hypertension, arteriosclerosis, or diabetes, but information on retinal changes among the general population is scanty (1,2).

The purpose of this study is to present the prevalence rate of hypertensive and arteriosclerotic retinal changes among the general adult Japanese population, and to correlate the findings with the incidence or mortality of cerebrovascular or hypertensive diseases in the same population.

The work presented here was started in 1957. During the first few years, the equipment for field surveys and a standardized diagnostic procedure were worked out (2,4,5).

In 1960, a committee for the epidemiological study of cerebrovascular diseases was organized with a research grant from the Ministry of Education. In 1961 and 1962, the Ministry of Health and Welfare organized a survey on the prevalence of cerebrovascular diseases on a 1% random sample of the population in the whole country. The classification of retinal findings proposed by the committee was adopted for this survey (6,7). In 1963, a new mirror-type fundus camera, adapted for field survey, was ready and began to be widely used for mass examination (8). From 1966 the follow-up study of cerebrovascular disease (CVA) in relation to retinal changes has continued under two study groups sponsored by the Committee on "Hypertensive Fundus" with a research grant from the Ministry of Education and by the Japanese Association for Cerebro- and Cardio-vascular Disease Control.

MATERIAL AND METHODS

About 9700 apparently healthy Japanese people have been examined by the author's team once every year for blood pressure, ECG, urine, and fundus examination by the use of fundus photographs (Table 1). Fundus photography for each person consisted of three or four colour pictures of the right eye, and in some places, ophthalmoscopic examination of both eyes was performed in addition to fundus photography. Retinal findings of subjects were classified according to the modified method of Scheie's classification which was proposed by the Japanese Association for Cerebro- and Cardio-vascular Disease Control (Table 2). Two classifications of the fundus changes, as modified from Scheie's and Keith-Wagener's classifications, are presented in an annex at the end of this paper (see pages 196-197).
Table 1. Number of subjects in the study (1971)

<table>
<thead>
<tr>
<th>Examination</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Casual blood pressure</td>
<td>17 224</td>
</tr>
<tr>
<td>ECG</td>
<td>9 762</td>
</tr>
<tr>
<td>Fundus photography</td>
<td>9 636</td>
</tr>
<tr>
<td>Urinalysis</td>
<td>11 119</td>
</tr>
<tr>
<td>Serum lipid analysis</td>
<td>2 038</td>
</tr>
<tr>
<td>Blood sugar estimation</td>
<td>2 048</td>
</tr>
</tbody>
</table>

Table 2. Classification of retinal findings

<table>
<thead>
<tr>
<th>Items</th>
<th>Grading</th>
</tr>
</thead>
<tbody>
<tr>
<td>Narrowing of arterioles</td>
<td>- + ++</td>
</tr>
<tr>
<td>Irregularity in calibre</td>
<td>- + ++</td>
</tr>
<tr>
<td>Haemorrhages</td>
<td>- +</td>
</tr>
<tr>
<td>Exudates except C-W-P and star figure</td>
<td>- +</td>
</tr>
<tr>
<td>Hard shiny exudates</td>
<td>- +</td>
</tr>
<tr>
<td>Cotton wool patches</td>
<td>- +</td>
</tr>
<tr>
<td>Oedema of retina</td>
<td>- +</td>
</tr>
<tr>
<td>Papilloedems</td>
<td>- +</td>
</tr>
<tr>
<td>Increase in arteriolar reflex</td>
<td>- + copper silver wire</td>
</tr>
<tr>
<td>Arteriovenous crossings</td>
<td></td>
</tr>
<tr>
<td>(1) Tapering</td>
<td>- + ++</td>
</tr>
<tr>
<td>(2) Deflection</td>
<td>- + ++</td>
</tr>
<tr>
<td>(3) Concealment</td>
<td>- + ++</td>
</tr>
</tbody>
</table>

RESULTS

I. Sensitivity of fundus photography in mass examinations

The feasibility of using fundus photography in mass examinations was assessed by the author's team, by the following steps:

(1) To evaluate the sensitivity and accuracy of mass examination with a fundus camera, the subjects of several populations were examined both by using an ophthalmoscope on both eyes, and by retinal photographs of the right eye which consisted of three pictures representing (i) the area of the optic disc (P); (ii) the area of the upper temporal arterioles (To); and (iii) the area of the lower temporal arterioles and the macula (Tu). The sensitivity of fundus photography was expressed in relation to the fundus changes (Scheie's classification, above grade 2) seen during ophthalmoscopic examination.
The result of this evaluation is as follows:

(a) the sensitivity of enlarged monochrome prints as compared to the ophthalmoscopic examination of both eyes was as follows (8):

- 77.7% with P, To and Tu
- 77.7% with To and Tu
- 72.2% with P and To
- 61.1% with P and Tu
- 38.8% with P
- 68.5% with To
- 46% with Tu

(b) the screening with three colour pictures was as follows (9):

- 80.3% with P, To and Tu
- False negative rate: 19.7%
- False positive rate: 4.7%

(2) The simplicity and convenience of the procedures are of crucial importance for use in mass examination. Table 3 shows the success rate of retinal photography in mass examinations; 95 to 99% of all the photographs were found to be adequate for the diagnosis of the retinal changes. The maximum number of examinees photographed per day was about 120 persons with exposure of three colour pictures per person.

<table>
<thead>
<tr>
<th>Photographic area</th>
<th>Excellent</th>
<th>Good</th>
<th>Fair</th>
<th>Poor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Papilla</td>
<td>13.8%</td>
<td>65.0%</td>
<td>16.2%</td>
<td>4.8%</td>
</tr>
<tr>
<td>Upper temporal</td>
<td>26.0%</td>
<td>65.0%</td>
<td>7.3%</td>
<td>1.6%</td>
</tr>
<tr>
<td>Lower temporal</td>
<td>18.0%</td>
<td>70.4%</td>
<td>10.6%</td>
<td>0.8%</td>
</tr>
</tbody>
</table>

II. Prevalence of retinal changes

(1) Retinal examination using a fundus camera was carried out on 2249 subjects above 30 years of age in three communities (Kamomura, Nishiizu, and Matuzaki), located on the west coast of the Izu peninsula in Shizuoka prefecture, in the middle of the main island of Japan (10). The crude death rate and the death rate from vascular lesions affecting the central nervous system for these districts were higher than those for the whole Japanese population. In 1964, the crude death rate was 9.1 (6.1 for the whole Japanese population) per 1000 and the death rate from CVA was 266.3 (171.7 for the whole Japanese population) per 100,000. The majority of subjects are engaged in agriculture and in forestry or fishing. In the Shizuoka survey, retinal examination was carried out not only on the hypertensives but also on the normotensives, and the interpretation of the retinal changes was made by the same ophthalmologist (the author).
Retinal changes (above Scheie's grade 2) were frequent in the adult Japanese population, but severe retinal changes (retinopathy of malignant hypertension) were rare (Table 4). The focal constriction of retinal arterioles, retinal haemorrhages, and arteriovenous crossing phenomena increased in severity and frequency with age up to the sixties. On the other hand, generalized narrowing of the arterioles and widening of the arteriolar light reflex did not show a significant change with age. It is worth noting that the frequency of focal constriction was less in persons over 70 years compared with that in persons in their sixties. The frequency of abnormal findings was somewhat higher in the males than in the females.

The hypertensive group revealed a significantly higher frequency of focal constriction, arteriovenous crossing phenomena, and widening of the arteriolar light reflex compared with the normotensive group (10).

(2) In the Shizuoka survey, retinal vessel calibre was measured on the fundus photographs of 394 subjects of both sexes aged 30 to 69 years (11). The mean and variance of the true dimension of the calibre of individual arterioles at 0.5 P.D. away from the disc margin were calculated by a simplified formula which determined the magnification of the retinal photograph using the value of keratometry and refractive error, as proposed by Abe (12). The means and standard deviations of the true dimension of the arterioles in each decade of age groups from the third to the sixth were respectively 65.7 (± 6.7) μm, 61.7 (± 6.5) μm, 62.3 (± 7.2) μm, and 59.3 (± 6.5) μm in the males, and 63.1 (± 7.3) μm, 61.4 (± 7.9) μm, 61.3 (± 6.5) μm, and 62.9 (± 8.5) μm in the females.

| Table 4. Prevalence rate of retinal changes (Mass survey of CVD among adult Japanese populations by Kamomura, Nishiizu, and Matuzaki) |
|---|---|---|---|---|---|
| Items | Age (years) |
| | 30-39 | 40-49 | 50-59 | 60-69 | 70+ |
| Male (874 subjects) | | | | | |
| Narrowing of arterioles ++ | 0.4% | 0.5% | 1.0% | 0.5% | 1.2% |
| Irregularity in calibre ++ | 1.2% | 5.2% | 11.1% | 24.5% | 18.2% |
| Haemorrhages | 0.0% | 1.0% | 2.5% | 6.4% | 10.9% |
| Copper wire and silver wire art. | 0.0% | 1.0% | 3.5% | 2.9% | 1.2% |
| Arteriovenous crossings ++ | 0.8% | 3.1% | 11.1% | 16.9% | 15.8% |
| Total of examinees | 234 | 190 | 197 | 171 | 82 |
| Female (1375 subjects) | | | | | |
| Narrowing of arterioles ++ | 0.0% | 0.2% | 0.3% | 0.8% | 1.0% |
| Irregularity in calibre ++ | 0.0% | 3.0% | 9.2% | 20.2% | 23.1% |
| Haemorrhages | 0.7% | 0.8% | 4.7% | 8.0% | 9.4% |
| Copper wire and silver wire art. | 0.0% | 1.1% | 1.8% | 3.7% | 1.0% |
| Arteriovenous crossings ++ | 0.4% | 2.2% | 9.5% | 14.7% | 14.7% |
| Total of examinees | 412 | 360 | 271 | 237 | 95 |
A noteworthy finding on the sum of individual arteriole calibres is that the means of the calibre became significantly reduced with age in both sexes. In the males, it was 480.6 (± 75.3) μm in the thirties, 454.5 (± 71.4) μm in the forties, 432.4 (± 70.0) μm in the fifties, and 420.5 (± 81.1) μm in the sixties; the means for the females were slightly less than those for the males; they were 455.3 (± 71.0) μm in the thirties, 453.1 (± 83.1) μm in the forties, 425.0 (± 67.7) μm in the fifties, and 379.2 (± 85.3) μm in the sixties.

III. Follow-up of the changes in retinal vessel calibre as measured on fundus photographs

The changes in retinal vessel calibre as measured on the fundus photographs were followed up for 3-4 years on the hypertensives of ages 30 to 59 years in several places in Tokyo and Yanagata prefecture. Measurements of the diameter of retinal arterioles were performed on four major vessels, each selected from the four quadrants of the fundus of the right eye (13). Table 5 shows the changes in diameter of the central retinal artery at 0.5 P.D. away from the disc margin during the observation period. Although there were no significant differences in the mean and variance for all the subjects, a different pattern was seen in the changes in the calibre of the arterioles related to the presence of Scheie's sclerotic changes.

During a 3-4 years follow-up, the sum of the calibres of four major arterioles was reduced in 77.7% of the subjects above grade 2 of Scheie's sclerotic changes and in 45.4% of those with grade 0 and 1. This difference is statistically highly significant and the same tendency was seen in each of the four major arterioles in the same individuals.

Table 5. Changes in the diameter of retinal arterioles during 3-4 years of follow-up

<table>
<thead>
<tr>
<th>Grade of Scheie's sclerotic changes</th>
<th>Subjects with reduction in calibre (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sum of 4 major arterioles</td>
</tr>
<tr>
<td>Above grade 2</td>
<td>77.7</td>
</tr>
<tr>
<td>Grade 0 and 1</td>
<td>45.4</td>
</tr>
</tbody>
</table>

Note: Above grade 2: Arteriovenous crossing ++
Copper wire and silver wire art.

No. examined:
- Sum of 4 major art., 62
- Upper temporal art., 75
- Lower temporal art., 73
IV. Retinal changes in relation to the prognosis of cerebro- and cardiovascular diseases

In the Shizuoka survey (the prevalence data described in section II), a prospective study on CVA and coronary heart disease (CHD) was performed on 1421 subjects above 40 years of age from 1964 to 1969(14).

During the observation period, CVA and CHD occurred in 72 cases. Of these, retinal examination had previously been performed in 47 cases: 33 with CVD and 14 with CHD. The distribution of retinal changes according to the Keith-Wagener classification are shown in Table 6. There were moderate or severe retinal changes (Scheie's H and/or S above grade 2) in 17 out of the 33 cases (51.6%) with CVD and in 4 out of the 14 cases (28.6%) with CHD. The prevalence rates of moderate and severe retinal changes in cases with CVA were more frequent than in those with CHD. Grade 2 of Scheie's hypertensive changes was found in 8 (24.2%) and grade 3 in 6 (18.1%) out of the 33 cases with CVA. Grade 2 of Scheie's sclerotic changes was found in 6 (18.1%) and grade 3 in 3 (9.0%) out of these same 33 subjects. Severe retinal changes, above grade 4 of Scheie, were not found in this population. The prevalence of focal constriction of arterioles, corresponding to Scheie's grade 2 and over ("++") was 39.3% in the cases with CVA, which was the most frequent of the retinal findings in the subjects with hypertension and sclerosis. Tables 7-9 show the incidence rate and relative risk of CVA and CHD based on each of the individual findings.

### Table 6. Distribution of retinal changes (Follow-up period, 1964-1969)

<table>
<thead>
<tr>
<th>Keith-Wagener</th>
<th>No. observed</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>662 (54.9%)</td>
</tr>
<tr>
<td>I</td>
<td>417 (34.6%)</td>
</tr>
<tr>
<td>IIa</td>
<td>89 (7.3%)</td>
</tr>
<tr>
<td>IIb</td>
<td>34 (2.8%)</td>
</tr>
<tr>
<td>III</td>
<td>3 (0.2%)</td>
</tr>
<tr>
<td>IV</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>1205 (100.0%)</strong></td>
</tr>
</tbody>
</table>

The presence of moderate or severe retinal changes was closely related to the incidence of CVA and CHD. The order by which the incidence rate of CVA is correlated to individual findings was: generalized narrowing, focal constriction, retinal haemorrhage, widening of arteriolar reflex, and arteriovenous crossing phenomena. It is worth noting that with the presence of even a slight generalized narrowing the incidence

a Relative risk = the incidence rate of cerebro- and cardio-vascular accidents among persons with retinal changes divided by the incidence rate among persons without retinal changes.

189
increased almost the same as with the severe grade of other retinal changes. The criteria of generalized narrowing we used is assumed to be more strict in the evaluation of severity than those of the other retinal findings.

The relative risk of CVA in the presence of moderate or severe retinal changes was as follows: 7.3 in generalized narrowing (above grade "+"), 5.5 in focal constriction (++), 5.0 in retinal haemorrhage, 5.9 in widening of arteriolar reflex (copper wire and/or silver wire), 3.8 in arteriovenous crossing phenomena (++ and +++), 4.4 in grade 2 of Scheie's sclerotic changes, 9.0 in grade 3 of Scheie's sclerotic changes, 4.0 in grade IIa of Keith-Wagener's classification (Keio University modification), and 10.5 in grade IIb of Keith-Wagener's classification (Tables 7-9).

The presence of generalized narrowing, focal constriction, and retinal haemorrhage, and widening of the arteriolar reflex were most useful in estimating the risk of patients for CVA.

Table 7. Incidence rate and relative risk of cerebral stroke based on Scheie's hypertensive changes

<table>
<thead>
<tr>
<th>Changes</th>
<th>Incidence rate (%)</th>
<th>Relative risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Narrowing of arterioles</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-</td>
<td>2.5</td>
<td>1.0</td>
</tr>
<tr>
<td>+ &amp; ++</td>
<td>18.2</td>
<td>7.3</td>
</tr>
<tr>
<td>Irregularity in calibre</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-</td>
<td>1.9</td>
<td>1.0</td>
</tr>
<tr>
<td>+</td>
<td>1.4</td>
<td>0.7</td>
</tr>
<tr>
<td>++</td>
<td>10.5</td>
<td>5.5</td>
</tr>
<tr>
<td>Haemorrhage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-</td>
<td>2.4</td>
<td>1.0</td>
</tr>
<tr>
<td>+</td>
<td>11.9</td>
<td>5.0</td>
</tr>
</tbody>
</table>

Table 8. Incidence rate and relative risk of cerebral stroke based on Scheie's sclerotic changes

<table>
<thead>
<tr>
<th>Changes</th>
<th>Incidence rate (%)</th>
<th>Relative risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase in arteriolar reflex</td>
<td>2.2</td>
<td>1.0</td>
</tr>
<tr>
<td>+</td>
<td>6.5</td>
<td>3.0</td>
</tr>
<tr>
<td>copper wire &amp; silver wire</td>
<td>12.9</td>
<td>5.9</td>
</tr>
<tr>
<td>Arteriovenous crossing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-</td>
<td>2.1</td>
<td>1.0</td>
</tr>
<tr>
<td>+</td>
<td>2.7</td>
<td>1.3</td>
</tr>
<tr>
<td>++</td>
<td>7.9</td>
<td>3.8</td>
</tr>
</tbody>
</table>
Table 9. Incidence rate and relative risk of cerebral stroke based on the Keith-Wagener classification (Keio-University modification)

<table>
<thead>
<tr>
<th>Group</th>
<th>Incidence rate (%)</th>
<th>Relative risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.4</td>
<td>1.0</td>
</tr>
<tr>
<td>I</td>
<td>3.1</td>
<td>2.2</td>
</tr>
<tr>
<td>IIa</td>
<td>5.6</td>
<td>4.0</td>
</tr>
<tr>
<td>IIb</td>
<td>14.7</td>
<td>10.5</td>
</tr>
<tr>
<td>III</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

DISCUSSION

According to the adult health survey by the Ministry of Health and Welfare in 1961, 39.2% of Japanese adults aged over 40 years had systolic blood pressures over 150 mmHg. Although at that time, a considerable amount of clinical research had appeared on the fundus changes of hypertension, little was known about their course and prognosis among the population(15-18).

In the 1950s, the majority of previous reports on the population study had been concerned with blood pressure or ECG. Nakajima(19) first reported in 1955 the prevalence of retinal changes in individuals working in a certain mining company located in the north-east of Japan, and detailed epidemiological and preventive studies have been carried out successfully since 1957 by the author's team.

In population studies, the fundus camera should be used in addition to examining the blood pressure, ECG, and urinalysis for the following reasons:

(1) Two populations with equal prevalence of high blood pressure sometimes differ in the prevalence of abnormal retinal findings. Thus, both the prevalence of retinal changes and the incidence of cerebral stroke were apparently lower in Shizuoka than in Akita (in the northern part of the main island of Japan) and Gunma (in the middle part of the main island of Japan); however, the prevalence of high blood pressure was the same in all three areas(20).

(2) While the severity of retinal changes is not always correlated to blood pressure level and ECG findings, the grade of retinal changes is closely related to the risk of future CVA. In the prospective study of CVA among the residents of Akita and Osaka by Komachi(21) the incidence rate of CVA in the group without hypertension, abnormal ECG findings, and abnormal retinal changes was extraordinarily low (0.7 per 1000 persons per year). On the other hand, the incidence rate was remarkably high in the group with all of these three factors (25.22 per 1000 persons per year); the latter was 34.0 times higher than the former (Table 10).
<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Blood pressure</th>
<th>ECG</th>
<th>Fundus photo</th>
<th>Subjects at risk (No.)</th>
<th>CVA observed (No.)</th>
<th>Incidence rate (per 100 persons per year)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>8474</td>
<td>25</td>
<td>0.74</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>N</td>
<td>HT</td>
<td>604</td>
<td>9</td>
<td>3.73</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>N</td>
<td>HT</td>
<td>115</td>
<td>1</td>
<td>2.17</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>N</td>
<td>IS</td>
<td>1007</td>
<td>18</td>
<td>4.47</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>N</td>
<td>HT</td>
<td>172</td>
<td>9</td>
<td>13.08</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>N</td>
<td>IS</td>
<td>135</td>
<td>11</td>
<td>20.37</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>N</td>
<td>HT</td>
<td>652</td>
<td>34</td>
<td>13.04</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>N</td>
<td>HT</td>
<td>228</td>
<td>23</td>
<td>25.22</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>N</td>
<td>HT</td>
<td>11387</td>
<td>130</td>
<td>2.85</td>
</tr>
</tbody>
</table>

**Notes:**

- Blood pressure: N = <159/<94 mmHg, H = 160 mmHg or over and/or 95 mmHg or over.
- ECG:
  - HT = ST depression and/or T wave inversion accompanied with LVH
  - IS = T wave inversion and/or ST depression of 0.05 mV or over (horizontal type only).
  - 3. Angina pectoris.
- Fundus photo:
  - HT = Scheie's classification H and/or S, above grade 2.
  - N = Scheie's classification H and S, grade 0 or 1.
- (HT) = ECG and/or fundus.
It is worth noting that the incidence rate of CVA in the group associated with hypertension and abnormal retinal changes but without an abnormal ECG was markedly high (13.04 per 1000 persons per year); this rate was 2.9 times higher than the rate in the group with hypertension alone (4.47 per 1000 persons per year).

(3) In following the epidemiology of CVA, fundus examination is of great value for the differential diagnosis of the type of stroke\(^{(14,20)}\).

Many problems in the survey methods remain to be solved. The previous WHO reports relating to cardiovascular diseases often indicated the difficulty with techniques and the poor reproducibility in the assessment of retinal changes\(^{(21,22)}\).

There is a need for a cost/benefit analysis of multiphasic mass examinations including the use of fundus photography. There is also a need to study systems designed to incorporate fundus examination in the line of multiphasic examination\(^{(23)}\). Instead of a hand ophthalmoscope, we adopted a mirror-system fundus camera designed specially for a mass survey.

The training of technicians in fundus photography for mass surveys is not difficult and we have some experience in training many such technicians. In 1971, two highly trained technicians of the author's team performed fundus photography on 9636 persons from several population groups. It is clear from this experience that the use of the fundus camera is feasible for a mass survey. Concerning the poor reproducibility of assessments, concerted efforts have been made by Japanese research workers to establish a standard of interpretation and classification of the retinal findings, e.g., the classification of retinal findings and criteria for the adult health survey directed by the Ministry of Health and Welfare in 1961 (Table 11 shows the observer variation of retinal findings in using this classification); the criteria for classification by using fundus colour photographs proposed in 1966 by the Tokyo Research Council for the Control of Cerebro-cardiovascular Diseases (the Council specially trained the technicians to interpret fundus photographs and obtained a high level of agreement in the processing of photographs); the classification and criteria of the Japanese Association for Cerebro- and Cardio-vascular Diseases Control (1967); and the colour atlas and criteria of fundus changes in hypertension by the Committee on "Hypertensive Fundus" in 1969 \(^{(23)}\). The more recent assessments of the results of fundus photography in mass examinations are expected to have a higher degree of agreement.

CONCLUSION

About 9700 healthy Japanese people have been examined by the author's team once every year for blood pressure, ECG, urine, and fundus examination by the use of fundus photographs and ophthalmoscopes. The records on 2249 of these individuals, living in the Izu Peninsula in Shizuoka prefecture and aged over 30 years, were analysed in detail for the prevalence of retinal changes and the correlation of these findings with prognosis.

The results were as follows:

(1) The 'sensitivity' of fundus photographs of a single eye was nearly comparable to that of an ophthalmoscopic examination of both eyes.
Table 11. Observer variation in grading the retinal changes

**Fundus photography** (Colour slides; 6 interpreters for 20 examinees)

<table>
<thead>
<tr>
<th>Scheie</th>
<th>Agreement</th>
<th>Disagreement (over two grades)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Perfect</td>
<td>Perfect + Fair*</td>
</tr>
<tr>
<td></td>
<td>15%</td>
<td>45%</td>
</tr>
<tr>
<td>H (0 - 3)</td>
<td>15%</td>
<td></td>
</tr>
<tr>
<td>S (0 - 3)</td>
<td>10%</td>
<td>75%</td>
</tr>
</tbody>
</table>

*Fair: difference in one grade

**Ophthalmoscopic examination of both eyes** (4 interpreters for 18 examinees)

<table>
<thead>
<tr>
<th>Scheie</th>
<th>Agreement</th>
<th>Disagreement</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>39%</td>
</tr>
<tr>
<td>H (0 - 3)</td>
<td>22%</td>
<td>61%</td>
</tr>
<tr>
<td>S (0 - 3)</td>
<td>28%</td>
<td>78%</td>
</tr>
</tbody>
</table>

Scheie's classification; modified for a mass survey
(Report of the Committee on Epidemiological Study on CVD)
Chairman: R. Yanagisawa 1960-1961

(2) The frequency of focal constriction of retinal arterioles and the arteriovenous crossing phenomena increased with age up to the sixties and decreased thereafter. Generalized narrowing of the arterioles and widening of the arteriolar light reflex did not increase very much with age. The arteriole calibre (calculated by simplified formulae which determined the magnification of the retinal photograph) reduced with age in both sexes.

(3) As observed in 3-4 years of follow-up by photomicroscopy on retinal vessels, the calibre of the retinal arterioles of the subjects with grade 2 and over of Scheie's sclerotic changes reduced more significantly than the arteriole calibre of the subjects with grade 0 and 1 changes.

(4) The presence of moderate or severe retinal changes (Scheie's H and/or S, above grade 2, or Keith-Wagener's group II and over) was correlated to the increased incidence of cerebro- and cardio-vascular accidents. Generalized narrowing, focal constriction, retinal haemorrhage, and widening of arteriolar reflex are suggested to be the most useful signs in estimating the risk for cerebral stroke.
REFERENCES

### CLASSIFICATION OF FUNDOUS CHANGES

#### A. Scheie's classification

<table>
<thead>
<tr>
<th>Grade</th>
<th>Hypertensive changes</th>
<th>Sclerotic changes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Grade 0</td>
<td></td>
<td>Grade 0</td>
</tr>
<tr>
<td>Grade 1</td>
<td>Arteriolar narrowing (+) and/or calibre-irregularity (+)</td>
<td>Arteriovenous crossing signs (+) and/or arteriolar reflex (+)</td>
</tr>
<tr>
<td>Grade 2</td>
<td>Arteriolar narrowing (++) and/or calibre-irregularity (+++</td>
<td>Arteriolar crossing (++) or copper-wired artery</td>
</tr>
<tr>
<td>Grade 3</td>
<td>Spotty or patchy haemorrhage except thrombosis of the retinal central vein</td>
<td>Arteriolar crossing and copper-wired artery, white line crossing signs (+++) or silver-wired (white lined)</td>
</tr>
<tr>
<td>Grade 4</td>
<td>Grade 3 + cotton-wool patches or retinal oedema</td>
<td>Arteriovenous crossing sign (++) and silver-wired or white lined artery</td>
</tr>
<tr>
<td>others</td>
<td>Grade 3 + retinopathy + papilloedema</td>
<td>N (not classifiable)</td>
</tr>
<tr>
<td>N (not classifiable)</td>
<td>H 0 or 1 grade + artery with haemorrhage, hard patch, soft patch on oedema</td>
<td></td>
</tr>
</tbody>
</table>

---

*As modified by the Tokyo Cerebro-Cardiovascular Research Committee (1966).*

* Cited by Irinoda, K. (26).*
B. **Keith-Wagener's classification**

<table>
<thead>
<tr>
<th>Grouping by KEITH-WAGENER's classification</th>
<th>Fundus change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal fundus</td>
<td>(S.H.) none (rare) (K-W 0 group)</td>
</tr>
<tr>
<td>Fundus hypertonicus</td>
<td>Slight narrowing and sclerosis of the retinal arteriole (SCHIEE's modification grade I)</td>
</tr>
<tr>
<td>Group II</td>
<td>Arteriolar sclerosis becomes marked (SCHIEE's grade II), and narrowing is more marked than Group I</td>
</tr>
<tr>
<td></td>
<td>Arteriosclerotic retinopathy or obstruction of the retinal central vein is added to the above-mentioned</td>
</tr>
<tr>
<td>Retinopathia hypertonica</td>
<td>An important criterion is the presence of angiospastic retinitis, together with definite sclerotic changes in the arterioles, namely retinal oedema, white spot, haemorrhage</td>
</tr>
<tr>
<td>Group III</td>
<td>The important retinal alterations are marked spastic and organic narrowing of the arterioles, with diffuse retinitis and oedema of the discs</td>
</tr>
<tr>
<td>Group IV</td>
<td></td>
</tr>
</tbody>
</table>

\[b\] As modified in Keio University
DISCUSSION

Dr Werko: Do you have any studies on observer errors of the interpretation?

Dr Arai: Concerning observer variation, please refer to Table 11. The data were taken in 1960 to 1962. We used the 4 classes in the Scheie classification. Regarding a one-grade variation in the Scheie classification, as agreed, two observers were in accord in about 80% of cases. Concerning the cost, I would say that a camera for mass examination would cost about US$ 2600 and three colour pictures would cost about 70 cents. In Japan, these are very popular now.

Dr Doyle: Can you tell us whether this camera can be used with fluorescein angiography?

Dr Arai: This camera can be used with fluorescein angiography as well. There are several kinds of camera all of which can be used with fluorescein angiography. Some of them are more suitable for mass examinations and some for clinical use. You have to choose according to your purpose.

Dr Freis: Do you have to use drugs to dilate the pupil, and if you do, does this hold up the turnover time for patients on mass screening?

Dr Arai: That is a very important question. Dilation of the pupil is necessary. We use a mixture of tropicamide and phenylepherine hydrochloride. In the mass examination we dilate the pupil of one eye and this can be done very easily. This could induce a raised pressure from glaucoma in one out of 20 000 or 30 000 subjects. However, if you question the subjects before instilling the medicine you can avoid this danger. There have been no problems so far in our experience.

Dr Reader: I was interested in the risk ratios. Is the population that you are reporting untreated? Do you have any information from this kind of study on improvement in the retinal picture with hypotensive therapy?

Dr Arai: The hypertensives who were found in mass examinations were treated afterwards. Improvement in the retinal pictures is sometimes seen but I think you do not find as much improvement as you might expect.

Dr Strasser: Clinicians, of course, are convinced that fundus examinations are extremely valuable. Epidemiologists, on the other hand, are convinced that it is a poor method, sometimes even a waste of time. Myself being both a clinician and an epidemiologist, I have a kind of ambivalent attitude towards fundus examinations in mass screening. I have three questions: Are you satisfied with 15% "perfect" agreement? Are you satisfied with Scheie's classification? Do you have any proposals for improving the international comparability of fundus examinations in cardiovascular epidemiological studies?

---

*R Mydriaticum "Roche"
Mydrin P.
Dr Arai: First concerning the observer variation I think an improvement has to be made. I am fairly optimistic on this point; the data I have shown are the old data and improvements were made afterwards. Some tests were conducted, but in the future we have to conduct tests based on new classifications. Secondly, concerning Scheie's classification, I prefer this to the Keith-Wagener because the observer variation was less; it is widely used in Japan. Fundus examination is used more and more and it is desirable to establish international comparability in the interpretation of these pictures. Considerable experience on this has been accumulated in Japan. I said yesterday that auxiliaries may be more objective in interpreting the data than the ophthalmologists; you can be optimistic in this respect too.

Dr Paul: I would just mention to Dr Strasser that the average clinician is probably much worse than the auxiliaries in evaluating the photographs.

Dr Toole: It is very important to remember that the retina is the only place in the body where one can actually see blood vessels and that the blood vessels we see are arterioles and capillaries, not large arteries. Do you distinguish diabetic retinopathy from those two which you have described? Is it recommendable to do fundus examination only on people who on screening have high blood pressure rather than attempting to do fundus examination on everybody.

Dr Arai: In Japan at the present time, we do the fundus examinations on the hypertensives only. The first screening is made before the fundus camera is used, but there are arguments about whether we should limit ourselves to hypertensives. I started with the examination of all subjects.

Dr Akinkugbe: One of the major advantages of a conference like this is to improve international comparability. I indicated in my presentation the rarity of severe retinopathy in the Africans, and I am particularly interested in this study because we are looking for parameters of severity of hypertension in seeing what risk factors are precipitating cerebrovascular accidents. In my own setting, ECG findings were not reliable as risk factors, nor did we find fundus examination helpful, although we have been using largely ophthalmoscopy, which is now being supplemented by retinal photography. In fact, is there a correlation between the pattern of cerebral atherosclerosis and the severity of retinopathy? We do know that in the African populations with a rather low prevalence of retinopathy cerebral atherosclerosis is certainly not common, and it may well be that the height of blood pressure and also other risk factors in cerebrovascular accidents may be related to the actual distribution of cerebral atheroma.

Dr Arai: Whether the fundus examination or the fundus pictures can be used for predicting stroke also depends on the countries. Fundus findings are considered to be extremely important in Japan, and a difference may be found in this respect between Nigeria and Japan. An epidemiological comparison would be of great value. I think there are international differences but we do not have enough data, and so we have to further pursue and explore this field.

Dr Paul: It might be of some interest before the next topic, since this is an international meeting, to find out how many colleagues outside of Japan are using fundus examination as part of the screening procedure. Would those from outside of Japan who are using this as a technique in screening raise their right hand? I see no one. Thank you very much.
From the etiological viewpoint, hypertension by itself is not considered as a disease entity but rather as one of the cardiovascular manifestations in various diseases. It has not been quite decided whether a deviation of blood pressure from "normal" is caused by a mechanism(s) qualitatively different from that operating in "normal" blood pressure homeostasis. It is well accepted that there is no dividing line between normal and raised arterial blood pressure. A temporary elevation of blood pressure should sometimes be considered as a homeostatic function of the cardiovascular system, not requiring active treatment. Blood pressure can fluctuate considerably according to environmental changes affecting physical or psychological conditions. Diurnal or seasonal variation in blood pressure is also present. In this paper some of the problems in diagnosis of hypertension in community studies will be discussed.

What does diagnosis of hypertension mean?

The question is connected with the problem of how to select hypertensive subjects for registration. The criteria for hypertension are clearly stated in a WHO technical report published in 1962. It has been stated that casual blood pressure over 160 mmHg in systolic and/or 95 mmHg in diastolic blood pressure should be accepted as hypertension. Systolic blood pressure of 140 to 159 mmHg and/or diastolic blood pressure of 90 to 95 mmHg is defined as border-line hypertension. Our prospective population study in Hisayama showed that 40.5%, 22.1%, and 10.5% of the subjects with hypertension, border-line hypertension, and normal blood pressure at entry died within 10 years, respectively. Blood pressure was measured three times at entry and the value of the third reading was taken for registration. Cerebrovascular accident occurred about 13 times and heart disease about 6 times more frequently in subjects with hypertension than in those with normal blood pressure. The frequency of occurrence of both diseases was intermediate in the subjects with border-line hypertension. The 10-year survival rate by the blood pressure at entry was 89.5%, 77.9%, 61.7%, and 57.7% for the subjects with normal blood pressure, border-line, systolic, and diastolic hypertension, respectively. The outcome of 99.7% of all the subjects (1621 subjects, aged 40 years and over of both sexes) was known in this study. Considering the systolic or diastolic blood pressure at entry, the survival rate was particularly low in the subjects with a systolic blood pressure of 180 mmHg and over, or a diastolic blood pressure of 110 mmHg and over. Since the population survey has been repeated every two years, the fluctuation in the blood pressure in each subject was considered in relation to the prognosis. The
survival rate was significantly higher in those with normal blood pressure at all determinations than in those having an elevated blood pressure in at least one determination. Therefore, the study indicated that hypertension detected at any time can be an important risk factor in the development of cardiovascular disease and an indicator of prognosis. About one-fifth of the hypertensive subjects under study were treated satisfactorily.

Diagnosis of hypertension may refer to either etiological diagnosis of a disease that causes an increased blood pressure or diagnosis of the severity of hypertensive cardiovascular disease. Although the frequency of essential hypertension is exceedingly high compared with that of well-defined diseases causing hypertension, the diagnosis of essential hypertension is made by excluding all the known causes of hypertension. This is a difficult task to accomplish in community studies. Secondary hypertension not infrequently mimics essential hypertension. Clinical and laboratory examinations are required to establish the etiological diagnosis of hypertension. This is particularly true for the diagnosis of renal parenchymal disease, renal artery stenosis, and some of the endocrine disorders such as Conn's syndrome, phaeochromocytoma, etc. Screening procedures applicable to the community study have not been established. Past medical history, inquiry of symptoms pertinent to certain diseases, physical examination, urinalysis, funduscopic examination, ECG findings, blood chemistry such as serum electrolytes, BUN, etc. will help in the diagnosis of secondary hypertension. If secondary hypertension is suspected, further examinations are required to reach a definite diagnosis. They include the determination of plasma renin activity, aldosterone in blood or urine, urinary catecholamines, and X-ray (intravenous pyelography, arteriography, venography, etc.) or radioisotope examinations (renogram or scintigram), etc.

For the diagnosis of the severity of hypertensive cardiovascular disease, the clinical symptoms, the functional status of the brain, heart, and kidney, and other major complications of vascular disease, such as aortic aneurysm and peripheral vascular disease, should be checked. However, the causal relationship between any of the major cardiovascular diseases and hypertension has not always been clear. This is a basic problem to be settled for defining the severity of hypertensive cardiovascular disease. Our experience shows that stroke has a closer relation with hypertension than with heart disease. Most of the cases with cerebral haemorrhage occurred among subjects who had diastolic hypertension. The occurrence of cerebral infarction was significantly higher not only in the subjects with diastolic hypertension but also in those with systolic hypertension compared with that in normotensive subjects. No significant correlation was found between the occurrence of myocardial infarction and the level of blood pressure.

Post-mortem examinations showed that renal diseases were much more frequently found in hypertensive subjects but they were not severe enough to cause renal failure. The frequency of proteinuria was significantly higher in hypertensive subjects than in those with normal blood pressure at any decade of age, although it steadily increased with advancing age in both groups of subjects. It is also worth noting that proteinuria was most frequently found in subjects with diabetes mellitus. Subjective complaints such as headache, light-headedness, vertigo, and dizziness did not seem to have a significant correlation with the blood pressure level. Females had in general more frequent complaints than males.
The frequency of renal and adrenal diseases found in autopsy material in the community

In 374 autopsy cases obtained from the Hisayama population during the period from November 1961 to October 1971, the following diseases were found in the kidney or adrenal gland. (The autopsy rate was 85.2%; therefore, the figures may be considered to be rather representative of the diseases occurring in the whole population aged over 40 in this community.)

Arteriolar nephrosclerosis, 81 (21.6%); renal arteriosclerosis, 49 (13.1%); chronic pyelonephritis, 17 (4.5%); hydronephrosis, 13 (3.4%); renal infarct, 12 (3.2%); focal suppurative interstitial nephritis, 5 (1.3%); and diabetic nephropathy, 4 (1.0%). There were 3 cases each of renal artery stenosis, polycystic kidney, renal hypoplasia, and cholemic nephrosis; 2 cases each of adrenocortical adenoma and urinary tract anomalies; and one case each of myeloma kidney, periarteritis nodosa, and renal tuberculosis. The criteria for the diagnosis of arteriolar nephrosclerosis and renal arteriosclerosis are described elsewhere. The renal diseases were neither detected nor even suspected at the time of the survey, unless proteinuria was present. Even when proteinuria was present, examinations to define the type of renal disease were not performed except for some hospitalized cases.

Arteriolar nephrosclerosis was found in close association with diastolic hypertension. Renal arteriosclerosis was caused by the aging process and aggravated by hypertension. The former was frequently associated with both cerebral haemorrhage and cerebral infarction but the latter merely with cerebral infarction. Although cerebrovascular accidents occurred more frequently in subjects having nephrosclerosis, heart diseases such as myocardial infarction or coronary artery disease occurred rather independently of the presence of nephrosclerosis.

The trend was shown that a more progressive rise in blood pressure was observed in those with renal diseases than in those without them, but it was not diagnostic for detecting the presence of certain types of renal disease in the community. Approximately two-thirds of the cases with renal diseases not including nephrosclerosis showed an increase in blood pressure at least once during the follow-up study. In the remaining cases blood pressure stayed below the level of border-line hypertension at all determinations. No definite correlation could be established between renal artery stenosis or adrenocortical adenoma and hypertension because of the small number of cases.

REFERENCES


DISCUSSION

Dr Marquardsen: It struck me that Dr Omae found the serious prognostic significance of hypertension to be present also in the old. In my own follow-up study of stroke patients I found that in women over the age of 70 the height of the blood pressure did not seem to influence the long-term prognosis at all. Could Dr Omae give information about the different age groups and for the two sexes separately?

Dr Omae: We actually did not analyse the effect of sex, particularly in the old age group, because the number of cases was not so large. Cerebral haemorrhage used to be very high in males compared with females, but the difference decreased with advancing age, as Dr Hirota mentioned yesterday. The point that Dr Marquardsen mentioned is very important, because when we divide the cases by each decade of age the significance of hypertension decreases with advancing age. In the subjects aged over 80 there was no apparent difference in cerebral infarction between normotensive and hypertensive patients.

Dr Fukuda: We have examined the age-specific incidence rate of strokes in more than 100,000 workers of the Japanese National Railways. In the older age group there was only a small difference in stroke incidence between the hypertensives and those with lower blood pressure. Systolic and diastolic blood pressure levels were analysed separately and the incidence rate of stroke varied, depending upon the levels of the diastolic and systolic blood pressures. Therefore both diastolic and systolic blood pressure levels have to be taken into consideration in the prognosis of an individual. I found that in the various centres which Dr Reader described in his paper, diastolic pressure only is used. I think it is desirable to include the systolic blood pressure, too, so that you can have a comprehensive judgement of the relationship between the blood pressure and the incidence of stroke.

Dr Omae: I quite agree with Dr Fukuda's opinion. We should consider both systolic and diastolic for a given patient.

Dr Kagan: I would just like to mention that in our Ni-Hon-San study an elevated blood pressure level (either systolic or diastolic) was one of the strongest risk factors for coronary heart disease, including myocardial infarction.
DIAGNOSIS OF HYPERTENSION:  
RECENT ADVANCES  
AND POSSIBLE APPLICATIONS  

by  
Hideo Ueda

I should like to begin with a brief outline of basic diagnostic procedures and then discuss the value of aortography and measurement of plasma renin activity for the diagnosis of hypertension in public health.

Fundamental diagnostic measures

Very briefly, the basic diagnostic procedures that are practicable in an epidemiological study are as follows:

(a) Blood pressure measurement with sphygmomanometer by auscultation or semi-automatically. Measurement of the blood pressure in both arms or in the legs is sometimes necessary for the diagnosis of aortitis and aortic coarctation.

(b) The second important procedure is, of course, eyeground examination by ophthalmoscopy or eyeground (fundus) camera.

(c) The detection of left ventricular hypertrophy (LVH) can contribute to the diagnosis and the evaluation of severity and duration of hypertension. LVH should be confirmed by physical examination, chest X-ray, and ECG.

(d) Auscultation and the phonocardiogram can offer valuable information for the diagnosis of essential and secondary hypertension. Auscultation of the renal artery in the abdomen is a useful manoeuvre to ascertain renovascular hypertension. About 76% of the renovascular hypertension cases (16 out of 21 cases) presented a vascular stenotic murmur according to the research done at the University of Tokyo. In young female hypertensives, auscultation of the aorta and renal artery is necessary to pick up Takayasu arteritis and renovascular hypertension.

(e) Urinalysis and blood urea nitrogen (BUN) measurement help in determining nephrogenic hypertension and its severity.

(f) Measurement of cardiac output by the dye-dilution method, among others, is necessary to diagnose the early stages of hypertension and the β-adrenergic hyperkinetic state of Frohlich.

(g) Laboratory study of serum potassium, urinary vanillyl-mandelic acid (VMA), and plasma renin activity (PRA) is useful to diagnose hypertension of adrenal origin resistant to treatment. When phaeochromocytoma and aldosterone-secreting tumours are suspected, catecholamines and aldosterone in the blood should be examined.
Aortography and renoarteriography

X-ray aortography and renoarteriography are recommended to clarify the cause of hypertension in young patients and in patients who do not respond to routine therapy.

The prevalence of stenotic renal artery in patients who underwent X-ray aortography in the University of Tokyo is shown in Table 1.

Table 1. Frequency of stenosis of the renal artery in hospitalized patients

<table>
<thead>
<tr>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertensives</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stenosis of renal artery</td>
<td>219</td>
<td>152</td>
</tr>
<tr>
<td>(10%)</td>
<td>(19%)</td>
<td>(14%)</td>
</tr>
<tr>
<td>Non-hypertensives</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stenosis of renal artery</td>
<td>76</td>
<td>11</td>
</tr>
</tbody>
</table>

Table 1 shows that about 14% of established hypertensives revealed narrowing of the renal artery in X-ray aortography and about 75% of these patients had a significant degree of stenosis with high PRA in the renal vein, on the same side.

Table 2. Pathology of renovascular hypertension in 51 cases

<table>
<thead>
<tr>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortitis (Takayasu arteritis)</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>Atherosclerosis</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>Fibromuscular hypertension</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>Aneurysm of renal artery</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Compression of renal artery</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Others</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>22</td>
<td>29</td>
</tr>
</tbody>
</table>

Table 2 shows the etiology of renovascular hypertension and Table 3 the classification of in-patient hypertension in the University of Tokyo.

Table 3. Frequency of various causes of hypertension in hospitalized hypertensive patients

<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 618 hypertensives (14%)</td>
<td>417 hypertensives (14.5%)</td>
</tr>
<tr>
<td>Essential hypert.</td>
<td>71%</td>
</tr>
<tr>
<td>Chronic nephritis</td>
<td>14.0%</td>
</tr>
<tr>
<td>Pyelonephritis</td>
<td>1.3%</td>
</tr>
<tr>
<td>Diabetic nephropath.</td>
<td>2.8%</td>
</tr>
<tr>
<td>Renovascular hypert.</td>
<td>2.6%</td>
</tr>
<tr>
<td>Endocrine hypert.</td>
<td>1.6%</td>
</tr>
<tr>
<td>Others</td>
<td>3.3%</td>
</tr>
</tbody>
</table>

Table 2 shows the etiology of renovascular hypertension and Table 3 the classification of in-patient hypertension in the University of Tokyo.
Diagnosis of hypertension in an occupational group

The following are the results of detection and detailed diagnosis of hypertension in an occupational group of 3313 subjects in the younger age group of 20 to 40 years. Dr Oobu and others carried out a hypertension detection programme in young male employees of Japanese National Railways in Kushiro Hospital. They detected 577 hypertensives whose blood pressure was over 140/90 mmHg at the first screening; 448 hypertensives over 150/90 mmHg were checked at the second screening. The suspected hypertensives received further, more thorough examination during 1-7 days of hospitalization, which included chest X-ray, ECG, eyeground, blood potassium level, and PRA and VMA in the urine. After these examinations, the final diagnosis of essential and secondary hypertension was made, as can be seen in Table 4.

Table 4. Frequency of various causes of hypertension in hypertensive patients detected by screening

<table>
<thead>
<tr>
<th>Cause</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential hypertension</td>
<td>389 (86.9%)</td>
</tr>
<tr>
<td>Chronic glomerular nephritis</td>
<td>27 (6.1%)</td>
</tr>
<tr>
<td>Hydronephrosis</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Mobile kidney (RVH)</td>
<td>3 (0.6%)</td>
</tr>
<tr>
<td>Aldosterone-secreting tumour</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Phaeochromocytoma</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>β-adrenergic hyperkinetic state</td>
<td>4 (0.9%)</td>
</tr>
<tr>
<td>Others</td>
<td>22 (4.9%)</td>
</tr>
<tr>
<td>Total</td>
<td>448</td>
</tr>
</tbody>
</table>

Diagnosis of renin subgroups in essential hypertension (epidemiological and prognostic meaning)

Recently, Brunner & Laragh described how essential hypertension could be classified into three renin-level subgroups which have different physiological and epidemiological features. \(^1\) Low-renin hypertensive patients are relatively protected from heart attacks and strokes. These patients are usually older and exhibit lower blood urea than the other groups, which suggests a normal renal circulation.

The normal- and high-renin groups are prone to stroke and heart attacks. The occurrence of cardiovascular complications in the three subgroups are as follows: low renin, 0%; normal renin, 11%; high renin, 14% (in 59 patients in five years).

The high-renin group reveals high mean diastolic blood pressure, high BUN, and low plasma potassium. This suggests that it may prove appropriate to retain the term "essential hypertension" only for the normal-renin and normal-aldosterone group, in which no abnormalities are yet identifiable. Now, it appears necessary to measure plasma renin activity (PRA) biologically or by radioimmunoassay to control and treat hypertensives and prevent the cardiovascular complications.

Table 5. Renin subgroups of hypertensive patients: epidemiological and physiological characteristics

<table>
<thead>
<tr>
<th>Renin subgroup</th>
<th>Prevalence in essential hypertension</th>
<th>Mean age (years)</th>
<th>Diastolic blood pressure (mmHg)</th>
<th>Incidence of heart attack and stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>low</td>
<td>27%</td>
<td>46.5</td>
<td>104.9</td>
<td>0%</td>
</tr>
<tr>
<td>normal</td>
<td>57%</td>
<td>37.5</td>
<td>103.5</td>
<td>11%</td>
</tr>
<tr>
<td>high</td>
<td>16%</td>
<td>43.1</td>
<td>124.0</td>
<td>14%</td>
</tr>
</tbody>
</table>

Kaneko, and the group in the University of Tokyo presented similar results in the same year as Laragh published his paper on renin subgroups. They measured PRA in 118 hospitalized patients with essential hypertension, and examined the occurrence of cardiovascular complications during one to eight years (average 4.8 years). There were a total of 18 CVA: 3 cases of uraemia, 15 strokes, 3 heart attacks, and 7 deaths. In 32 patients with low PRA (average, 2.1 ng/ml) only one stroke (3.1%) occurred and none died.

In 69 patients with normal PRA (average, 8.7 ng/ml), 8 (11.6%) developed cardiovascular complications, including 6 strokes (8.7%), and 3 (4.4%) died: the average blood pressure, severity, and observation period were comparable in both groups.

In the high-renin group of 17 patients (PRA average, 42.7 ng/ml), 8 (47.1%) developed vascular complications, including 6 strokes (35.5%), and 4 (23.5%) died during the comparable period. The average blood pressure and severity were higher than the normal-renin and low-renin subgroups. Twenty-four patients with blood pressure and severity almost compatible with those of the high-renin group were selected from the normal-renin group. The incidence of complications and death was still higher in the high-renin group than in the selected normal-renin group.

The level of plasma renin seems to be an important factor influencing the prognosis and vascular complications of patients with essential hypertension.

Table 6. Incidence of stroke in renin subgroups of hypertensive patients

<table>
<thead>
<tr>
<th>PRA (µgAT/ml)</th>
<th>Low renin</th>
<th>Normal renin</th>
<th>High renin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (average years)</td>
<td>2.1</td>
<td>8.7</td>
<td>42.7</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>47.8</td>
<td>39.5</td>
<td>37.9</td>
</tr>
<tr>
<td>190/109</td>
<td>185/112</td>
<td>211/127</td>
<td></td>
</tr>
<tr>
<td>Severity score</td>
<td>6.3</td>
<td>6.1</td>
<td>9.9</td>
</tr>
<tr>
<td>1.8</td>
<td>4.8</td>
<td>4.4</td>
<td></td>
</tr>
<tr>
<td>Period of follow-up (years)</td>
<td>1.8</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Stroke</td>
<td>0</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Death</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The incidence of stroke in essential hypertension is closely related to the level of PRA and the severity score of hypertension, and is to a lesser degree related to the levels of blood pressure and BUN. Therefore, stroke could be predicted in the hypertensive patients from data on PRA and the hypertension score which is calculated by the grade of blood pressure, eyeground changes, and complications of heart, kidney, and brain.

The level of PRA contributes, as is well known, to a diagnosis of renovascular hypertension and primary aldosteronism. The measurement of PRA may be used to classify essential hypertension into three renin subgroups and to predict cardiovascular complications in the near future.

DISCUSSION

Dr Paul: Is it correct that in the low-renin group the follow-up period averaged 1.8 years and in the normal- and high-renin groups the follow-up period was, I think, 4.8 and 4.4 years? There was a significant difference in the follow-up periods.

Dr Ueda: The follow-up periods are as you have indicated.

Dr Richard: In what conditions did you measure plasma renin activity? Second, did you exclude in your groups people who were treated or not and particularly did you take into account the diuretic treatment, because people who take diuretics have usually high plasma renin levels?

Dr Ueda: The data on the last slide were obtained from resting in-patients whose sodium intake was usually between 5 and 10 g daily. From an epidemiological viewpoint, it is sometimes difficult to take rest for several hours. In future, we need to compare the data of ambulatory subjects who take from 10 to 15 g salt, like the average Japanese. We first take a casual blood sample after 4-5 hours' rest and then after a workload of 3 or 4 hours. We may compare the values of the plasma renin activity in these three stages. The plasma renin value may either increase by work loading or may remain in the normal range. After having obtained the normal ranges in three stages we are able to evaluate casual values. The measurement of renin activity may thus be available for the epidemiology of hypertension. However, we have many problems to solve.

Dr Doyle: This question of plasma renin and prognosis is a very complicated matter. I think most of us would agree that patients with high plasma renins who have malignant hypertension of severe renal disease do in fact have a worse prognosis than other patients; but if one excludes those particular patients, there seems to be little evidence that the ordinary patients with a high plasma renin without other complications would have a poor prognosis.

The second problem relates to the proposition that a low plasma renin protects individuals from either stroke or coronary artery disease. In our experience it is first of all extremely difficult to do more than define in an arbitrary way which patients have low plasma renins and which have normal levels. In other words, there seems to be a continuum between low renin and normal renin; there are not two discrete groups. We have done two studies: one involving a five-year follow-up of patients originally studied for another purpose. Taking an arbitrary distinction of low and normal renins, we were unable to find any difference at all in the incidence of either stroke or coronary artery disease. I think the other point that
needs to be made is that, as far as I know, there is no obvious sex difference between plasma renin levels and yet it is well known that for given levels of blood pressure the outlook is much worse in men than in women. I think your study is the only one that I am aware of, which supports the original concept of Laragh. I wonder, like Dr Paul, whether the short follow-up could have something to do with it. And I wonder whether you have excluded malignant hypertension from your high-renin group?

Dr Ueda: In the last slide, we diagnosed malignant hypertension by examination of the eyeground and evaluation of blood pressure level. The patients with over 70 mg/dl BUN and over 70 years of age were excluded from the high-renin group. When we classify the three groups we must consider many causes of high blood renin. For the second question regarding the low-renin subgroup, some subclinical hyperaldosteronism could be concealed in the low-renin group. For the third question, I do not have enough numbers to comment on the sex difference.

Dr Gross: I should like to know how often plasma renin levels were determined in your patients; was it only once or was it during the whole observation period? Because, during a prolonged period, the method of determination of plasma renin activity has probably been changed. My second point is: what was the renal function in these patients, and what was the intravascular volume in the patients with a low renin activity? This may be the group of patients who, or at least some of whom, have a suppressed renin response, and these hypertensive patients respond well to diuretic treatment. After they have eliminated a certain amount of fluid or normalized the intravascular volume, plasma renin returns to normal, and so does the renin response. Thus, I think various factors are involved, and I should like to say, or to repeat what I said already yesterday, namely, that a single determination of plasma renin activity can be misleading. Therefore I should like to warn again against trying to establish far-reaching conclusions on the basis of such a determination.

Dr Ueda: The data on the final slide were obtained from hospitalized patients. Plasma renin activity was measured 5-7 days after admission and we maintained the daily salt-intake constant (between 5-10 g). The plasma renin activity was measured by the same bioassay method. The patient was at first not given diuretics or hypotensive drugs. After the initial measurement of plasma renin activity, the effects of upright position, hydralazine, dioxane, and hypotension induced by sodium nitroprusside were examined. The changes of renin release induced by these procedures have been published in several journals. As to the second question, the data of the first measurement were presented. We examined albuminuria, BUN, Fishberg's concentration test, and so on. The severity of the hypertension was scored in each case from eyeground findings, blood pressure, and the complications in the heart, brain, and kidney. Nephrogenic secondary hypertension was excluded.

Dr Freis: We do not know the true prevalence of renal vascular hypertension and other forms of curable hypertension in the general populations of young hypertensive patients. We badly need this information because we need to know how important the problem really is. Mostly information has come from referral centres or from hospitals that specialize in curable forms of hypertension, and the prevalence has been estimated as high as 20%. I notice that in your own interesting data the Tokyo University Hospital had about 3 to 4% incidence of renal vascular hypertension, but when you surveyed the Railway employees, who were also mostly young - under the age
of 40 - there were less than 1% who had renal vascular hypertension, and even these were apparently not due to renal arterial disease but rather to a sliding kidney. Including all forms of curable hypertension, they seem to account for less than 2% of all the hypertension that you saw in these young male hypertensives. I think that is very important epidemiological information.

Dr Ueda: Dr Dustan of Cleveland showed that about 20% of hospitalized hypertensives are of renal vascular origin, but the frequency of about 3% seems to be a reasonable general figure in Japan; however, it differs by sex and age. In young female hypertensives who are resistant to routine treatment, about 40 or 50% of them have renal vascular hypertension. I think Dr Omae may have some idea about the frequency of renal vascular hypertension in Japan.

Dr Omae: My impression is that renal vascular hypertension is less frequent in Japan than in the USA, but we do not have exact figures, particularly on a community basis. We have more aortitis syndrome (Takayasu arteritis) than atherosclerosis as a cause of renal artery stenosis. As I told you when I presented my paper, we have three cases with renal artery stenosis but it is not very clear whether it is a cause of hypertension or not. We have to make a further study in order to detect the incidence of renal vascular hypertension in the community.

Dr Akinkugbe: Tables 3 and 4 are not strictly comparable: the one is a University study, a clinical study, and the other is a screening study in a young male population, but I am struck by the contrast in the percentages of essential hypertensives. In the one it is about 70%, in the other it is 87%. I think that the explanation may be that the subjects shown in Table 3 went through a finer sieve, because it was a clinical study, and thus was more likely to find secondary forms of hypertension. In any screening study one expects a higher percentage of people with essential than with secondary hypertension. The other point is that in the younger population there appears to be a higher prevalence of essential hypertension than in the overall population. Normally, one has the impression that in younger groups renal causes are more important than non-renal causes. Finally, in Table 3 there is a column on pyelonephritis, but there is none in Table 4. I wonder if there was no single case of pyelonephritis in the young male adult population of the Japanese National Railways, and on what was the diagnosis of chronic glomerulonephritis based?

Dr Ueda: The sources of these studies are different. Table 3 shows data from a University hospital and Table 4 is based on the screening of the employees in the Japanese National Railways. Hypertension might be present in some cases with pyelonephritis. In the last column of Table 4 you will find that the hypertensives from other causes accounted for 22%; the hypertensives in this group may include those with pyelonephritis.
FREQUENCY AND DIAGNOSIS OF CEREBROVASCULAR DISEASES IN AGED PEOPLE

by

Masakuni Kameyama

Cerebrovascular diseases (CVD) are of great concern in Japan, especially in the field of geriatrics. As a cause of death, CVD is estimated at 31.2% for subjects aged more than 65 years in 1971. The real features of CVD in the elderly population, however, are not clearly known, because of diagnostic difficulties. The purpose of this report is to point out the frequency and clinical characteristics of CVD in elderly subjects, based on a large number of autopsies at the Yokufukai Geriatric Hospital, Tokyo. This hospital was founded as an Institute of the Social Welfare Corporation for the Aged, and the in-patients consist mainly of the inhabitants within the Yokufuen Yard. The autopsy rate in this hospital has been almost 100%, so the data obtained from this Institute may represent the average pattern of CVD in the aged in this part of Japan.

The results obtained are as follows:

1. **Age and atherosclerosis of the major cervical arteries**

Histological preparations were made from the portion of maximal stenosis of the internal carotid and vertebral arteries. The degree of stenosis was measured on cross sections with a planimeter. The average degree of stenosis was calculated from the arteries on the right and left sides. The frequency of more than 50% average stenosis of the internal carotid was 29.4% in subjects in the sixties, 25.5% in the seventies, and 27.2% in the eighties or more, and that of the vertebral was 19.6%, 15.7% and 15.7%, respectively (Table 1).

2. **Age and cerebral atherosclerosis**

Of the basal cerebral arteries, the middle cerebral and vertebral (basilar?) arteries were chosen and the degree of atherosclerosis in them was measured by the stenosis from atheroma formation; stenosis over 50% was defined as severe. In subjects over 65 years old, the frequency of severe atherosclerosis in the middle cerebral artery increased almost linearly with age, but in the basilar artery this tendency was not observed (Table 1).

It is concluded that severe stenosis of the major cervical or basilar arteries seems to be life-threatening; while that of the middle cerebral does not.
Table 1. Relative frequency of cerebrovascular diseases at Yokufukai Geriatric Hospital, Tokyo

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>60-64</th>
<th>65-69</th>
<th>70-74</th>
<th>75-79</th>
<th>80-84</th>
<th>85-89</th>
<th>90+</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of cases examined</td>
<td>38</td>
<td>119</td>
<td>282</td>
<td>383</td>
<td>372</td>
<td>193</td>
<td>82</td>
<td>1469</td>
</tr>
<tr>
<td>Severe atherosclerosis:</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Middle cerebral arteries</td>
<td>57.9</td>
<td>54.6</td>
<td>63.1</td>
<td>69.1</td>
<td>73.6</td>
<td>75.6</td>
<td>85.4</td>
<td>70.1</td>
</tr>
<tr>
<td>Basilar artery</td>
<td>42.1</td>
<td>47.0</td>
<td>47.9</td>
<td>47.2</td>
<td>48.6</td>
<td>53.3</td>
<td>43.9</td>
<td>48.2</td>
</tr>
<tr>
<td>Fatal cerebral haemorrhage(^a)</td>
<td>7.9</td>
<td>9.2</td>
<td>7.4</td>
<td>5.7</td>
<td>5.9</td>
<td>5.2</td>
<td>3.6</td>
<td>6.0</td>
</tr>
<tr>
<td>Fatal cerebral infarction(^a)</td>
<td>2.6</td>
<td>4.2</td>
<td>7.0</td>
<td>6.3</td>
<td>3.2</td>
<td>8.3</td>
<td>9.8</td>
<td>5.8</td>
</tr>
<tr>
<td>Non-fatal cerebral haemorrhage(^a)</td>
<td>28.9</td>
<td>19.3</td>
<td>17.7</td>
<td>15.4</td>
<td>9.9</td>
<td>6.2</td>
<td>9.8</td>
<td>13.6</td>
</tr>
<tr>
<td>Non-fatal cerebral infarction(^a)</td>
<td>39.4</td>
<td>38.6</td>
<td>42.9</td>
<td>38.1</td>
<td>35.4</td>
<td>32.1</td>
<td>36.6</td>
<td>29.5</td>
</tr>
<tr>
<td>More than 50% stenosis:</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Internal carotid artery</td>
<td>15/51 (29.4%)</td>
<td>57/223 (25.5%)</td>
<td>33/121 (27.2%)</td>
<td>105/395 (26.6%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vertebral artery</td>
<td>10/51 (19.6%)</td>
<td>35/223 (15.7%)</td>
<td>19/121 (15.7%)</td>
<td>64/395 (16.2%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) Fatal: death within 3 months of the onset of stroke.
Non-fatal: death later than 3 months of the onset of stroke.
3. Prevalence of cerebral haemorrhage and infarction in elderly autopsy cases

Cerebral haemorrhage and infarction were divided into two groups according to their severity: fatal and non-fatal with clinical manifestations. No cerebrovascular lesions were found in 22-25% of every age group after 60 years. Fatal cerebral haemorrhage was found in 7.7% of patients aged 60-64 years; thereafter it decreased gradually with the advance of age. The prevalence of fatal haemorrhage was 6.0%. The prevalence of fatal infarction was 2.6% in the subjects aged 60-64 years; thereafter it increased gradually with the advance of age. In total, the number of fatal cerebral haemorrhages was almost equal to that of fatal infarction (Table 1).

Non-fatal cerebral haemorrhage with clinical manifestations was observed in 29.8% of patients aged 60-64 years; 19.3% of those aged 65-69 years; 17.7% of those aged 70-74 years; 15.4% of those aged 75-79 years; 9.9% of those aged 80-84 years; 6.2% of those aged 85-89 years; and 9.8% of those aged 90 years or more. The overall frequency was 13.6%.

The frequency of non-fatal cerebral infarction was 39.4, 38.6, 42.9, 31.8, 35.4, 32.1, and 36.6% respectively, according to the age order given in the previous paragraph. The overall frequency of non-fatal infarction was 29.5%. The frequency of non-fatal infarction was more than twice that of haemorrhages.

The frequency of fatal subarachnoid haemorrhage (SAH) was 1.4% in this series, all of which were due to a rupture of cerebral aneurysms.

4. Prognosis of CVD and sites of lesions confirmed by autopsy

The relation between the sites of lesions confirmed at autopsy and the clinical cause of the disease was investigated (Table 2). Of 588 cases of first stroke, 115 (19.5%) died of CVD within three months after the onset. Among the fatal cases extensive infarctions in the area of the internal carotid or middle cerebral arteries were most frequently observed, followed by haemorrhage in the putamen, thalamus, pons, and cerebellum. Of the patients with non-fatal stroke, 24% were bed-ridden, 38.6% fairly and 17.9% markedly improved.

5. Some diagnostic clues for stroke in the aged

We have a guideline for the diagnosis of cerebrovascular diseases, made several years ago by a research group supported by the Ministry of Education (Chairman: Emeritus Professor Dr S. Okinaka). This guideline is also useful for diagnosis of CVD in the aged. However, there are many pitfalls in the signs and symptoms of aged patients, because extracranial factors may play an important role in the pathogenesis and clinical picture. Millikan and his co-workers proposed two criteria of practical utility in the identification of cerebrovascular stroke: (1) evidence of focal brain disease; (2) the temporal profile of the clinical syndrome. As a focal character of brain disease, the following findings are important: hemiplegia, sensory disturbances on one side of the body including the face, agnosia, homonymous hemianopsia or monocular blindness, unilateral cerebellar ataxia, ocular or gaze palsies, dysphagia, or dysarthria. The temporal profile can usually be ascertained by a clear history of the mode of onset, evolution, and course of each symptom taken in relationship to the medical
Table 2. Sites of vascular lesions and prognosis (autopsy findings)

<table>
<thead>
<tr>
<th>Site of lesions</th>
<th>Non-fatal&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Total</th>
<th>Fatal&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Degree of improvement</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Good</td>
<td>Fair</td>
<td>Poor</td>
<td>Total</td>
</tr>
<tr>
<td>Internal carotid or middle cerebral artery</td>
<td>10</td>
<td>20</td>
<td>14</td>
<td>44</td>
</tr>
<tr>
<td>Anterior cerebral artery</td>
<td>2</td>
<td>9</td>
<td>12</td>
<td>23</td>
</tr>
<tr>
<td>Posterior cerebral artery</td>
<td>2</td>
<td>6</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>Centrum semiovale</td>
<td>6</td>
<td>12</td>
<td>7</td>
<td>25</td>
</tr>
<tr>
<td>Internal capsule: anterior half</td>
<td>27</td>
<td>58</td>
<td>12</td>
<td>97</td>
</tr>
<tr>
<td>Internal capsule: posterior half of the posterior limb</td>
<td>13</td>
<td>57</td>
<td>60</td>
<td>130</td>
</tr>
<tr>
<td>External capsule and internal capsule</td>
<td>6</td>
<td>17</td>
<td>17</td>
<td>40</td>
</tr>
<tr>
<td>Thalamus</td>
<td>9</td>
<td>15</td>
<td>6</td>
<td>30</td>
</tr>
<tr>
<td>Nucl. lenticularis</td>
<td>7</td>
<td>9</td>
<td>0</td>
<td>16</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>11</td>
<td>5</td>
<td>1</td>
<td>17</td>
</tr>
<tr>
<td>Pons</td>
<td>12</td>
<td>19</td>
<td>12</td>
<td>43</td>
</tr>
<tr>
<td>Total</td>
<td>105</td>
<td>227</td>
<td>141</td>
<td>473</td>
</tr>
</tbody>
</table>

<sup>a</sup> Fatal: death within 3 months of the onset of stroke.
Non-fatal: death later than 3 months of the onset of stroke.
status at the time of examination. Without a satisfactory knowledge of the clinical course, it may be impossible to distinguish cerebrovascular diseases from other diseases of the brain, such as tumour, subdural haematoma, abscess, encephalitis, and acute demyelinating disease of the brain. In aged subjects, however, these two points are frequently uncertain. In occasional cases of CVD, disturbance of consciousness showing generalized metabolic failure may dominate the clinical picture. Reliable information may not be obtained concerning the mode of onset, the evolution of the stroke, or past history. Symptoms and signs are often clouded by deafness, visual disturbances, or dementia; but, nevertheless, there are some clues useful in daily practice to reach a correct diagnosis of CVD in aged persons. These are:

(1) If a patient shows severe hemiplegia with disturbances of consciousness, he most likely has cerebral infarction. However, in cases of cerebral infarction with extensive lesions in the territory of the internal carotid or middle cerebral arteries, deep coma with flaccid hemiplegia is often observed.

(2) If hypertension is not confirmed at the onset of stroke, cerebral haemorrhage is less likely.

(3) If a patient shows focal cerebral signs such as aphasia, hemianopsia, agnosia, or apraxia with disturbances of consciousness, he most likely has cerebral infarction. There are some patients who show dementia, urinary incontinence or retention, and frontal signs with abrupt onset; multiple or large infarctions are occasionally found in the anterior frontal regions in these patients.

(4) Epileptic seizures are not uncommonly encountered in cerebral infarction (about 24% of cortico-subcortical lesions). However, in the EEG of these patients, spiky or sharp waves are rarely seen. The latter are usually seen with other cerebral diseases such as tumours or encephalitis.

(5) The acute brain syndrome, in which disturbances of water and electrolyte balance are frequently found, is a common phenomenon in the aged. In such conditions, a focal character of brain disease is not a rule, but in some cases with old vascular lesions in the brain, the acute brain syndrome may be accompanied by some focal neurological manifestations and it is difficult to differentiate it from acute stroke. Neurological, biochemical, electrophysiological, and radiological examinations are needed in order to reach an accurate diagnosis.

(6) More frequently associated with carotid bruits is cerebral infarction than cerebral haemorrhage.

(7) Subdural haematoma is not rare in the aged. The signs and symptoms are highly variable; in our experience, headache is rather rare, while a motor disturbance or clouding of consciousness with a fluctuating course is more or less characteristic.

(8) Normal pressure hydrocephalus is conceivable if a patient shows dementia after a subarachnoid haemorrhage.

(9) Meningitis of various origins is not rare in the elderly. However, meningitis is often diagnosed as "dementia". Disturbance of consciousness often dominates the clinical picture. On the other hand,
there are some cases which show numerous leucocytes in the CSF after stroke; in such cases a diagnosis of meningitis is likely to be suspected. Polymorphonuclear leucocytes were said to be found in 70% of the patients with haemorrhagic infarction and lobar haematoma, with a peak three to four days after the onset.²

(10) Typical subarachnoid haemorrhage is exclusively a manifestation of rupture of cerebral aneurysms; however, more than half the cerebral aneurysms are clinically silent, being found only at autopsy. Therefore, in order to diagnose ruptured aneurysms, the exact findings of rupture or the related picture of a cerebral angiogram is important. Cerebellar haemorrhage and thalamic haemorrhage which had ruptured into the ventricles were occasionally misdiagnosed as a rupture of intracranial aneurysms.

(11) Bloody cerebrospinal fluid (CSF) is an important finding in suspected intracranial haemorrhage, but there are many cases which do not show bloody CSF, regardless of actual intracranial bleeding. In such cases, however, the protein value of the fluid usually exceeds 80 mg/dl, an important finding to help differentiate between haemorrhage and infarction.

(12) At the beginning of stroke, care must be given to excessive hypotension. In such cases severe extracranial illness is common, especially acute myocardial infarction, peptic ulcer with bleeding, or sepsis of unknown origin. In the aged, the disseminated intravascular coagulation syndrome is not so rare.

(13) Non-fatal cerebral infarction is very frequent in diabetics with hypertension. In diabetics without hypertension, the incidence of fatal or non-fatal infarction is almost equal to that in the controls. Cerebral haemorrhage is more frequent in the hypertensives without diabetes mellitus than in the diabetic hypertensives.

(14) In subarachnoid haemorrhage, headache is most severe at the beginning of stroke, while in cases of intracerebral haemorrhage, headache may increase with the lapse of time. This is important in the differentiation of subarachnoid haemorrhage from cerebellar haemorrhage.

(15) There are cerebral tumours which mimic a transient focal cerebral attack in showing recurrent manifestations of stereotyped symptoms and signs. In these cases, a brain scan is a useful tool for differential diagnosis.

REFERENCES


DISCUSSION

Dr Toole: I am interested to know whether or not in your autopsies you were able to dissect the carotid artery in the neck and the vertebral arteries extracranially, and also whether you found any possible correlation between more advanced extracranial disease and less intracranial pathology because some people have suggested that extracranial artery stenosis protects the intracranial circulation from the effects of hypertension.

Dr Kameyama: I have investigated the frequency of complete occlusions of the major cervical arteries in 400 cases aged 60 years or more at general autopsy and 2% of this series showed occlusion of the internal carotid artery. As pointed out by Dr Katsuki in his population-based autopsy study (Neurology, 13: 279 (1963)), I too found more occlusions in the intracranial than in the extracranial arteries. In Japan, however, extracranial occlusion of the carotid artery is not as uncommon as it was supposed to be. The figure of 2% of occlusion in the internal carotid artery in the general autopsies of the aged subjects does not appear to be very small.

Dr Marquardsen: It is very valuable that Dr Kameyama emphasized the differences in the reaction of the brain that exist between various age groups. In old people the manifestations of raised intracranial pressure are often very mild and inconspicuous. In fact, an old person may die from a subdural haematoma without having shown the usual clinical signs of increased intracranial pressure, such as a rise of blood pressure, bradycardia, or a high pressure of the cerebrospinal fluid. This is an important pitfall in the differential diagnosis between stroke and subdural haematoma or cerebral tumour. Further, I was impressed by the very low fatality rate among Dr Kameyama's patients. Can this be explained by particularly effective treatment, or by some selective factors? Finally, I have a short comment on Dr Toole's remark about the possibility of an extracerebral arterial stenosis protecting the homolateral side of the brain against the effects of high blood pressure. In a series of my patients I observed that cerebral haemorrhages, which occurred in patients who had survived a cerebral infarction, nearly always affected the opposite hemisphere. This observation seems to support Dr Toole's statement.

Dr Kameyama: I have read your article, "Natural History of Cerebral Infarction", and have compared my data with yours. The death rate was about 20% in our series. We were dealing with the prognosis of patients from among all cases of stroke; even the slightest cases were admitted to a particular geriatric ward. As you know, many of the stroke deaths result from recurrences; if we deal with all the stroke deaths, the rate may perhaps be close to yours. As for subdural haematoma, it is more or less common in the elderly patients; about 2 or 3% of this autopsy series showed fresh or old subdural haematoma. The correct diagnosis may be missed unless one is keen to differentiate it. The symptoms and signs of chronic subdural haematoma are atypical in many old subjects.

Dr Paul: Dr Kameyama, what is the definition of a non-fatal cerebral haemorrhage found at autopsy? I suppose you would have found instances of fibrosis which could have been residues of a haemorrhage or of an infarction. How did you decide which was which, and how much blood or how large an area of involvement was classified as a haemorrhage?
Dr Kameyama: Concerning the pathological-anatomical distinction between cerebral haemorrhage and infarction, there are some clues proposed by Scholz et al. of the German School, as I have already pointed out. We call a stroke fatal when a person dies within 3 months after the onset without any other obvious cause and the autopsy confirms cerebrovascular lesions as a major finding. The "non-fatal" cases are the ones who survive longer than 3 months after the onset and in whom cerebrovascular lesions are confirmed at autopsy.

Dr Akinkugbe: In Table 1 I would like you to confirm that in your crude figures there are 10 times as many patients (autopsy cases) between 75 and 79 years of age as compared with those between 60 and 64 years. Were these autopsies done over the same period? It seems interesting comparing this age pattern with the pattern of atherosclerosis. We find that there is a steady increase from 60 years right up to 90.

Dr Kameyama: Our hospital is for elderly patients only and the average age of the autopsied cases is about 78 years. I have mentioned that we do not have many patients between 60-64 years of age and that the number of autopsies in that age group is quite small. We have 75-84-year-old people mostly. We can investigate the patients for a long period of time and we do autopsy examinations on almost all the subjects when they die. As for the connexion between age and atherosclerosis, the frequency of severe atherosclerosis (i.e., showing more than 50% stenosis on cross sections of the arteries) of the middle cerebral arteries increased after 60 years of age; however, this trend was not seen in the major cervical and basilar arteries. We can have many interpretations on these results, but I think that severe atherosclerosis in the cervical as well as basilar arteries would be life-threatening, while that in the middle cerebral would not be directly related to the survival of patients.
EXPERIENCE OF HOSPITAL CARE
FOR STROKE PATIENTS

by
Keiichi Ito

Our hospital, a medical centre for cerebrovascular disease (CVD), was established in 1969 in Akita prefecture, because Akita has had the highest CVD death rate in Japan.

The hospital has 70 beds, and, as shown in Fig. 1, the patient is transported to the hospital by our hospital ambulance as soon as possible after receipt of the call from the patient's family or the family doctor. After arrival at the hospital, cerebral angiography and, if necessary, brain scans are performed on all patients in addition to careful clinical examination, to confirm the diagnosis of the type of stroke and the site of the lesion. After that, the patient is treated in one of the stroke intensive care units (ICU) or sub-ICUs or in a surgical unit depending on the type of stroke and the severity.

Deaths of stroke patients are not always attributable to brain damage alone, but may appear frequently to be due to non-neurological complications such as asphyxia from vomiting, pneumonia, urinary tract infection, or gastrointestinal bleeding. Moreover, as mentioned later, we can assist the survival of some patients with intracerebral haemorrhage by surgical evacuation of the haematoma.

Therefore, it is essential to differentiate the type of stroke, detect the complications early, and treat patients intensively at a well-equipped hospital.

On the other hand, there remains an idea in Japan that for stroke patients, strict bed rest should be enforced for a few days after the onset; and, as yet, more than 80% of stroke deaths occur in the patients' own homes.

Therefore, in this paper, our experience in the intensive care of stroke patients is reported considering the following three points: (1) to evaluate the effect of early transport of stroke patients, within 24 hours after the onset; (2) to evaluate the value of angiographic studies in the early stage of stroke; (3) to evaluate the effectiveness of setting up an intensive care unit in a hospital, i.e., the effectiveness of a Stroke ICU itself.
Fig. 1. Our scheme for the management of acute stroke patients

Call from patient's family or the family doctor → Mobilization of the ambulance to patient's home → Arrival at our hospital → Special radiological examinations → Radiological examinations → Diagnosis of type and site of lesion → Stroke sub-ICU 12 beds → Stroke ICU 5 beds → Surgical intervention → Recovery room → General ward

Physical examination First-aid
Neurological and laboratory examinations
Carotid angiography Vertebral angiography
Group discussion

Brain scan Tomoangiography Pneumoencephalography Regional CBF
I. EARLY TRANSPORT WITHIN 24 HOURS AFTER THE ATTACK

Materials and methods

Acute stroke patients admitted within two weeks after the attack were divided into four groups, according to the time intervals between the onset and transporting to our hospital, as follows: the first group contained patients who were admitted within 24 hours after the onset, the second group during the second or third days, the third group during the fourth or fifth days, and the fourth group was transported five days or more after the stroke. The mortality rates were compared among these four groups, and the effect of early transportation was evaluated from these mortality rates. At the same time, evaluation was based on the change in the level of consciousness and eye signs, such as conjugate deviation, anisocoria, etc., before and after transport.

In the ambulance there are an Ambu-bag, tracheal tubes, oxygen bombs (oxygenator), an aspirator, and an electrocardiograph; and the ambulance staff consists of a doctor, a nurse and a driver. The distance of transportation was usually within 50 km, and all cases were divided into three groups according to the distance, that is: the first group was carried 5 km or less, the second group from 6 to 30 km, and the last 31 km or more. Whether the prognosis for survival varied according to the distance transported or not will also be discussed.

Results

As shown in Table 1, in patients with intracerebral haemorrhage or with cerebral infarction, there is no difference in the mortality rates between the group transported within 24 hours and the one during the second or third days after the onset; but the group brought in after four days or more showed a better prognosis.

In patients with subarachnoid haemorrhage, however, the mortality rates in the group transported within 24 hours was 72.7%; and the rates in the groups transported after two days or more ranged from 25% to 50%. Though the difference between the two values was not significant statistically, the patients transported within 24 hours after the onset fared slightly worse.

Some investigators(1) have reported that transporting within 24 hours after the onset was not suitable for patients with acute stroke because of the risk of developing brain oedema or herniation and the potential hazard of rebleeding. In this series, however, there was no significant difference in the prognosis between the group transported within 24 hours and the group during the second or third days, in both cerebral haemorrhage and cerebral infarction.

In general, it would be expected that the group transported in the early stage, within 24 hours after the onset, showed the worst prognosis for survival, since the mortality rate is highest within 24 to 48 hours after the onset, especially in patients with cerebral haemorrhage. However, there was no statistical difference in the prognosis between the group transported within 24 hours and the group transported within two or three days in our cases, and this might be due to the efficacy of early transport and suitable early treatment.
It should not be a surprise to find that the prognosis was better in cases brought in four or five days after the onset. It also seems suggestive that the decision for the early transport of patients with subarachnoid haemorrhage has to be made carefully, since such patients transported within 24 hours showed a higher incidence of death, as mentioned above.

There was no correlation between the distance transported and the mortality in any of the types of intracerebral haemorrhage, cerebral infarction, and subarachnoid haemorrhage, as shown in Table 2.

In Table 3, the effect of transport on acute stroke is evaluated by comparing the level of consciousness and the eye signs before and after transportation. While a deterioration of clinical signs and symptoms was observed in the range of 4.8 to 19% during transport, clinical signs and symptoms improved in the range of 4.8 to 12.2% during transport. This means that the influence of early transport on the patients' level of consciousness and eye signs is, on balance, not always considerable.

II. CEREBRAL ANGIOGRAPHIC STUDIES IN ACUTE STROKE

Materials and methods

Serial carotid angiography was performed through a needle inserted percutaneously, and 8 ml of the contrast medium (60% meglumine iotalamate) was injected by using an automatic injector (Cisal I). A total of 14 films was exposed over about 11 seconds with two exposures per second for the first four seconds for each angiography.

Vertebral angiography was carried out either through a catheter inserted into the femoral artery by the Seldinger method or through a needle puncture into the brachial artery with retrograde filling in the older patients (over 60 years old).

The incidence of complications of cerebral angiography was studied in 632 patients with acute stroke within three weeks of the onset. Distribution of patients by ages and stroke type is shown in Table 4.

Results

Eight patients (1.3%) developed complications in the central nervous system, such as hemiplegia, dysarthria, disturbance of consciousness, etc., within 24 hours after the angiography; six of them had subarachnoid haemorrhage, and two had cerebral infarction. Therefore, it could be said that complications were observed more frequently in subarachnoid haemorrhage; and they could be, in part, correlated with the state of so-called "angio-spasm" which developed easily. The incidence of complications according to the age of the patients was as follows: 1.8% under 40, 2.2% between 40 and 49, 0.7% between 50 and 59, 0.9% between 60 and 69, and 1.3% aged 70 years and over. The incidence of complications was not necessarily higher in the older ages.

Cerebral angiography was found to be very useful for diagnosing the type of stroke and the site of the lesion in the acute stage; since it was found that a misdiagnosis had been made in only four cases (4%) by stroke type and five cases (5%) by focus in the comparative studies of clinical diagnoses and the results of autopsies performed on a total of 104 cases (46 with intracerebral haemorrhage, 23 with cerebral infarction, and 35 with subarachnoid haemorrhage).
Table 1. Mortality rate by the time interval from the onset of the stroke to transport to hospital

<table>
<thead>
<tr>
<th>Interval from onset to transport (days)</th>
<th>Intracerebral haemorrhage</th>
<th>Cerebral infarction</th>
<th>Subarachnoid haemorrhage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of patients</td>
<td>Mortality (%)</td>
<td>No. of patients</td>
</tr>
<tr>
<td>0 - 1</td>
<td>30</td>
<td>33.3</td>
<td>18</td>
</tr>
<tr>
<td>2 - 3</td>
<td>24</td>
<td>29.0</td>
<td>20</td>
</tr>
<tr>
<td>4 - 5</td>
<td>10</td>
<td>25.0</td>
<td>6</td>
</tr>
<tr>
<td>6 - 14</td>
<td>8</td>
<td>12.5</td>
<td>4</td>
</tr>
</tbody>
</table>

<sup>a</sup> 0.2 > P > 0.05

Table 2. Mortality rate by the distance the acute stroke patient was transported

<table>
<thead>
<tr>
<th>Distance of transportation (km)</th>
<th>Intracerebral haemorrhage</th>
<th>Cerebral infarction</th>
<th>Subarachnoid haemorrhage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of patients</td>
<td>Mortality (%)</td>
<td>No. of patients</td>
</tr>
<tr>
<td>&lt; 5</td>
<td>15</td>
<td>40.0&lt;sup&gt;a&lt;/sup&gt;</td>
<td>16</td>
</tr>
<tr>
<td>6 - 30</td>
<td>28</td>
<td>25.0&lt;sup&gt;a&lt;/sup&gt;</td>
<td>18</td>
</tr>
<tr>
<td>&gt; 31</td>
<td>26</td>
<td>23.0</td>
<td>11</td>
</tr>
</tbody>
</table>

<sup>a</sup> P > 0.3
<table>
<thead>
<tr>
<th>Type of stroke</th>
<th>Number of patients</th>
<th>Level of consciousness</th>
<th>Eye signs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Unchanged (%)</td>
<td>Improved (%)</td>
</tr>
<tr>
<td>Intracerebral haemorrhage</td>
<td>48</td>
<td>77.1</td>
<td>8.3</td>
</tr>
<tr>
<td>Cerebral infarction</td>
<td>41</td>
<td>70.7</td>
<td>12.2</td>
</tr>
<tr>
<td>Subarachnoid haemorrhage</td>
<td>21</td>
<td>90.5</td>
<td>4.8</td>
</tr>
</tbody>
</table>
Table 4. Age distribution of acute stroke patients having cerebral angiography and the incidence of side effects

<table>
<thead>
<tr>
<th>Type of stroke</th>
<th>&lt;40</th>
<th>40-49</th>
<th>50-59</th>
<th>60-69</th>
<th>70+</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracerebral haemorrhage</td>
<td>20</td>
<td>58</td>
<td>55</td>
<td>53</td>
<td>16</td>
<td>202</td>
</tr>
<tr>
<td>Cerebral infarction</td>
<td>7</td>
<td>27</td>
<td>66</td>
<td>114</td>
<td>52</td>
<td>266</td>
</tr>
<tr>
<td>Subarachnoid haemorrhage</td>
<td>30</td>
<td>44</td>
<td>32</td>
<td>50</td>
<td>8</td>
<td>164</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>57</strong></td>
<td><strong>129</strong></td>
<td><strong>153</strong></td>
<td><strong>217</strong></td>
<td><strong>76</strong></td>
<td><strong>632</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>No. of side effects</th>
<th>Percentage of side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.8</td>
</tr>
<tr>
<td>3</td>
<td>2.2</td>
</tr>
<tr>
<td>1</td>
<td>0.7</td>
</tr>
<tr>
<td>2</td>
<td>0.9</td>
</tr>
<tr>
<td>1</td>
<td>1.3</td>
</tr>
<tr>
<td>8</td>
<td>1.3</td>
</tr>
</tbody>
</table>

Table 5. Mortality rate by level of consciousness and type of stroke

<table>
<thead>
<tr>
<th>Type of stroke and level of consciousness</th>
<th>Our hospital</th>
<th>Control hospital</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of patients</td>
<td>Mortality (%)</td>
</tr>
<tr>
<td>Intracerebral haemorrhage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coma - Semicoma</td>
<td>141</td>
<td>30.3&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Stupor - Somnolence</td>
<td>65</td>
<td>58.5&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Alert</td>
<td>65</td>
<td>7.7&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>0.0</td>
</tr>
<tr>
<td>Cerebral infarction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coma - Semicoma</td>
<td>94</td>
<td>12.7</td>
</tr>
<tr>
<td>Stupor - Somnolence</td>
<td>46</td>
<td>40.0</td>
</tr>
<tr>
<td>Alert</td>
<td>43</td>
<td>21.7&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Subarachnoid haemorrhage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coma - Semicoma</td>
<td>60</td>
<td>36.6</td>
</tr>
<tr>
<td>Stupor - Somnolence</td>
<td>23</td>
<td>78.2</td>
</tr>
<tr>
<td>Alert</td>
<td>27</td>
<td>14.8</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>0.0</td>
</tr>
</tbody>
</table>

<sup>a</sup> P < 0.05  <sup>b</sup> P > 0.3  <sup>c</sup> P > 0.1
It has generally been known that the reliability of cerebral angiography for the diagnosis of stroke decreases with the course of time from the onset. Positive findings found angiographically in intracerebral haemorrhage have been noticed to decrease after three or four weeks from the onset. This tendency was more markedly shown in cerebral infarction, since the positive findings observed in cases after four or five days decreased to about a half of that seen in the first 24 hours.

It is therefore apparent that cerebral angiography has to be performed in the earlier period after the onset in order to make satisfactory diagnoses of the stroke type and to make a correct location of the lesion. The ultimate purpose of early transport and early diagnosis should be to improve the survival rate of patients. Although there is the possibility of some transient deterioration in the patients' clinical condition, if early transport and angiographic studies can lead to a more favourable prognosis by making effective treatment possible, then they should be recommended. However, the usefulness of early transport and cerebral angiography seems to vary depending on the kind of treatment carried out thereafter, i.e., whether the patient could be admitted to the most suitable institution or not.

As reported below, the acute strokes showed good survival rates because of correct diagnoses of the types of stroke and the site of the lesions and because appropriate treatments were available, including the surgical removal of haematoma in many cases of haematomas in the region of the basal ganglia and in the cerebellum.

III. RESULTS OF STROKE INTENSIVE CARE

Materials and methods

The Stroke ICU had five beds. These were equipped with two positive pressure respirators, a defibrillator, an aspirator, and oxygen supply at the bedside. Two nurses are on duty at all times in the unit; and blood pressure, pulse rate, respiration rate, level of consciousness, and the conditions of the pupils on all patients are recorded every two hours by them. Moreover, if need arises, cardiac and blood pressure monitorings are performed at each bedside. Besides the Stroke ICU, we have two Stroke sub-ICUs with six beds each. Although there is no defibrillator or respirator, other medical care is available to almost the same extent as in the Stroke ICU.

Semicomatose and more severe patients are treated in the Stroke ICU; less serious patients and patients who improved in the Stroke ICU were treated in the Stroke sub-ICUs.

Craniotomy was carried out in about half of the patients with haemorrhage in the putamen of the basal ganglia and in the cerebellum, and the haematoma in the brain was evacuated.

Patients with subarachnoid haemorrhage who were found to have aneurysms in the cerebral angiogram were operated on, as a rule, within two to three weeks after the onset.
We had no definite programme for conservative treatment. However, adrenocortical steroids were administered in the majority of patients in whom the appearance of cerebral oedema was anticipated; and urokinase was injected intravenously in some patients with cerebral infarction. Two hundred and ninety-five patients, who were admitted to our hospital within 24 hours of the onset and for whom the type of stroke was confirmed, have been included in the study for a comparison of mortality rates. They comprised 141 cases with intracerebral haemorrhage, 94 with cerebral infarction, and 60 with subarachnoid haemorrhage.

In order to evaluate the effectiveness of Stroke Intensive Care, the acute stroke patients who were admitted within 24 hours of the onset to a 600-bed general hospital located in Akita prefecture served as controls. Cerebral angiography was carried out in this hospital also in order to differentiate between the types of stroke. Therefore, the reliability of the diagnosis for the type of stroke was of the same order as that in our hospital, and it indicated 94% accuracy as compared with the autopsy findings; but surgical procedures were not performed in this hospital.

Results

The mortality rates in the two hospitals within one month of the onset, by the type of stroke and the level of consciousness, are shown in Table 5. As compared with the control hospital, the rate for the coma group of patients with intracerebral haemorrhage was lower in our hospital (P < 0.05). The prognosis for the other groups was nearly the same in both hospitals. Although a comparison with the results of other series may not be satisfactory because of variation in the subjects studied, the results from the Stroke ICU reported by Kennedy et al. indicated one-month mortality rates of 77.8% for patients with intracerebral haemorrhage, 21.6% for patients with cerebral thrombosis, and 41.7% for patients with subarachnoid haemorrhage. The mortality rates of patients with cerebral thrombosis or subarachnoid haemorrhage did not differ significantly between our hospital and the Stroke ICU of Kennedy et al. But, for patients with intracerebral haemorrhage, the prognosis observed in our hospital was better.

Okinaka et al. surveyed 132 patients who had attacks of intracerebral haemorrhage and found one-month survival rates of 13% in the severe group (those in coma), 58% in the moderate group, and 94% in the mild group (consciousness: alert). Marquardsen followed up 769 patients with various types of stroke and found three-weeks survival rates of less than 1% in comatose patients, 13% in semi-comatose patients, and 29% in stuporose patients.

We have obtained a one-month mortality rate of 88.6% from a survey of 34 comatose patients with acute stroke in Akita. From these observations, the Stroke Intensive Care carried out in our hospital seems to reduce the one-month mortality rate in severe cases of acute stroke, particularly those with intracerebral haemorrhage. Our results of a better survival rate for patients with intracerebral haemorrhage is, in part, associated with surgical treatment.
Table 6 shows a comparison of the mortality rates with conservative and surgical treatment of patients with haemorrhage in the putamen of the basal ganglia. As seen in this table, the one-month mortality rate of cases treated conservatively for the coma group is 80.0% and bears close agreement with the rates in previous reports. On the other hand, the mortality rate of cases treated surgically was 33.3% and indicates a better result as compared with the conservatively treated cases.

Comment

There have been several reports(2,5-8) on intensive care for stroke patients. Except for Taylor's results(5), other observations(2,6-8) have suggested that the establishment of ICUs for stroke patients was of little value.

If we consider the value of a Stroke ICU in a narrow sense, i.e., as limited care in a small room modelled after a Coronary Care Unit, then the effectiveness of a Stroke ICU appears not to be so great in our experience. Because we have not encountered a single patient who required a defibrillator in the Stroke ICU, and because emergency tracheotomy has not been performed more than a few times, the difference in the prognosis between our hospitals (excluding the surgically treated cases) and the control hospital became insignificant. However, if one includes in the intensive care system the following elements: the early transportation of patients, the measures leading to a correct diagnosis of the type of stroke and the site of the lesion, and the availability of reasonable treatment including surgical therapy, then the results seem to make such a unit worth while.

Therefore, a comprehensive Stroke ICU, whose activities range from transportation to treatment of acute stroke patients and which is staffed by a neurosurgeon and a neuroradiologist as well as a physician, can be recommended in future health service plans.

Summary

We have evaluated intensive care for stroke patients from the viewpoint of regarding the Stroke ICU as a well-integrated part of our hospital, which is a centre for cardiovascular diseases. Thus, our Stroke ICU is concerned with transportation, accurate diagnosis by angiographic studies, and treatment including surgical procedures.

As compared with conservative treatment, in which absolute rest comes first, it seems that active and intensive care, as defined above, leads to better results. This better outcome was particularly marked in caring for patients with intracerebral haemorrhage. On the other hand, the value of a stroke ICU which is managed like a coronary care unit, is doubtful.
### Table 6. Mortality rate by conservative and surgical treatments for patients with intracerebral haemorrhage

<table>
<thead>
<tr>
<th>Level of consciousness</th>
<th>Conservative treatment</th>
<th>Surgical treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of patients</td>
<td>Mortality (%)</td>
</tr>
<tr>
<td>Coma - Semicoma</td>
<td>35</td>
<td>80.0&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Stupor - Somnolence</td>
<td>32</td>
<td>12.5&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> P < 0.01  
<sup>b</sup> 0.1 > P > 0.05

### REFERENCES

1. Mihara, H. Some problems on transport of acute stroke patients.  
4. Marquardsen, J. The natural history of acute cerebrovascular disease,  
   a retrospective study of 769 patients.  
8. Cooper, S. W., Olivet, J. A. & Woolsey, F. M. jr. Establishment and operation of a combined intensive care unit for patients with cardiac and cerebrovascular disease.  
DISCUSSION

Dr Doyle: Could you tell us about the effects of surgical and conservative managements on residual disability, dependence, and so on?

Dr Ito: While other hospitals may have a rehabilitation unit, our hospital has not. Therefore, we did not compare residual disability. In the comparison of disability between patients with surgical intervention and patients with conservative management, we found that surgical procedures resulted in less disability for stuporous and more severe patients and non-surgical management produced better results for somnolent and milder patients.

Dr Paul: Do I gather, Dr Ito, in response to Dr Doyle's question that there was less disability in the non-operated cases?

Dr Ito: The non-operative management of mild cases had a better prognosis on disability; however, the stuporous and more severe cases would show better results if operation is carried out.

Dr Hatano: In the situation in Japan where stroke is more common and ischaemic heart disease is rather rare, I wonder what type of care should be provided. You did not mention what type of specific services are provided in the so-called stroke intensive care unit. Is there any difference between the ordinary type of intensive care and that in the stroke intensive care unit? Do you have any specific provision in the ambulance car? There may be some more convenient type of mobile care in the Japanese situation.

Dr Ito: In the narrow sense of the word, the stroke intensive care unit is nearly the same as the ordinary intensive care unit, as was mentioned in the paper. We have ECC monitors, an oxygen inhaling system, respirators and aspirators, and according to the symptoms we record the vital signs every two hours. Ambulances are equipped with ECC apparatus, ambu-bag, tracheal tubes, oxygen bomb and an aspirator. However, it is better to transport the patient to the hospital earlier than to operate in the ambulance.

Dr Shmidt: Did you operate on cases of haemorrhage in deep coma? Second, did you have any deaths during transportation? Third, did you have any deaths immediately after angiography?

Dr Ito: We have operated on patients in deep coma and we have rescued the life of these patients, but in such cases it has frequently resulted in a "vegetable" life. As for death in the ambulance, there was one such case; when we arrived at the patient's home, the family was told that the patient was too ill and would probably die in the ambulance, but the family insisted on our taking him and he did in fact die in the ambulance. We did not have any deaths immediately after angiography but there were several cases with no filling of the cerebral arteries in angiography.
Dr Strasser: Mr Chairman, Dr Ito's results may be interpreted as encouraging if one is an optimist and they may be interpreted as discouraging if one is a pessimist. This is an extremely important issue, at least for WHO. And if we are going to give some conclusions at the end of the meeting, we should state our ignorance on this topic. I do not want to prejudice further discussion, but I just want to stress the very great importance of evaluating the role of intensive care in the management of patients with acute stroke.

Dr Ito: The benefits may also depend on the country. In countries such as Japan where the general practice is to keep a stroke patient at home under complete rest, the stroke ICU would be very effective. However, in countries where stroke patients are transferred to hospital, I do not think that intensive stroke care can offer significant benefits.

Dr Weiss: We believe that a stroke is an emergency case and a patient with a stroke should be transported with special care in a special car, accompanied by a doctor. Intensive care of stroke is much closer to spinal cord injury care. For instance, in both a special bed which is different from a coronary care bed and which can be tilted or turned is needed. In the team for an emergency care unit there should be a physiotherapist to see to breathing exercises and also postural treatment. I would therefore ask our speaker: do you use a special bed to enable tilting? And do you, like Douglas and others, apply breathing exercises or use special equipment for unconscious cases?

Dr Ito: We do not use special beds, but the beds have wheels and we can transport the patient while lying on the bed in order to be examined in other units. We have not conducted breathing exercises.

Dr Toole: Mine is more of a comment than a question. You will notice in Dr Taylor's figures that the mortality rate from stroke in his hospital was listed as 49% before there was any stroke intensive care unit and 12% after. To me, that means that the level of care provided for the average patient in the hospital where he served had been very poor, and that the improvement with the intensive care unit is attributable to better diagnosis and management, rather than to the specific equipment available in the intensive care unit. It would seem to me, therefore, that the true test of what an intensive care unit might do is not to be found in the speciality hospitals where many people are interested in the field of stroke practice, because they have already instituted good measures even on the general floors before the patients come to the intensive care units. The true measure therefore would be comparing the practice in very average hospitals and in putting intensive management units in them. In the USA the concept of intensive care is now different from what it had been a few years ago when people used the coronary care model. It really means intensive management rather than special equipment. The intensive management is provided by nurses more than physicians and by psychiatrists and physical therapists. It is a concentration of a group of people who are devoted to keeping the airway open, providing breathing exercises, and seeing to the movement of the patient; basically it is a prevention of the complications of the stroke rather than a management of the stroke itself. In Dr Taylor's figures much of the mortality was due to neglect of the patients and misdiagnosis, so that we have two factors: one is the accuracy of the diagnosis, and the other is the personnel to give good management, not of the stroke but of the general patient.
Dr Ito: I agree with Dr Toole. When we make comparisons of different ICUs we should examine first of all the standard of medical services that is given at the control hospital. If the control hospital has good facilities, the ICU might show a low benefit, but if the standard of services in the control hospitals is low, the Stroke ICU will be of significant value.

Dr Kagan: The suggestion from Tables 1 and 2 would be that the more severe cases and the people who were closer to the hospital were the ones who tended to be transported and admitted to the hospital. What proportion of strokes occurring in the community were hospitalized and what were the criteria for admitting them to the hospital and to the intensive stroke unit?

Dr Ito: We do not have a specially defined population in an epidemiological sense. We serve the entire Akita prefecture and practically all the patients within reach of our ambulance service, i.e., within a radius of about 50 km; whenever there is a call within that radius, we go there with medical help. We have only 70 beds for this purpose and we are probably only covering a part of all the patients who need hospitalization in the area. The original goal of our centre was for research and reference rather than to establish a therapeutic centre.
MANAGEMENT OF STROKE
IN POPULATIONS*

by

J. F. Toole

I will introduce two documents for consideration concerning the management of stroke in population groups. The first is a report compiled by the Joint Committee for Stroke Facilities, sponsored by the American Neurological Association. The second one consists of the guidelines which are used by the North Carolina Comprehensive Stroke Programme for the provision of nursing care and medical care in hospitals throughout the State (see Annex, page 347).

No single health problem places as heavy a demand upon as wide a range of community services as does stroke, and it was correctly mentioned yesterday that stroke is a team problem rather than a single-physician problem. In the USA, for example, at any one time there are likely to be more than 2.5 million persons who suffered varying degrees of stroke, and during any year another half million new cases occur. In our country, somewhat fewer than half of these will survive the first 30 days; and of those who live longer than a month, 10% recover with no discernible disability, 40% have mild disability, another 40% are severely impaired and require special care, and the remaining 10% must be in institutions for the rest of their lives. Stroke occurs at any age: we have stroke in infancy, childhood, adolescence, and young adults as well.

The first point that I wish to make is that care can be given in a local hospital and need not be provided in special hospitals. We do not advocate the care of stroke patients in the home. The second point is that only certain categories of patients require special care, i.e., care that must be provided by neurologists or a neurosurgeon. However, the third point, the accuracy of diagnosis, is the prelude to correct management and one cannot speak of stroke in epidemiological terms when one considers the management of a patient. We have been speaking of stroke in populations; now we are speaking of stroke in an individual, and of the care of a person, so that we can no longer apply epidemiological concepts. This means we must have an accurate diagnosis early on as to whether a patient has an infarction, whether he has subarachnoid haemorrhage, or intracerebral haemorrhage, or subdural haematoma, since we can prevent the progression of these disorders in many patients by the early institution of appropriate management. This is described in the report by the Joint Committee for Stroke Facilities, which was referred to above. This Committee was accredited by the

---

* Based on a speech delivered at the meeting.

US Department of Education and Welfare and the report is distributed by the American Heart Association and the American Neurological Association, emphasizing the fact that stroke has been falling between these two special groups of people, cardiologists on one side and neurologists on the other, because in our country there are very few people who consider themselves to be specialists in the field of stroke.

On the title page of this particular report, the names of the people who contributed to the report are listed: cardiovascular surgeons, internists, general practitioners, and even psychiatrists. I cannot go through the entire report on how we manage stroke in populations in our country except to give a few broad hints. Transient attacks of neurologic dysfunctions, otherwise known as transient ischaemic attacks (TIA), are a prelude to approximately 35% of patients who had cerebral infarction in our country. This may contrast to the findings among the Japanese population. However, this warning signal TIA, is broadly misinterpreted by both the patients and the physicians. Very often patients do not realize the seriousness of the dizzy spell or the blurring of vision and, unfortunately, all too often the physician does not either. The attacks seldom, if ever, occur before the eyes of a doctor, and as a consequence we are dependent upon what the patients tells us about the attack which he had; so there is no screening device which we can use for TIA's other than talking with the person at length.

Transient attacks of neurological dysfunction

Most important in the evaluation of transient attacks of neurological dysfunction are an adequate history and a careful neurovascular examination. In every case a triggering mechanism such as polycythaemia, a decrease in the oxygen-carrying capacity of the blood, episodic hypoglycaemia, hypotension, carotid sinus hypersensitivity, or cardiac arrhythmia should be sought. Thereafter, consultation with an internist, ophthalmologist or otolaryngologist may be indicated. Accessory studies, including lumbar puncture, skull X-rays, electroencephalogram, and brain scan, all have their places. The differential diagnosis should be pursued as far as possible with these techniques before the patient is subjected to complicated, expensive and potentially dangerous diagnostic procedures.

Angiography is indicated if there is reasonable suspicion of a cerebral mass lesion, or if a clinical diagnosis of TIA (see next paragraph) has been made. The latter could be due to a surgically accessible atherosclerotic stenosis of the extracranial cerebral arterial tree. Angiography should be performed only in hospitals where personnel with considerable experience in dealing with cerebrovascular disease are available (see: Section on Special Procedures and Equipment in the Diagnosis and Management of Stroke. *Stroke*, 4: 111-137 (1973)).

TIA

Episodes of neurological dysfunction followed by complete recovery within 24 hours are consistent with a diagnosis of TIA. Persistence of

---

1 For reference, see footnote 1 on the previous page.
minor neurological signs (for example, reflex changes) beyond that period indicates the presence of a permanent brain lesion, but does not necessarily alter management procedures.

(Distinction between TIA of the carotid artery system and the vertebrobasilar artery system, variety of conditions to be differentiated from TIA, and the methods for reproducing TIA for diagnostic purposes are described in the text of the report.)

In the report of the Joint Committee we described the management of the patient, i.e., on the decision to hospitalize him, when to ask for consultation, when to transfer him elsewhere, and in contrast with what the practices in Japan are, we emphasize that almost every single patient must be hospitalized. That is not what happens in the USA, but it is what we advocate. We also talked about what categories of patients should be transferred. An emergency admission, meaning a special ambulance to get the patient to the hospital within minutes of the occurrence of the attack, is not necessary. This stands in contrast to the patient with myocardial infarction where, because of the arrhythmia and the possibility of ventricular fibrillation and sudden death, rapid transportation is vital. We do not think we save lives by transferring our patients with the red light flashing and the siren blowing and getting the patient to the emergency room quickly. However, admission to the hospital within hours is necessary.

MANAGEMENT OF THE PATIENT

Decision to hospitalize

Almost all clinicians admit stroke patients to the hospital during the acute phase of the illness when further diagnostic or special therapeutic programmes are contemplated. However, three interrelated aspects of the natural course of acute ischaemic cerebral infarction should be reemphasized: (1) the probability of some recovery in most cases and of total recovery in a few; (2) the probability of progression of neurological disability during the first few days, sometimes after a minor episode; and (3) the probability that in many cases systemic complications (congestive heart failure, myocardial infarction, aspiration of gastric contents, pneumonia, or hyponatremia) will follow shortly after a major stroke. Failure to appreciate these considerations is implied in the traditional dictum that nothing can or should be done for a stroke, a cliché often implemented in classical emergency room management: "If the patient can swallow, send him home; if he cannot swallow, insert a nasogastric tube and send him home." Such a disposition might have been adequate in the past for patients with strokes for which a definite etiological diagnosis had been established and which had been stable for several days. At the present time, reasoning of this nature is decidedly inadequate for all stroke patients, particularly for those with acute stroke of less than 48 hours' duration, whether initially mild or severe, and regardless of diagnostic certainty.
Consultation and decision to transfer

Consultation

The following conditions might call for immediate consultation with a specialist in neurological or vascular disorders.

Semicoma or coma. If a cardiac, metabolic, or infectious cause is not evident, a neurological specialist should be consulted. Many patients in this state have mass lesions (subdural, extradural, or intracerebral haematoma, or brain tumour). Consultation is essential for diagnosis and treatment.

Stroke-in-evolution. If the signs of stroke are progressing, active intervention by a specialist in vascular surgery may be indicated.

Subarachnoid haemorrhage. This condition requires prompt diagnosis and effective management, and may necessitate surgical treatment of an aneurysm, intracranial clot, or arteriovenous malformation.

TIA. These disorders require careful evaluation, clinical diagnostic measures, and possibly angiography, and treatment by the vascular surgeon.

Transfer

Any of the following conditions constitutes a need for transfer of the patient to an institution with specialized personnel and facilities:

1. The comatose or semicomatose condition of the patient cannot be attributed to cardiac, metabolic, or infectious disease;

2. An exact diagnosis remains in doubt after appropriate laboratory evaluation and consultation locally with available specialists;

3. Abnormal and unanticipated laboratory findings cannot be explained;

4. The patient's condition is deteriorating and proper management is uncertain;

5. Management requirements of the patient are beyond the capabilities of the local hospital;

6. Specialized evaluation is indicated; and

7. Adequate facilities for rehabilitation are not available locally.

In most cases, the following conditions should be handled in the local hospital:

1. Massive intracranial haemorrhage. If the patient will not survive transfer, then he should be given the best possible treatment available in the community hospital.
2. Cerebral embolism. If a cardiologist is available for consultation, the underlying cardiac or peripheral vascular disease can be treated in the community hospital, unless cardioversion and other special procedures beyond local capabilities are considered (see: Section on Clinical Prevention of Stroke. *Stroke*, 3: 803-825 (1972)).

3. Completed stroke. Most cases in which the diagnosis is clearly established and emergency transfer is unnecessary require appropriate help with the rehabilitation programme and with recommended therapy designed to prevent further episodes (see: Section on Stroke Rehabilitation. *Stroke*, 3: 373-407 (1972)).

In the summary of the report, our study group made a variety of recommendations for further action, because we agreed that the treatment of stroke in the USA is very inadequate in most places. Not only is there a diversity of opinion about what is the best form of management, but the level of care in different hospitals varies enormously, and as a consequence, I would point out to you several of the recommendations and leave the rest for you to study at leisure.

We also advocate that programmes of education to heighten public awareness of the known risk factors and warning symptoms associated with cerebrovascular diseases be implemented in the same way as the warning signals for hypertension and for coronary artery disease. Specifically, the meaning of transient ischaemic attacks must be brought to the attention of the public. We also recommend, as in the patients with hypertension, that they be identified early, and I was intrigued when I heard this morning that the identification of high blood pressure in youth and adolescence might be very important.

There is very little teaching at the undergraduate level about stroke in the USA, a surprising oversight. Stroke is usually taught in our medical schools as a single disease category where all the varieties of stroke are lumped together and it is therefore not surprising that the treatment of stroke by general physicians is very poor. I know for a fact that hardly in any medical school are medical students taught to listen to the neck and to the head with their stethoscopes. This is a simple screening device, very valuable, and yet neglected.

Methods must be sought to implement the stroke team concept, which is again to reiterate that many people are required to care for what I consider to be the most complicated of all diseases. The guidelines which we used for the North Carolina Regional Comprehensive Stroke Programme are very complicated but you might be interested in the way we collect information. Of more importance to you is the material which talks about stroke admission orders, and this continues on to what the physician, what the nurse, and what the physical therapist should do and at what stage they should be brought into the treatment programme. I do not intend to go into this, but it might be of interest to you to contrast what you do with what we do and possibly informally we could then consider these things at another time.
DISCUSSION

Dr Doyle: Dr Toole, you said that TIA seldom occurs in the presence of a doctor and one is entirely dependent on the history. I guess it is clear enough if the patient has an episode of aphasia or loss of use of an arm or leg for 5 or 10 minutes, but how far are you prepared to go in accepting that an episode of dizziness or something of that sort was a TIA? One of the problems in my life is that I constantly see patients who have had episodes of dizziness and not all of them have noises in their neck; the other implication is, if one sees this kind of problem, how far are you prepared to go in diagnosing it?

Dr Toole: With regard to isolated phenomena such as vertigo and dizziness, we have to make a very clear distinction between postural hypotension, labyrinthitis, and cerebral vascular insufficiency, at least as best we can. Regarding this diagnosis, I have become less sure of myself the longer I stay in the field; and in the diagnosis of transient ischaemic attack I look for a constellation of phenomena, not just a single symptom unless it happens to be blindness in one eye. In most patients you will find at least two symptoms, and if I have two of a better of possibilities, then my suspicion is greatly heightened. Many patients have a bruit in the neck and they do not have symptoms, and unfortunately very many have symptoms and no bruit, so that this is just an added diagnostic device.

Dr Reader: Dr Toole and others have been very careful to emphasize the non-specific approach to the management of a stroke. Where do we stand on the specific approach to the intracerebral lesion? I am thinking of hyperosmolar solutions and that kind of thing.

Dr Toole: You will recall that I emphasized the necessity for an accurate differential diagnosis before one can institute local management, and in talking about increased intracranial pressure, we are talking about a specific variety of intracranial catastrophe. Most people that I know do attempt to reduce intracranial pressure with hyperosmolar solutions. If you are talking further about the reduction of cerebral oedema in cerebral infarction, most will use steroids, but if intracranial pressure is raised because of a localized intracranial haematoma, others might remove it surgically.

Dr Weiss: I am a little bit concerned with a physiatrist being called at the very early stage because it removes some responsibility of the treating doctor if we introduce a physiotherapist at this stage. I believe that basic management and an activating form of therapy should be the responsibility of a treating doctor and of a nurse. Probably later, when the danger for life is over and a patient can adapt to living with hemiplegia, then the physiatrist is a good consultant. I have one question: Do you try general body cooling as a treatment in the acute stage?

Dr Toole: I have never done it but I have been intrigued by the possibilities. It makes good sense. One thinks that reducing cerebral metabolism would reduce the extent of infarction, but I have no experience. It may have been done in the USSR; maybe you could ask Professor Shmidt.
Professor Shmidt: Hypothermia was not used. The question concerning cerebral vasodilators is very important from a practical point of view. I believe that their negative effect in patients with ischaemic lesions has not been proved. A big and long experience has shown the effectiveness of the cerebral vasodilators and we continue to use them. I think that cerebral vasodilators improve cerebral blood flow in general and so the blood supply of the ischaemic regions. At the last international neurological congress in Madrid several months ago, Professor John Mayer with his collaborator reported that, using the isotopic method in patients with ischaemic cerebral lesions, they could not ascertain the presence of the well-known "luxations-perfusion syndrome" around the ischaemic area of the brain and they recommended the use of a cerebrovasodilator. I think that this question is still in dispute.

Dr Toole: I do not remember the exact phraseology in the report, but there are people on both sides of the fence with regard to what Professor Shmidt has just said. The counter-argument is that increase in blood flow does not necessarily mean increase in neurological function. We all agree that vasodilators increase cerebral blood flow, but the question is whether the patient's neurologic function is improved too.

Dr Yoshikawa: Many cases are diagnosed as cerebral arteriosclerosis in Japan and it is my impression that, especially in elderly patients, the differential diagnosis of TIA, cerebral arteriosclerosis, and cerebral thrombosis is very difficult. Dr Hirai, an experienced neurologist in our department, classified about 1000 patients with CVA, of whom about 500 cases were diagnosed as cerebral arteriosclerosis. I think TIA is included in this group, and it is very difficult to apply the clinical diagnostic method for cerebral arteriosclerosis in an epidemiological study. The number of these patients is very large. Can I have your comments on this problem?

Dr Toole: I believe that cerebral arteriosclerosis is probably present in every one of us in this room and the question is, "Does it produce symptoms?" I suspect that some better methods for screening those with symptoms from those who only have atherosclerosis have to be devised, and up to this point, at least in the USA, the only method that we use on a practical basis is identifying patients with symptomatic complaints. It has not yet been shown whether listening for bruits in the neck or measuring retinal artery pressure or some other test has any prognostic significance.
III. BORDERLINE PATHOLOGY

A. MILD HYPERTENSION

THE DILEMMA OF MILD HYPERTENSION

by

A. E. Doyle

In the last quarter of a century there has been a revolution in the therapeutics of high blood pressure. This has largely been due to the introduction of pharmacological agents capable of producing large falls of blood pressure in hypertensive patients and to the demonstration that such treatment improves prognosis and alters the pattern of mortality and morbidity in patients with severe hypertension. The earlier drugs, notably the ganglion blocking drugs, had grave disadvantages. They needed to be given by injection, produced large and often unpredictable falls in blood pressure, often of a magnitude to promote cerebral or cardiac ischaemia, and additionally had a high incidence of severe side effects which caused numerous symptoms. It is therefore not surprising that, in the early phase of antihypertensive drugs, treatment was generally offered only to those in whom the short-term prognosis was clearly very poor. Since that time, numerous new antihypertensive drugs have been introduced; these have been easier to use, have led to easier control of blood pressure, and have mostly had side effects of a less dramatic nature than did the earlier ganglion blocking drugs. Nevertheless, all drugs at present available for the treatment of hypertension have some disadvantages and most still require comparatively skilled administration, although for most patients this can be of a lower order than was formerly the case.

The administration of any form of treatment for any disease always involves a cost-benefit analysis being carried out. In the case of the patient with mild hypertension the most important questions to be resolved are, firstly, what are the risks of not treating the patient; secondly, what diminution of these risks is to be expected from treatment; and thirdly, what, if any, are the disadvantages and disabilities which may result from the treatment? There are also a number of logistical questions which have to be answered in relation to the patient with mild hypertension. These relate to methods of detecting the symptomless mild hypertensives within the community, and to the very high costs, both of drugs and of medical supervision, involved in managing all cases of mild hypertension. Clearly, these questions only become of importance if the benefits of treatment can be shown to be worthwhile and to outweigh the disadvantages of prolonged treatment with drugs. Finally, perhaps the most important question to be considered is the possibility that patients with mild hypertension may be divisible into subsets, each carrying a different prognosis unrelated to the levels of blood pressure. Linked with this question is the important aspect of pathogenesis of hypertension.
and the possibility of defining several distinct etiological types of hypertension, each carrying a different prognosis and each amenable to a specific form of therapy. Finally, there exists the important question of the presence of definable risk factors other than the level of blood pressure; this matter, although linked with pathogenesis, may exist independently of the causes of hypertension and may relate to genetic or environmental factors.

It is comparatively easy to define these dilemmas. It is considerably more difficult to evaluate the present evidence, and it is at present impossible to provide definite answers to them.

There is quite strong evidence, which mostly derives from life insurance statistics, that any elevation of blood pressure leads to earlier death from cardiovascular disorders. Thus, figures published by the Metropolitan Life Insurance Company,\(^1\) based on casual estimates of blood pressure in several million people examined for life insurance purposes, show a very close relationship between the level of diastolic blood pressure and excess mortality. In this study, individuals with diastolic blood pressure of about 75 mmHg were shown to exhibit the expected mortality (100%) in life insurance terms. People whose diastolic blood pressures were 88-92 mmHg had an increased mortality of 150%, and those with diastolic pressures between 103-117 mmHg had a mortality rate two-and-one-half times the average. Significantly, also, individuals with diastolic blood pressures lower than 75 mmHg showed decreased mortality. There is thus clear evidence that the level of blood pressure has an important effect in inducing early death, and also that quite modest elevations of diastolic pressure are associated with early death.

Other evidence is available to show the effects of such marginal elevations on life expectancy, and on the effect of blood pressure rises in the two sexes, and at various ages. Thus the Metropolitan Life Insurance Company's figures show that for American men aged 35 years with blood pressures of 120/80 or below presenting for life insurance, the average life expectancy was 42 years, and for men in the same age group, the life expectancy with a presenting blood pressure of 150/100 was reduced by 17 years to 25 years. At the age of 45 for men, the average life expectancy was a little over 30 years; with blood pressures of 150/100 it was reduced to about 20 years. For women of 45 years, average life expectancy was about 35 years, and a blood pressure of 150/100 reduced the average life expectancy by 8.5 years.

Figures published by the Society of Actuaries, Chicago, provide further evidence on the relationship between casual insurance blood pressure readings and mortality at various ages of presentation.\(^2\) These indicate that at the age of 30-39 years there is a steady increase in mortality as the initial systolic pressure rises, so that whereas deaths in individuals of this age average only 1 per 1,000 per annum when the systolic blood pressure is 125 mmHg, deaths in persons with initial systolic pressures of 165 mmHg are about 10 per 1,000 per annum. At 50-59 years the deaths rise from about 20 per 1,000 per annum to 50 per 1,000 per annum. Such figures indicate that when very large numbers of persons are involved, quite modest elevations of blood pressures in people of 50-59 years lead to an excess mortality of 30,000 per million per annum. Moreover these mortality figures, impressive though they are, take no account of morbidity. Studies by the Metropolitan Life Insurance Company\(^1\) indicate that the mortality increase is accounted for mainly by stroke and cardiovascular disease, and that the increased mortality from stroke in persons with blood pressures in the range 148/93 - 177/102 is six times that of individuals with diastolic pressures below 83 mmHg.
It is likely, although few figures are currently available, that the incidence of non-fatal but disabling stroke is equally raised.

There is therefore little doubt about the adverse effect of even modest rises of blood pressure on mortality and morbidity in American individuals, and most evidence suggests that these figures are applicable to other westernized communities. The magnitude of the problem has already been mentioned. Prevalence studies carried out in a number of areas of the world have demonstrated that as many as 15% of the population aged 50 or more years have casual diastolic pressures of 95 mmHg or more. Thus, Prineas, Stephens & Lovell(3), in a study in an Australian country town, found a percentage of this order in a population sample aged 50-59 years.

It is thus evident, therefore, that there exist in many communities large numbers of patients with mild hypertension and that in these patients morbidity and mortality from cardiovascular diseases and stroke can be expected to be substantially greater than in the population at large.

Leaving aside the logistical problem of identification of patients at risk and the problems of administering treatment to such patients, I now wish to examine the evidence as to the risks and benefits which may accrue from any attempt to offer widespread treatment to such patients.

It may be useful initially to attempt to assess the effects of treatment on the severely hypertensive patient, since this may offer some guidelines to the problem of deciding at what blood pressure level treatment can be justified.

There is clear evidence that in severe hypertension, drug treatment relieves symptoms, prolongs life, and reduces the incidence of many morbid events. The most convincing study was that of the Veteran's Administration Cooperative Study(4) which had to be abandoned after 20 months because of the high incidence of major complications in the untreated group. Few other controlled trials of antihypertensive drug treatment have been undertaken in severe hypertension. There have also been a number of studies in which the prognosis of treated patients has been examined. Thus, Breckenbridge, Dollery & Parry(5) examined the prognosis of patients treated for hypertension at the Postgraduate Medical School, London. Several striking points emerged. Firstly, a comparison of five-year survival rates for the periods 1952-59 and 1960-67 showed that in the latter period there had been a substantial improvement in outlook for treated patients; this seems likely to be due to the improved drugs available in the latter period with consequent improvement in blood pressure control. Secondly, patients who presented with diastolic pressures in excess of 140 mmHg had a much lower five-year survival than the less severely hypertensive patients, mainly because of a higher incidence of renal failure. Patients with diastolic pressures from 90 to 130 mmHg seemed to have five-year survival periods which were about 90-95% and which were little affected by the initial height of the diastolic pressure within this range. In all series so far reported it has been found that the major reduction in mortality and morbidity has been due to a reduced incidence of stroke and congestive heart failure. Deterioration of renal function is uncommon in treated patients unless moderate renal insufficiency is present at the start of therapy. Although the incidence of stroke is greatly reduced by treatment, the incidence of myocardial infarction is little affected by treatment of severe hypertension, and there is general agreement that myocardial infarction is
the commonest major complication in the treated hypertensive patient. It is not clear whether this reflects that a degree of reduction in blood pressure adequate to control heart failure or stroke is not adequate to prevent continuation of the vascular disease of the coronary arteries, or whether it can be taken as an argument to suggest the need for earlier treatment. It is also possible that hypertension and myocardial infarction are closely associated diseases rather than hypertension predisposing to myocardial infarction. Finally, it is possible that treatment of hypertension may in some way be concerned in the process of actually inducing myocardial infarction.

It seems likely that the results which have been obtained in treating the more severe hypertensive patient will prove applicable to the patient with less severe or mild hypertension. Indeed, the results obtained in the Veteran's Administration Cooperative Study of patients with diastolic blood pressures between 90 to 114 mmHg(6) strongly suggest that this will prove to be the case. In this study there were 19 deaths in the placebo-treated group compared with 8 in the treated group, the difference being almost entirely attributable to a reduction in death from stroke. It is necessary to be cautious about accepting this study as conclusive evidence in favour of early treatment for mild hypertension since the patients were all male, mostly black, and their blood pressures were assessed after five days of hospital treatment, which makes them not comparable to a group with similar casual blood pressures. In spite of these difficulties, the study remains the best evidence so far available that treatment of mild to moderate hypertension is likely to benefit the patient by reducing mortality and morbidity. It has to be emphasized, however, that final proof of the benefits of antihypertensive drugs on a widespread scale in the borderline mild hypertensive patient has not yet become available.

On the possible debit side of the decision several factors have to be considered. Aside from the expense and the practical difficulties of the enormous numbers of patients to be treated, the side effects, both pharmacological and psychological of life-long treatment with antihypertensive drugs have to be considered. From what is known of the mortality rates of mild hypertension, if a marginal benefit were conferred, most patients would need drugs for 20 years and some for 30 years or more. Firm evidence on the effects of taking drugs for 20-30 years is not available, but it is clear that a side effect with quite a small incidence could result in a major incidence of disability. An example of this sort of problem is the problem of hypokalaemia or hyperuricaemia induced by the thiazide diuretics. Most diuretic drugs induce some reduction in total body potassium with or without hypokalaemia. The long-term (20-30 year) effect of this is quite uncertain, and the methods of establishing its presence are currently quite impracticable on a large scale. An incidence of death of one to two per thousand per annum owing to a reduction of total body potassium is conceivable, but would probably escape detection and be attributed to myocardial infarction, sudden death, pyelonephritis, or to whatever its clinical manifestation might be. Hyperuricaemia is a more tangible problem resulting from diuretic therapy. The serum uric acid rises to levels above 7.0 mg per 100 ml in about 50% of patients taking thiazides on a long-term basis. Clinical gout occurs in about 10-15% of patients, often requiring allopurinol or other therapy. The long-term effects of hyperuricaemia are not established but there is suspicion that it may cause renal tubular disease, and it has been linked epidemiologically with myocardial infarction. These are examples of the difficulties in
assessing the long-term effects of known metabolic effects of a very useful and widely used group of drugs. It hardly needs to be emphasized that other metabolic effects may occur which are unknown. The essential problem is that if, for example, the thiazide drugs already cause a mortality of 0.5% per annum in treated hypertensive patients, such a fact would be submerged in the mortality attributed to the hypertension itself unless it were of a distinctive and characteristic type such as an aplastic anaemia. In such an event, in the treatment of milder hypertension one cause of death might merely be substituted for another.

A second problem lies in the still comparatively high incidence of side effects. There is no doubt in my mind that alpha-methyl dopa is one of the most effective and least objectionable of hypotensive drugs, yet even this model drug is not without problems. The rare incidence of haemolytic anaemia or jaundice might be more spectacular if several million patients took the drug. More serious, however, is the comparatively high incidence of disorders of sexual function in men taking alpha-methyl dopa: impotence is a common symptom. In the severe hypertensive the benefits of the drug are sufficiently obvious to both physician and patient to make continuation acceptable. In mild hypertension, males are more at risk than females, yet impotence is a symptom not likely to be well tolerated in the young, symptomless man whose benefit from treatment may not be apparent for 20 years, if at all. Similar objections can be raised to almost all other pharmacological agents.

The empirical approach to the therapeutics of high blood pressure has served the community well in the last 20 years. The doctrine that reduction of blood pressure, irrespective of mechanism, will improve prognosis has proved to be sound when applied to the severe hypertensive. Over the same period, it has also become evident that when an underlying pathological cause is evident such as renal artery stenosis or primary aldosteronism, specific curative therapy is to be preferred. In dealing with the patient with mild hypertension, an increased mortality rate of 1% per annum involves 10 000 extra deaths per million, but leave 990 000 per million alive and well per year. In the face of such figures, given the uncertainties of the long-term effects of treatment, the way ahead must surely be to try to define more closely the factors other than casual blood pressure which distinguish those most at risk from those least at risk. Are the ones most at risk those whose blood pressures rise steadily over a few years? If this is the case, regular assessment rather than treatment for all might be appropriate. Are there metabolic or discernible biochemical disturbances evident in those most at risk? The proposition that plasma renin levels might be such a factor seems unfortunately to be discredited, but some such differentiation may yet be possible on other grounds.

It seems difficult to avoid the conclusion that the only solution to the dilemma of the mild hypertensive patient lies in the long run in solving the problems of pathogenesis and pathophysiology of the disease. While it may be possible to demonstrate that, overall, mortality from mild hypertension is significantly reduced by antihypertensive treatment, such a conclusion is less to be desired than a solution to the problems of defining more precisely the risk factors and underlying causes of this disease, and to developing a series of specific treatments for the different varieties of essential hypertension.
REFERENCES


DISCUSSION

Dr Werkö: The mild hypertensive may not be hypertensive at all. The question is whether the blood pressure is increasing with age or not. In the on-going study in Göteborg we screened a population of men around 50 years of age and followed up those whom we called "borderline hypertensives". All together, 531 men out of 1800 were within this group and this is almost 30% of the population. Two years later, 3% had developed symptoms of hypertension and were on treatment; 7.5% had progressed to elevated pressure above 160-175/95-115 mmHg; but 46% were on the same level and 38% had decreased down to normal blood pressure (below 160/95) without any treatment. What Dr Doyle said is thus important, that patients who are in the lower range of hypertension should be followed up, observed, and not necessarily treated from the start.

Dr Paul: Dr Doyle has expressed a conservative view and I think there is no question that this is one area in which we have a great deal of knowledge to be gained. I would believe it unfortunate, however, if the meeting left with the view that under no circumstances would we treat the patient with a blood pressure of modest elevation. I believe there are circumstances where with our current state of knowledge, some treatment is appropriate and that this should be done on a selective rather than on a routine basis. I was struck that the end-point that he was discussing was death which is a rather formidable change in status. If you have a 30-year-old man whose blood pressure either progresses or persists, with observation, at a level which is distinctly above the optimum, and particularly if this individual has other factors which make this risk factor more important, such as family history or hyperlipidaemia, one has
as a physician to consider the benefits of medical treatment. Accepting our lack of appropriate knowledge, I do not entirely agree with him that the use of thiazide diuretics is accompanied with as many disadvantages. It seems to me that the disadvantages are really very modest and that when one considers the individuals in the world today under treatment with thiazides it is remarkable how well they are tolerated rather than how badly. I would agree with him that with other agents we have more serious problems. I would just remind the group that I believe a person with a modest elevation, particularly in the younger age group, has to be considered on a selective basis and I believe it is appropriate for us, accepting the limitations of our knowledge, to treat certain of these patients because the alternatives may be worse.

Dr Doyle: Could I just comment briefly on Dr Paul's remarks, particularly about the thiazides. A number of the patients whose deaths were attributed to myocardial infarction indeed died of sudden death. I have no means of knowing any more than anybody else does whether that is in fact due to the reduction of total body potassium that almost all patients taking thiazides can be shown to have, if one uses a total body counter, or is indeed due to myocardial infarction. Now, clearly, if we are going to try to apply that kind of thinking to mild hypertension, one is really not in possession of the fact that a number of patients are already not being killed by thiazides: they have been given thiazides for treatment which is associated with heart failure and sudden death. The only point I want to make is that before we embark on treating people for 30 years with these drugs, we have to be pretty confident that we are not actually causing 100 people to survive and another 50 to die.

Dr Gross: A major problem is to follow up the patients carefully and to measure plasma potassium levels occasionally when they are on long-term treatment, and perhaps also to stop treatment when their blood pressure comes down, or to apply periods of treatment and of non-treatment instead of continuing long-term treatment for years. One of the most intriguing matters is what Dr Doyle called the additional risk factor. It is still enigmatic to me what turns a borderline case of hypertension into a more severe or even malignant case of hypertension. We still do not know why hypertension may suddenly become a malignant and rapidly progressing disease. On the other hand, high blood pressure can be stable for 30 years and nothing happens, and I think this is one of the most fascinating aspects of the pathogenesis of hypertension.

Dr Freis: I want to make a comment about thiazides and sudden death. I do not think one can say anything about it unless one has a control series of patients who are not taking thiazides and who have a similar degree of hypertension and heart disease. Of course, we had that opportunity in the Veteran's Administration Cooperative Study, and in that experience there were 6 patients who died suddenly in the control group and 4 in the treated group. Since all of the treated patients were getting thiazides and none of the control group were, this would indicate that there was no evidence to suggest that the sudden deaths were associated with the thiazides. Concerning the serum uric acid and hypokalaemia, we had an excess of hyperuricaemia of 20% in the treated patients; however, this was mild and asymptomatic in all cases, and it would fluctuate back and forth so that for one year the patient would be hypokalaemic and in another year he would not be. With respect to hyperuricaemia, if we took a value of 8 mg, we had in the beginning about 12% in both the control and treatment groups prior to randomization. During the post-randomization period the control
group had a 16% incidence and the treated group 30%, indicating that in 15% of the 30% that had hyperuricaemia it was probably due to the thiazide diuretics. On the other hand, there were only two patients who had developed gout out of 180 treated patients.

Dr Doyle: I would just like to make it clear that I think that thiazides are probably the best drug available at the moment for this particular problem; but I believe that since they were introduced only 12 or 13 years ago, we cannot say what their effects are over 30 years.

Dr Akinkugbe: In those who are involved in total community studies, the problem of size becomes real, for when you have screened your patients you have then to decide on a cut-off point for subjects with mild hypertension and how to start management. If you can, in fact, break these into two or three groups in whom the blood pressure does not rise much with age in the same community and another group in which it rises very fast, then you might be nearer to answering the problem. I also wonder whether one should not be looking at specific figures for specific age groups in order to determine the prognosis rather than taking a cut-off point which affects a very wide spectrum of ages.

Dr Strasser: Dr Werktö mentioned an important point, which was that about 30% of mild hypertensives were later found to be normotensive. Is there similar experience from other countries also and what do we really know about spontaneous regression of hypertension when random variation and so-called regression towards the mean is excluded? May I just add that there are several studies going on in which investigators are looking for haemodynamical parameters other than blood pressure. I understand that Dr Robertson is doing something of the kind and he might wish to make a brief comment?

Dr Robertson: At ABCC (Atomic Bomb Casualty Commission, Hiroshima) we have begun measuring systolic pressure at time intervals in a subgroup of the adult health study. The major purpose of the study was to look for some possible radiation effect; however, as a side product of this, we hope in the future to analyse the incidence of cardiovascular events by the systolic pressures with the concept that flow and the instantaneous flow rate may be related to endothelial surface damage in the arteries and may give sharper differentiation of those at higher risk, particularly in the hypertensives; those with higher flow might be at higher risk than those with normal flow.
It is generally conceded that elevated levels of blood pressure play an important role in the pathogenesis of stroke including cerebral haemorrhage and cerebral infarction, which are the most prominent causes of mortality in Japan. Mortality from cerebral haemorrhage has been more prominent than that from cerebral infarction, although the morbidity and mortality from atherothrombotic diseases have been increasing in recent years. Stroke, ischaemic heart disease, and cardiac failure in hypertension play a role as a direct and/or indirect cause of death, especially in the aged. Antihypertensive treatment in younger people have been evaluated to be effective in controlling accelerated hypertension, although this is not certain for mild hypertension. The effects of antihypertensive treatment in the aged have not been established. It would seem to be ineffective or rather harmful according to several investigators.

This report is concerned with the prognosis and pathology of untreated hypertension in patients in the older age group who were referred with mild hypertension and systolic hypertension, and also with the results of antihypertensive treatment on morbidity and mortality in these older hypertensive patients. This study was made at the Yokufu-kai geriatric home for the aged in Tokyo. All of the patients admitted in the annexed hospital were, after their death, autopsied. The subjects were aged over 60 years.

1. Survival and causes of death in untreated mild hypertension and systolic hypertension in the aged: 10-year prospective study

The clinical material investigated comprised 22 men and 33 women, aged from 60 to 69 years, and 38 men and 71 women, aged from 70 to 79 years. They were in good health and working in the home and were free from cerebrovascular and coronary heart disease on examination. The blood pressure was measured every week through two years. Thereafter these subjects were followed up over the ensuing ten years.

The survival rates after ten years decreased in order of both systolic and diastolic blood pressure levels. The periods at which the survival rate became 50% are shown in Table 1.

248
Table 1. Survival in old age of patients with mild hypertension

<table>
<thead>
<tr>
<th>Blood pressure</th>
<th>Age 60 - 69 years</th>
<th>Age 70 - 79 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of cases</td>
<td>Years to 50% survival rate</td>
</tr>
<tr>
<td>Systolic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;160 mmHg</td>
<td>28</td>
<td>10</td>
</tr>
<tr>
<td>160-199 mmHg</td>
<td>21</td>
<td>8.7</td>
</tr>
<tr>
<td>≥200 mmHg</td>
<td>6</td>
<td>3.0</td>
</tr>
<tr>
<td>Diastolic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;90 mmHg</td>
<td>29</td>
<td>10</td>
</tr>
<tr>
<td>90-109 mmHg</td>
<td>22</td>
<td>7.0</td>
</tr>
<tr>
<td>≥110 mmHg</td>
<td>4</td>
<td>2.4</td>
</tr>
</tbody>
</table>

Ten-year survival rates according to the grade of high blood pressure are shown in Table 2. The prognosis of grade 2 hypertension was the poorest and that of systolic hypertension in those aged 70-79 years was poor.

Causes of death during the 10-year follow-up are shown in Table 3. The incidence of cardiovascular deaths was high in systolic hypertension (S) and diastolic hypertension (G₁, G₂).

2. Causes of death and pathology of mild hypertension and systolic hypertension in the aged: retrospective study

Eight hundred and ninety-nine consecutive autopsied cases were investigated for the direct causes of death (Table 4) and the frequency of pathologically proved cerebral haemorrhage, cerebral infarction, and myocardial infarction related to the type and the grade of hypertension in the aged. The vascular lesions in the brain and the heart were taken into account when they were larger than a finger-tip in size (one diameter of the lesion was over 1 cm). The category and the grade of hypertension were classified as follows by the average values of blood pressure through one year from the time of admission to the geriatric home:

N No hypertension: \( S <160 \) / \( D <90 \)
S Systolic hypertension: \( S >160 \) / \( D <90 \)
G₁ Grade 1 hypertension: \( S >160 \) / \( D >90 \)
G₂ Grade 2 hypertension: \( S >180 \) / \( D >100 \) (exclude \( G_3 \))
G₃ Grade 3 hypertension: \( S >200 \) / \( D >110 \)
<table>
<thead>
<tr>
<th>Classification of hypertension</th>
<th>Age 60 - 69 years</th>
<th>Age 70 - 79 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of cases</td>
<td>10-year survival rate</td>
</tr>
<tr>
<td>N: No hypertension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S&lt; 160 D&lt; 90</td>
<td>33</td>
<td>52.1%</td>
</tr>
<tr>
<td>S: Systolic hypertension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S~160 D&lt; 90</td>
<td>6</td>
<td>66.6%</td>
</tr>
<tr>
<td>G1: Hypertension Grade 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S<del>160 D</del>90-109</td>
<td>17</td>
<td>23.6%</td>
</tr>
<tr>
<td>G2: Hypertension Grade 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S<del>160 D</del>110</td>
<td>4</td>
<td>0</td>
</tr>
</tbody>
</table>
Table 3. Causes of death during the 10-year follow-up period

<table>
<thead>
<tr>
<th>Classification of hypertension</th>
<th>No. of cases initially</th>
<th>No. of cases that died during 10 years</th>
<th>Causes of death&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Other causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>65</td>
<td>22 (33%)</td>
<td>0 (4.6%) 3 (4.6%) 0 2 (3.1%)</td>
<td>17 (26%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S</td>
<td>22</td>
<td>11 (50%)</td>
<td>2 (9.1%) 0 1 (0.5%) 2 (9.1%)</td>
<td>6 (27%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>G&lt;sub&gt;1&lt;/sub&gt;</td>
<td>64</td>
<td>22 (34%)</td>
<td>4 (6.2%) 3 (4.7%) 2 (3.1%) 6 (9.4%)</td>
<td>7 (11%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>G&lt;sub&gt;2&lt;/sub&gt;</td>
<td>13</td>
<td>8 (62%)</td>
<td>2 (15%) 1 (8%) 0 0</td>
<td>5 (38%)</td>
</tr>
</tbody>
</table>

<sup>a</sup> CH: cerebral haemorrhage
CI: cerebral infarction
MI: myocardial infarction
HF: heart failure
Table 4. Causes of death

<table>
<thead>
<tr>
<th>Classification of hypertension</th>
<th>No. of cases</th>
<th>Direct causes of death</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CH</td>
<td>CI</td>
<td>MI</td>
</tr>
<tr>
<td>N</td>
<td>256</td>
<td>7</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S</td>
<td>177</td>
<td>6</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>G₁</td>
<td>221</td>
<td>16</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>G₂</td>
<td>180</td>
<td>22</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>G₃</td>
<td>65</td>
<td>11</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a CH: Cerebral haemorrhage
b CI: Cerebral infarction
MI: Myocardial infarction
CVD: Cerebrovascular diseases
HD: Heart disease
RD: Renal disorders

Figures in parentheses are percentages.

The number and frequency of pathologically confirmed cases of cerebral haemorrhage, cerebral infarction, and myocardial infarction in this autopsy population is shown in Table 5.

On the whole, cardiovascular diseases as a cause of death were more frequent in systolic hypertension than in normotension, and were also more frequent in diastolic hypertension. Among them, the most prominent lesion as a cause of death was cerebral vascular diseases, especially cerebral haemorrhage. The frequency of cerebral haemorrhage was well correlated with the grade of diastolic hypertension.

Cerebral infarction was more frequent as a cause of death and pathologically proved lesion in systolic hypertension; it seemed to be frequent in diastolic hypertension. However, it was not so much correlated with the grade of diastolic hypertension as was cerebral haemorrhage.

The frequency of myocardial infarction was higher in systolic hypertension, but it was not related to the grade of diastolic hypertension.
Table 5. Pathologically proved incidence of CH, CI and MI

<table>
<thead>
<tr>
<th>Classification of hypertension</th>
<th>No. of cases</th>
<th>Pathologically proved</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CH</td>
<td>CI</td>
</tr>
<tr>
<td>N</td>
<td>256</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td>(7.4)(^a)</td>
<td>(14.1)</td>
</tr>
<tr>
<td>S</td>
<td>177</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>(6.8)</td>
<td>(19.2)</td>
</tr>
<tr>
<td>G(_1)</td>
<td>221</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>(11.3)</td>
<td>(20.0)</td>
</tr>
<tr>
<td>G(_2)</td>
<td>180</td>
<td>34</td>
</tr>
<tr>
<td></td>
<td>(18.9)</td>
<td>(15.0)</td>
</tr>
<tr>
<td>G(_3)</td>
<td>65</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>(20.0)</td>
<td>(18.5)</td>
</tr>
</tbody>
</table>

\(^a\) CH: cerebral haemorrhage; CI: cerebral infarction; MI: myocardial infarction.

\(^b\) Figures in parentheses are percentages.

3. Arteriosclerosis of the kidneys in mild hypertension and systolic hypertension in the aged

The narrowing index \((W/r)\) is calculated as the ratio of the thickness of the arterial wall \((W)\) and the radius of the artery \((r)\). Since direct measurement of \(W\) and \(r\) cannot give accurate values, the diameter of the artery \((D_a)\) and of the lumen \((D_l)\) are measured; \(W\) is then calculated from \(1/2 (D_a-D_l)\) and \(r\) from \(1/2 D_a\).

The narrowing index of arterioles \((<50 \mu m)\) and small arteries \((50-200 \mu m)\) was thus calculated. Eighty to 100 vessels were measured in one or two specimens of kidneys. Average values of \(W/r\) were presented as a narrowing index. The narrowing index of small arteries in the kidneys was investigated in relation to the type and grade of hypertension. The classification of hypertension was the same as that given in the previous section. The blood pressure in the aged was classified by mean values of blood pressure measured every week for one or two years before death. The controls were selected autopsied cases of subjects aged from 20 to 29 years and 40 to 49 years who had had normal blood pressure and no cardiovascular or renal disease. The narrowing indices of the small arteries in the various types and grades of hypertension are shown in Table 6.

Narrowing of the small arteries in the kidneys developed with advancing age. There were no definite differences in the narrowing index of the small arteries between cases of normotension and borderline hypertension in the aged. The narrowing index of the small arteries increased in systolic
hypertension. It was more prominent in diastolic hypertension than in systolic hypertension. The grade of narrowing seemed to be related to the grade of diastolic hypertension.

Table 6. Narrowing index of small renal arteries in hypertension of the aged

<table>
<thead>
<tr>
<th>Hypertension Grade</th>
<th>Age (mean) (years)</th>
<th>No. of cases</th>
<th>Narrowing index of small arteries ( \frac{W}{r} ) (mean) ± (SE) (μm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normotension: S &lt; 140 D &lt; 90</td>
<td>24</td>
<td>5</td>
<td>0.416 ± 0.02</td>
</tr>
<tr>
<td>Normotension: S &lt; 140 D &lt; 90</td>
<td>43</td>
<td>5</td>
<td>0.479 ± 0.03</td>
</tr>
<tr>
<td>Normotension: S &lt; 140 D &lt; 90</td>
<td>70</td>
<td>5</td>
<td>0.496 ± 0.03</td>
</tr>
<tr>
<td>Borderline hypertension: S 140-159 D &lt; 90</td>
<td>81</td>
<td>5</td>
<td>0.494 ± 0.01</td>
</tr>
<tr>
<td>Systolic hypertension: S ≥160 D &lt; 90</td>
<td>82</td>
<td>20</td>
<td>0.554 ± 0.01</td>
</tr>
<tr>
<td>Grade 1 hypertension: S ≥160 D 90-99</td>
<td>80</td>
<td>15</td>
<td>0.601 ± 0.02</td>
</tr>
<tr>
<td>Grade 2 hypertension: S ≥180 D ≥100</td>
<td>78</td>
<td>12</td>
<td>0.573 ± 0.01</td>
</tr>
<tr>
<td>Grade 3 hypertension: S ≥200 D ≥110</td>
<td>74</td>
<td>5</td>
<td>0.633 ± 0.01</td>
</tr>
</tbody>
</table>

\( W \) = thickness of the wall.
\( r \) = radius of the vessel.
4. Atherosclerosis of coronary arteries and cerebral arteries in mild hypertension in the aged

One hundred and thirty-two cases with a history of blood pressure measurement regularly for 10 years or longer were selected for the study. There were 33 males and 99 females and all the cases were over 70 years of age. Determination of serum total cholesterol was performed at least five times in 95 cases.

The coronary arteries were classified into six grades of narrowing and the cerebral arteries into four grades.

Correlation coefficients of severity of atherosclerosis with blood pressure and total serum cholesterol are shown in Table 7.

<table>
<thead>
<tr>
<th>Artery</th>
<th>Systolic pressure</th>
<th>Diastolic pressure</th>
<th>Total serum cholesterol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary</td>
<td>0.319*</td>
<td>0.064</td>
<td>0.284*</td>
</tr>
<tr>
<td>Cerebral</td>
<td>0.434*</td>
<td>0.284*</td>
<td>0.149</td>
</tr>
</tbody>
</table>

* P < 0.01.

A significant correlation was observed between the mean annual systolic pressure and the narrowing of both coronary and cerebral arteries. On the other hand, the diastolic blood pressure was significantly correlated with the narrowing of cerebral arteries, but not with that of coronary arteries. The serum total cholesterol was significantly correlated with the narrowing of coronary arteries but not with that of cerebral arteries.

5. Effects of antihypertensive treatment for systolic hypertension and mild hypertension in the aged: 5-year study

All the patients were outpatients who were healthy and working in the geriatric home. Their ages were from 60 to 90 years. Control subjects were matched in age, sex, blood pressure, and ECG findings. Blood pressure was measured every week for one or two years in each individual. Thereafter, the type and the grade of hypertension were classified. An antihypertensive drug (diuretics) was given to 63 patients and a placebo to 49 control patients.

The results of the 5-year follow-up study are as follows: in mild systolic hypertension, the incidence of cardiovascular attacks and deaths was 8.3% in the treated group and 28% in the control group. In moderate systolic hypertension (S = 180; D = 90), the incidence was 7.2% in the treated group and 44% in the control group. In mild diastolic hypertension, the incidence was 16.3% in the treated group and 23% in the control group.
In summary, the incidence of cardiovascular attacks including deaths was 12.7% in the treated group and 32.5% in the control group. Antihypertensive treatment for hypertension in the aged seems to be effective in preventing cardiovascular attacks and the resulting deaths. However, the 5-year survival rates could not be improved.

DISCUSSION

Dr Gross: May I ask you: What was your antihypertensive treatment? Was it standardized?

Dr Ikeda: Diuretics.

Dr Gross: Only diuretics, nothing else?

Dr Ikeda: Nothing else. We used only diuretics in this group.

Dr Freis: I just want to ask whether you had many cases of sudden cardiac death in your group receiving diuretics?

Dr Ikeda: I have had no case of ventricular fibrillation nor sudden cardiac death in this group. It may be argued whether hypotensive drugs should be given to the aged or not. The decrease of potassium or the increase of uric acid are considered to be side effects. Overdoses of hypotensive drugs would be dangerous and we have to be careful in applying hypotensive therapy to populations at large, because there are individual differences and it would be very difficult to control all the conditions.

Dr Kagan: It is commonly expressed clinical knowledge that a lowering of blood pressure in aged people may lead to serious cardiovascular consequences. I would like somebody who has such evidence to cite it.

Dr Werko: Lowering of the blood pressure, as long as it is controlled, is not dangerous in the aged. Many old people have more orthostatic hypotension, which makes it necessary to measure blood pressure both standing and sitting or lying down, both before you start treatment and while on treatment.

Dr Toole: Dr Hoobler will address himself to that problem tomorrow. I believe that he will say that lowering the blood pressure of patients who have had a stroke is not dangerous.

Dr Fries: There is confusion about lowering the blood pressure and the incidence of stroke. If the blood pressure is lowered by acute blood loss this is highly dangerous in producing thrombotic stroke, particularly in old people. However, if the blood volume and cardiac output are normal and the blood velocity is normal, as is the case when you lower blood pressure with any hypotensive agent, it is an entirely different haemodynamic situation from haemorrhagic hypotension and it rarely leads to stroke. It occasionally will and there are clearly defined instances in old people where the blood pressure was lowered drastically with drugs. For example, this was reported with the ganglion blocking drugs resulting in thrombotic stroke but this is quite unusual.
Dr Kameyama: We have to deal separately with cerebral haemorrhage and infarction. Dr Ikeda said that a distinction should be made between cerebral infarctions, big and small ones. I agree with him on this point. In our results, the frequency of fatal cerebral infarctions is not always directly related to the presence of high blood pressure, while that of the small or non-fatal ones was closely related to hypertension.

Dr Ashizawa: We have to define the concept of old people. Who are the old people? The concept varies or differs from one country to another. We can use neither the chronological age nor the physiological age unless these are properly defined. Do you have any criteria?

Dr Ikeda: A definition of old age is also needed when making international comparisons. I think one can use 65 or 70 years of age as objective criteria, but I do not have a clear-cut answer to exactly which age should be taken.
NINE THERAPEUTIC TRIALS
IN MILD HYPERTENSION

by
R. Reader

The general principle that a raised blood pressure is associated with shortened life expectancy, and its corollary that the reduction of hypertension will lead to increased life expectancy are now widely accepted. Because raised blood pressure is so common in many countries throughout the world, the opportunity to reduce morbidity and mortality from hypertensive disease by community control programmes must be seriously considered by health authorities in such countries.

Primary prevention of hypertension is not yet feasible since it requires information about etiological mechanisms which are not yet available. This important aspect is the subject of other papers in this seminar.

In the meantime, there is good evidence that pharmacological control of hypertension, both presymptomatic and after symptoms have developed, will significantly improve the prognosis. In some countries there has been a fall in national mortality rates from hypertensive diseases, very probably reflecting the benefit of hypotensive drugs which were introduced about 1950 (Epidemiological and Vital Statistics Report, WHO, 1967, Vol. 20, Nos 9 and 10). In Australia, for example, the mortality rate between 1950 and 1971 for men and women aged 30 to 64 years has fallen from 82 to 60 per 100,000 for cerebrovascular diseases and from 32 to 8 for hypertensive heart disease.

Population surveys in many countries have shown a high prevalence of unrecognized hypertension, and also a high prevalence of known hypertensives who are inadequately controlled. Data from three studies in the USA are summarized in a report of the Intersociety Commission for Heart Disease Resources. One such study in Australia showed that in a sample of 1515 (total community, 1744) men and women, aged 50 to 59 years, 21% had diastolic pressures greater than 110 mmHg or were on treatment for hypertension, and one-third of these were unaware that their blood pressure was raised.

All of this points to the need for public health programmes involving the identification of unrecognized hypertensive subjects by some form of screening, and the institution of effective treatment. However, the simple approach, to conduct a mass screening of all adults and to provide treatment for all subjects with systolic or diastolic blood pressure above a given threshold, is clearly not acceptable on the basis of present knowledge.
Because treatment involves the possibility of undesirable side-effects of the pharmacological agents, long-term and possibly a lifetime of medical care for the subjects, and great expense of drugs and medical care, it is important that studies should be made in the hypertensive population to identify subgroups who will respond to pharmacological treatment on a scale to justify the programme. Such studies should be based on the efficacy of medical care and the cooperation of patients commensurate with that likely to apply in the community programme envisaged. It is clear that the benefits that might be expected from a fully effective mass screening programme with ideal patient cooperation and medical management will be considerably attenuated in the practical situation.

The most significant predictive factor, which still needs evaluation in the light of the above, is the actual level of blood pressure, particularly in relation to age and sex. While there are no doubts about the benefits of treatment in severe hypertension, the problem of mild or borderline hypertension is by no means clear. There is little doubt that prognosis is impaired even at these levels, but the net benefit of therapy is not clear.

The one very important study bearing on this is the therapeutic trial conducted by the Veterans' Administration Cooperative Study Group. This gave certain clear guidelines. It dealt with men aged from 24 to 75 years with a level of hypertension that persisted through a period of four to six days' bed rest. Non-cooperative subjects were excluded. The men were treated by a fixed dose regimen of hydrochlorothiazide, hydralazine, and reserpine (alternative regimens were available if side-effects occurred). Under these circumstances, in those with diastolic pressures from 90 to 114 mmHg there were 28.9% with complicating events among those on the placebo compared with 11.8% in treated subjects during an average period of 3.3 years (there were respectively 9.8% and 4.3% deaths).

The scale of benefit in both studies was thus considerable. However, multiple regression studies showed that the benefit was less in those of lower age groups and blood pressures at commencement, and with no complicating cardiovascular or renal conditions.

Many have assumed from these results that benefit on a significant scale would arise from treating every person in a community with diastolic blood pressures (DBP) greater than 90 mmHg. However, it is likely that the Veterans' Administration study in the USA refers to subjects with more severely affected circulatory systems than those with similar blood pressure levels determined at casual examination. This is supported by the considerable number of subjects with existing cardiovascular or renal complications (219 of 380 subjects with DBP, 90-114), and the high incidence of complications in the control group (56 of 194 in 3.3 years).

The study provided no data for females, nor could it provide information relating the effectiveness of treatment in a large-scale community programme provided by non-specialized medical services.

Largely stimulated by the Veterans' Administration study, but requiring more essential information relevant to extensive open community programmes, groups in a number of countries independently have commenced or are planning to commence screening and therapeutic trials to provide such data. These include:

2. Medical Research Council of Great Britain (MRC), United Kingdom. Dr W. Miall, Secretary, Planning Committee, London.


4. National Heart Foundation of Australia Hypertension Screening and Therapeutic Trial (NBFS). Dr Ralph Reader, Chairman, Management Committee, Canberra.

5. Veterans' Administration Cooperative Study (VA) on Antihypertensive Therapy: Mild Hypertension. USA. Dr Mitchell Perry, Chairman, St Louis.

6. United States Public Health Service Hospital Study (USPHS). Dr W. McFate Smith, San Francisco.

7. The Hypertension Detection and Follow-up Study (HDFP), National Heart and Lung Institute, USA. Dr W. Zukel, Director for Community Programs, NHLI, Washington. Dr A. Shapiro, Chairman, Policy Committee, Pittsburgh. Dr H. Langford, Chairman, Coordinating Committee, Jackson. Dr Richard Remington, Director, Coordinating Centre, Houston.

The first six were specifically oriented to mild or borderline hypertension; the seventh, the HDFP study in the USA, covered all levels of hypertension, including mild hypertension. Two other groups are conducting multifactor intervention trials, the results of which will include data on the treatment of mild hypertension. These are:

8. The Göteborg Trial. Sahlgren's Hospital, Göteborg. Dr G. Tibblin and Dr Berglund.

9. Heart Disease Prevention Project. St Mary's Hospital. Professor G. Rose and Dr D. Christie, London.

At the invitation of the Cardiovascular Disease unit of WHO in May 1973, I visited each of these groups and the following summaries and Tables are taken from my report on those visits. The protocol for the nine trials is given in Table 1 and the baseline parameters being recorded are shown in Table 2.

GREA STUDY, PARIS

The study is sponsored by the French National Institute for Health and Medical Research. The populations studied are the personnel in the Civil Police of Paris, which includes some office workers and a few females. Some 8000 persons aged over 40 years will be screened in the first year and the remainder, between 22 and 40 years, over the next three years.

Stated objectives

To obtain information on the prevalence, natural history, and prognostic factors of severe, moderate, and labile hypertension; to evaluate
### Table 1. Protocol for the nine therapeutic trials in mild hypertension

<table>
<thead>
<tr>
<th>STUDY POPULATION</th>
<th>Paris (GREA)</th>
<th>London (St Thomas')</th>
<th>London (MRC)</th>
<th>USA (IDFP)</th>
<th>USA (VA)</th>
<th>USA (USPHS)</th>
<th>Australia (NBPS)</th>
<th>London (St Mary's)</th>
<th>Orebro</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>M</td>
<td>F</td>
<td>M</td>
<td>F</td>
<td>M &amp; F</td>
<td>H</td>
<td>F</td>
<td>M &amp; F</td>
<td>H</td>
</tr>
<tr>
<td>No. in defined pop. (n)</td>
<td>35 000</td>
<td>1 612</td>
<td>84 400</td>
<td>98 500</td>
<td>160 000</td>
<td>62 000</td>
<td>19 000</td>
<td>30 000</td>
<td></td>
</tr>
<tr>
<td>Estimated No. screened (ns)</td>
<td>35 000</td>
<td>1 400</td>
<td>63 300</td>
<td>73 800</td>
<td>100 000</td>
<td>200 000</td>
<td>43 000</td>
<td>15 000</td>
<td></td>
</tr>
<tr>
<td>No. rand. (2N)</td>
<td>2 000</td>
<td>160</td>
<td>8 800</td>
<td>9 000</td>
<td>10 500</td>
<td>8 000</td>
<td>312 78</td>
<td>3 640</td>
<td></td>
</tr>
<tr>
<td>Ell%</td>
<td>5.7</td>
<td>10</td>
<td>6.5</td>
<td>6.5</td>
<td>7+</td>
<td>4</td>
<td>7+</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Duration (years)</td>
<td>5+</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>10</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>BLOOD PRESSURE RANGE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP</td>
<td>160-180</td>
<td>&lt;200</td>
<td>&gt;90</td>
<td>90-104</td>
<td>&gt;90-104</td>
<td>90-114</td>
<td>95-109</td>
<td>&gt;115</td>
<td></td>
</tr>
<tr>
<td>DBP</td>
<td>95-115</td>
<td>90-114</td>
<td>&gt;90</td>
<td>90-104</td>
<td>&gt;90-104</td>
<td>90-114</td>
<td>95-109</td>
<td>&gt;115</td>
<td></td>
</tr>
<tr>
<td>Diastolic phase</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>DESIGN OF STUDY</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p&lt;</td>
<td>0.05</td>
<td>(not appl.)</td>
<td>0.01</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
<td>0.05</td>
<td>(not appl.)</td>
</tr>
<tr>
<td>q</td>
<td>0.05</td>
<td>0.05</td>
<td>0.1</td>
<td>0.05</td>
<td>0.05</td>
<td>0.1</td>
<td>0.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estimated av. drop-out p.a.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estimated reduction trial-end-points</td>
<td>20%</td>
<td>40%</td>
<td>40%</td>
<td>50%</td>
<td>25%</td>
<td>40%</td>
<td>157</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subjects &amp; &quot;Blind&quot;</td>
<td>-</td>
<td>X</td>
<td>X</td>
<td>-</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Treatment management &amp; &quot;Blind&quot;</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>X</td>
<td>X</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Evaluation of end-points &amp; &quot;Blind&quot;</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>EXCLUSION FACTORS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>On therapy for hypertension</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>-</td>
<td>X</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of CVA</td>
<td>-</td>
<td>X</td>
<td>X</td>
<td>-</td>
<td>X</td>
<td>X</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of M.I.</td>
<td>-</td>
<td>X</td>
<td>X</td>
<td>-</td>
<td>X</td>
<td>X</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of A.P.</td>
<td>-</td>
<td>-</td>
<td>X</td>
<td>-</td>
<td>X</td>
<td>X</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gout</td>
<td>-</td>
<td>X</td>
<td>X</td>
<td>-</td>
<td>X</td>
<td>X</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>-</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Asthma</td>
<td>X</td>
<td>X</td>
<td>?</td>
<td>-</td>
<td>X</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral contraceptives</td>
<td>X</td>
<td>?</td>
<td>-</td>
<td>?</td>
<td>X</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other factors</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>-</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

---

* R.Z: Random zero; LSH: London School of Hygiene; S: Standard sphygmmomanometer.  
* In some cases exclusion is qualified according to the interval since the event or the presence of objective signs.
Table 2. Parameters recorded at baseline

<table>
<thead>
<tr>
<th></th>
<th>Paris (GREA)</th>
<th>London (St Thomas')</th>
<th>London (MRC)</th>
<th>USA (HDFP)</th>
<th>USA (VA)</th>
<th>USA (USPHS)</th>
<th>Australia (NBPS)</th>
<th>London (St Mary's)</th>
<th>Göteborg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood urea</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Electrolytes</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cholesterol</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resting (ECG)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exercise (ECG)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minn. code</td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>X-ray chest</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.G.O.T.</td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spirometry</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

These parameters are recorded partly for evaluating whether the subject is suitable or not for admission to the trial and partly as baseline data for monitoring the subjects' experience, either as a control or treated subject. As well as the items listed in the table, all nine studies include: a general history and physical examination (though the detail varies considerably), enquiry as to the knowledge of existing hypertension and whether on treatment for it, whether or not the subject is a tobacco smoker, fundal examination (except at Göteborg), and recording of height and weight. Examination of renin status is carried out on all subjects in the Paris study and may be included as local options in some other studies.

Other special studies for which data are recorded at baseline include: physical activity status of the subject (St Mary's; GREA; HDFP, USA and VA, USA), employment status (HDFP and VA studies, USA), education status (USPHS), and the effect of hypertension and its treatment on the patients' economic situation and work performance (GREA; St Thomas'; MRC). A special study of psychological factors in the hypertensive treated and control subjects and also in a reference group of matched normal subjects is being made in a subset of the Paris study population. The HDFP includes frozen storage of a sample of serum in case further tests have to be carried out in the future.
the screening methods, benefits and costs of treatment, and adherence to treatment regimen; and to obtain information on the etiology and pathogenesis of hypertension with particular reference to obesity, psychological factors, tobacco, renal pathology, and hereditary factors, and the renin-angiotensin and adrenergic systems.

Screening

There are two screening visits, the first, conducted simultaneously at three centres, staffed by 11 doctors, aims to screen 80 patients per day. Blood pressure is taken by technicians with the subject seated in a comfortable armchair, the first reading after five minutes' rest. This is followed by a detailed history and physical examination by a doctor. If one or both readings are greater than 160 SBP and/or 95 DBP (150/90 under 30 years), the subjects are seen at the second screening. If not, they are dismissed.

At the second screening a single blood pressure measurement is taken. This will take place at one centre and in the first instance consists of blood pressure measurement after five minutes in an armchair. Subsequently, a three-hour examination by a doctor involves detailed supplementary history and physical examination, blood sample for biochemistry and renin (PRA) taken after one hour sitting in the armchair. Blood pressure is taken after one hour of sitting, then after 10 knee-bending exercises (pulse rate is taken by the BP technicians at each blood pressure measurement throughout the screening). If the BP exceeds 180/115, the subject is admitted to hospital for detailed investigation. If it is between 160/95 and 180/115 and there are no exclusion factors, the subject is admitted to the trial. There are subclassifications depending on whether one, two, or three of the readings are above 160/95. If below this level, the subject is regarded as labile hypertension and dismissed.

At this examination a detailed psychological examination is made in a subgroup of hypertensives by a psychologist and also a detailed examination of economic factors including the cost of medical care in the previous 12 months. For the purposes of the two latter observations and also other physiological examinations a comparable control group (non-hypertensive) will also be recalled for examination at this time.

Management

All persons under 40 years of age will be seen at the clinic at three-year intervals. All those over 40 years of age will be seen at the clinic at one-year intervals. In the meantime, all hypertensives will be referred to their own doctor for treatment according to the doctor's own practice. No directions as to treatment are given.

Evaluation is made at the yearly or three-yearly visits to the study clinic. However, information in intermediate events will be available through the normal police medical service. There is no clear-cut definition of the duration of the trial but it is envisaged that it will go on indefinitely and subjects will be followed up to, perhaps, the age of 65 years.
ST THOMAS' STUDY, LONDON

The study is conducted by the Department of Epidemiology and Social Medicine of St Thomas' Hospital, London. It was originally intended to be a cooperative study in a number of general practices. Because of difficulty in gaining cooperation, a feasibility study has now been set up in the St Thomas' Medical School General Practitioner group in Lambeth. There are six doctors in the group. The total practice list is 9500 of whom 1612 are men aged between 35 and 64 years, the base population. The trial has been undertaken with the object of demonstrating practicability to other practitioner groups. It is not, as presently designed, capable of answering a question about the effectiveness of treatment, but it is hoped to pool the results with the MRC trial.

Stated objectives

To measure the effect of drug treatment on mortality and morbidity, to measure the prevalence of hypertension, known and unknown, in a medical practice, to evaluate long-term adherence to hypotensive therapy, and to assess feasibility and the cost of screening and treatment.

Screening

Subjects are invited to attend at special screening clinics. At the first visit, blood pressure is taken twice with the subject sitting. The first reading is taken by a doctor or a nurse immediately on entry and the second two to three minutes later. In the interval a brief history is taken. Those with a mean diastolic pressure of 90 mmHg or more are invited to a second visit. The definitive pressure is the mean of the four readings, unless at the subsequent clinic visit DBP is less than 90 or more than 114, in which case the mean of six readings is taken.

Management

Subjects are seen monthly for the first three months and then three-monthly. Annual examinations include ECG and blood tests. All tablets have riboflavine incorporated. Experience so far has been that this has not helped assessment of adherence because of difficulties in evaluating the urine appearance.

Progress results

Of the 900 who attended the first screening, details of 700 have been analysed: 75% had diastolic pressure below 90, 22% between 90 and 114, and 2% above 114. Of 24% attending the second screening, half were accepted into the trial. Exclusions at the second screening were because the mean DBP on this occasion was below 90 (80%) or above 114 (8%), and for other reasons (12%). It is of interest that of 40 in the treated group, only six have required a second drug during the first six months of the trial.

MRC TRIAL, LONDON

The trial is under the sponsorship of the British Medical Research Council. It is a multicentric trial in which hypertensive subjects are recruited from industrial groups, lists of patients in several general practitioner groups, or simply the hypertensive patients of a hospital.
There are eight or nine groups involved. In some centres, subjects will be related to a total base population; in other centres they will not. In the first instance a pilot trial of some 500 to 1000 subjects will be conducted for one to two years.

**Stated objectives**

The primary objective is to determine whether the regimen of treatment reduces morbidity and mortality from cardiovascular renal complications. A second objective is to determine whether early effective treatment alters the subsequent course after discontinuation of therapy.

**Screening**

Blood pressure will be taken seated and after a period of three minutes. It will be taken twice at each of two screening attendances. The definitive pressure is the average of the four readings. A random zero sphygmomanometer will be used.

**Therapeutic regimen and management**

The subjects will be managed by the centre staff in some cases, general practitioners, hospital specialists, and industrial medical officers in others. Patients will be seen at fortnightly intervals for the first three months, and at three-monthly intervals for the first year, and at six-monthly intervals subsequently. The placebo dose will not be manipulated. There will be two separate drug regimens and one objective will be to test the efficacy of one against the other. The first consists of a thiazide diuretic with alpha-methyldopa as the second-order drug, the second regimen consists of a beta-blocker with guanethidine as the second-order drug. Assessment will be by a panel unaware of the subject's treatment group. As well as the end-points (indicated in Table 3) analysis will be made of the control of blood pressure levels, the duration of and reasons for sickness causing absence from work, the adherence rate of patients, and the magnitude of adverse psychological effects.

**NHLI STUDY, USA**

This is a study in 14 centres, the number of subjects in each centre varying from 600 to 1200. The trial is managed by a Steering Committee, of which Dr Herbert Langford is Chairman, with representatives from each of the 14 centres, from the coordinating centre, the biochemical laboratory, and the ECG centre. A Policy and Advisory Committee is chaired by Dr A. P. Shapiro. While the trial is concerned with all levels of hypertension, the study population will be stratified into three levels of diastolic blood pressure, 90-104, 105-114, and >114 so that analysis of the results for mild hypertension will be possible.

**Stated objectives**

The primary objective is to assess the ability of a step-care programme (compared with regular care) to reduce mortality and morbidity associated with high blood pressure. The primary end-point is mortality and the secondary end-point is cause-specific mortality. Intermediate end-points (hard) include malignant hypertension, ischaemic heart disease (on ECG), cardiac enlargement on X-ray, left ventricular hypertrophy (ECG).
Table 3. Specified end-points and drugs used for treatment

<table>
<thead>
<tr>
<th>SPECIFIED TRIAL END-POINTS</th>
<th>Paris (GREA)</th>
<th>London (St Thomas')</th>
<th>London (MRC)</th>
<th>USA (HDFP)</th>
<th>USA (VA)</th>
<th>USA (USPHS)</th>
<th>Australia (NRPS)</th>
<th>London (St Mary's)</th>
<th>Göteborg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death: all causes</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Death due to hypertension</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Angina pectoris</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Stroke</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Congestive cardiac failure</td>
<td>?</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Malignant or accelerated hypertension</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal failure</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Retinopathy</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Hypertensive encephalopathy</td>
<td>?</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>

TREATMENT (Number indicates 1st, 2nd, 3rd order drugs)

<table>
<thead>
<tr>
<th>Controlled by</th>
<th>GP</th>
<th>GP</th>
<th>GF or Ind.MO</th>
<th>Clinic staff</th>
<th>Clinic staff</th>
<th>GP &amp; clinic staff</th>
<th>GF or Ind.MO</th>
<th>Clinic staff</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fixed dose (F) or Step-care (S)</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>F</td>
<td>F</td>
<td>S</td>
<td>F</td>
</tr>
<tr>
<td>Thiazide diuretic</td>
<td>U</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>β-blocker</td>
<td>U</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>α-methyldopa</td>
<td>U</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Reserpine or rauwolfia</td>
<td>U</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Hydralazine</td>
<td>U</td>
<td></td>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Guanethidine</td>
<td>U</td>
<td></td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>-</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>-</td>
</tr>
</tbody>
</table>

Commencement date

| Number screened (May 1973) | 3 433 | 900  | 23 000 | 390  | 400  | 6 316 | 6 846 |
| Number randomized (May 1973) | 38  | 80   | 1 500  | 390  | 400  | 6 316 | 6 846 |

* U = unspecified.
Intermediate end-points (soft) include positive Rose questionnaire for myocardial infarction or angina pectoris, serum creatinine levels, congestive cardiac failure, retinopathy, elevation of DBP, and deterioration in life style. Side-effects and toxic effects of drugs will also be evaluated. Finally, it is proposed to evaluate the influence of the intervention in hypertension on the total mortality of the community in which the programme is implemented. Other objectives are to further the knowledge on the clinical course and prognosis of raised blood pressure and to determine the resources in terms of health manpower, organization, administration, and cost of a public health programme of this kind and the rate of participation of individuals in it.

Screening and recruitment

Screening will be by house-to-house visits by trained screeners who will take a brief history and measure blood pressure three times. Those in whom diastolic pressure on the second and third readings average 95 mmHg or more will be requested to attend the clinic within one to two weeks. At the clinic visit, further examination and biochemical tests, ECG, and X-ray are arranged. The blood pressure is taken four times, twice by standard sphygmomanometer and twice by random zero machine. The definitive blood pressure is the average of two random zero readings. If the average DBP is 90 mmHg and if the patient agrees to participate, a randomization envelope is allocated but not opened. A second clinic visit leads to more detailed examination and a repeat of blood tests including fasting blood sugar, postural effects on ECG, etc. There are no exclusions.

Management

The treatment regimen consists of up to five steps using a diuretic, an anti-adrenergic, hydralazine, guanethidine, and other drugs if necessary. The target of treatment is to reduce diastolic blood pressure to 90 mmHg or to 10 mmHg below the baseline, whichever is the lower. All definitive blood pressure readings are taken sitting.

A step-down procedure is laid down for those subjects who remain well controlled for periods of eight months and longer.

THE COORDINATION CENTRE, HOUSTON

Coordination is the responsibility of the members of the Disease Control Section of the School of Public Health, University of Texas, Houston, who undertake training of screeners and interviewers, collection of data from all centres, editing, key punching, programming, and surveillance of quality control for all centres. The programme has now been in operation for slightly more than two months. Some 43 000 forms have been received so far.

VETERANS' ADMINISTRATION STUDY, USA

This trial has been planned under the auspices of the Veterans' Administration as a follow-up to the Freis study. A decision to implement it has not yet been taken.

The study population of hypertensive subjects will be recruited from all possible sources. These will include all subjects attending Veterans' Administration hospitals for whatever cause, both inpatients and outpatients and their families. Efforts will also be made to recruit patients from the general community. There will be no attempt to define a population
base. The full trial will involve 20 centres. A feasibility study involving four centres for two years is envisaged in the first instance.

**Stated objectives**

The object of the study is to determine the advantages and disadvantages of treating mild hypertension in relatively young subjects. It particularly asks the question whether treatment before progression to complications is effective in preventing myocardial infarction and other evidence of coronary heart disease. Other objectives are to find the incidence of complications in untreated mild hypertension, the extent of iatrogenic disease, and whether treatment in the early stages (while pressure is low and there are no complications) has advantages over delaying treatment until the blood pressure rises to higher levels.

**Screening**

The screening procedure will consist of three visits one month apart, at each of which three readings will be taken. All subjects with average diastolic pressure between 90-115 mmHg at the first visit will be reviewed at the second and third screening visits. The definitive pressure will be taken as the average of all nine readings and those with diastolic pressures of 90-105 mmHg will be randomized into the trial. It is also necessary that subjects to be accepted must have readings between 90-105 mmHg at the third screening visit. During screening visits, the subjects' compliance will be tested by pill counts and urinary fluorescence.

**Treatment**

Treatment will be by the clinic staff. The regimen will be a fixed two-step regimen using chlorthalidone 50 or 100 mg daily with reserpine 0.25 mg daily as the second-order drug. The procedure will be double-blind. Subjects in either group whose blood pressure rises above 105 will be dealt with as follows: a single reading above 120 will lead to cessation of randomized treatment. Two readings above 115 at monthly intervals will also lead to this procedure.

**ST MARY'S HOSPITAL, LONDON**

The trial is a multifactor intervention trial, although a subgroup study will investigate the effect of treatment in several hundred mild hypertensives with low risk profiles for coronary heart disease. It is based on factory groups and 24 such groups have been identified. They are divided into two groups of 12 factories, each pair matched as far as possible. One of each pair is then randomized to the intervention and the other to the non-intervention group.

**Stated objectives**

1. To determine the effect of such a programme on the incidence and mortality from coronary heart disease, the incidence of all cardiovascular diseases, and total mortality.
2. To determine the degree of risk-factor reduction that is possible in high risk individuals as a result of a community education programme.

Screening

All members of the factories in the intervention group and 10% of members in the non-intervention group are screened by questionnaire and personal interview. The data recorded is minimal for the objectives of the programme. Sitting blood pressures are taken twice at each visit by a nurse. If the SBP is less than 150 at the first reading, the patient is dismissed. If the mean of two readings is greater than 150 the subject is requested to return the following day. At the second visit two further readings are taken under similar conditions and if the mean of four is greater than 160, the subject is considered for entry to the trial.

Entry to the trial depends on a combination of risk factors (raised blood pressure, raised blood cholesterol, cigarette smoking, physical inactivity, and obesity). The scoring system involving all these factors is applied and the top 15% are recalled for further examination. Those whose blood pressures are below 160 at this examination are not treated but reviewed in three months' time. Those with SBP between 160 and 199 and who are in the upper 15% of risk are treated either by their own doctor or the factory doctor. Those with SBPs above 199 or DBPs above 114 are referred to their own doctor for treatment. Those with SBP 160 to 199 and not in the upper 15% at-risk group are randomized to treatment or non-treatment groups. This constitutes a subgroup study of treatment of mild hypertension within the overall intervention group.

Management

The object of treatment is to lower the blood pressure below 160. Other risk factors are dealt with in various ways, mainly involving individualized education for the top 15% at risk. A general education programme on risk factor reduction is directed at the entire factory staff. The treatment regimen consists of bendrofluazide 5 mg plus a potassium supplement daily and reserpine 0.125 mg tablets, one or two daily.

A 10% sample of the control factories are examined in a similar way at the outset and after two years.

End-point evaluation

End-points are identified by surveillance of the factory sickness absentee records of all individuals from the intervention and control factories who were absent for three weeks or more. Where the certificate indicates a cardiovascular illness, special follow-up enquiries of the patient's doctor or hospital are made. A final examination of all subjects in the intervention groups and the same 10% in the control factory groups is made at the end of five years. Mortality surveillance is based on the central records of the National Health Services.

Progress

Observations were started in April 1971 and screening was completed in April 1973. There was an 85% response rate. Eight thousand and ninety-six in the intervention group have been screened and 684 in the control group.
Comparison of baseline data showed good comparability between the two groups. It was noted that at the recall examination some 60% of those with SBPs above 160 had fallen below this level. On preliminary analysis of the first eight intervention factories, there were 7371 on nominal role, 6315 were screened, and 400 were hypertensive. Of those offered treatment 95% accepted. In 90% of those treated there was a good response to the diuretic alone, and in the other 5% a good response with added reserpine. These are preliminary figures.

GÖTEBORG STUDY

Observations on the effect of blood pressure control are being made as part of a multifactor intervention trial. All men between the ages of 45 and 55 years in the city of Göteborg are identified (30 000) and 10 000 of these are randomized into an intervention group. A second 10 000 were to be contacted by questionnaire only, to obtain baseline data. This procedure was abandoned and the current design is to monitor the control subjects (20 000) by the AMI register, stroke register, and death reporting procedure in Göteborg. Intervention is also made in subjects with a high risk owing to the serum cholesterol level or cigarette smoking.

Stated objectives

The objectives of the trial are to determine the extent of reduction of risk factors and secondly to measure the effect of the intervention programme on the total death rate and on fatal and non-fatal myocardial infarction and stroke.

Screening

Blood pressure at screening is taken once, sitting, under standardized conditions using a conventional mercury sphygmomanometer. Subjects are accepted into the treatment group if SBP > 175 or DBP > 115 mmHg.

Management

Treatment is conducted by seven doctors working in the clinic and is individualized for each patient; each doctor has his own regimen but mostly this involves a beta-blocker as the first-order drug, hydralazine as second, and a thiazide diuretic as third.

Progress

Screening was started in 1968 and was completed in 1972. Analysis of the results (preliminary) for men born in 1916-1921 inclusive show a primary population of 6117; 4658 (76%) attended for screening; and 682 were hypertensive (11.1% of the base population, 14.6% of those screened). Results of blood pressure treatment in 87 in the cohort born in 1915 after 12 months showed that 34% had blood pressures below 160/95, 36% had blood pressures between this level and 175/115, and 12% had blood pressures above 175/115. No therapy was applied in 18%.

USPHS HOSPITALS STUDY, USA

This study which commenced in September 1966 has been undertaken in six centres throughout the USA. Each centre is based on a USPHS
hospital. The average follow-up period at the present time is four years. The study population consists of mariners, hospital employees, coastguards, etc. There is no defined population base and the hypertensive population is recruited actively from patients attending the hospital and any other subjects submitting to screening examination.

The study was designed for evaluation on a sequential analysis design. As yet a conclusion has not been reached.

Stated objectives

To determine whether chlorothiazide-rauwolfia treatment of mild hypertension reduces the rate of development of degenerative vascular complications of the disease.

Screening

All subjects suspected to be hypertensive were started on a self-taken home blood pressure regimen for six weeks. The pressure was taken twice daily in the sitting position after 10 minutes' rest. The subjects whose average pressure over the last two weeks of this period was between 90-115 mmHg were considered for the trial provided a clinic blood pressure reading during the fifth or sixth week also exceeded 90 mmHg. The subjects then entered a second control period in which they were admitted to hospital for laboratory studies. Patients were not excluded if they became normotensive in hospital. A third control period was then started in which the subjects were observed for three months with three clinic visits. During this period they took a placebo tablet twice daily. If pill counts indicated poor adherence, the subjects were excluded. If two or more of the three clinic diastolic blood pressures were less than 90 mmHg, the subject was excluded. Clinic blood pressures were taken by a nurse on two occasions and the result was averaged. The subject was sitting.

Management

The study was double blind with a fixed treatment regimen consisting of 500 mg chlorothiazide and 100 mg rauwolfia twice daily, or a pharmacological placebo. Supervision was monthly or two-monthly and full physical examination and laboratory tests were conducted annually.

Subjects whose diastolic blood pressure exceeded 130 mmHg on three consecutive visits at intervals determined by the observer, or on one visit if complicating symptoms were present, were reviewed by the referee in consultation with the observer and the question of ceasing protocol therapy discussed.

Progress

The experience in the control group was reviewed and published in 1972. The drop-out rate averaged 4.7% per annum. There have been 17 terminations because of drug intolerance, 14 in the treated, and three in the placebo group. Fourteen subjects in the control group have developed accelerated hypertension (DBP greater than 130). Eight of these were
asymptomatic and six symptomatic. The fixed therapeutic regimen has controlled approximately 80% of the subjects. The event rate including all morbid events, both hypertensive and atherosclerotic has been about 8% per annum.2

NATIONAL BLOOD PRESSURE STUDY, AUSTRALIA

The study is being conducted under the auspices of the National Heart Foundation of Australia in association with the National Health and Medical Research Council, Life Insurance Medical Research Fund, the Ramaciotti Foundations, and the Raine Medical Research Fund. It will be conducted in five centres, each using a different screening procedure.

Stated objectives

To determine whether treatment of mild hypertension under ordinary conditions of medical practice is of benefit. The second objective is to evaluate various screening procedures in terms of the number of hypertensive subjects previously not knowing of their condition who are brought under effective treatment.

Screening

There will be two screening visits. Blood pressures will be taken in a seated position by trained non-medical screeners. Those who at the first visit have diastolic blood pressures greater than 95 mmHg will be recalled for a second screening two weeks later. Two blood pressure readings will be taken at each visit. If the average of four diastolic pressures is between 95 and 109 mmHg and the subjects have no other exclusion factors, they will be invited to enter the trial. The random zero sphygmomanometer will be used.

Management

Subjects qualifying will be randomized to active or placebo treatment groups. Management will be by the patients' family doctor in consultation with clinic centres after an initial stabilization by clinic staff. Subjects will be reviewed at four-monthly intervals at the clinic and tablets provided by the clinic.

Subjects in either group whose diastolic pressure rises above 109 mmHg will be removed from randomized treatment and placed on individualized treatment. They will, however, continue to be observed and any end-points occurring will be counted in their original randomized group.

DISCUSSION

Each of the studies was designed to answer various key questions relevant to the group concerned. Some of the questions were common to all groups; others can be answered by data from only one or two groups (see Table 4).
Table 4. Questions with respect to mild hypertension relevant to planning public health programmes in hypertension control

<table>
<thead>
<tr>
<th>Questions</th>
<th>Paris (GREA)</th>
<th>London (St Thomas')</th>
<th>London (NIH)</th>
<th>USA (MDPP)</th>
<th>USA (VA)</th>
<th>USA (USPHS)</th>
<th>Australia (NBPS)</th>
<th>London (St Mary's)</th>
<th>Orebro</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Does the general intention to treat with pharmacologic agents applied in the &quot;ordinary medical care&quot; situation improve prognosis?</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>-</td>
<td>-</td>
<td>X</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2. Does the general intention to treat with pharmacologic agents in a specialized clinic improve prognosis compared to:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(a) ordinary medical care?</td>
<td>-</td>
<td>-</td>
<td>X</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>x ubiquitous</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>(b) no treatment?</td>
<td>-</td>
<td>-</td>
<td>X</td>
<td>X</td>
<td>-</td>
<td></td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>3. Does the general intention to treat with pharmacologic agents from time of diagnosis improve prognosis compared with observation and institution of treatment if blood pressure rises above &quot;mild&quot; levels?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(a) in the &quot;ordinary medical care&quot; situation?</td>
<td>-</td>
<td>X</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>X</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>(b) in a specialized clinic?</td>
<td>-</td>
<td>-</td>
<td>?</td>
<td>- X</td>
<td>X</td>
<td>X</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>4. Does reduction of blood pressure to normal levels by pharmacologic agents improve prognosis?</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>5. What is the natural history (rate of progression and development of complications) of untreated mild hypertension?</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>- X</td>
<td>X</td>
<td>X</td>
<td></td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>6. What predictive factors will indicate favourable response of blood pressure to pharmacologic treatment?</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>- X</td>
<td>X</td>
<td>X</td>
<td></td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>7. What is the relative effectiveness of individual antihypertensive agents in control of high blood pressure and improving prognosis?</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>8. What is the relative effectiveness of various screening methods in identifying symptomless hypertension, and implementing effective treatment?</td>
<td>-</td>
<td>-</td>
<td>X</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>9. Does a community programme for the control of hypertension influence the general health of the community in which it is implemented?</td>
<td>-</td>
<td>?</td>
<td>- X</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>10. Does early treatment halt progression of disease allowing cessation of treatment eventually?</td>
<td>-</td>
<td>-</td>
<td>X</td>
<td>X</td>
<td>?</td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

St Thomas' study will provide data as shown but will not give statistically significant conclusions.

This implies that the placebo control group is not treated. However, if DBP rises above mild levels, treatment is instituted. In this case all controls who remain untreated serve as reference for the original treatment group and the result is diluted by loss of that segment of the controls going on treatment.

This implies that the placebo control group is not treated unless DBP rises above mild levels. However, the entire control group, whether eventually treated or not, serves as reference for comparison with the original treatment group.

Note: In the MRC study those control subjects whose DBP rises above mild levels are treated to bring the BP to the mild hypertension level.

Some details of the baseline data recorded by each study, and relevant to this question as shown in Table 2, or discussed in text.

i.e., subgroups randomised to different pharmacological regimens.

Data could show whether the intention to screen and treat severe hypertension in a community improves the prognosis compared to situations in which hypertension may be treated by the ordinary medical services on chance diagnosis, or symptomatic presentation, i.e., the usual situation.
The primary question is that set out in question 4 in Table 4: "Does reduction of blood pressure to normal levels by pharmacologic agents improve prognosis?" However, this may be regarded as somewhat academic and indeed a judgment could confidently be made that it would. Questions 1 and 2 are concerned with the "pay off" under field conditions and if they give contrary answers to that of the primary question, then there will be an indication to undertake a community programme only if high levels of management skill and patient cooperation are available.

The data likely to arise concerning the natural history of untreated hypertension with respect to the rate of progression of pressure levels, rate of onset of complications, etc. is of the greatest importance and offers one of the most valuable results of this combined series (Table 4, question 5). Each study, by defining its baseline data, has indicated its view as to the most likely predictive factors (Table 2). These, of course, have been modified to a considerable extent by financial and other constraints.

Such obvious factors as age, sex, initial level of blood pressure, general history and physical examination, and certain biochemical, electrocardiographic, and X-ray observations are all included. As indicated in the footnote to Table 2, various other special studies have also been included. Renin status, physical activity status, and response to physical stress, education status, and other socioeconomic matters are the subject of a special enquiry by a few groups in each instance.

The use of the same baseline data to provide predictive factors for the response of blood pressure to treatment (Table 4, question 6) and also of the rate of complications in the treated groups is equally important.

A great deal of practical information will be available from these studies during the next six years. It is hoped that this will be helpful, not only for health programmes of the study groups themselves, but in many other countries also. There will, no doubt, be problems of interpretation. The results and the conclusions may conflict or appear to conflict. However, a rational evaluation of the combined results should ensure confidence in the guidelines drawn for community programmes.

Except in one or two instances (e.g., MRC and NBPS, which have planned their studies with a view to subsequent pooling), there has been no attempt to coordinate or match the study plans. Nevertheless, it should be possible to test the comparability of many aspects of the data, e.g., population characteristics, age and sex distribution, BP profiles, progression of control group blood pressures, rate of complications in the control groups, blood pressure responses to therapy, etc., as well as methodological aspects.

It seems important that efforts should be made to document this comparative data prospectively by continuing conference between the principals of each of the studies.

274
REFERENCES


DISCUSSION

Dr Reader: Could I just finish, Mr Chairman, by a sort of postscript, not to give you the information so much as to provide an illustration as to how one of these trials has progressed over a period of eight months. I refer to the Australian study. Let me remind you that the format of the study involved a casual screening (S1) in the first instance. Those who were hypertensive, as defined, say, by a diastolic pressure of 95 mmHg and over were invited back to a second screening (S2). If they were still mildly hypertensive and were not subject to a number of exclusion factors which were dictated partly for ethical reasons and partly for practical reasons, they were invited to a more detailed physical and biochemical examination and subject to no further exclusions on that score. They were then invited to volunteer for a randomized therapeutic trial on a placebo basis. What became of that involved a number of surprises for us because the planning of such a trial is difficult and detailed and one has to layout among other things a lot of money based on the number of people involved. It is a multicentric trial and two of the centres have completed their screening now, Professor Doyle's and Professor Lovell's, with a total of 36,489 subjects. If you regard that number as 100%, there were 8,301 or 22% who were hypertensive at the defined level, quite a high figure. There were in fact 2,600 (7.3%) under treatment. After certain exclusions there were 5,052 eligible to go to a second examination. All of these were more or less what we estimated at the outset. At the second examination there were a number of exclusions for blood pressure and this was the first surprise, which is relevant to remarks made by Professor WerkO, Dr Strasser, and several others earlier today. If you now regard the figure of 5,020 as a new population (100%), in 1,734, i.e., in one-third of them, the blood pressure had dropped to normal and they were therefore not eligible to come into the trial. There were in fact 471, i.e., 9% of the hypertensives or 1.3% of the original screened population, who were above the proper level of what we regard as mild hypertension. Now, following through, there were a number of exclusions for medical factors and we were left with 36%, that is to say, 1,827 who were eligible to go on to a detailed physical examination and that is as far as we can go from the first 36,489 because some of those are still going through the S1 examination, but the final point is that, of about 33,000 that have been fully processed, 3.8% from the initial screening go into the trial and this was really the figure we wanted right from the beginning. We estimated that it would be nearer 8% and consequently we have had to recalculate the number screened. Nevertheless, we have accommodated for this and the trial is now going well.

Dr Gross: You did not mention one multicentre trial that is going on in Europe organized by the Belgian Society on Hypertension. This is aiming at the evaluation of treatment of elderly hypertensives. Dr Amery Leuven is the coordinator and about 15 centres are participating.

Dr Kagan: You found a group of 1,734 people who originally had elevated diastolic blood pressure but who were found on the second examination to have a diastolic pressure below 95 mmHg; does your protocol permit you to follow them for morbid and mortal events?

Dr Reader: It is a very good point. I would have thought one of the most interesting outcomes of any of these studies is not so much to follow up the hypertensive subjects but to follow up those who were found to be normal. We will have these people registered and may be able to study them if our resources allow.

276
Dr Hatano: How will morbid events be evaluated in the Australian National Blood Pressure Study, at one-year intervals or in which way? If an annual review or some kind of placebo is given, that means a certain kind of intervention is provided for the control group as well.

Dr Reader: The subjects are reviewed at 4-monthly intervals through the 5 years, and more intensively in terms of biochemistry and electrocardiograms annually. Both the active and control groups are taking tablets, either active or placebo; this trial is purely to evaluate pharmacological treatment. It excludes any psychological or other benefit from continuing medical supervision.

Dr Paul: You are treating one group and you are not treating the other. Do I understand that the family physician will likewise not treat the control group and he has agreed or the patient has agreed there will be no medication? How do you get that agreement? I am quite amazed. How do you get the participant to agree that he and his physician will not give him any medication?

Dr Reader: There is very careful discussion with the physicians in the district beforehand. Many of them, all of them who would come to meetings, discussed the trial and they all agreed to the protocol. That is not to say that they will all follow it. There will be drop-outs. Every person is of course entitled to withdraw from the trial. We estimate that the drop-outs over the 5 years will be 25%. This is a problem that all trials have. We were very much encouraged by the response in the US Public Health Study of Dr McFate Smith which has now 5 years' experience and their drop-out rate was relatively low; we hope we can achieve the same thing.

Dr Strasser: How do you monitor for unwanted effects and do you foresee any placebo toxicity?

Dr Reader: We certainly do foresee placebo toxicity. The question of monitoring for drug side-effects is not an easy one. At the four-monthly examinations either you say nothing and wait for the patient to volunteer, or you have a series of leading questions in which case there may be a problem of suggestive questions. We have tried to steer a middle course in which the examining physician simply asks, "Are you well? Have you had any problems or symptoms?" without specifying any particular ones. It is well known that the placebo population get many side effects in placebo trials of this kind.

Dr Freis: One of the things that bothers me is that treatment might be beneficial and you will not be able to show it for the following reasons: one is that you have exclusion criteria for patients whose blood pressures rise above a certain level. This would mean that the people who enter the high-risk group will then be removed from your trial. I know you have to do that, but still it bothers me. The other thing is that if you are just going to include the patients whose blood pressures remain in a certain range, a very mild range below 110, then the main type of complication that you probably get will be the complications of coronary atherosclerosis. Do you think that giving antihypertensive drugs in a 5-year trial or any trial that does not run 10 years or longer would be fair as far as the ability to prevent coronary atherosclerosis?
Dr Reader: The first question of course is a very thorny one. There is a control group not being treated, and it is certain that many - we do not know how many - will go above the mild hypertension level and must be treated. How do you handle that situation in terms of counting end-points in the control group? Are they failures? We will treat them and continue to observe them for other end-points. Any such end-point will be a score against the control group. Now your second question, "are five years long enough?" If no benefit is observed within 5 years, I think we are getting fairly close to making a judgement that you do not treat unless blood pressure rises above the threshold.
TRANSIENT CEREBRAL ISCHAEMIA AS A COMMUNITY PROBLEM
by
J. Marquardsen

Introduction

Transient cerebral ischaemia, being one of the earliest manifestations of atherosclerotic cerebral disease, is often a harbinger of major stroke. The early detection, investigation, and treatment of patients with transient ischaemia would therefore seem to be appropriate measures in the prevention of stroke in the community. It is the purpose of the present paper to review and discuss some epidemiological and clinical aspects of transient cerebral ischaemia in the context of the community control of cerebrovascular disease.

Definitions

The term "transient cerebral ischaemic attacks" (TIA) - synonymous with "intermittent cerebral circulatory insufficiency", "little strokes", "cerebral angina", etc. - usually refers to episodes of focal neurological deficit of sudden onset and of less than 24 hours' duration. It is unfortunate that some workers also include diffuse cerebral manifestations such as fainting or vertigo, which may have many causes other than vascular. The time interval 24 hours represents the dividing line between TIA and "definite stroke".

Frequency of TIA

Little is known about the incidence and prevalence of TIA in the community, mainly because most of the patients are not hospitalized, and many do not seek medical advice at all. In some retrospective stroke studies about 40% of the patients with completed strokes gave histories of previous TIAs, although such episodes were sometimes merely prodromes immediately preceding the ultimate stroke. In a community with a stroke incidence of 2 per 1 000 population per year (as found in several European countries) the incidence of TIA can thus be expected to be 0.8 per 1 000 per year as a minimum. An incidence rate of this magnitude was actually found in one community in the USA(2). In three other community surveys in the USA(8,11,12) the incidence of TIA ranged from 0.3 to 1.1 per 1 000 per year, the prevalence rate being 13 per 1 000. TIA seemed more frequent in the white than in the black population. It should be noted that these studies were not concerned with total populations, but only with the age groups beyond 40 or 50 years.
As suggested by the above findings, the frequency of TIA may be strongly influenced by ethnic factors and TIA may be rare in parts of the African and Asian population. For example, in a review of cerebrovascular disease in Singapore published by Gwee (2), cases of "cerebral ischaemia" represented less than 10% of the patients. Such findings would suggest that TIA, like ischaemic heart disease, is a community problem particularly in the developed countries in Europe and the USA.

Pathogenesis

Vasospasm was originally considered as a possible cause of TIA but has now only few protagonists. According to a later theory, the episodes are due to haemodynamic changes, i.e., temporary systemic hypotension, causing the perfusion pressure to fall below a "critical" value in those parts of the brain supplied by stenotic vessels. This theory, although undoubtedly valid in some cases, was challenged by Eastcott et al., and Adams et al. (1) since they failed to provoke clinical episodes in TIA-patients by lowering the BP. It is now almost universally agreed that most cases of TIA are caused by small platelet emboli capable of traversing the cerebral or retinal circulation without permanent damage being done. The source of such emboli can be atherosclerotic plaques in the walls of the large or medium-sized extracranial arteries or an endomural thrombus in the heart after myocardial infarction. Dramatic evidence in favour of this theory was provided by Fisher (7) and Ross Russell (16) who actually saw small emboli pass the retinal vessels of patients who were examined during the ischaemic episodes. Indirect support was given by Millikan (11) who reported a favourable effect of anticoagulants in patients with TIA.

Clinical aspects

The symptoms of TIA depend on the site of the responsible vascular disturbance. Episodes originating from the carotid circulation are usually characterized by unilateral paresis, paraesthesia, or numbness affecting the face and/or the limbs, often combined with cortical symptoms, such as dysphasia. Of particular diagnostic interest are the visual disturbances caused by small emboli entering the retinal circulation. These are episodes of sudden blindness in one eye of only few minutes' duration, followed by total recovery. TIAs caused by vertebrobasilar lesions present a variety of symptoms: vertigo, visual hallucinations, drop attacks, diplopia, visual field defects, etc. (18). The term "drop attacks" refers to sudden and extremely brief impairment of consciousness, causing unexpected falls. A very special type of vertebrobasilar attacks are those caused by a stenosis of the subclavian artery medial to the origin of the vertebral artery; the characteristic feature is that vertigo, caused by reversed blood flow in the vertebral artery, is provoked by exercise of the ipsilateral arm; this is the "subclavian steal" syndrome.

Before a safe diagnosis of TIA can be made, it is necessary to include a number of other conditions, each of which can simulate ischaemic episodes: epilepsy, migraine, Menière's disease, hypertensive crisis, hypoglycaemia, blood dyscrasia, collagenosis, etc. This can usually be achieved by a painstaking history, combined with physical examination (including BP measurement in both arms and auscultation of the cervical region) and simple laboratory tests.
Once a diagnosis of TIA is established, the important thing is to decide whether a surgically accessible arterial stenosis is the responsible lesion. In most cases this will require angiography. When a carotid stenosis is suspected, the investigation may be limited to the carotid artery on the relevant side; when the symptoms appear to involve the vertebrobasilar territory, an arch aortogram must be considered. The fact that angiography is not completely without risk of complications has caused a search for alternative methods to detect extracranial arterial disease, but hitherto such methods, including ophthalmodynamometry and thermography, have not been able to supplant angiography.

In the absence of any relevant lesion in the extracranial arteries, a search should be made for possible disorders of cardiac function, including hypersensitive carotid sinus, episodes of transient cardiac standstill, and cardiac sources of emboli. The role of cardiac dysrhythmia was recently reviewed by Reed et al. who found that, although many such patients had symptoms of general cerebral ischaemia, mainly syncope, only very few experienced TIA with focal symptoms.

Most workers agree that in young or middle-aged patients with TIA the diagnostic field is so wide that hospital investigation is usually indicated.

**Prognosis**

In some patients the ischaemic episodes after having occurred once or twice, are absent for several years, while in others the episodes continue for varying lengths of time, being eventually followed by major cerebrovascular accidents. In several studies, about 20-30% of patients with untreated TIA experienced major strokes within five years of observation. Apart from stroke, ischaemic heart disease was an important cause of death in these series. TIA within the carotid territory seem to carry a higher risk of subsequent strokes than attacks originating in the vertebrobasilar system. It is an interesting fact that the long-term excess mortality associated with TIA is found mostly at ages under 65 years, whereas the survival of elderly patients with TIA is almost equal to that of the corresponding general population.

The prognostic significance of angiographically demonstrated carotid stenoses is not clear.

**Treatment**

The aims of the treatment of TIA are twofold: to relieve the patient of symptoms causing trouble or anxiety, and to prevent subsequent major strokes. Fortunately, most therapeutic procedures will serve both purposes. Whereas the need for treatment of heart disorders, diabetes, or other underlying generalized disease is self-evident, some comments are needed on the choice of treatment in cases of verified lesions in extracranial arteries. When stenosis of an artery is so severe that it interferes with blood flow - as in the subclavian steal syndrome - vascular surgery is the treatment of choice. Experiments have shown, however, that the lumen of the internal carotid may be reduced by as much as 90% without interference with flow. Most cases of stenosis or atheromatous ulceration are therefore important mainly as sources of emboli. In such cases the therapeutic dilemma is the choice between surgery and anticoagulant therapy.
A comparison of large numbers of anticoagulant-treated patients and controls gave the result that 4% of the treated patients had cerebral infarction as against 29% of the controls\(^{(14)}\). Of patients followed up after carotid endarterectomy, about 5% died of cerebrovascular disease over 5 years and 10% over 10 years\(^{(6)}\). The two types of treatment seem to carry similar risks of complications. The choice of therapy is thus not easy, although the general trend seems to be in favour of surgical treatment.

Very recently, attempts have been made to treat TIA with platelet-suppressing drugs, such as dipyridamole and anti-inflammatory agents (aspirin, phenylbutazone, etc.). This type of therapy, although theoretically well-founded, should probably not be widely used until more practical experience has been accumulated.

Control of cerebral ischaemia in the community

The pertinent question is whether large-scale efforts to find and treat cases of TIA in the community will be worth while, in terms of prevention of stroke? In order to get a rough idea of the answer, let us assume that the incidence of new TIA cases is 0.8 per 1 000 per year; that appropriate investigation and treatment of all such cases can be achieved; that most people over the age of 70 years are not eligible for surgical treatment; that one-fourth of untreated patients with TIA will subsequently develop major, disabling strokes; and that medical or surgical treatment can prevent or at least delay such events. Based on these rather optimistic assumptions, the maximum number of patients in whom major strokes can be prevented will be 0.1-0.2 per 1 000 per year. In other words, a campaign against TIA may, in developed communities, be able to reduce the incidence of completed strokes by 5-10%. The extent to which such a prospect will justify the investment of efforts and money clearly differs from one community to another, depending on the availability of resources and the priority given to the prevention of vascular disease.

It appears from this review that, until more information about the epidemiological and therapeutic aspects of TIA has been collected, it remains an open question how much the control of TIA will contribute to the prevention of major cerebrovascular disease in various communities.

REFERENCES

NATURAL HISTORY
OF TRANSIENT CEREBRAL ISCHAEMIA
AS OBSERVED AMONG THE JAPANESE
by
Teruo Omae

The pathogenesis of transient cerebral ischaemic attacks (TIA) has not been fully understood. Atherosclerosis of the brain, together with some other factors including circulatory alteration, may play a role in the development of TIA. They include vasospasm, transient hypotension such as orthostatic hypotension, kinking or external compression of the neck arteries by cervical spondylosis or neoplasms, temporary hypoglycaemia, and thrombosis or embolism. Although TIA has been considered as a warning sign of cerebral thrombosis, its significance has not been fully established. The frequency of cerebral thrombosis occurring among those who have had episodes of TIA was reported to vary greatly (1.6-76.0%). This may have been caused at least in part by the lack of uniform criteria in the selection of patients. The selection of patients by a hospital, differences in study procedures (whether retrospective or prospective), and the duration of the observation period may have caused a wide variation in the results reported. Some racial differences may also exist. A United States/Japan collaborative study on stroke revealed that the Japanese population had less frequent extracranial arterial disease than the Caucasian population in the USA, but the situation was the reverse for intracranial arterial disease (2).

A follow-up study of 28 Japanese patients with TIA was carried out for a period of 9 to 144 months, averaging 48 months. There were 21 males and 7 females, aged from 30 to 80 years and averaging 57 years at entry. The criteria for admission to the study were as follows: (1) focal cerebral symptom considered to be due to cerebral circulatory disturbance, (2) the symptom completely subsided within 24 hours, (3) the patients who had a cerebrovascular episode lasting for more than 24 hours were not included, (4) dizziness or disturbance of consciousness was not accepted as TIA unless it was accompanied by other focal neurological symptoms. Symptoms caused by vasculitis (Takayasu arteritis, etc.) or valvular heart disease were not included. Among the 28 cases, 8 patients were invited to the University Clinic for a periodic check-up every year and the remaining 20 were followed up by letter or telephone. Cases of death were examined retrospectively by consulting the attending physicians and reviewing the protocols or autopsy records of their ante-mortem physical conditions and causes of death. The cases still alive underwent physical examinations. The final outcome of the 28 cases is shown in Table 1. Cerebral thrombosis developed in 6 patients (21.6%), 2 of whom had two episodes; but none of the
patients died from this. Seven out of eight episodes of cerebral thrombosis occurred in the same area of the arterial system as TIA. The time interval from the initial episode of TIA to cerebral thrombosis was 3 hours, 20 hours, 1.5 months, 2.5 months, 4 years and 4 months, and 8 years. Six patients (21.6%) died from stomach cancer, myocardial infarction, arteriosclerotic heart disease, acute renal failure, etc. Of the 22 survivors, 15 were engaged in gainful work and 7 were unable to work or were bedridden.

Table 1. Fate of 28 patients with TIA during a follow-up period of 9 to 144 months, averaging 48 months

<table>
<thead>
<tr>
<th>Development of cerebral thrombosis</th>
<th>6 (21.4%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>6 (21.4%)</td>
</tr>
</tbody>
</table>

Cause of death: stomach cancer (2), myocardial infarction (1), arteriosclerotic heart disease (1), acute renal failure (1), and cause undetermined (1)

<table>
<thead>
<tr>
<th>Occupational work or housework</th>
<th>15 (53.6%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No occupational work or bedridden</td>
<td>7 (25.0%)</td>
</tr>
</tbody>
</table>

Table 2. Clinical findings in TIA relating to the development of cerebral thrombosis (prospective study)

<table>
<thead>
<tr>
<th>Findings</th>
<th>No. of cases</th>
<th>No. of cases developing cerebral thrombosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex: male</td>
<td>21</td>
<td>4</td>
</tr>
<tr>
<td>female</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Age: over 60 years</td>
<td>15</td>
<td>4</td>
</tr>
<tr>
<td>below 60 years</td>
<td>13</td>
<td>2</td>
</tr>
<tr>
<td>Diseased area: Int. carotid</td>
<td>20</td>
<td>5</td>
</tr>
<tr>
<td>Vertebrobasilar</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>Duration of symptoms in TIA:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>less than 1 h</td>
<td>22</td>
<td>5</td>
</tr>
<tr>
<td>over 1 h</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>both</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>No. of episodes: 1</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>2-9</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>10+</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Blood pressure: elevated</td>
<td>19</td>
<td>4</td>
</tr>
<tr>
<td>normal</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>unknown</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>ECG: abnormal</td>
<td>14</td>
<td>4</td>
</tr>
<tr>
<td>normal</td>
<td>11</td>
<td>2</td>
</tr>
<tr>
<td>unknown</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>
The clinical findings relating to the development of cerebral thrombosis are summarized in Table 2. No definite statement can be made because of the small number of cases, but it appeared to us that the patients who had frequent episodes of TIA may have been more prone to developing cerebral thrombosis.

Our experience showed that about 15% of all the patients with cerebral thrombosis had a preceding episode of TIA(1). The time interval between the initial episode of TIA and the completion of stroke is illustrated in Table 3(4). The Table also includes the observations reported by Mori and his associates among their Japanese cases. About one-third of the patients developed cerebral thrombosis within one week and more than half within a few months after the episode of TIA. However, this retrospective study could not give us a definite answer as to how much importance should be placed on TIA as a warning sign of cerebral thrombosis.

Table 3. Time interval between the initial episode of TIA and the development of cerebral thrombosis (retrospective study)

<table>
<thead>
<tr>
<th>Time interval</th>
<th>Nishimaru &amp; Omae (1970)</th>
<th>Mori et al. (1966)</th>
</tr>
</thead>
<tbody>
<tr>
<td>within 1 week</td>
<td>8 (30%)</td>
<td>15 (38%)</td>
</tr>
<tr>
<td>1 week - 1 month</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>1-6 months</td>
<td>12</td>
<td>9</td>
</tr>
<tr>
<td>6 months - 1 year</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>1 year +</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>26</td>
<td>38</td>
</tr>
</tbody>
</table>

The pathogenesis of TIA is not fully explained, but the most plausible theory speaks of basic arterial lesions with thrombotic or embolic formation. This view is supported by Millikan(2) who considered that TIA might be due to platelet thrombi forming locally in an area of the diseased endothelium, becoming dislodged, impacting at a bifurcation, and obstructing the blood flow. On the other hand, others have supported the idea that atherosclerosis or occlusion plus haemodynamic changes as in transitory relative hypotension might lead to significant ischaemia in the brain. The relationship between heart rate and cranial blood flow in patients with TIA and various cerebrovascular diseases is shown in Fig. 1 and 2.
Fig. 1. Relationship between heart rates and cranial blood flow in patients with cerebral transient ischaemic attacks.

At heart rate below 60/min, cranial blood flow decreased. In one case having atrial fibrillation (af), the reduction of blood flow was much greater than that in those having sinus rhythm, even at heart rate above 60/min (6).
Fig. 2. Relationship between heart rates and cranial blood flow in 115 patients with various types of cerebrovascular diseases.

At heart rate below 50/min, cranial blood flow decreased.
REFERENCES


DISCUSSION

Dr Strasser: Is a case of TIA an emergency?

Dr Marquardsen: This is a very pertinent question. It may be answered as yes, considering Dr Omae's observations of very short intervals between TIA and stroke in some cases. However, to carry out all the relevant examinations and to consult a vascular surgeon during such short intervals will seldom be possible. It is therefore doubtful whether TIA, in general, could be called an emergency in the strict sense of the word, but I should strongly advocate that young or middle-aged patients with TIA should as soon as possible be referred to a competent specialist, preferably in hospital. What is the opinion of Dr Omae?

Dr Omae: Yes, I agree. Transient ischaemia itself is not an emergency but, as I said, the time interval between the episode of TIA and the development of a completed stroke was relatively short in many cases.

Dr Toole: In Table 3 of your report, the time interval between the onset of TIA and the development of the thrombosis was within one week in 30% and 38% in another series. Does that not make it an emergency? What is going to lead to a stroke in a very short interval of time sounds to me an emergency.

Dr Omae: It depends on the definition of the emergency.
Dr Werkö: Is this not almost the same as pre-infarction angina, which I think is an emergency because it can develop into an infarction at any time? Similarly, TIA can lead to complete stroke at any time and the patient has to be taken care of as soon as possible.

Dr Schmidt: I should like to inform you about our work on TIA. We carry out research on the structure of cerebral vascular disease in cooperation with 30 neurological clinics and hospitals in Moscow. During the screening of the population, composed of men aged 40-49 years, TIA was found in 1.5 per 1,000. Out of 9,200 patients hospitalized with cerebrovascular disease, the patients with TIA consisted of 15%. In the patients with essential hypertension TIA cases were most frequently registered in the age group 40-49 years and in atherosclerotic patients in the age group 50-59 years. In patients with combined arterial hypertension and atherosclerosis, TIA predominated in the age group 60-69 years; it is, therefore, possible that hypertension plays a protective role in these patients. The percentage of TIA in all cerebrovascular diseases decreases with age, whereas the frequency of stroke increases; the decrease in the frequency of the attacks with age is insignificant. In a retrospective stroke study, out of 7,240 patients with completed stroke, 17% of patients give histories of previous TIA. This percentage is less than in other reports. We have not included the cases in which the time interval from the TIA to stroke was less than 24 hours. In 36% of cases, the time interval from the first attack to stroke was 2.4 years and in 22% more than 5 years. This interval can therefore be very long. Patients with ischaemic stroke and having TIA in their past history were often in an older age group than patients who had not TIA. The death rate from stroke of the former was about half the latter. This suggests that transient vascular disturbances resulting from breakdown of compensation at the same time stimulate the appropriate mechanisms and in particular contribute to the development of collateral circulation. TIA occurs a little more often in the vertebrobasilar arterial system than in the carotid arterial system; 47% and 38%, respectively. In atherosclerosis, the attacks were twice more often in the vertebrobasilar arterial system, whereas in essential hypertension they occurred more frequently in the carotid arterial system; strokes occurred in the carotid arterial system 8 times more often than in the vertebrobasilar arterial system.

Dr Reader: Do I understand that 30% of all cerebral infarctions were preceded by a TIA?

Dr Omae: No, in our experience only 15% out of all the thrombotic cases had a preceding episode of TIA, and of these patients with preceding TIA, 30% had it within one week prior to stroke. In the other 85% of cerebral thrombosis there was no episode of previous TIA.

Dr Reader: That is not the same thing as saying that 15% of all TIAs will go on to a cerebral thrombosis. It may be very much lower.

Dr Toole: The 30% was an estimate I have this morning. Dr Marquardsen has written in his paper that about 40% of patients who have completed stroke have shown TIAs as a prelude to the stroke. Dr Omae has just said 15%. You now have a figure of somewhere between 15 and 40% of all patients with ischaemic stroke who had a preceding TIA. Then you take the other side of the coin, that of those who had TIAs; how many of them will go on to have an infarction? Our studies suggest that about one third of patients with TIAs will eventually have infarction.
Dr Omae: This is very important, I think, because only a prospective study can give the answer. We had 20% of TIAs who developed stroke during an average period of 4 years' observation.

Dr Marquardsen: As an answer to Dr Reader's question; a few prospective studies have shown that 20-30% of patients with TIAs proceeded to major strokes within a few years.

Returning to the problem of emergency, the chairman made an apparently very good point in referring to Dr Omae's findings. It should be remembered, however, that Dr Omae's report dealt with patients who were hospitalized because of completed stroke and who gave a history of previous TIA; 30% of such patients had experienced their first TIA less than one week before the stroke. This does not allow the conclusion that 30% of patients with an initial TIA will proceed to a stroke within one week. Such a statement can only be based on a prospective follow-up of TIA patients. Based on the prospective studies hitherto available I should say that the average interval between the first TIA and the major stroke is about one to two years. Generally, I should therefore still hesitate to consider the first TIA that a patient has as an emergency.

Dr Akinkugbe: Our own limited experience in Nigeria shows that TIA does occur, but the prognosis is much worse than is found in a number of data on the white populations. Eleven out of 15 cases that were observed between the period of 6 months and 10 years went on to complete stroke and one died. I am interested in the ones who die from ischaemic heart disease or something else quite separate from stroke.

Dr Hatano: Are you actually treating all patients who come to the hospital with a history of TIA with anticoagulant or surgical procedures? If you treat only some of them, what are the criteria for selection? Can we define more vulnerable TIAs?

Dr Strasser: May I stress that here we can do something for preventing stroke. I am again coming back to the question of emergency and I should very much appreciate it if we could have a clear-cut answer. Should transient cerebral ischaemic attacks be considered as an emergency? I think they should; perhaps not an emergency where you need hospitalization with an ambulance with flashing lights and a siren, but certainly within an hour or two such a patient should receive appropriate attention. If there is any possibility of preventing a catastrophe then this kind of a patient is much more important than the one in coma with cerebral haemorrhage.

Dr Werktø: At what time do you decide that this is a TIA if you see a patient within 2 hours of the start of the attack? At that time it must certainly be considered as an emergency, would it not?

Dr Marquardsen: Dr Werktø's remark is very vital to the whole question of emergency, since many patients with TIA are in fact hospitalized as emergencies because they are thought to have a full stroke. This is a common experience in our stroke register. In many cases a safe diagnosis of TIA cannot be made until the patient has been observed for several hours. Further, I am convinced that many of the patients with very short intervals between initial TIA and stroke are in fact cases of so-called "impending stroke", in which the initial neurological symptoms are the very first manifestations of the major stroke and not separate vascular episodes.
Whether or not TIA should be called an emergency depends on how you define the word. If it implies ambulances and flashing lights, I should still not consider TIA as an emergency, but I can heartily agree with the statement that those patients should be given high priority regarding access to specialized diagnostic and therapeutic procedures.

Dr Doyle: I should just like to go back to the question of episodes of neurological deficit associated with high blood pressure. One of the difficulties about TIA is that it is always difficult to know whether the patient should be seen by a neurologist or a vascular surgeon, or somebody who is interested in high blood pressure. If you are in the high blood pressure field, it is quite evident that there are a number of patients who, when they have very high blood pressure, develop episodes of neurological deficit and it is possible to induce precisely the same kind of neurological deficit in those patients if you drop their blood pressure too far. It implies that there is an organic vascular disease somewhere in the brain. What I should like to ask Dr Marquardsen is: if you have a patient who is admitted to hospital having a neurological deficit which then cleared up in the next 24 hours, would you decide immediately to go ahead and investigate that patient fully or would you say there is no great problem, nothing will probably happen now for 2 or 3 years: which would you do?

Dr Marquardsen: If a patient is admitted with his first TIA and at the same time has a very high blood pressure, I should not advocate immediate angiography, but the patient should be followed up closely for the next few days. If no further neurological symptoms develop, he should be given antihypertensive drug treatment, taking care not to provoke a too sudden drop of the blood pressure. As to Dr Hatano's question about the criteria for thorough diagnostic and therapeutic procedures, in my district of Copenhagen, when cases of TIA are referred to us, we admit them to the Department of Neurology within a few days. If they are in a clinical state that makes them suitable candidates for treatment, we will go through the full range of examinations, including those intended to disclose heart disease, blood dyscrasias, etc. If the symptoms are suggestive of disorder in the carotid arterial system, angiography is performed in all patients who are within reasonable age limits. Cases of relevant arterial stenosis are referred to the vascular surgeon, and the remaining patients are treated with either anticoagulant drugs or aspirin.

Dr Omae: We are doing the same thing on patients with TIA. As a rule we do not give active antihypertensive treatment in an acute stage of stroke of any type within several days to one week, because cerebral ischaemia can produce a transient elevation of blood pressure.

Dr Doyle: Can I just ask for a little clarification there? What about a hypertensive patient with cerebral haemorrhage? Do you regard that as not a good thing to treat?

Dr Omae: We do not have enough data to show the effect of an active antihypertensive treatment in an acute stage of stroke, including cerebral haemorrhage. Blood pressure not infrequently rises after severe cerebral haemorrhage probably caused by ischaemia of the brain stem.

Dr Doyle: I must say I quite agree with you that the blood pressure often goes up after a cerebral haemorrhage. However, I think that if the blood pressure is still high it is logical and sensible to reduce it. In our
experience it certainly does not increase the degree of neurological
deficit, and there are occasionally patients with very high blood pressure
when they come in with what appears to have been a stroke and the symptoms
disappear when the blood pressure is reduced. It seems to me that in the
face of an established neurological deficit and high blood pressure, there
is little to be lost by taking the optimistic view that they may improve
and they are unlikely to get worse.

Dr Omae: However, when we reduce the blood pressure too much, cerebral
blood flow may decrease accordingly. There is loss of autoregulation of
cerebral blood flow.

Dr Doyle: I think that is the point for which there really is not a great
deal of evidence. When I say one should reduce the blood pressure, I
would not advocate getting it down to 40 systolic; that would be too much,and there are limits. If somebody comes in with a blood pressure higher
than 100 mmHg diastolic it does not do any harm to get it down to 100.

Dr Paul: As one who practises as a cardiologist, I would just like to
remind the group of some of the precipitating factors of TIA. We have
seen people with TIA precipitated by bouts of atrial flutter, atrial
fibrillation, or ventricular tachycardia and we have also seen them
triggered off by episodes of a sick sinus node with bradycardia or with
intermittent A-V block. We are missing a certain number of these people
because we have not really monitored them enough. There was an exhibit of
this at the American College of Cardiology about a year ago pointing out
the yield when you are looking for a precipitating factor in these patients.
We say a patient has a TIA, but there may be a basis for it. We have also
seen patients in whom TIA has been brought on by the onset of congestive
heart failure and where, with appropriate treatment of congestive heart
failure, the symptoms cleared. We have also seen this with acute blood
loss where a volume contraction from acute blood loss is associated with
focal neurological signs which cleared. I would end by saying that we
also see patients like Dr Omae's very interesting case with the hypotension
accompanied by neurological symptoms. We have seen these too and it does
indicate that it is necessary to take the blood pressure both standing as
well as sitting, particularly in older people.

Dr Marquardsen: A very important point is whether these attacks you
mentioned, precipitated by a cardiac standstill for example, were focal or
non-focal because this was the crucial point in the controversy on the
prognosis of TIA between John Marshall and the American group. It seems
to be that nearly all the cases that are precipitated by cardiac
dysrhythmia or block are of the non-focal type. Of course, these are
caused by transient cerebral ischaemia, there is no doubt about that; but
they have no particular significance in the prevention of major stroke;
they are simply manifestations of a failure of the heart and constitute
another problem. This is why we wanted to confine the problem to the
focal TIA because, as far as I can see, hitherto very few of these patients
were precipitated by the cardiac conditions you mentioned.

Dr Freis: Have there been any controlled trials on the effectiveness of
surgical treatment and of anticoagulant treatment in the prevention of
stroke and, if so, quantitatively how effective are these treatments?

Dr Marquardsen: Millikan has reported that cerebral infarction occurred in
only 4% of patients who received long-term anticoagulant treatment because
of TIA but in 29% of untreated controls. As far as I remember, the Joint

293
Study of Stroke and Extracranial Arterial Disease in the USA gave similar results. However, it seems to be very difficult, in spite of appropriate treatment, to influence the long-term mortality of TIA patients. As Dr Akinkugbe remarked, a surprisingly high proportion of these patients died from other cardiovascular manifestations, which probably shows that TIA, like completed stroke, is only a more or less incidental manifestation of an underlying progressive vascular disease.

Dr Omae: In answer to the questions by Dr Freis, we have never tried vascular surgery because, as Dr Kameyama and Dr Ikeda said, we had more intracranial than extracranial vascular occlusions. The possibility therefore exists that the mechanism of TIA is not the same in our cases as those in Americans or Europeans.

Dr Paul: Could I just reply to Dr Marquardsen that some of these I described are focal. For example, just before leaving Chicago, I saw a patient who in the course of acute myocardial infarction with a hypotension and a drop in cardiac output developed focal signs which then cleared. I suppose this might have been embolic. I agree with him that the majority are episodes of brief unconsciousness or faintness. I am indicating, however, that some of them have focal signs and are classified as TIA because of the transient hemiplegia, because of transient aphasia, or because of symptoms and signs consistent with this definition of TIA.

Dr Toole: I would like to make one point, that to a certain extent I think we are confusing two issues: first, transient ischaemic attacks, at least the ones in the USA, are felt most often to be the result of microembolism from atheromatous plaques in the precerebral circulation and are not related to hypertension per se; second, hypertensive encephalopathy is excluded from our definition of TIA. Consequently, we would not treat patients who are having TIA with hypertensive agents; we would use anticoagulants. Now, on the other hand, if we feel that the patients had severe stenosis and not microembolism, we might even be tempted to raise blood pressure but not to lower it. This is true in the white population. In the black population in the USA the incidence of extracranial vascular lesions is very low and their lesions are mostly intracranial; the complications that might be considered to be TIA usually lacunar infarcts which are small infarctions of penetrating cerebral arterial regions, and in them a reduction of blood pressure is the treatment that is most often advocated.

Dr Doyle: Mr Chairman, I have a problem that when I see a patient who has hemiparesis which has lasted for 2 or 3 hours, I find it very difficult to be sure whether this is due to platelet emboli going up somewhere or what it is due to. The presence of the high blood pressure does not in fact exclude the possibility of a carotid stenosis. I am sure that the mechanisms may be quite different, but faced with the clinical problem I think that it is often extremely difficult to know exactly what to do at first sight. We always would use antihypertensive drugs, but when we have got the blood pressure down we would also do cerebral angiography immediately. We would therefore regard this as an emergency in Dr Strasser's terms.

Dr Toole: We must, unfortunately, conclude this session on transient ischaemic attacks despite the fact that there is so much material which remains to be covered. It is my personal belief that all patients with an acute neurological deficit deemed to be vascular in nature should be
hospitalized. My practice is first to eliminate other treatable causes for TIAs such as cardiac dysrhythmia, cranial arteritis, hypoglycaemic attacks, etc., and then to initiate therapy with heparin when an evolving infarction is most likely and when there is no contraindication.

After recovery from the ictus, I discontinue the heparin and evaluate the extracranial circulation for carotid stenosis or thrombus, particularly when a bruit is heard in the region of a carotid bifurcation. When one is dealing with vertebrobasilar insufficiency, there is less justification for angiography because the yield of remedial lesions is so low. I have largely abandoned performing angiograms for vertebrobasilar TIAs as a consequence.

Now for the patient who has had a TIA which has subsided; how urgent is his situation? Professor Omae showed that over 30% of patients have a permanent infarction within a week after a previous transient ischaemic attack. Professor Shmidt, in his retrospective study of over 7200 patients with completed stroke, found that 17% gave a history of previous TIAs. Yet in 36% of cases, the time interval from the first attack to the stroke was between two and four years; and in 22%, more than five years. How can we reconcile these findings? First, one might suspect that the disease may be different in the two populations in Japan and in the USSR. Secondly, as Professor Shmidt suggests, TIA occurs more often in the vertebrobasilar system than in the carotid and yet in the basilar system they are more benign than those in the carotid. Third, Dr Reader correctly surmises "that of all cerebral infarctions only 15% are preceded by TIAs" and with Dr Omae he concludes that we must have a prospective, not a retrospective study to provide us with the answer as to how urgent a situation TIAs are.
IV. GUIDELINES FOR ACTION

PERSPECTIVES OF HYPERTENSION AND STROKE CONTROL

by

Edward D. Freis

Evidence bearing on the effectiveness of drug treatment in the prevention of stroke in hypertensive patients has been accumulating over the past decade. The information is not yet complete particularly as it relates to the effectiveness of treatment in elderly patients with mild hypertension. However, the evidence is very good if not conclusive that antihypertensive drug treatment significantly reduces the incidence of stroke in patients with moderate to severe hypertension, especially in those under 60 years of age. This paper will summarize the studies that lead to the above conclusions.

Although a number of investigators (Leishman, for example) reported a decrease in the occurrence of stroke in treated patients with severe hypertension, such studies were uncontrolled and, therefore, open to question. The first controlled trial was reported by Hamilton and his associates in 1964. This prospective study included patients with severe diastolic hypertension averaging approximately 130 mmHg prior to treatment who exhibited no clinical evidence of cardiovascular damage. Alternate patients received either antihypertensive drugs or no antihypertensive treatment.

Over a follow-up period of approximately five years, 4 of 12 male patients in the untreated or control group developed strokes of which one was fatal. None of the 10 treated male patients developed cerebrovascular complications. In the female patients strokes occurred in 3 of the 19 control patients and in 3 of the 20 treated patients. However, treatment was unsatisfactory in reducing the diastolic blood pressure below 110 mmHg in the three treated females who developed strokes.

The results were also analysed by comparing those patients whose diastolic pressures were reduced to below 110 mmHg with those whose blood pressures were not, irrespective of the regimen. For both sexes combined, 6 of 31 patients with inadequately controlled blood pressures developed complications as compared to none of 30 whose blood pressures were controlled. These results, however, must be interpreted with some caution because some patients are in effect being moved from the treated to the control group in order to demonstrate a significant benefit from treatment.

A prospective, randomized trial was carried out by Carter in 97 stroke survivors who had hypertension. Mortality from all causes at the end of two to five years of follow-up was 46% in the control group and 26% in the treated group. Non-fatal strokes occurred in 23% of the control group as
compared to 14% of the treated patients. The evidence for the preventive
effect of treatment was seen primarily in patients under 60 years old.
Carter observed little or no benefit from treatment in the patients over
the age of 65 years.

The most carefully controlled primary prevention trial carried out to
date is the Veterans' Administration Cooperative Study on Antihypertensive
Agents.\textsuperscript{4,2} This prospective randomized double-blind trial encompassed 523
male patients with initial diastolic blood pressures in the range of
90-129 mmHg.\textsuperscript{4,2} All patients were hospitalized initially. Those whose
diastolic blood pressure averaged below 90 from the fourth through the sixth
hospital day were excluded from the trial, thus limiting the trial to
patients with fixed diastolic hypertension. Five per cent. of the patients
in both the control and treated groups had suffered a prior stroke from
which they had made a good recovery with minimum residual signs.

The evidence for the preventive
treatment in the patients over
The most carefully controlled primary prevention trial carried out to
date is the Veterans' Administration Cooperative Study on Antihypertensive
Agents.\textsuperscript{4,2} This prospective randomized double-blind trial encompassed 523
male patients with initial diastolic blood pressures in the range of
90-129 mmHg.\textsuperscript{4,2} All patients were hospitalized initially. Those whose
diastolic blood pressure averaged below 90 from the fourth through the sixth
hospital day were excluded from the trial, thus limiting the trial to
patients with fixed diastolic hypertension. Five per cent. of the patients
in both the control and treated groups had suffered a prior stroke from
which they had made a good recovery with minimum residual signs.

The design of the trial included a prerandomization outpatient obser­
vation period of two to four months. During this period the patients
received known placebos containing riboflavin which causes fluorescence of
the urine when it is viewed under ultraviolet light. To be randomized into
the trial the patient had to demonstrate adherence and compliance on the
basis of pill counts and urine fluorescence tests. Treatment consisted of
a combination of hydrochlorothiazide, reserpine, and hydralazine.

The trial was terminated after an average follow-up of only 18 months
in the subgroup of patients with initial diastolic blood pressure in the
range of 115-129 mmHg. There were 143 such patients, 70 in the control
group and 73 in the treated group. The reason for discontinuing the trial
was because of a highly significant difference in morbid events in the
control group as compared to the treated patients. With respect to stroke
this complication occurred in five of the control patients and in one of the
treated cases.

The remaining 380 patients whose initial diastolic blood pressures were
in the range of 90 to 114 mmHg were observed for an average follow-up period
of 3.3 years although some were observed for longer than five years. The
number of patients developing strokes was 20 in the control group and five
in the treated group, a ratio of four to one.

The ratio of incidence of stroke, therefore, between the control and
treatment groups was four or five to one in both subgroups of patients, that
is, those with initial diastolic pressures averaging 115 to 129 and those
averaging 90 to 114 mmHg. Because of the similar effectiveness of treat­
ment in the two subgroups and also for convenience in presenting the results,
the data for the two groups will be combined in the subsequent discussion.
When the two groups are combined there were 264 patients at risk in the
control group and 259 among the treated cases.

The overall incidence of strokes was 25 in the control group and six
in the treated patients. Of this number in the control group, seven were
fatal, seven others survived but were quite disabled and were terminated
from the trial, and 11 others had non-disabling strokes including two who
had transient ischaemic attacks. Among the treated patients there was one
fatal stroke, no nonfatal disabling strokes, and five patients who had
cerebral thromboses from which they made a good recovery.

Cerebral haemorrhage was diagnosed clinically or pathologically in four
and subarachnoid haemorrhage in two control patients. The clinical diag­
nosis of cerebral haemorrhage entailed the neurological evidence of a

297
localizing lesion and the finding of blood in the spinal fluid. Haemorrhagic strokes were not diagnosed in any of the treated patients. These results are consistent with prior observations that antihypertensive drug therapy is more effective in preventing haemorrhagic than in preventing atherothrombotic stroke.

The effectiveness of treatment was greatest in patients under the age of 60 years although effectiveness was demonstrated in all age groups. The percentage effectiveness of treatment in preventing stroke was estimated from the following relationship: percentage incidence in the control group minus percentage incidence in the treated group divided by the percentage incidence in the control group. A value of zero would indicate no difference, of 50% a 2 to 1 difference favouring treatment, 66% a 3 to 1 difference, 75% a 4 to 1 difference, and so on. By this criterion treatment was 84% effective in the patients under 60 years and 63% effective in the patients aged 60 years or older. Although the effectiveness of treatment drops off somewhat in patients over 59 years old there is still good protection since the incidence ratio of control to treated patients is nearly 3 to 1 in the older patients.

With respect to the severity of the hypertension, treatment appeared to be more effective in the patients with diastolic blood pressures of 105 or higher than in those with diastolic levels below this value. The percentage effectiveness of treatment was 86% in the subgroup with initial diastolic pressures of 115 to 129 mmHg and 91% in the patients with initial diastolic pressures averaging 105 to 114 mmHg. Although a difference favouring treatment was still indicated in the subgroup with 90-104 diastolic blood pressure, the ratio was much less since the effectiveness of treatment was 51%.

A recent controlled trial failed to demonstrate a significant benefit from treatment with antihypertensive drugs. This was the Hypertension-Stroke Cooperative Study Group under Dr Hoobler. This group compared deserpidine-thiazide and placebo in 452 patients who had a cerebrovascular episode in the previous year. Mean blood pressure was 167/100 mmHg and the average age was 59 years. The majority of the patients were black. Over a mean follow-up period of three years stroke recurrence rates were 16% on the drug and 19% on the placebo. Treatment was more effective among whites (two to one difference favouring treatment) than among blacks who showed no real difference between treatment and no treatment.

The reason for the discrepancy in the results found by the Hypertension-Stroke Study Group and by other investigators is not clear. Their patients probably had a preponderance of atherosclerotic cerebrovascular disease. The blood pressures averaged rather low at 100 mmHg diastolic and the mean age of 59 years indicated that most of the patients were in the age group where atherosclerosis was prevalent. Finally, the patients already had experienced at least one cerebrovascular episode and therefore probably manifested considerable atherosclerotic cerebrovascular disease. The greater benefit from treatment which they observed in whites as compared to blacks is not corroborated by the Veterans' Administration Study where blacks achieved as much therapeutic benefit as whites.

With only one exception, the accumulated evidence from these various studies agree that antihypertensive drug treatment is effective in reducing the incidence of stroke in patients with hypertension. Treatment appears
to be more effective in preventing haemorrhagic stroke than in preventing atherothrombotic stroke. The protective effect of treatment is greater in patients with diastolic blood pressures above 105 mmHg than in those with diastolic blood pressures below this level. It also appears to be more effective in patients below the age of 60 than in those above this age.

On the basis of the evidence presently available we can conclude that antihypertensive drug treatment has been proved effective in reducing significantly the incidence of stroke in patients with moderate and severe hypertension, particularly in patients under the age of 60 years. In patients with diastolic blood pressures in the range of 90-105 mmHg the evidence is conflicting. The Veterans' Administration Study indicates some benefit, although the degree of protection is considerably less than in the patients with higher diastolic blood pressures. The Veterans' Study also indicated a stroke preventive effect of treatment in patients above the age of 60, although it was less than in younger patients.

At the opposite extreme the Hypertension-Stroke Study indicated no significant benefit in the prevention of recurrent stroke. These patients had mild diastolic hypertension (average blood pressure 167/100) and an average age of 59 years. Dr Carter indicates that patients over the age of 65 did not benefit from treatment although there was evidence to suggest that those with diastolic blood pressures of 110 mmHg or higher did.

Because of such discrepant results we are forced to conclude that the effectiveness of antihypertensive treatment in preventing stroke in older age groups and in patients with mild elevations of diastolic blood pressure is still unproven. The question is of great importance because a very large proportion of the hypertensive population has diastolic blood pressures in the range of 90-105 mmHg. From the public health point of view the financial burdens and logistic problems would be much greater if patients with mild hypertension required treatment than it would be if treatment could be limited to patients with diastolic levels of 105 or 110 mmHg or greater.

For the above reasons it is of greatest importance that the extent of the benefit of treatment in patients with mild hypertension and in patients in the older age groups be determined as soon as possible. Fortunately, some studies are in progress. Controlled trials are being conducted by the Public Health Service in the United States, by the Medical Research Council in the United Kingdom and Australia, and by Dr Amery's group. These studies should supply us with the data needed to make appropriate therapeutic decisions in patients with mild hypertension.

At the present time there is more or less general agreement that patients with diastolic blood pressure levels of 105 mmHg or higher who are below the age of 60 should receive treatment. There is as yet, however, no well defined mechanism in any country whereby these patients may be identified and cared for in the current health care delivery system. Recent surveys such as the one by Schoenberger and his associates indicate that in the USA half of the hypertensive population go unrecognized. Of those who know they have hypertension only half were under medical supervision at the time of the survey.
The first task, therefore, is to establish some mechanisms for the screening and identification of hypertensive patients, particularly those with diastolic values above 105 mmHg who fall into the high-risk group. Various approaches can and have been used although not yet in a systematic and organized way. Physicians in all specialities including ophthalmologists, orthopaedists, and others should record the blood pressure routinely on all of their patients. Other health personnel who do not routinely take blood pressures such as podiatrists, optometrists, and dentists should be doing random screening. In addition, there should be organized screening programmes utilizing specially trained teams of allied health workers, including housewives who can be taught to record blood pressures. These teams would screen from house to house, at shopping centres, and at churches or wherever else people tend to congregate. Industry is another likely area for screening.

The task of treating the patients, even the limited number with diastolic blood pressures in the 105 and above range, will be both difficult and expensive but not impossible of accomplishment. In the author's opinion the most important step will be to educate and convince the physicians in the various communities that preventive treatment of the high-risk patient is important. In the USA at the present time a nationwide government sponsored educational programme is in progress. Its purpose is not only to make the public aware of the importance of hypertension but also to educate physicians in matters relating to the management of hypertension. Among other techniques public television is used extensively with often repeated short messages concerning hypertension for the public. Nationwide closed circuit television is being employed to bring lectures and conferences on hypertension to physicians. The latter are supported by pharmaceutical companies who have also supported live symposia on hypertension for practising physicians on a local or regional level.

Education of both patients and physicians is the necessary first step in developing an effective preventive programme. It has been well said that physicians must learn to be as compulsive about the treatment of hypertension as they are presently compulsive about the treatment of diabetes. How may this be done? The National Hypertension Program in the United States feels that this may best be done by frequently and repeatedly broadcasting to the public and the profession alike in a variety of ways the message that hypertension increases risk and that it can and must be controlled. Its purpose is to change pre-existing attitudes towards hypertension. In this way a climate of opinion will be created where treatment becomes the accepted practice and therapeutic nihilism will be regarded by both the physician and patient as medical neglect. Once this climate of opinion has been achieved, which is quite different from that existing at present, physicians themselves in the various local communities will begin to take the steps needed to cope effectively with hypertension as a public health problem.

For those segments of the population who do not have a private physician but rather are accustomed to obtain health care at state or city operated clinics a different approach may be needed. Currently, there has been considerable experimentation with the use of nurse clinicians or specially trained allied health personnel in the management of patients with uncomplicated hypertension. Finnerty operates a hypertension clinic in the city hospital in Washington, DC, with allied health personnel. Screening teams cover the surrounding neighbourhoods and refer in patients. Finnerty
has found that the dropout rate was greatly reduced if patients were seen promptly and given their medications without waiting at a satellite pharmacy in the clinic. Identification of the patient with a single therapist whether that be an allied health worker or a physician was also important in improving compliance.

The Veterans' Administration has established screening, work-up, and treatment clinics in a number of its hospital centres. Nurse clinicians provide primary medical care under the supervision of the clinic physician. The nurses receive an intensive one-month course in hypertension including a review of the relevant anatomy and physiology, the pathogenesis and pathology of the complications of hypertension, a description of the curable forms of hypertensions, and the clinical pharmacology of the antihypertensive agents. In addition, they are taught to do physical examinations including optic fundoscopy and auscultation of the heart. Practical aspects of management including education of the patient and evaluation of side effects of drugs are also stressed. Periodic refresher courses are planned after these nurses gain more experience in the field.

The experience to date from the various clinics that use nurses or allied health personnel for the management of uncomplicated or stable hypertensive patients suggests that this might be the most effective and most efficient way of managing the low-income patient with asymptomatic hypertension. However, more practical experience will be required before a well defined protocol can be established for the optimum method of managing such patients.

In summary, the effectiveness of antihypertensive drug treatment in the prevention of stroke has been demonstrated for patients with diastolic blood pressures of 105 mmHg or higher who are under the age of 60 years. The problem of providing adequate preventive treatment will depend first of all on overcoming present attitudes towards hypertension among both the profession and the public. Screening needs to be increased to include all physicians as screeners, as well as dentists, optometrists, podiatrists, and trained volunteers. A large segment of the population seeks medical care in clinics rather than from a personal physician. Hypertension clinics need to utilize nurse clinicians or allied health personnel to a greater extent in order to take care of the large number of asymptomatic patients with uncomplicated hypertension.

REFERENCES


5. Ibid. II. Results in patients with diastolic blood pressure averaging 90 through 114 mmHg. J. Am. med. Ass., 213: 1143 (1970).


DISCUSSION

Dr Hoobler: I am very pleased to see Dr Freis limiting the range under which treatment should be initiated, and I think this is an excellent advance over unrestricted enthusiasm for treating all diastolic hypertension. In the overloading of screening clinics it would perhaps be wise to set a lower age limit for actually taking blood pressures, such as below the age of 35 or 40 years; the likelihood of picking up hypertension is extremely low relative to the amount of work involved. However, younger individuals who have one parent with hypertension should be encouraged at any age to come in for screening.

Dr Toole: Dr Freis, once you start screening people you have to do it every year or at least at some intervals throughout the remainder of their lives to see whether they become hypertensive; this makes an enormous number to be examined.

Dr Freis: The Intersociety Commission recommended that persons with borderline hypertension should be rescreened yearly, but for persons with a pressure below 90 diastolic and 140 systolic, five years would be a sufficient rescreening interval.

Dr Werkt: We cannot go too much into the sophisticated method as in the USA because the screening will put an overload on existing medical facilities. We do not have as many medical facilities all over the world as you have in the USA.

Dr Komachi: I am concerned about the differences between the USA and Japan. The training of nurses and paramedical people in hospital to treat hypertension patients is one possible approach. However, can this be done on a wide basis in the USA? Concerning the general practitioners, what kind of measures are you planning to take?

Dr Freis: The allied, specially trained health personnel are to work in specialized clinics. By education programmes, we hope to have the general practitioners handling hypertension confidently and we are encouraging them to use their nurses more extensively than in the past. But it is strictly up to them whether they want to do so or not.
Dr Hatano: Concerning the size of the problem, my question is: how much less frequently can patients be seen or can blood pressure be measured?

Dr Freis: That has not yet been worked out. In the cooperative study, however, we could see the patients once every two months after they were well established and I would think even once every six months would be sufficient.

Dr Werktô: I can add that we have worked out a special hypertensive clinic programme in Sweden where we use auxiliary health personnel who are specially trained. They can take care of most of these problems and the physician in the hospital can see the patient only once every three or four months, which would be about the same as in the USA.
ANTIHYPERTENSIVE THERAPY FOR STROKE PATIENTS

by

S. W. Hoobler

Our cooperative group made a study of the effects of antihypertensive therapy on stroke recurrence. A fixed drug combination of deserpidine-methyclothiamide was administered in a randomized double-blind fashion to lower the blood pressure in one half of 452 patients who had a mean blood pressure of 167/100 (with a range of 140/90 to 220/115) and who had had a cerebrovascular episode in the preceding year. Patients were seen eight times per year for a mean period of three years in the eleven cooperating clinics. The mean age was 59 years and 80% were black. The treated and control groups with respect to blood pressure and to other risk factors associated with stroke were similar. The blood pressure in the placebo groups was identical to that which was found during the pretreatment period, whereas those who were treated had a sustained reduction in blood pressure over the three-year period with very little variation. The annual recurrence rates for stroke among the treated and control groups were similar. There was a 7.8% recurrence rate in the treated group in the first year and 10% in the placebo group. In the second year of treatment, they were almost identical; in the third year of treatment, the drug treated group had a lesser recurrence rate, 3%, against 6.7% in the placebo group; and in the fourth year this ratio was reversed. The overall recurrence rate was almost identical for the two groups.

The type of the initial cerebrovascular episode did not affect the outcome. The patients were classified as to whether they had only a completed stroke, or transient ischaemic attacks, or both. In the patients with a completed stroke, 176 were in the placebo group and 185 in the treated group. Small numbers had only transient ischaemic attacks and they were distributed seven in the placebo group and ten in the drug treated group. Some had had both a completed stroke and a transient attack in the preceding year and they were 36 and 38 in the placebo and treated groups, respectively. There was basically no difference in the recurrence rate. The group that had a completed stroke only and was treated with the drug showed a recurrence rate of 14%. The patients who had transient ischaemic attacks only and were treated with the drug ended up with 10% of them having a completed stroke. In fact they fared better than the individuals treated with the placebo, so that drug treatment did not appear to increase the frequency of stroke in patients who had had transient ischaemic attacks initially. However, none of these differences was significant.

The level of initial blood pressure in the untreated group did not affect the outcome either. The patients treated with placebo were classified according to the initial blood pressure range. The mildest hypertensives had a 16% recurrence rate; the next group, 22%; and the more severe hypertensive group, only 20%. This seems to contradict the general opinion about the relationship between high blood pressures and stroke occurrence, but our group of stroke recurrence was in a population in which one stroke had already occurred.

Thirty-seven strokes occurred in the treatment group and 42 in the placebo group. There were 12 cardiovascular endpoints in the treatment group and 19 in the placebo group, this difference being largely made up of 6 cases of congestive heart failure in the placebo group and none in the treatment group. A significant reduction was found only in congestive heart failure. There was a slight reduction in the stroke recurrence rate among the males who had more strokes than in the females who had fewer strokes, but neither was of statistical significance. Now the blacks had about an 18% recurrence rate for stroke and the whites had an almost 30% recurrence rate for stroke, but this is not of statistical significance because the whites were only 20% of the study population. The whites, being at a greater risk of recurrence, seem to have a greater reduction with treatment than the blacks who were hardly affected by hypotensive treatment.

The incidence of new strokes was higher in the older age groups and treatment of hypertension did not make much difference in the recurrence rate in the various age groups. In a small sub-sample of patients aged over 70 years, 25 were treated with the placebo and 19 received hypotensive drugs. The reduction in stroke recurrence rate was considerable.

Summary

1. Treatment of mild hypertension in stroke survivors is not beneficial, but is not harmful either in respect of stroke recurrence rates.

2. The occurrence of transient ischaemic attacks before treatment does not affect the stroke recurrence rates in patients with mild hypertension under hypotensive treatment.

3. Congestive heart failure was significantly reduced by the treatment.

4. In patients with mild hypertension who had survived one or more strokes, the stroke recurrence rates are not related to the blood pressure. It is possible that these patients had a greater degree of cerebral atherosclerosis before treatment and were therefore less able to benefit from hypotensive therapy.

These observations emphasize the great importance of early treatment of hypertension before the occurrence of stroke, since reduction of blood pressure in stroke survivors with mild hypertension is not of great value in preventing a stroke recurrence.
DISCUSSION

Dr Doyle: Dr Hoobler, as you point out, these results are extraordinary in that they differ from those which have been reported in severe hypertension following stroke by Hamilton and by the group at the National Hospital for Nervous Diseases in London. Do you have any data as to how effective the reduction in blood pressure was? Secondly, to what extent was there adherence by the patients to the drug regimen?

Dr Hoobler: The blood pressure reduction brought more than 50% of patients into the normal range according to WHO criteria. The compliance was almost exactly the same in the drug and placebo group; it reached approximately 85% based on pill counts.

Dr Werk: It is important to point out what Dr Hoobler and his colleagues did, that is, they have studied a predominantly black population and they did not find much difference in the blacks in contrast to the whites. Is not that true?

Dr Akinkugbe: Yes, I would like to emphasize that point because you have taken one-half of 452 patients and this means that you are dealing with only about 50 whites really. I therefore wonder what the statistical significance is of the rather radical conclusions. The distribution of atherosclerosis, particularly cerebral atherosclerosis, might have some effect on the outcome of your results. It is just possible that one is dealing with the superimposition of stroke over the pre-existing combination of mild hypertension and cerebral atherosclerosis.

Dr Hoobler: We are not claiming that the white population was of a significant number, nor was any significance demonstrated. The only thing that was surprising to us is that the blacks did not appear to benefit from antihypertensive treatment and there was a large enough sample of the blacks to make this result meaningful.

Dr Freis: We do not want to generalize about the blacks and the results of treatment because in the VA cooperative study 42% were blacks. Effectiveness of treatment was the same in black and white patients. I say "do not generalize".

Dr Ikeda: Concerning the people who are older than 70 years, what were the target values for the blood pressure? The second question: In the strokes among the blacks or whites, were there any differences seen between those with cerebral hemorrhage and those with cerebral infarction or thrombosis?

Dr Hoobler: The subjects did have to meet the inclusion criteria of having above 140 and 90 mmHg blood pressure for at least a two-month period of observation when free of all drugs. My recollection is that the blood pressure for persons over the age of 70 was about the same as that for other individuals in the study. With respect to the second question, according to the requirements for being entered in the study, almost all of these patients must have had cerebral thrombosis as the first event. It was impossible to be sure because the data on many patients were based on previously recorded data and lumbar punctures had rarely been carried out on the occasion of the first attack. I am quite sure from looking into the cases of second stroke in the study that 95% of these were cerebral
thrombosis by the usual criteria. Even though these cases were under close surveillance, it was surprising how seldom the examiners were actually able to see the patients who had the stroke; they always seemed to have had the stroke when somewhere else and we were not able to get lumbar punctures on these patients.

Dr Toole: In line with what was discussed yesterday, I think it is worth observing that patients with fixed hypertension have changes in cerebral circulation that are different from the atherosclerotic changes about which we have been talking up to this point. In contrast to atherosclerosis which is a large vessel disease, hypertensive vascular disease is a disorder of the penetrating arterioles and predisposes to lacunar strokes. They form an entirely different category from thromboembolic strokes resulting from atherosclerosis because the zone of infarction is very small and because there is no opportunity for collateral circulation to develop. Consequently, because of the different pathogenesis there may be a difference in the frequency of recurrence and in the prognosis for the two categories of infarctions.

Reduction of blood pressure in patients with thromboembolic disease owing to atherosclerosis should not affect recurrence; it is logical to lower blood pressure in this situation because hypertension is a risk factor for atherosclerosis and also leads to other target organ complications.

In the case of lacunar strokes reduction of blood pressure may not be beneficial, particularly if the hypertension is fixed and if secondary changes have occurred in the penetrating arterioles. In this case, reduction in pressure may further predispose to another lacunar infarction.

What about the cases in which both processes are active? In these, there is no ready answer and special tests of regional blood flow may be needed before instituting therapy.
STROKE AS AN EMERGENCY PROBLEM

by

E. V. Shmidt

1. The magnitude of the stroke problem for society is well demonstrated in the papers presented at a WHO meeting in Geneva on 6-13 December 1973. It suffices to recall a few figures: the annual incidence rate was 1.5 to 3 per 1000 inhabitants. The case fatality rate was over 40%; from the economic viewpoint it is important to draw attention to the fact that about 30% of patients had engaged in some gainful work before suffering from stroke, and of the survivors 75-80% were not working at all and only 13% were working at their former jobs. Three months after a stroke about one-third of patients required assistance from others and 17% depended entirely on such assistance, since they could not look after themselves.

The prevalence of invalidity of some degree after stroke is thus extremely high. In the USA in 1958, for example, there were about two million persons with some degree of invalidity after a stroke.

From the above figures it is clear that the stroke problem is not merely a medical one but an extremely important social problem.

2. The high case-fatality rate in stroke (and it is particularly high in the first few days of the illness) is due not only to the severity of the pathological process but also to the fact that the necessary properly differentiated care is not given quickly enough. Hence the importance of establishing a form of emergency care which ensures that urgent specialized care is given to the patient in the first few hours after the beginning of the stroke. This care, which differs according to the nature of the stroke (i.e., whether it is haemorrhagic or ischaemic), must be given at the place where the stroke occurred, before the patient is taken to hospital; it is only after it has been given that the patient is taken to hospital with special transport.

3. Ten years' experience of the work of the specialized neurological emergency services in the Soviet Union has shown that the establishment of a service of this kind is possible and rational. The service is based on the so-called "stroke teams" which operate in a number of Soviet cities at the emergency care centres.

1 WHO unpublished document, No. CVD/74.3(1).
4. The tasks of a stroke team are as follows:

(a) establishment of the diagnosis of stroke and its nature;
(b) giving first aid on the spot;
(c) determining whether it is possible to transport the patient and deciding on the type of ward for treatment to which he should be sent (specialized department for patients with disturbances of the cerebral blood circulation, neurological, general medical or neurosurgical department);
(d) transport of the patient and providing necessary care during transport; and
(e) emergency consultation with specialists at a general or other type of hospital, if no neurologist is on duty.

The stroke brigade consists of a neurologist skilled in resuscitation methods, a feldscher and a laboratory worker (who have been given special training and are permanently attached to the neurologist), and a driver. The team goes to the spot where the stroke has occurred, after being called out by the district doctor or doctor in a nonspecialized emergency service or at the request of a patient's relative or other citizens. Arrangements for dispatch of the stroke team are made by the senior physician on duty at the main emergency care centre.

As shown in Table 1, about a half of the patients (42%) received care in the first six hours after the beginning of the stroke and 84% of them within the first 24 hours.

Table 1. Length of time before care was given to patients with acute disturbances of the cerebral blood circulation

<table>
<thead>
<tr>
<th>Time</th>
<th>No. of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 1 hour</td>
<td>80</td>
<td>4.0</td>
</tr>
<tr>
<td>1-3 hours</td>
<td>279</td>
<td>13.6</td>
</tr>
<tr>
<td>4-6 hours</td>
<td>494</td>
<td>24.1</td>
</tr>
<tr>
<td>7-12 hours</td>
<td>481</td>
<td>23.5</td>
</tr>
<tr>
<td>13-24 hours</td>
<td>386</td>
<td>18.8</td>
</tr>
<tr>
<td>Total in first 24 hours</td>
<td>1 720</td>
<td>84.0</td>
</tr>
<tr>
<td>1½ - 2 days</td>
<td>166</td>
<td>8.1</td>
</tr>
<tr>
<td>3 days and more</td>
<td>162</td>
<td>7.9</td>
</tr>
</tbody>
</table>

5. In establishing a diagnosis at the patient's home a urine analysis is carried out and blood tests are made (clotting time, prothrombin index, white blood cell count).

In cases where the diagnosis is uncertain, if there are no indications requiring immediate hospitalization, a lumbar puncture is carried out to determine whether there is any blood in the cerebrospinal fluid.
a number of cases blood elements can only be detected upon microscopic examination. There has not been a single case of complications caused by lumbar puncture performed under home conditions.

The neurologist gives immediate general care at home (the sort of care which can be given without determining the nature of the stroke), when there are vital indications for doing so. This consists in the administration of cardiac agents, hypotensive or vasopressor drugs, diuretics, perfusions of aminophylline, and aspiration of mucus and other secretions from the mouth and pharynx. In a number of cases, some measures of resuscitation have to be taken: intubation, tracheotomy, intravenous or intra-arterial infusion of blood substitutes, mechanical artificial respiration, etc.

According to the Moscow stroke team (N. K. Bogolepov et al.), among a thousand patients with acute disorders of cerebral circulation, 23 had to be treated for collapse and 62 for pulmonary oedema; intubation was carried out in 76 cases and tracheotomy in 14; 54 patients were put on mechanical artificial respiration.

If a diagnosis of ischaemic stroke is beyond doubt, cerebral vasodilators are administered and, if there are no contraindications, anticoagulants are given (whether fibrinolytic preparations should be given under domiciliary conditions is still a moot point).

Some believe that if the stroke is embolic in nature and there are severe focal symptoms the doctor should refrain from giving anticoagulants, since in such cases the stroke often turns out to be of haemorrhagic type.

If it is established that the stroke is of the haemorrhagic type, suitable care is given: ganglion-blocking agents or other hypotensive agents, diuretics, and sedatives. It has been found that chlorpromazine or similar substances improve the patient's ability to withstand transport in the acute and critical period of a haemorrhagic stroke.

The average length of time the team spends in the patient's home is two to three hours.

After these first aid measures have been given it is decided whether hospitalization is indicated and is possible and what type of establishment the patient should be sent to. The condition of the roads is taken into account when this decision is being considered.

The safety of transport is ensured by a combination of measures taken at the patient's home. The already wide experience of stroke teams has shown not a single recorded instance of death during transport to hospital. No case of a worsening of focal symptoms has been recorded either. According to the Sverdlovsk stroke team, arterial pressure increased during transport in 19%, in 69% there was no change, and it decreased by 15 mmHg or more in 12%.

Most stroke patients are sent to the neurological department of a hospital or, if cardiac disorders predominate, to the general medical department. In some cases of cerebral haemorrhage, if surgical operation is indicated, such as in acute occlusion, or if stenosis of the extracranial portion of the carotid artery is suspected, the patient is sent immediately to a neurosurgical or surgical department, thus making it possible to carry out the urgent operation that is required in many cases. Wherever
specialized departments for cerebrovascular disorders exist, patients are usually sent there.

6. The proportion of stroke patients hospitalized by stroke teams was 40-75%, differing according to cities and the number of calls. According to the Leningrad team, the percentage of haemorrhagic stroke patients left at home was 72.7%, as against 25.3% for those with ischaemic stroke (personal communication by M. A. Messel).

Very serious cases with a profound disturbance of vital functions, or chronic severe cardiac decompensation, or the open form of pulmonary tuberculosis, or patients with purulent diseases should not be sent to hospital. Temporary contraindications to immediate transport are pulmonary oedema, acute cardiac insufficiency, and an attack of angina pectoris that cannot be improved. In the rare cases where it is possible to ensure the necessary care and full-scale treatment under domiciliary conditions, the patient is left at home. The reasons for leaving the patient in his own home are the mildness of his complaint and its rapid improvement, or the refusal of the patient himself to go into hospital, or the refusal of his relatives to allow him to be taken there.

The emergency calls for complaints other than stroke accounted for as many as one third of all calls in some stroke teams.

7. The diagnosis established by the physician in the stroke team proved to be correct in the overwhelming majority of cases. An analysis of 785 verified cases has shown that the percentage of divergences was only 13.3%. In 6.3% of cases one type of stroke was taken for another; most frequently a corrected diagnosis of cerebral infarction was established from a tentative diagnosis of haemorrhagic stroke. In 5.8% of cases the physician was not certain of the nature of the stroke or another disease was diagnosed. In 1.2% of cases the diagnosis of stroke was not confirmed on autopsy (D. G. Sefer et al.). The percentage of misdiagnoses cannot be considered as high in view of the conditions in which they were established.

According to D. G. Sefer et al., a comparison of patients taken to hospital by the stroke teams and patients left at home shows that the former group has a considerably lower case fatality rate (Table 2).

<table>
<thead>
<tr>
<th>Type of stroke</th>
<th>Persons taken to hospital</th>
<th>Persons left at home</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>Deaths</td>
<td>%</td>
</tr>
<tr>
<td>Haemorrhage</td>
<td>101</td>
<td>53</td>
</tr>
<tr>
<td>Embolism</td>
<td>98</td>
<td>44</td>
</tr>
<tr>
<td>Ischaemic stroke</td>
<td>195</td>
<td>24</td>
</tr>
<tr>
<td>&quot;Stroke&quot;</td>
<td>22</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>416</td>
<td>124</td>
</tr>
</tbody>
</table>

Table 2. Case fatality rate (within 40 days) in different types of stroke

Lower case fatality rates among hospitalized patients were striking for all degrees of severity, particularly in the case of ischaemic stroke. It is only in severe haemorrhages that no difference was found (Table 3).
Table 3. Case fatality rate in relation to the severity of the condition

<table>
<thead>
<tr>
<th>Type of stroke</th>
<th>Condition, (degree of severity)</th>
<th>Persons taken to hospital</th>
<th>Persons left at home</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Number</td>
<td>Deaths</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>extremely serious</td>
<td>25</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>serious</td>
<td>44</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>moderately serious</td>
<td>32</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>satisfactory</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Embolism</td>
<td>extremely serious</td>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>serious</td>
<td>48</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>moderately serious</td>
<td>38</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>satisfactory</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ischaemic stroke</td>
<td>extremely serious</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>serious</td>
<td>33</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>moderately serious</td>
<td>127</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>satisfactory</td>
<td>31</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
<td>extremely serious</td>
<td>41</td>
<td>34</td>
</tr>
<tr>
<td></td>
<td>serious</td>
<td>125</td>
<td>59</td>
</tr>
<tr>
<td></td>
<td>moderately serious</td>
<td>137</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>satisfactory</td>
<td>31</td>
<td>-</td>
</tr>
<tr>
<td>Overall total</td>
<td></td>
<td>416</td>
<td>532</td>
</tr>
</tbody>
</table>
8. **Staff requirements.** A team consists of three persons:
   - one physician
   - one feldscher
   - and one laboratory worker.

   All members of the team work for 24 hours in every 72. Thus, for a stroke team to be available for work continuously throughout the year five physicians, five feldschers and five laboratory workers are required. In addition, the team includes a driver who has a different time schedule.

   **Equipment.** Patients are transported in a specially equipped minibus containing:

   I. A medical kit with:
      
      (1) an instrument case containing instruments for tracheotomy, intubation, arterial and venous section, and lumbar puncture, as well as syringes and other instruments;
      (2) dressing materials; and
      (3) medicaments for giving first aid.

   II. A laboratory kit with sets of equipment for examining urine, blood, and cerebrospinal fluid; and a microscope.

   III. Apparatus:
      
      (1) electrocardiograph;
      (2) oxygen inhaler;
      (3) apparatus for artificial respiration;
      (4) anaesthesia apparatus; and
      (5) echo-encephalograph.

9. The data obtained by several stroke teams thus support the usefulness of this form of emergency care for patients with acute disorders of cerebral blood circulation. The fate of a patient largely depends on how soon a correct diagnosis is made and adequate therapy is begun. An example is the administration of anticoagulants or fibrinolytic agents in patients with ischaemic stroke, since the effectiveness of such treatment decreases with every hour of illness. Of equal importance is the immediate hospitalization of patients with carotid occlusion in the neck which is developing or has just occurred, since an operation in such cases is effective only in the first six to twelve hours. The complications from which patients sometimes die in the first few days - cardiac or pulmonary insufficiency, aspiration asphyxia, and pneumonia - can be more efficiently prevented and cured in hospital.

10. To sum up, it may be said that early transport of stroke patients by a stroke team is safe and to be recommended, particularly when the patients can be sent to a neurological department where it is possible to carry out all the requisite diagnostic and therapeutic measures, including angiography and surgery. For that reason such departments should be sited in the immediate vicinity of neurosurgical or surgical departments or else their staff should include a resuscitation and surgical group; (a description of the structure and staffing of a specialized neurological department for patients with cerebrovascular disorders is beyond the scope of this paper).
The data obtained in the stroke registry will show to what extent the outcome of the stroke, in terms of the case fatality rate or disability, depends on the speed and the nature of first aid and on the stay in therapeutic establishments of different types.

The organization of stroke teams and also of myocardial infarction teams is an example of one of the main principles of the Soviet health services, which is to bring specialized medical care as close as possible to the public.

Sefer believes that stroke teams should be set up in towns with a population of 300,000 to 500,000 inhabitants. If the teams are not fully occupied, they may be used for other emergency calls as well.

In conclusion:

1. the establishment of an emergency service for stroke patients is possible;
2. the type of service to be recommended, in our opinion, is the mobile stroke team and specialized departments for the treatment of patients suffering from vascular disorders of the nervous system;
3. the effectiveness of the stroke teams' work justifies their establishment. It is difficult to estimate the cost of these services, which is made up of the pay for the staff for day and night duty, the cost of the vehicle, and the cost of the equipment.

DISCUSSION

Dr Okada: Dr Shmidt, I quite agree with your emphasis on the importance of establishing such an emergency care system for new stroke patients. Establishing such a system in Japan would be very important. I should like to ask you two points. First, who has the responsibility in treating the patient at the first stage; who decides the transfer of the patient to the hospital or CVD centre from home? I think the first doctor who takes care of the patient must customarily have the responsibility in the treatment of the patient. I ask your opinion on the desirability for which of the doctors - home doctor or the emergency care doctor - should have the responsibility in this critical period. Second, when such patients in your country have improved in health and have entered the rehabilitation stage, do you send the patient back to the home doctor as early as possible?

Dr Schmidt: The responsibility for the fate of the patient lies on the doctor of the stroke brigade, and after the patient is admitted to a hospital, on the doctor in the hospital. We have no special family doctors, but have district doctors who take care of the stroke patients at home. In some hospitals there are specialized departments for rehabilitation. We have also special health resorts.

Dr Ito: We also transport our stroke patients, but it is very difficult to admit them to a hospital within a few hours after the onset, except for a few cases. In these patients we have sometimes found extravasation on angiogram, that is, leakage of contrast medium from a cerebral vessel; if such patients were left alone, almost 100% of them died. When we stopped this leakage by surgical methods, the fatality rate dropped to 37%. It is therefore essential to transport these patients immediately to a hospital.
with a neurosurgical department. How many cases of extravasation did you observe in patients who were transported within a few hours and on whom angiography was carried out? We observed extravasation in 30% of the patients within 5 hours and we did not see any extravasation in patients after 5 hours.

Dr Werktl: The question concerns haemorrhage. What proportion of cases were cerebral haemorrhage in those you transported?

Dr Shmidt: The percentage of haemorrhagic stroke was about 24% and ischaemic stroke 68%.

Dr Kagan: How big does a community have to be before it can have a hospital with a specialized neurological and neurosurgical institute, and from how broad an area is it reasonable to draw patients who can be transported to this institute?

Dr Werktl: I see in the paper the statement that a stroke team should be set up in towns with a population of 300 000 to 500 000 inhabitants, which partly answers your question.

Dr Kagan: Could you tell us how many such institutes are present in the Soviet Union?

Dr Shmidt: I do not know exactly. Special brigades for urgent aid have been organized in 6 or 7 towns in the Soviet Union.

Dr Paul: In the USA we have emergency cardiac resuscitation teams, which sometimes do only cardiac resuscitation but in some communities serve various functions; thus, they do cardiac resuscitation but they also take care of other illnesses. Do stroke teams service stroke cases only or do the personnel have other functions?

Dr Shmidt: They sometimes have other functions but mainly serve the stroke patients.

Dr Weiss: I would like to add a little bit from our experience. We do not actually have the home doctor system in our country. We are returning to this system because we think that it is a good one, which enables the home doctor to carry the medical problems of the family and to advise on other social problems as well. When a stroke happens the emergency station is informed. All the information received at the emergency station is sent to a chief doctor who sends a special group according to the information obtained. A stroke patient would be transported to the neurological division on duty.
REHABILITATION OF STROKE PATIENTS IN THE COMMUNITY

by

M. Weiss

Musculoskeletal impairment resulting from stroke is one of the most serious problems in rehabilitation. After a stroke, in addition to persisting, severe damage of all vital functions, the patient lives under the constant threat of a new attack. This is particularly true for younger patients. However, in practice, this younger age group has a greater recovery potential because of a greater compensatory capacity and more favourable social situation.

The studies conducted in Poland on 1000 stroke cases treated at the Konstancin Centre show that stroke demands a long-term rehabilitation programme, particularly in community life.

Unfortunately only a very small number of stroke cases leave the rehabilitation institute without any significant handicap. These handicaps, particularly impairment of the upper extremities, always change the total functional situation and sometimes create difficulties in communication. This situation influences the entire social outlook, and in some cases can break up family life. The patient has to struggle with emotional instability, and with behavioural and psychological mechanisms aiming to obtain a state of equilibrium. It is most important to have complete insight into the nature of the illness or disability in the course of the stroke.

One of the most important research aspects could be the recovery potential of younger patients at a productive age, i.e., their emotional and psychological reactions to their environment. A modern, comprehensive rehabilitation programme should cover both social and vocational aspects. Even the most sophisticated medical rehabilitation programme would not be successful if it did not pay attention to this goal.

MEDICAL REHABILITATION

In order to enable the patient to return to the community, any impairments should be reduced to a minimum. Some stroke cases would not be disabled or dependent on others if the medical programme was comprehensive enough and the community properly prepared to accept them. Medical rehabilitation must be very intensive and complex. Experience has shown that stroke patients cannot be treated together with patients with other musculoskeletal disabilities, since their psychological reactions are different. For example, stroke patients do not accept a very active programme and are unable to participate in group exercises.
A medical rehabilitation programme for a stroke patient is an example of team work. Every medical and allied profession participates in this activity, and emphasis should be placed on problems of nursing, physiotherapy, occupational therapy and speech therapy. New trends have been introduced into this team such as orthosis technicians and orthopaedic surgeons. No less attention should be paid to psychotherapy, under the supervision of a psychologist. All members of the team contribute to the final result.

The modern stroke rehabilitation team should consist of a specialist in rehabilitation or a physiotherapist who is oriented towards neuro-orthopaedics, nurses fully trained in therapeutic procedures, physiotherapists who have a good knowledge of neuropathology, an occupational therapist well trained in the treatment of spasticity, bioelectricity specialists, a speech therapist trained in psychology, a clinical psychologist able to synthesize all the information obtained from other members of the team, an orthopaedic surgeon to treat spasticity, medico-social workers, and a vocational counsellor.

Few ways of correcting brain damage are available at present. Some neurosurgical schools propose a direct approach and total removal of the haematoma. Also thrombectomy is now a popular operation, using a high oxygen supply to the brain and local cooling or other means to attack the focus directly in the early stages of stroke.

However, the only consistent source of improvement is spontaneous compensation. This can appear basically by recruiting nerves into a new action which slightly differs from their previous function. Cells and nerves destroyed by the primary or secondary ischaemia have no capacity for regeneration. Medical and allied therapists must stimulate all the existing peripheral proprioceptive and interoceptive reactions in the best possible way. Simultaneously all non-physiological impulses must be eliminated. Joints maintained in certain positions become painful when adhesions develop between the fascia and the capsule. Special techniques of neurophysiological facilitation developed by Kabat and others are among the best methods for stimulating compensation after stroke.

EARLY REHABILITATION

One of the first theses of the Sorbonne Faculty of Medicine in the eighteenth century touched upon the problems of early activating therapy for stroke patients. The author presented the results obtained by applying a standing position and passive movements very soon after the attack. Modern rehabilitation must follow this path. In early activating therapy we cannot neglect the status of the individual patient and his reactions to treatment. For this reason the initiator and creator of an early therapeutic programme must be an experienced neurologist. In this paper I should like to present new possibilities of rehabilitating stroke patients. The basic idea which must be stressed as strongly as possible is that rehabilitation starts from the moment when the life-threatening stage of stroke is over. Of course, even in the acute stage, some breathing exercises and adequate maintenance of airways can be executed by a physiotherapist.

INITIAL PHASE

Routine physiotherapy and activating therapy start three to four days after the attack. There is unjustified fear on the part of many doctors or family members if this active therapy is undertaken at home. Maximum
damage has already been done to the brain by the local ischaemic process. Secondary changes can be prevented only through an active approach with intensive, individually programmed physiotherapy. Because voluntary movement is lacking, all possible external stimuli should be applied, as follows:

(a) early tilting of the bed repeated a few times daily;
(b) passive motions to train all joints;
(c) exercises of intact limbs against resistance;
(d) breathing exercises.

Early attention should be paid to preventing contractures – particularly those found typically in the shoulder joints and in drop-foot with external total limb rotation.

Active nursing includes:

(a) prevention of contractures by physiological positioning of limbs;
(b) prevention of bedsores;
(c) encouraging self-feeding and self-hygiene;
(d) developing of bowel and urine control.

Because of the shortage of experienced physiotherapists, nurses should be aware of all the programmes described here. This is particularly important when we consider the growing number of stroke patients in the modern community. A very important general rule is to avoid any "sick-room atmosphere" around the patients; both the family and medical personnel should be involved in this task. Our experience and that of many authors show that simple tests, such as Wortenberger's or Treanoy's, may be used to assess prognosis in the first 10 days. In contrast to older patients with previous small strokes, younger patients after a massive cerebral attack would normally be left with a severe permanent deficit.

In cases where the dominant hemisphere has been damaged, a breakdown in the ability to use speech or to communicate occurs; the patient also loses his primary means of relating himself to his fellow men and to his environment. This complication, of course, requires the identification of what type of communication disturbance has occurred.

If a patient is thought of simply as being aphasic, the staff have a tendency to approach him with the preconceived notion that he does not understand and is unable to talk. As a consequence, the personnel usually ignore the fact that a stroke patient is able to communicate. Very often, the staff of a neurology department treat such a patient as being mentally intact but physically disabled.

Symptoms of difficulty in communication are common in the early stage, and the therapeutic approach, the techniques of presenting instructions, and the environment of treatment should be based on an evaluation of the speech pathology.

Recent studies have shown that the degree of recovery in communication is related to many factors:
(1) degree and type of disorder of the communication centre;
(2) degree of patient's physical involvement;
(3) general status of the patient;
(4) degree of neurological deficit;
(5) emotional adjustment to the stroke;
(6) family involvement and reactions.

Our experience and that of others indicate the need for speech diagnosis and speech therapy in the early stages to prevent the mental and frequently irreversible problems in communication. Patients who have a damaged brain have confused thoughts and are limited in their verbal expression, and they have an internal struggle to organize and express their thoughts. To prevent this mental self-destruction, stroke cases with speech impairment must receive some means of communication as soon as they become conscious.

In a comprehensive stroke rehabilitation unit a patient who has no visual comprehension deficit and can understand speech is given a set of picture cards which depict the things that he or the nurse wishes to communicate to each other. For patients who are able to read, the pictures would have words printed on them.

Both motivation and the learning of rehabilitation procedures require understanding between all members of the rehabilitation team and the patient. All staff dealing with a multidisciplinary approach and family members must be made aware of:

(1) prevention of the conditions of non-communication;
(2) development of simple techniques of immediate communication;
(3) the fact that the patient must be taught and not conditioned.

Normally, contact with a speech pathologist or a therapist starts only after the patient has been in total isolation for a few weeks. Experience shows that this is much too late.

STANCE AND WALKING

It is not possible to make an objective assessment of a hemiplegic patient until he is able to stand and walk. We see again no contraindications for this procedure at the very early stage. No muscle examination or dynamometry can give answers to basic questions such as which compensatory synergic activities to develop, which groups of muscles need therapy, etc.

After studying large numbers of hemiplegics, Gracianin, Dimitriovic, Mooney, Perry and others came to the conclusion that technically we can influence the development of new compensatory patterns. With the lower extremities use of a bio-electric brace permits phasic stimulation of the peroneal nerve and helps most hemiplegic patients to walk in a normal manner. This field of bio-electric stimulation opens up new horizons in rehabilitation and has potential for wider application, but further clinical study is needed.
SPASTICITY

One of the most difficult conditions for rehabilitation and a determinant of long-term results is spasticity. Severe spasticity of the upper extremities incurs both a psychological and a physical handicap. Improvement cannot be obtained in extensive physiotherapy and occupational therapy programmes because of spasticity. The patient is continually under the influence of a flow of pathological impulses, thereby creating tension and neurosis, and thus becomes dependent. Clinical methods of control of spasticity involve techniques of "deafferentation". Some drugs do influence spasticity, but simultaneously the patient's ability for active training is reduced. Local muscle cooling is widely used and should be applied more often, particularly in the early stages of spasticity. The basic theory that even with spasticity certain compensatory movements exist demands a more active approach in research. In this field, some new trends are seen:

(1) local nerve blocks with phenol;
(2) surgical adjustment of muscle length;
(3) resectioning of nerves.

After these operations, even where there is a total lack of normal reciprocal inhibition, progress in activities of daily living can be observed in all cases: hemiplegics can easily learn to manage with one hand only.

HEMIPLEGICS IN THE COMMUNITY

A sophisticated treatment and rehabilitation programme is not always available. Probably most stroke patients have no possibility of obtaining the minimum of the programme described above. For a better understanding of all the difficulties and to enable the formulation of practical proposals, the behavioural sequelae associated with cerebral vascular damage are listed here:

(1) intellectual deficits;
(2) emotional lability;
(3) perceptual distortions;
(4) impairment in learning ability;
(5) problems in self-conceptions.

Stroke patients can represent one of the three basic types of neuropsychological errors, sometimes in combination:

(1) input errors;
(2) faulty process of interpretation;
(3) output errors.
We know from practice that many of these important behavioural pathological symptoms would regress completely. Most improvement is seen during the first three to six months. After this time the new personality of the patient is rather fixed and should be accepted by the community.

One of the most striking features of stroke patients is their apparent emotional lability. Patients sometimes cry on the smallest provocation, and just as easily stop crying: they are unable to explain why, being so embarrassed at their behaviour. This condition is very difficult to cope with in the community, because it is very frequently connected with:

(a) loss of self-control;
(b) reduced tolerance of stress;
(c) inability to tolerate other members of the family, or co-workers.

Some degree of mental impairment always exists in a stroke patient with cerebral vascular disease. The patient's adaptation to his new bodily functions needs great patience and understanding from all members of his family and co-workers. The social and vocational readjustment of a stroke patient must always be worked out systematically. When a hemiplegic has gained an accurate picture of what he can or cannot achieve and when functional compensation has begun, he can begin to maximize his residual potential. Very frequently the social result is not equal to the physical one. The improvement depends more upon his ability to find new ways of dealing with the environment.

Some motivation for returning to an independent life is one of the most important elements in the rehabilitation programme. Patients in hospital must participate in the overall planning of their future way of life. Our experience has shown that it is necessary to prepare a patient with practical tests; we call this "social and vocational confrontations". In every case the observations of the patient and his family should always be taken into consideration.

COMMUNITY ASPECTS OF REHABILITATION OF STROKE PATIENTS

Stroke is a serious disease at its onset and needs the application of all the techniques that are used in emergency cases. Ideally, every stroke patient should be transported to a hospital where the necessary equipment and trained personnel are available. In cases where such facilities are not available, general practitioners and family members must try to:

(a) save life;
(b) prevent disability;
(c) prevent disabling complications; and
(d) develop conditions for a simple home-rehabilitation programme.

As far as medical education is concerned, we all know that not very much time is reserved for this most common disease and its sequelae in our civilized world. Appeals should be made for educating and training nurses and doctors in early rehabilitation programmes for stroke cases. The
Techniques used are very simple; no equipment is needed, just common sense and medical thinking on the lines of prevention. In all hospitals stroke cases should be concentrated in one service and all possible active forms of rehabilitation techniques should be applied as soon as possible. Family members should participate in the rehabilitation programme as early as possible, and should help where possible in encouraging passive movements, sitting-up in bed, walking, etc.

Organized, progressive care for stroke cases in hospital is one of the best ways of ensuring a good environment around hemiplegic patients. This same environment should be created at home after the patient returns from hospital or for patients who are not hospitalized. We all know that excellent results can be achieved by family members given the proper guidance. Many hemiplegics would demand from the community resources prolonged comprehensive rehabilitation services in special institutions. Because of the psychological problems involved this type of impairment needs to be treated separately in large rehabilitation centres or it can be treated on an outpatient basis. The outpatient rehabilitation departments or physiotherapy departments should continually assess the future rehabilitation programme on an individual basis. These services are also responsible for social and vocational adjustment.

Conclusions

The total rehabilitation of a stroke patient in the community must include consideration of his adjustment on a personal basis, with the family, and in some cases vocationally. These are bound inextricably on the one hand with the patient's ability to adjust, comprehend, and accept his new functional status, and on the other hand with the attitudes as well as the overt emotional reactions of family members, friends, and co-workers towards the patient and his disability, all of which play a very important part in his readjustment to community life.

The emotional, intellectual, educational, vocational, and social status before the stroke also contributes to the individual adjustment of stroke patients. They gain more in their physical functions when they have been treated early enough in a comprehensive stroke rehabilitation centre. A general feeling of repugnance is often associated with hospitals for chronic diseases. This stigma is largely associated with standards of care that are less stringent than those in other hospitals. Just as with modern obstetric or trauma care, which entail basically routine preventive measures, so prevention of complications in stroke must become a disciplined routine before efforts in rehabilitation can be successful. Knowledge of the basic management of stroke patients should be a part of the education in general medicine, neurology, orthopaedics, neurosurgery, and nursing. Without a large education and teaching programme in minimum rehabilitation for the medical and allied professions, full rehabilitation of stroke cases in the community can never be achieved. Much responsibility must be delegated to the family members and home therapists. Everyone must work actively and positively to implement a complete rehabilitation programme. Every member of the community must be made aware of the continuous and dynamic integration needed in their actions. From beginning to end, the personnel in public health, private hospitals, outpatient departments, etc. must make concerted efforts to enable the stroke patient to make the best use of his physical, intellectual, and emotional capacities, and thereby become again a productive, active, independent, and useful member of the community.
REFERENCES


DISCUSSION

Dr Isomura: In your country, what type of orientation programme is under way to enhance the understanding of general practitioners about early rehabilitation? Our experience shows that the effects of a rehabilitation programme are less significant for patients with mental disturbances, particularly aged persons. What kind of approach is made in your country?

Dr Weiss: You presented a very interesting point because you placed attention on the early stage. When rehabilitation is neglected at the early stage a higher degree of dependence develops. These patients would need a very expensive rehabilitation programme with surgery and other long-term techniques. You can compare stroke cases to spinal cord cases; if we admit a patient with a spinal cord injury to a proper comprehensive institution, many complications can be prevented. Now, I think that early rehabilitation is good treatment for stroke. We are able to tell very soon if a patient will be able to return to the community to continue an independent life.

A speech therapist should engage in this difficult task when a patient has a problem in speech. In this case we must provide him with some simple means of communication to facilitate contacts with nurses, the cleaning personnel, and with the doctor. Our colleagues from the USA and the USSR express a strong view that we should start speech therapy as soon as possible. Now, what do we do with severe cases? Severe cases that cannot be transferred to the community from hospital and those who are treated at home should be controlled in a special centre. We have a special hospital for the rehabilitation of stroke cases in Konstantin. Because this unit is placed close to us we are able to supply them with orthosis to do small surgeries. So much about rehabilitation, in which we would rather stress the prevention of disabilities.

Concerning the last question about how we train medical personnel in this programme, we convinced our University in Warsaw to give a six-day intensive course to every student before he leaves the university.

Dr Werktl: This only takes care of the medical students and the question was how do you take care of the general practitioners?

Dr Weiss: We train general practitioners with short courses or postgraduate courses on rehabilitation.

Dr Strasser: Two short questions. One to my Japanese colleagues: I had the opportunity to see in a rehabilitation centre near Beppu the system in which the spouse of the patient was also in the hospital; besides helping in the hospital, the spouse learns the methods of kinesitherapy and what to do about further rehabilitation. My question is, has this very interesting
system been evaluated and do you think it is useful? Another question to Dr Weiss: stroke is largely a geriatric condition; are there any differences in the approaches to the old and very old concerning rehabilitation?

Dr Weiss: In our conditions we do not differentiate between geriatric and non-geriatric cases. We would like to have all of them back home. Of course there are cases which should be transferred to nursing homes because of their family situations. The trend is even to redesign conventional nursing homes and we are reserving one full floor for nursing care in a new quarter in our town which is now under construction. We would prefer this system instead of building expensive and big old villages like the existing ones in some countries.

Dr Isomura: The cooperation of family members is essential for restoring normal living pattern to stroke patients. With respect to a patient who has recovered to some extent, thanks to a hospital rehabilitation programme, he may still be kept bed-ridden unless the training is successively carried on after discharge. Consequently, we encourage family members to be with the patient for a certain period before his discharge so that they may realise what type of training is required at home. Another point is that Japanese style houses require much modification to suit the physically handicapped. Guidance, therefore, is provided on the remodelling of toilets, beds, and bathing facilities.

Dr Kobayashi: In answer to Dr Strasser, I think that scientific evaluation of family attendance in hospital has not yet been done.

Dr Kameyama: In our hospital we have a lot of old people and their rehabilitation is a serious problem. One of the biggest worries is that about a quarter of the elderly patients with cerebrovascular stroke are bed-ridden and we have to devise appropriate treatment, as Dr Weiss has just mentioned. We are planning the establishment of half-way houses in Japan. In our country, every patient in hospital is exposed to the western style of living, but at home he will live in the ordinary Japanese style and to this he must be adapted before his discharge from hospital.
In 1971, the Japanese Government conducted a nationwide survey on cardiovascular diseases in order to collect accurate information. Persons aged 30 years or older were surveyed in the 197 areas which were randomly selected from all Japanese census tracts. A follow-up survey was repeated on the same subjects in 1972 to study serial changes during the one year period. Some of the results have been introduced during this meeting by Dr. Kobayashi.

The remarkable progress in prevention and care of cardiovascular diseases enables us to reduce the number of deaths from cardiovascular diseases and to improve the quality of life of a patient by modern rehabilitation.

The national Government has therefore decided to improve the present medical care system for cardiovascular diseases by:

1. Improving or creating special clinics or facilities for cardiovascular diseases in 62 national hospitals;

2. Establishing a national centre for cardiovascular diseases in Osaka. This national centre will serve as a central scientific institute for research, training, and medical care for cardiovascular diseases, as well as contributing to the expansion and completion of such facilities throughout Japan.

Mass examinations for cardiovascular diseases, especially hypertension, have been conducted by health centres in many parts of Japan with the aim of preventing stroke and heart disease (Table 1). The proportion, as well as the number of examinations for "adult diseases" (mainly cardiovascular diseases) has been increasing year by year, accounting for 13.7% of total health examinations in 1971. Besides medical care, modifications in diet and living conditions are necessary in controlling high-risk subjects who are detected in case-finding programmes. For this purpose, public health nurses visit patients in their homes and give them individual instructions on dietary habits and living conditions. The number as well as the proportion of home visits for "adult diseases" by public health nurses has been increasing annually (Table 2). However, the increasing number of patients has made home visits difficult with the limited number of public health nurses. It would be desirable to organize, with the cooperation of local physicians, a number of group sessions in each district, and to eventually establish a community-wide stroke prevention system.
From 1969 to 1972, the national Government conducted special stroke prevention programmes with the aim of reducing the number of stroke patients. In the first year for such programmes (1969), six prefectures were selected where the death rates from cerebrovascular diseases were twice or more than twice the national average. In the next year (1970), six other prefectures were added for such special programmes. In this programme, examinations were conducted in two steps. In the first examination blood pressure and personal history were obtained from all persons aged 40 to 64 years who lived in the designated districts, and persons with abnormal findings were screened for the second examination. The number of patients examined in the special stroke prevention programmes is given in Table 3. After the second examination, the persons who were judged to require medical treatment or guidance were referred to local physicians with the suggestion that they should receive continuous medical care; they were also given instructions on dietary habits and living conditions. The detection of persons with hypertension and its complications is important, but the effective aftercare of these patients is as important as detection. The success of these special pilot programmes led to the establishment of a nationwide stroke control programme and the Government has planned an annual hypertension screening programme (measurement of blood pressure and urine test) to be enforced in conjunction with the existing tuberculosis control programme in all parts of Japan.

Thus, after careful evaluation, various pilot studies on cardiovascular diseases have been expanded to nationwide control programmes. It is hoped that such programmes will result in reducing the number of deaths from stroke.

Table 1. Health examination for cardiovascular diseases carried out by health centres

<table>
<thead>
<tr>
<th>Year</th>
<th>(A) Total number who received all health examinations</th>
<th>(B) Number who received CVD examination</th>
<th>B/A (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1967</td>
<td>20 906 077</td>
<td>1 579 763</td>
<td>7.6</td>
</tr>
<tr>
<td>1968</td>
<td>20 574 575</td>
<td>1 820 084</td>
<td>8.8</td>
</tr>
<tr>
<td>1969</td>
<td>19 336 619</td>
<td>2 053 017</td>
<td>10.6</td>
</tr>
<tr>
<td>1970</td>
<td>18 731 998</td>
<td>2 314 606</td>
<td>12.4</td>
</tr>
<tr>
<td>1971</td>
<td>18 079 501</td>
<td>2 481 959</td>
<td>13.7</td>
</tr>
</tbody>
</table>
Table 2. Visits by public health nurses for cardiovascular diseases

<table>
<thead>
<tr>
<th>Year</th>
<th>(A) Total number of visits for all cases</th>
<th>(B) Number of visits for CVDs</th>
<th>B/A (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1967</td>
<td>3 778 319</td>
<td>467 603</td>
<td>12.4</td>
</tr>
<tr>
<td>1968</td>
<td>3 765 505</td>
<td>529 390</td>
<td>14.1</td>
</tr>
<tr>
<td>1969</td>
<td>3 713 951</td>
<td>586 675</td>
<td>15.8</td>
</tr>
<tr>
<td>1970</td>
<td>3 683 787</td>
<td>639 347</td>
<td>17.4</td>
</tr>
<tr>
<td>1971</td>
<td>3 608 536</td>
<td>693 739</td>
<td>19.2</td>
</tr>
</tbody>
</table>

Table 3. Special stroke prevention programme, 1971

<table>
<thead>
<tr>
<th>First examination:</th>
<th>Number of persons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number to be examined</td>
<td>Total</td>
</tr>
<tr>
<td>207 449</td>
<td>119 254</td>
</tr>
<tr>
<td>Those actually examined</td>
<td>144 454</td>
</tr>
<tr>
<td></td>
<td>88 195</td>
</tr>
<tr>
<td>Second examination:</td>
<td></td>
</tr>
<tr>
<td>Total number to be examined</td>
<td>Total</td>
</tr>
<tr>
<td>71 032</td>
<td>42 061</td>
</tr>
<tr>
<td>Those actually examined</td>
<td>56 785</td>
</tr>
<tr>
<td></td>
<td>28 971</td>
</tr>
<tr>
<td>Those found to require medical treatment</td>
<td>30 692</td>
</tr>
<tr>
<td></td>
<td>12 391</td>
</tr>
<tr>
<td>Those found to require medical advice and guidance</td>
<td>11 138</td>
</tr>
<tr>
<td></td>
<td>4 363</td>
</tr>
<tr>
<td>Those found to require periodic examination</td>
<td>14 937</td>
</tr>
<tr>
<td></td>
<td>5 513</td>
</tr>
</tbody>
</table>
DISCUSSION

Dr WerkH: What kind of medical treatment did you provide for this vast number of patients?

Dr Komachi: I am participating in the hypertension control programme of communities supported by the Ministry of Health and Welfare. Simple anti-hypertensive drugs such as rauwolfia alkaloids, chlorothiazide, and hydralazine are most frequently used but the choice of drugs is left to general practitioners and to local hospitals.

Dr Reader: I think that, after screening, your population was either given advice, given treatment, or reviewed at some subsequent date. What were the cut-off points to divide the population into those three groups?

Dr Shimada: The three groups were: a group requiring medical treatment, one requiring observation, and one requiring neither treatment nor observation. We have criteria for each group based on the combination of diastolic pressure, systolic pressure, symptoms and signs of cardiovascular diseases including ECG and eyeground findings and proteinuria. After the first screening, public health nurses visit hypertensive patients in their homes, give guidance concerning food and general living, tell them about the importance of treatment, and refer the patient to hospital, if necessary.
HYPERTENSION AND STROKE CONTROL
IN A LARGE OCCUPATIONAL GROUP

by

Yasuyuki Chiba

INTRODUCTION

The major role of hypertension control is to prevent the possible occurrence of cerebral stroke and ischaemic heart attacks. Mortality from these two complications reached the top place in Japan and countermeasures are an urgent national necessity. To cope with this need, our study team began, in 1960, hypertension control for 450,000 employees in the Japanese National Railways (JNR) throughout the country, using the network of the well-organized JNR health control system which was initially established for antituberculosis measures. The JNR Central Health Institute with which we are affiliated functions as the headquarters of the health programmes as well as an operating health centre for 80,000 workers in Tokyo, while each of the local JNR health centres deal with about 10,000 to 20,000 workers. Formulating a uniform methodology, pooling the results, and having the support of the company in regulations and budget can be counted as the advantages of studies in an occupational group such as the JNR.

SUBJECTS

Subjects were employees of working age, from 18 to 55 years. These workers have somewhat better dietary and environmental conditions than the general population who still work hard and whose diet is mostly rice and salt with a poor protein and fat content. Such a difference may have an influence upon the incidence rates of cerebral stroke and heart attack, which was half that of the general population in Japan but was still higher than those in Europe or America.

METHODS OF EXAMINATION

1. Age for hypertension control

In order to obtain the maximum benefit with the minimum effort, the target age group for hypertension control was decided by considering the number of workers who would need hypertension control and the incidence of stroke and heart attacks in that age group. Workers aged over 40 years comprised 30% of the total workers and 75% of the total cases of stroke and heart attacks when our hypertension control was begun in 1960. Therefore, workers aged 40 years and over were selected as the target population.
2. **Blood pressure limits for hypertension and control screening** (Fig. 1)

The limiting levels of blood pressure in screening should be decided on the basis of what percentage of the cases of stroke and heart attack would be expected to occur. When the 150 mmHg systolic and/or 90 mmHg diastolic pressure limits were set up, the workers with pressure above these levels amounted to 30% of the total workers and 75% of the cases of stroke and heart attacks. Therefore, these levels were considered to be the practical and effective limits in screening for hypertension control.

3. **Other items for examination**

A sample of 900 workers over the age of 40 years were examined for blood pressure, ECG, and cardiothoracic ratios on chest X-ray films. As shown in Fig. 2, a single measurement of blood pressure did not prove to be a sensitive enough method for the identification of persons at risk of developing cerebral infarction or heart attack. Therefore, multifacet cardiovascular examinations have been made on a large number of workers in Tokyo at the ages of 40, 45, 50, and 55 years for the past few years.

4. **Frequency of cardiovascular examinations for train drivers**

Since a cerebral stroke or a heart attack could occur in a train driver on duty and lead to an accident, train drivers are requested to undergo cardiovascular examinations every two years, a shorter interval than medical examinations for workers with other jobs.

5. **Registry of cerebral stroke and heart attack**

If a worker takes sick leave owing to a stroke or a heart attack for six or more days, he must by the regulations present a report to the JNR health centre. Less than six days' sick leave is not yet registrable for technical reasons. The registry document for Tokyo workers follows the format of the WHO stroke record form.

6. **Health education**

The employees who need no medication but only regular checkups in the future are sent to the JNR prevention clinic for three days for practical health education on high blood pressure, including advice on salt-reduced meals and on general living.

**OBSERVATIONS ON CARDIOVASCULAR DISEASE STATUS**

1. **Type of cerebral stroke**

At the same blood pressure level, the incidence rate of cerebral infarction was higher among older persons than among younger ones. However, cerebral haemorrhage is the most frequent complication in our occupational group with the upper age limit at 55 years.
Fig. 1  Screening efficiency during a year

40—54 years (144,553 person-years)

Screening line of blood pressure →

Systolic and/or diastolic

HI

Rates of the cases required with detailed examinations (Rates of the cases over the screening line)

Notes: 1. Screening efficiency = Number of episodes occurring from cases beyond the screening level × 100
Number of episodes occurring within a year after screening test

Fig. 2  Relationship between blood pressure, ECG and cardiothoracic ratio (40—55 years)

Cardiothoracic Ratio (53% or more)

(12.9%)

Hypertension (150/90)

(19.3%)

Abnormal ECG

(20.6%)

5.4

2.5

4.5

5.4

10.8

9.8

10.8

(61.8%)

(41.8%)

Notes: 332
2. Incidence rate of cerebral stroke and heart attack according to blood pressure and age (Fig. 3)

At the same levels of blood pressure, the incidence rates of stroke or heart attack were higher among older persons than among younger ones. The higher the blood pressure, the smaller the difference in incidence rates by age.

3. Incidence rate of cerebral stroke according to the degree of physical labour (Fig. 4)

The incidence rate of stroke was higher in the heavy labour group than in the light labour group and might be related to the fact that heavy labourers requiring more calories tend to take an unbalanced diet with a large amount of salt.

4. Regional differences (Fig. 5)

According to the statistics of the Ministry of Health and Welfare, the mortality rates of stroke showed a significant difference by geographical regions. A similar regional difference in mortality rates was observed among the JNR workers.

Fig. 3 Incidence of episodes according to systolic blood pressure and age
Labour condition and incidence of cerebral and coronary heart episodes (40–55 years)

- Cerebral haemorrhage
  - Incidence rate per 10,000: 8.7 (22)

- Other cerebral stroke
  - Incidence rate per 10,000: 9.5 (24)

- Coronary heart attack
  - Incidence rate per 10,000: 3.6 (57)

Person-year
- Group of night shift and medium degree of work: (156,506)
- Group of night shift and heavy degree of work: (25,332)
RECENT CHANGES IN PHYSICAL STATUS

(a) Living

Living conditions among the Japanese have improved during the past 10 years as a result of economic development. This may have contributed to the reduction in the occurrence of strokes and heart attacks.

(b) Body weight

The average body weight of 40 year-old employees at the initial cardiovascular examinations has been increasing by 1 kg every three years.

(c) Cholesterol levels (Fig. 6)

After a period of six years the average serum cholesterol level was 20 mg/dl higher, regardless of the subjects' age.

(d) Blood pressure

The prevalence of hypertensive persons and of those with a history of treatment for hypertension among the employees aged 40 years was higher in 1971 than in 1962 (Fig. 7).

(e) Drinking habits

The number of drinkers of 360 ml or more of Japanese "sake" has increased among the 40 year-old employees after a period of six years.
Fig. 6 Serum cholesterol in JNR employees in 1963 and 1969

<table>
<thead>
<tr>
<th>Age in years</th>
<th>Number of subject</th>
<th>Cholesterol (mg/dL)</th>
<th>After 6 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-25</td>
<td>(154)</td>
<td>180.7</td>
<td>158.0</td>
</tr>
<tr>
<td>26-31</td>
<td>(231)</td>
<td>167.4</td>
<td>169.4</td>
</tr>
<tr>
<td>32-37</td>
<td>(173)</td>
<td>182.9</td>
<td>184.1</td>
</tr>
<tr>
<td>38-43</td>
<td>(354)</td>
<td>170.5</td>
<td>181.7</td>
</tr>
<tr>
<td>44-49</td>
<td>(87)</td>
<td>171.0</td>
<td>184.7</td>
</tr>
</tbody>
</table>

Fig. 7 Distribution of systolic blood pressure in JNR employees in 1962 and 1971

Obesity ± 9%

1962 (388 Cases)
1971 (335 Cases)
(f) Smoking habits

The number of smokers of more than 20 cigarettes a day increased during the six-year period.

(g) Diet (Fig. 8)

The fat intake of the Japanese population has increased since 1960 according to a census taken by the Ministry of Health and Welfare.

![Fig. 8 Changes of calorie intake among the Japanese](image)

EFFECT OF HYPERTENSION CONTROL

1. Changes in blood pressure

The mean blood pressures, according to age groups, were compared between 1965 and 1970 (Fig. 9). In the 40-44 years age group, the mean blood pressure was higher in 1970 than in 1965, but among the workers aged 50 years and over it showed a decrease during the same period. This could be interpreted to mean that there is an overall tendency towards elevation of blood pressure, as shown by the workers in the 40-44 years age group, who had not been enrolled into the hypertension control programme. The older workers had been subjected to hypertension control and this may have been effective enough to cancel out the general rising trend in blood pressure levels.
2. Changes in the incidence rate of cerebral stroke

The incidence rates of cerebral stroke in the initial examination period (1960-63) and in a later period (1968-69) were compared. Those workers in the 30-39 years age group, who had not undergone cardiovascular examinations, showed a higher incidence rate of cerebral haemorrhage in the later period; and those aged 45 years and over showed a lower incidence between the same two periods, which may have been due to effective hypertension control (Fig. 10). As for cerebral infarction, as shown in Fig. 11, the incidence rates rose in all ages between the two periods; the rising tendency was less marked, however, in the age group that received hypertension control.

3. A trial of preventive medication for mild hypertensive subjects

The effect of treatment of mild hypertensive subjects was investigated in 1961 by a double blind method. The subjects were persons with systolic 150-169 mmHg and/or diastolic 90-109 mmHg by the first and second surveys and with no marked abnormalities in the ECG or cardiothoracic ratio. The treated group comprised 426 cases and the placebo group 408. Medication
Fig. 10  The incidence rate of cerebral haemorrhage according to age in 1960-1963 and 1968-1969

Initial observation in 1960 - 1963  
Incidence of cerebral hemorrhage: 479/1,730,000 person-years

7 years after in 1968 - 1969  
Incidence of cerebral hemorrhage: 281/920,000 person-years

Fig. 11  Incidence of cerebral infarction according to age in 1960-1969

Initial observation in 1960 - 1963  
Incidence of cerebral infarction: 202/1,730,000 person years

7 years after in 1968 - 1969  
Incidence of cerebral infarction: 202/920,000 person years
lasted three months and the results obtained two years later were as follows:

(a) As shown in Fig. 12, the treated group showed lower blood pressure than the placebo group during the three months after the drug discontinuation.

(b) No rebound phenomenon was found.

(c) During a two-year observation period, not a single case of stroke or heart attack was found in the treated group, but two cases of cerebral haemorrhage and one cerebral infarction occurred in the placebo group.

(d) No serious side-effects were observed.

Although these favourable results were obtained, preventive medication has not yet been applied to all mild hypertensive employees in the JNR.

Fig. 12 Results of preventive medication for mild hypertensives - a double blind test
V. SUMMARY AND RECOMMENDATIONS

Recent progress in the control of hypertension and stroke has been reviewed, and the research needs and knowledge to be applied in the community control of hypertension and stroke have been summarized.

1. Control of hypertension in the community

High blood pressure is a prevalent condition in most parts of the world, with a few exceptions. Prevalence data presented from Japan did not appear to be essentially different from that from other areas.

Moderate and severe rises in blood pressure must be adequately treated, but more studies are needed to determine the effectiveness of treatment in the prevention of ischaemic heart and brain disease.

Hypertensive patients comprise 10-20% of the total population in many countries, and their management requires a community approach. The use of registers, screening, treatment, and follow-up in the WHO hypertension control programme was presented as a model, and similar programmes in other areas were also presented. Whereas single, casual blood pressure measurements have epidemiological significance, several measurements should be taken before the diagnosis of hypertension is established for therapeutic purposes. The role of allied health personnel was emphasized. Inviting doctors specializing in fields other than internal medicine to take blood pressure measurements, depending on the local resources and social situation, and using trained nurses or volunteers under a physician's supervision were proposed. Devices for automatic blood pressure recording and eyeground photography were presented. Their possible application merits consideration, pending further refinement and standardization.

Mild hypertension is defined as a diastolic blood pressure of 90-109 mmHg, based on multiple blood pressure measurements under standard conditions and on separate days. It is accepted that patients with a diastolic blood pressure above this (or with a systolic blood pressure of 180 mmHg or over) should in most circumstances be treated. Patients with mild hypertension should be rescreened at yearly intervals as a minimum, and those manifesting additional risk factors should be considered for active treatment.

The current treatment of hypertension by drugs is by no means ideal, but primary prevention is hindered by lack of knowledge on the etiology of essential hypertension. Epidemiological study is expected to provide an insight into the etiology. In some less industrialized societies blood pressure levels do not rise with age; however, when people from these societies move into an urban environment their blood pressure distribution approaches that in other developed societies. None of the changes associated with life-style, however, could explain the underlying mechanisms. Environmental and behavioural factors are of significance and should be taken into consideration in any community study.
Recommendations

More information is needed on the geographical prevalence of high blood pressure. Standardization of sampling and diagnostic techniques is required to obtain comparable data. Due regard should be paid to the circumstances of recording blood pressure.

Communities which have a low prevalence rate of high blood pressure need to be studied further so that the relative importance of environmental and hereditary causative factors may be identified.

Further studies of geographical and environmental factors, such as temperature and salt intake, are recommended.

Studies aimed at understanding the mechanism of essential hypertension should be pursued, because these would assist our approach to primary prevention.

Weight control as an approach to the management of hypertension in communities is also recommended.

More studies are needed on the treatment of women patients and of younger and elderly population groups.

Longitudinal studies to provide insight into the natural history of hypertension should be encouraged.

WHO should, as previously recommended, collate information on the natural history of mild hypertension from the therapeutic studies now being conducted throughout the world, and should promote contacts and exchange of information between the study centres.

Projects aimed at developing and evaluating optimum methods for obtaining adherence and compliance of patients undergoing long-term treatment should be actively pursued.

The training of allied health personnel for the detection, follow-up, and treatment of high blood pressure under professional supervision should be encouraged.

2. Control of stroke in the community

In many countries cerebrovascular disease is still one of the three leading causes of death and control measures should be taken from the public health point of view.

Patients with transient cerebral ischaemic attacks (TIA) with focal symptoms of unknown cause require rapid referral to a competent specialist for diagnostic investigation and treatment, and they are considered as emergencies. An information campaign for physicians on primary medical care, and for the general public on the symptoms, significance, and treatment of TIA should be promoted. Since the prevalence of TIA is rather small and no effective method of screening has been developed, mass screening of TIA seems to be premature.
The diagnosis and treatment of stroke is a complex problem and it cannot often be handled effectively by a single physician. It is desirable that all acute stroke patients should have intensive care, for which highly trained staff must be provided for diagnosis and treatment. Such care can be established within the general hospital by the organization of a dedicated team. Aggravation of a patient's condition by medically supervised transportation per se has not been experienced. The availability of, and access to, such a service should be made well known to primary care physicians and the public.

In spite of the high rate of mortality from cerebrovascular disease, education on this condition is generally insufficient. Early treatment and early initiation of rehabilitation of stroke patients should be emphasized in the undergraduate medical curriculum, and achievements should be evaluated.

Information on the treatment of acute stroke patients should be provided to general practitioners, nurses, and health personnel who play a decisive role in the early transfer and early initiation of rehabilitation of stroke patients. Medical societies and public health authorities should be alerted to the need for education on these topics.

Rehabilitation must be started as soon as the life-threatening stage is over. Calling a family member to the hospital may be encouraged in order to teach ways of assisting the patient. Simple physical training supervised by a family member under the guidance of a specialist is very helpful. Sending the patient back home is always the goal, irrespective of the age of the patient. The use of "half-way houses" between hospital and home may be helpful. Extended care facilities at home or in outpatient clinics should be provided wherever resources permit. Although simple techniques are very useful in rehabilitation, further research into the ways of compensating for impaired function needs to be promoted.

Recommendations

The etiology of cerebral infarction has not been sufficiently explored and methods of prevention are still unknown. Research on the etiology and pathogenesis of atherosclerosis has to be pursued.

Further efforts to establish a standardized diagnostic method for TIA should be made.

Studies on the natural history and effect of treatment of TIA in many areas are desirable.

Identification of a group of TIA patients who are more prone to cerebral infarction, and of additional factors which increase the risk of a major stroke need to be studied.

A study on the geographical, ethnical, or social class differences in the frequency of arterial bruit in the neck in relation to stroke morbidity and mortality in different areas is worth while.
Intensive care should be available to every acute stroke patient. The establishment of a competent team for diagnosis and treatment should be promoted.

More specialists in rehabilitation are needed. The training of auxiliary personnel, such as nurses, or the involvement of family members may be considered in order to supplement the shortage of rehabilitation specialists.

Collection of systematic information on cerebrovascular disease in a well-defined community should be promoted in different areas. The use of standardized methods in diagnosing various kinds of stroke, uniform collection of data, and central processing may facilitate the comparison of the data collected.

3. Comprehensive cardiovascular disease control programme

Hypertension and stroke control should logically be unified and it is desirable to organize community programmes as comprehensive systems from the very beginning, including coronary heart disease, pulmonary heart disease, etc. However, there is lack of experience until now with such a system and it is important to make operational studies of this kind.
Dr Werko: Before I give the word to Dr Soda for his closing speech, I should like to express the foreign guests' thanks to the interpreters who made the discussions possible during the past three days and to the Japanese organizing committee who made our stay here so fruitful. Thank you very much indeed.

Dr Soda: Dr Strasser and the secretariat of WHO, and all the participants at this meeting, it is a very great pleasure and a privilege for me to be able to speak for a few minutes. First I have to congratulate you for your successful achievement and for the effective promotion of the world-wide study on the prevalent conditions and various control measures enabling all the member countries of WHO to develop a systematic and well-organized programme against the ravages of cerebral vascular and cardiovascular diseases. Cerebrovascular diseases have been and still are the most important cause of death in Japan accounting for nearly a quarter of all deaths. This is why all the people in Japan, not only physicians and members of the national and local government, but also lay people and civil and private organizations are very enthusiastic to have a solution to this problem. They are very eager to know how to develop the most efficient national and community programme for prevention, detection, first-aid and subsequent treatment, rehabilitative care, and so forth, based upon the results of the studies and the experiences obtained in any country of the world.

Various studies have been carried out in Japan and more and more experiences are being accumulated to be used for a campaign against cerebrovascular diseases and hypertension. Besides the research and surveys reported and discussed during the meeting, some data are available from other sources. I should mention to you the blood pressure measurements made annually in the National Nutrition Survey in this country on randomly sampled 13,000 households with over 50,000 household members. Other sources of information on the prevalence of and the status of treatment and care for hypertensives and for patients with cardiovascular and cerebrovascular diseases are the results of the annual health examinations given to old persons aged 65 years and over, according to the aged persons welfare roll which was started in 1963. This examination is not compulsory and is only of an advisory nature for the old people. The roll requires that local communities, such as the city, town and village authorities, should provide the occasion and the provisions for such annual health examinations for the old people, according to the standard procedure indicated by the Ministry of Health and Welfare, free of charge, at least for the first screening. Of nearly seven and a half million people aged 65 years and over, 1,740,000
(that is more than one-fifth of this population) received such a health examination, including the measurement of blood pressure, in 1971. Data links between these individual records thus obtained and other cerebral and cardiovascular disease study programmes are not yet established. Though these data may be lacking in accuracy for other purposes, it may be advisable to consider some ways of utilizing the information obtained from the routine health and welfare services in the clinical and epidemiological research on hypertension and stroke, especially from the community point of view.

I hope that the results from this meeting will be distributed widely to the many persons concerned and will be utilized for the further development of programmes in every country. I am very pleased to have been a member of the Preparatory Committee which helped in preparing for this WHO symposium on hypertension and stroke held in Tokyo, from which meeting both the Japanese and foreign participants have derived much profitable information.

I hope that you will have some spare time to look around the country before you return safely to your homes with pleasant memories of this meeting in the city of Tokyo and the country of Japan. Thank you very much.

Dr Strasser: Dr Soda, may I shake hands with you and may I express the deepest appreciation of the World Health Organization to you, personally, and to the Japanese Preparation Committee for the wonderful help you gave us in organizing this meeting: thank you very much. I hope the results of this meeting will contribute even to a modest extent to the enormous activity which is being displayed in Japan in the struggle against hypertension, stroke, and other cardiovascular diseases, and also other chronic diseases.

I wish to express my deepest thanks to all the participants who took the trouble to undertake this long trip and who wrote all the excellent working papers. I hope we shall meet again.
ANNEX

HOSPITALIZATION AND NURSING CARE FORMS, AND GUIDELINES USED IN THE COMPREHENSIVE STROKE PROGRAMME OF THE NORTH CAROLINA REGIONAL MEDICAL PROGRAMME

Presented by

J. F. Toole
### COMPREHENSIVE STROKE PROGRAM

#### NORTH CAROLINA REGIONAL MEDICAL PROGRAM

**Hospitalization Form**

<table>
<thead>
<tr>
<th>Part</th>
<th>(To be completed by Stroke Exec. Secty.)</th>
<th>ADMISSION</th>
<th>DISCHARGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Hospital No. of Patient</td>
<td>Age</td>
<td>Adm. Date</td>
</tr>
<tr>
<td>2</td>
<td>Name of Hospital</td>
<td>Sex</td>
<td>Disch. Date</td>
</tr>
<tr>
<td>3</td>
<td>Physician's Name</td>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>County Code No.</td>
<td>Adm. Date</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>County Code No.</td>
<td>Disch. Date</td>
</tr>
<tr>
<td>6a</td>
<td>Social Security No.</td>
<td>County Code No.</td>
<td>Length</td>
</tr>
<tr>
<td>6b</td>
<td></td>
<td>County Code No.</td>
<td>Of Stay</td>
</tr>
<tr>
<td></td>
<td></td>
<td>County Code No.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Part</th>
<th>(To be completed by Stroke Exec. Secty.)</th>
<th>ADMISSION</th>
<th>DISCHARGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>Hospital No. of Patient</td>
<td>Age</td>
<td>Adm. Date</td>
</tr>
<tr>
<td>8</td>
<td>Name of Hospital</td>
<td>Sex</td>
<td>Disch. Date</td>
</tr>
<tr>
<td>9</td>
<td>Physician's Name</td>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td></td>
<td>County Code No.</td>
<td>Adm. Date</td>
</tr>
<tr>
<td>11</td>
<td></td>
<td>County Code No.</td>
<td>Disch. Date</td>
</tr>
<tr>
<td>12</td>
<td>Reason for Hospitalization</td>
<td>Disch. Date</td>
<td>Length</td>
</tr>
<tr>
<td>13</td>
<td>Stroke</td>
<td>Disch. Date</td>
<td>Of Stay</td>
</tr>
<tr>
<td>14</td>
<td>&quot;Risk&quot;</td>
<td>Disch. Date</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>Admission Date</td>
<td>Disch. Date</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>Discharge Date</td>
<td>Disch. Date</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>Length of Stay</td>
<td>Disch. Date</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Part</th>
<th>(To be completed by Stroke Exec. Secty.)</th>
<th>ADMISSION</th>
<th>DISCHARGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>18</td>
<td>Permanent residence:</td>
<td>Adm. Date</td>
<td>Disch. Date</td>
</tr>
<tr>
<td>19</td>
<td>Reason for Hospitalization</td>
<td>Disch. Date</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>Hospital bill paid by:</td>
<td>Disch. Date</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>Complications in Hospital</td>
<td>Disch. Date</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>Name of local responsible individual:</td>
<td>Disch. Date</td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>Relationship to patient:</td>
<td>Disch. Date</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>Discharge Status:</td>
<td>Disch. Date</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>Remarks</td>
<td>Disch. Date</td>
<td></td>
</tr>
<tr>
<td>26</td>
<td>For CSP Office Use Only Stroke Code</td>
<td>Disch. Date</td>
<td></td>
</tr>
</tbody>
</table>

**Exec. Sec. mails original copy to Comprehensive Stroke Program**

Carbon copy is for Exec. Sec. records

Rev. 12/72
### Patient Identification

**Name:**

- LAST: 
- FIRST: 
- MIDDLE: 

**Social Security No.:**

- I I I I I I I I I I

### Hospitalization Form

**Name of Hospital:**

---

### COMPREHENSIVE STROKE PROGRAM

**NORTH CAROLINA REGIONAL MEDICAL PROGRAM**

**Hospitalization Form**

---

### Part III

**TO BE COMPLETED BY NURSE**

- No. children

---

### Part IV

**PHYSICIANS' ADMISSION NOTES**

- Name of Hospital:
- Part UI

---

### Part V

**PAST HISTORY**

- Date of this stroke: 19

---

### Part VI

**NEUROLOGICAL EXAMINATION**

- RATE WEAKNESS as:
  - 0 = normal strength
  - 1 = mild
  - 2 = moderate
  - 3 = severe

---

### Part VII

**CONSULTATIONS REQUESTED**

- P. T.: 
- Cardiology: 
- Neurol./Neuro. Surg.: 
- Speech: 
- Other: 

---

### Part VIII

**LABORATORY STUDIES**

- SUGAR
  - 2 hr. p.p.: 
  - FBS

---

**Signature of examining physician:**

---

**Original copy for hospital records**

Fee: Sec. mails duplicate copy to Comprehensive Stroke Program

**Rev. 2/73**
Date of this report ____________

COMPREHENSIVE STROKE PROGRAM

NORTH CAROLINA REGIONAL MEDICAL PROGRAM

Follow-up Report Form

1. Name of Patient:

2. Age at Time of Stroke:

3. Sex:

4. Race:

5. "Stroke Code" at Discharge:

6. Occupation:

7. Address (Current) ____________________________

8. Hospital No. ____________________________

9. Age: ____________

10. Sex: ____________

11. Race: ____________

12. "Stroke Code" at Discharge:

13. Occupation:

14. Address (Permanent) ____________________________

15. Hospital No. ____________________________

16. Age: ____________

17. Sex: ____________

18. Race: ____________

19. "Stroke Code" at Discharge:

20. Occupation:

21. Address (Current) ____________________________

22. Hospital No. ____________________________

23. Age: ____________

24. Sex: ____________

25. Race: ____________

26. "Stroke Code" at Discharge:

27. Occupation:

28. Address (Permanent) ____________________________

29. Hospital No. ____________________________

30. Age: ____________

31. Sex: ____________

32. Race: ____________

33. "Stroke Code" at Discharge:

34. Occupation:

35. Address (Current) ____________________________

36. Hospital No. ____________________________

37. Age: ____________

38. Sex: ____________

39. Race: ____________

40. "Stroke Code" at Discharge:

41. Occupation:

42. Address (Permanent) ____________________________

43. Hospital No. ____________________________

44. Age: ____________

45. Sex: ____________

46. Race: ____________

47. "Stroke Code" at Discharge:

48. Occupation:

49. Address (Current) ____________________________

50. Hospital No. ____________________________

51. Age: ____________

52. Sex: ____________

53. Race: ____________

54. "Stroke Code" at Discharge:

55. Occupation:

56. Address (Permanent) ____________________________

57. Hospital No. ____________________________

58. Age: ____________

59. Sex: ____________

60. Race: ____________

61. "Stroke Code" at Discharge:

62. Occupation:

63. Address (Current) ____________________________

64. Hospital No. ____________________________

65. Age: ____________

66. Sex: ____________

67. Race: ____________

68. "Stroke Code" at Discharge:

69. Occupation:
North Carolina Comprehensive Stroke Program

STROKE
ADMISSION
ORDERS
(For further details see obverse side)

1. Stroke Management: Phase ______
2. Airway: Suction PRN ______
4. Nutrition: __ I.V. 5% Dextrose/water, 2000-2400 ml/day, and/or ______ ml/day
   __ Oral ___
   __ Tube feeding ___
5. Medications (circle dosage and route desired):
   ____ None
   ____ ASA 10 gr. orally/rectally q. 4 hrs. PRN for pain and/or fever
   ____ Librium 25-50 mg. oral/I.M. q. 4-6 hrs. for restlessness
   ____ Demerol 50-100 mg. I.M. q. 4 hrs. for pain
   ____ Codeine 60 mg. oral/I.M. q. 4-6 hrs. for pain
   ____ Other ___
6. Bladder: _ Foley catheter _ Condom to straight drainage _ Other ___
7. Bowel: _ SSE q. d./q.o.d. _ Mineral oil 30 cc q. H.S., PRN _ Other ___
8. Laboratory: _ CBC _ Urine _ VDRL _ BUN _ FBS _ EKG _ Other ___
9. X-rays: _ Chest __ A.P. and ______ lateral stereo of skull _ Other ___
10. Obtain Physical Therapy Consultation ______
11. Discharge Planning Conference to be scheduled: ______ later;
    ______ for DAY MONTH YEAR
12. Other: _____________________________________ ___
13. Notify Stroke Executive Secretary of this admission ______

Date: __________________ Signed _______________________ M.D.
CSP-1/70
The Stroke Admissions Order Sheet is modified from that developed by the Northern Hospital of Surry County, N. C., according to the Guidelines of the Comprehensive Stroke Program. This side of the Order Sheet contains facts of immediate use to the physician in determining procedures, dosages and rationale of treatment.

1. **STROKE MANAGEMENT PHASES**
   I. (Acute): First 48 hours after onset of the stroke or until constant surveillance is no longer required.
   II. (Post-Acute): Vital signs are stable, life is not endangered, but the patient is unable to participate fully in his own program.
   III. (Rehabilitative): Patient consciously and actively participates in his own rehabilitative program.
   IV. (Maximum Benefit): 3 months after the progress of the patient has plateaued or 2 years after the onset of the stroke.

2. **AIRWAY**
   If suction is ineffective, use endotracheal tube; if tube is needed > 3-4 days, consider tracheostomy with cuffed endotracheal tube (permitting intermittent positive pressure breathing, IPPB); remove as soon as possible.

3. **VITAL SIGNS**
   Report significant changes (especially in B.P., pupillary inequality, and responsiveness) to physician. Mild hypertension may persist for 24 hrs. after a stroke, and usually requires no treatment. Observe respirations for 30-second periods to detect irregularities in breathing pattern.

4. **NUTRITION**
   (a) Use I.V. feeding only if necessary; replace by tube or oral feeding as soon as possible.
   (b) Many stroke patients have cardiac disease; do not overload the circulation.
   (c) Check electrolytes before giving saline infusion (not > 1000 ml./day) since acute cerebral lesions may be associated with hypernatremia and hyperchloremia.

5. **MEDICATIONS**
   (a) Elderly patients may over-react to medications given in normal doses, and rarely require analgesics or sedatives.
   (b) Librium may cause hypotension in ambulatory patient; also ataxia, dizziness.
   (c) Demerol: contraindicated in increased intracranial pressure, auricular flutter, or in presence of monoamine oxidase inhibitors (e.g. Eutonyl, Nardil). Respiratory depression due to Demerol: counteract with Nalorphine (Nalline): 5-10 mg. I.V. q. 10-15 mins. (not to exceed total of 40 mg.).

6. **BLADDER**
   (a) Indwelling catheter required in comatose patient and incontinent female; remove as soon as possible.
   (b) Condom to straight drainage in incontinent male helps nursing care.

7. **BOWEL**
   Specific treatment often unnecessary if nurse can restore patient’s bowel habits.

8. **LABORATORY**
   Stroke patients may have cardiac disease or diabetes mellitus; EKG and fasting blood sugar (FBS) may suggest specific treatment.

9. **X-RAYS**
   (a) Repeated chest x-rays may reveal developing pneumonitis, requiring prophylactic antibiotic treatment.
   (b) Skull x-rays are often inadequate in bed-ridden patient; but if fracture or increased intracranial pressure is suspected, these may be helpful.

10. **NURSE AND PHYSICAL THERAPIST**
    Will follow Guidelines furnished by the Comprehensive Stroke Program with any changes suggested by the physician.

11. **DISCHARGE PLANNING CONFERENCE**
    Can be held within 4-5 days after admission in most cases (cerebral thrombosis); the Stroke Executive Secretary will notify members of time and place.

12. **OTHER**
    For further instructions, or changes in Nursing Management Plan.

13. **EXECUTIVE SECRETARY**
    Discharge and follow-up plans will be hastened, with economy of physician’s time, if Secretary is notified when Order Sheet has been completed.

352
GUIDELINES OF MANAGEMENT OF THE STROKE PATIENT

PHASE 1: ACUTE

(The Acute Phase is the first 48 hours after onset of the stroke or until constant surveillance is no longer required. Refer to "Management of the Acutely Ill Stroke Patient" for details.)

<table>
<thead>
<tr>
<th>PHYSICIAN</th>
<th>NURSE</th>
<th>PHYSICAL THERAPIST</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Check items 32-35, 36a, 37a, 38a, 39 and 40 on Hospitalization Form 1b.</td>
<td>1. Surveillance Measures</td>
<td></td>
</tr>
<tr>
<td>2. Check Stroke Admission Orders Sheet or order &quot;Treatment according to Guidelines.&quot;</td>
<td>a. ELEVATE FOOT OF BED, 6-10 inches, OF COMATOSE PATIENT (contraindicated in cerebral hemorrhage)</td>
<td></td>
</tr>
<tr>
<td>3. Recommendations: a. Elevate foot of bed 6-10 inches for postural drainage, (except in cerebral hemorrhage) b. Avoid use of indwelling catheter if possible. c. Desirable initial studies include: Chest x-ray E. K. G. F. B. S., or 2 hr. post-prandial sugar</td>
<td>b. Place stroke patient’s bed in space providing maximum visibility to nursing staff.</td>
<td></td>
</tr>
<tr>
<td>4. Lumbar puncture, if not contraindicated by papilledema, and if: a. The diagnosis is in doubt (cerebral hemorrhage? tumor? subdural hematoma?) b. Anticoagulation therapy is being contemplated.</td>
<td>c. Maintain open airway 1) Tracheal suction P.N 2) Pulmonary resuscitation equipment and personnel readily available.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>d. Observe, report, and record any change in sensorium.</td>
<td>e. Vital signs as per physician’s orders</td>
</tr>
<tr>
<td></td>
<td>e. Vital signs as per physician’s orders</td>
<td>f. Request admission CBC, urinalysis, blood sugar and BUN</td>
</tr>
<tr>
<td></td>
<td>f. Request admission CBC, urinalysis, blood sugar and BUN</td>
<td>2. Nutrition</td>
</tr>
<tr>
<td></td>
<td></td>
<td>a. NPO until individual orders written.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>b. Record intake and output.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3. Bowel and Bladder Management</td>
</tr>
<tr>
<td></td>
<td></td>
<td>a. Observe for bowel and bladder control. Avoid use of indwelling catheter if possible.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>b. Obtain history of bowel and bladder habits prior to illness.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>c. Utilize a. and b. in management to keep dry and regulated.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4. Skin Care</td>
</tr>
<tr>
<td></td>
<td></td>
<td>a. Alter position from prone, affected, non-affected side and supine at least q. 2 hours.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>b. Inspect skin and give care with lubricating lotion and massage pressure points q. 4 hours.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5. Positioning</td>
</tr>
<tr>
<td></td>
<td></td>
<td>a. POSITIONING SHOULD BE STARTED ON ADMISSION.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5. Positioning</td>
</tr>
<tr>
<td></td>
<td></td>
<td>a. Contact family members</td>
</tr>
</tbody>
</table>

NORTH CAROLINA COMPREHENSIVE STROKE PROGRAM
Page 2

b. Utilize high-low bed and place bed board under mattress.
c. Support involved foot in well-padded aluminum splint, secure with ace bandage.
d. Support leg in neutral position by means of trochanter roll. (Do not place pillow under knee.)
e. Emphasize shoulder abduction and external rotation (arm resting overhead).
f. Emphasize elbow extension and supination.
g. Use large hand roll to maintain wrist extension and fingers open.
h. Apply side rails to both sides of bed.
i. Restraining patient only if required for safety in side-lying position.

6. Mobilization
   a. RANGE OF MOTION EXERCISES SHOULD BE STARTED ON ADMISSION. Exercise at time of daily bath, plus at least two additional times daily. Coordinate with Physical Therapist.
   b. Alter position from prone, affected, non-affected side, and supine at least q. 2 hours.
   c. Approach patient from uninvolved side, place bedside table, signal device on uninvolved side.

7. Communication
   a. Observe and evaluate understanding of conversation and directions.
   b. Begin assisting patient to express himself by speech, signals or in writing according to his abilities.
   c. Observe reaction to voice or pain; patient may be aware but cannot respond.
   d. Patient care plan to include key words to be used by all personnel.

8. Planning with Family
   b. Interpret labile emotional status to family.
   c. Urge hopeful but realistic approach to patient.

9. Start Nursing Care Plan.

10. Add Stroke Forms to Chart.

11. Notify Stroke Executive Secretary of Admission.

b. Work with nurse on positioning and skin care.

b. Physical Therapist evaluates patient and initiates more dynamic treatment.
GUIDELINES OF MANAGEMENT OF THE STROKE PATIENT

PHASE II: POST-ACUTE

(Vital signs are stable, life is no longer endangered, but the patient remains unable to participate fully in his own program).

<table>
<thead>
<tr>
<th>PHYSICIAN</th>
<th>NURSE</th>
<th>PHYSICAL THERAPIST</th>
</tr>
</thead>
</table>

1. Surveillance Measures
   - Continue observations of sensorium and airway
   - Remind physician of need to alter orders for vital signs and discontinue sedation if possible.

2. Nutrition
   - Continue intake and output
   - Consider dentition, previous eating habits, mastication and swallowing in resuming regular diet as soon as possible
   - Assist with feeding as required
   - Maximize regular meal times and minimize between meal feedings to facilitate bowel retraining as necessary

3. Bowel and Bladder Management
   - Utilize history and observation of control to establish regular voiding and evacuation time
   - Begin retraining program if indicated. (See nursing manual for outline). Use American Rehabilitation Foundation "A Nursing Guide for Bowel and Bladder Care" as basis for this Section
   - If catheter is in place, check with physician before clamping off to start bladder training
   - Place conscious patient on bedpan in supported sitting position (bed rolled up) at 2-hour intervals, increasing time span as pattern emerges and is established

4. Skin Care
   - Alter position from prone, affected, non-affected side and supine at least q. 2 hours

   c. Evaluate patient regarding ability to feed self and make recommendations to nursing staff

   b. Evaluate abdominal muscles and ability to elevate pelvis for using bedpan

   Evaluate stability of sitting balance. Make recommendations to nursing staff
5. Positioning (continue all previous measures if patient is inactive)
   a. Utilize high-low bed and place bed board under mattress.
   b. Support involved foot in well-padded aluminum splint, secure with ace bandage.
   c. Support leg in neutral position by means of trochanter roll. (Do not place pillow under knee).
   d. Emphasize shoulder abduction and external rotation.
   e. Emphasize elbow extension and supination.
   f. Keep fingers open with hand roll.
   g. Restrain patient only if required for safety.
   (In side lying)

6. Mobilization in bed
   a. Continue normal range of motion exercises at the time of daily bathing. CAUTION: Check with physical therapist as intensive physical program is initiated at this time. Coordinate necessity of ROM with level of Physical Therapy treatment. Communicate any change in muscle tone to physician and physical therapist.
   b. Alter position from prone affected, non-affected side, and supine at least q. 2 hours.
   c. Place in supported sitting position for bedpan use as outlined in 3d, Par. 3, above.
   d. Approach patient from uninvolved side, place bedside table, signal device, on uninvolved side. Encourage participation in self-care and feeding activity.
   e. Assist to supported sitting position on the patient's non-affected side, using a low bed.
   f. Utilize sling for affected arm if indicated when in sitting position or out of bed.
   g. Involve family in exercise program, set up teaching schedule with family members.

b. Note skin condition and make recommendations regarding positioning.

5. Observe and make recommendations to nursing staff.

a. Exercise patient at his highest level of cooperation. Resistive exercises should be given, if possible.

b. Evaluate patient regarding his ability to initiate and perform change of position in bed:
   1) rolling
   2) side to side
   3) up and down

d. Evaluate ability to maintain supported sitting position. Recommend assistive devices.

e. Evaluate ability to come to a sitting position and maintain unsupported sitting balance.
7. Mobilization out of Bed  
   a. Assist from bed to chair as sensorium and condition allow. *Use Kenny Rehabilitation Institute Rehabilitation Nursing Techniques.

8. Communication  
   b. Continue use of patient care plan. (7d, Phase I)

9. Planning with Family  
   a. Request that family bring patient's personal articles appropriate for hospital use and capabilities. Shoes, shirt, pants, open-front dress, clock, pipe, etc., to assist in restoring self image.
   b. Teach and involve family in care techniques:  
      1) Feeding
      2) Skin care and positioning
      3) Bowel and bladder retraining.
      4) Exercises
      5) Turning and transfer procedures.
      6) Communication

10. Revise Nursing Care Plan continuously during daily team conference.

11. Review total patient care plan at regular intervals with physician, physical therapist, family and others participating. (This could be accomplished in Medicare Utilization conference by including stroke nurse and physical therapist for all stroke patient discussions).

   Re-evaluate patient and treatment program at regular intervals.

---

<table>
<thead>
<tr>
<th>PHYSICIAN</th>
<th>NURSE</th>
<th>PHYSICAL THERAPIST</th>
</tr>
</thead>
</table>
| 7. Mobilization out of Bed  
   a. Assist from bed to chair as sensorium and condition allow. *Use Kenny Rehabilitation Institute Rehabilitation Nursing Techniques.
| 8. Communication  
   b. Continue use of patient care plan. (7d, Phase I) |
| 9. Planning with Family  
   a. Request that family bring patient's personal articles appropriate for hospital use and capabilities. Shoes, shirt, pants, open-front dress, clock, pipe, etc., to assist in restoring self image.
   b. Teach and involve family in care techniques:  
      1) Feeding
      2) Skin care and positioning
      3) Bowel and bladder retraining.
      4) Exercises
      5) Turning and transfer procedures.
      6) Communication |
GUIDELINES OF MANAGEMENT OF THE STROKE PATIENT

PHASE III: REHABILITATIVE

(The patient is consciously and actively participating in his own rehabilitation program).

PHYSICIAN

1. If patient is admitted in this phase, indicate in Stroke Admission Orders Sheet or order "Treatment according to Guidelines." Complete Hospitalization Form 1b, according to directions noted in Phase I.

2. If patient has passed from the post-acute to the rehabilitative phase while hospitalized, note the procedures which the Nurse and Physical Therapist will follow except as modified by you.

3. The following should be specifically considered:
   a. Vital signs: according to hospital policy (e.g., b.i.d.).
   b. Oral feeding in almost all cases.
   c. Bladder training with catheterization as required. If unable to train, use condom drainage.
   d. Review with Nurse and Physical Therapist status and progress of patient, and state of Patient-Family Education, especially with respect to continuation of therapy at home.
   e. Discharge plans should have been completed. Discharge patient as soon as feasible.

4. Check items 36b, 37b and Part VII, Hospitalization Form 1b.

NURSE

1. Surveillance Measures
   a. Vital sign observation (unless physical changes or institutional policy require them)

2. Nutrition
   a. Discontinue intake and output recording.
   b. Encourage resuming preferred eating habits.

3. Bowel and Bladder Management
   a. Proceed with instituted retraining programs required as outlined in a nursing guide, "Bowel and Bladder Care".
   b. Utilize bathroom toilet facilities with handrails and individualized self-help devices only if patient has sitting and standing balance; otherwise, use bedside commode.

4. Skin Care
   a. Encourage patient to gradually assume responsibility for position changes within physical limitation.
   b. Encourage patient, and assist if necessary, with massage of pressure points q.4 hours.
   c. Begin increasing patient's participation in tub bathing, or shower, utilizing appropriate devices.

5. Positioning (If indicated)
   (Follow Par. 5, Phase II-a, thru b.)
   i. Substitute short siderails if not previously used.
   j. Keep bed in low position whenever nursing measures not being performed.
   k. Utilize sling or pillow support for affected upper extremity, if indicated, whenever patient is in sitting position or out of bed.

PHYSICAL THERAPIST

1. Surveillance Measures
   a. Vital sign observation (unless physical changes or institutional policy require them)

2. Nutrition
   a. Discontinue intake and output recording.
   b. Encourage resuming preferred eating habits.

3. Bowel and Bladder Management
   a. Proceed with instituted retraining programs required as outlined in a nursing guide, "Bowel and Bladder Care".
   b. Utilize bathroom toilet facilities with handrails and individualized self-help devices only if patient has sitting and standing balance; otherwise, use bedside commode.

4. Skin Care
   a. Encourage patient to gradually assume responsibility for position changes within physical limitation.
   b. Encourage patient, and assist if necessary, with massage of pressure points q.4 hours.
   c. Begin increasing patient's participation in tub bathing, or shower, utilizing appropriate devices.

5. Positioning (If indicated)
   (Follow Par. 5, Phase II-a, thru b.)
   i. Substitute short siderails if not previously used.
   j. Keep bed in low position whenever nursing measures not being performed.
   k. Utilize sling or pillow support for affected upper extremity, if indicated, whenever patient is in sitting position or out of bed.

Observe and recommend positions where indicated.
<table>
<thead>
<tr>
<th>PHYSICIAN</th>
<th>NURSE</th>
<th>PHYSICAL THERAPIST</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>6. Mobilization in Bed</strong>&lt;br&gt;a. Encourage patient and/or family to assume their responsibility in carrying out exercise program.</td>
<td></td>
<td>a. Instruct patient and his family in preferred exercise program at patient's highest level of cooperation and recovery. Re-evaluate patient as necessary.</td>
</tr>
<tr>
<td><strong>7. Mobilization out of Bed</strong>&lt;br&gt;a. Establish schedule for increasing periods out of bed, in chair for meals, to bathroom, and other activity, as condition warrants.</td>
<td></td>
<td>a. Evaluate patient's posture and balance and his level of mobility. Treat at appropriate level. Recommend necessary equipment.</td>
</tr>
<tr>
<td><strong>8. Communication</strong>&lt;br&gt;a. Encourage visits by family and close friends who have been made aware of communication limitations.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>9. Planning with family (and with patient whenever possible).</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
PHASE IV: MAXIMUM BENEFIT

This phase starts 3 months after the progress of the patient has plateaued or 2 years after onset of the illness.

<table>
<thead>
<tr>
<th>PHYSICIAN</th>
<th>NURSE</th>
<th>PHYSICAL THERAPIST</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Note the periodic evaluation conducted by the Public Health Nurse and, when available, the Community Physical Therapist.</td>
<td>1. Re-evaluate patient and family situation every 3 months if possible.</td>
<td>1. Patient has usually reached plateau of function. Efforts directed at maintaining highest functional level possible.</td>
</tr>
<tr>
<td>2. Suggested physician schedule: Evaluate the patient about once a month for the first 3 months; once every 2 months for the next 6 months, and twice a year thereafter unless circumstances alter the suggested schedule.</td>
<td>2. Surveillance Measures</td>
<td></td>
</tr>
<tr>
<td></td>
<td>a. If emboli, or history of cardiac involvement, be alert to early symptoms of congestive heart failure; cough, loss of appetite, fatigue.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>b. Avoid Upper Respiratory infections.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3. Supportive Measures</td>
<td></td>
</tr>
<tr>
<td></td>
<td>a. Encourage outside interests.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>b. Continue exercises, use of self-help devices, if needed.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>c. Be alert to emotional aspects such as anxiety, dependency, depression.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>d. Continue interpreting to family the need to understand and accept the patient.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4. Safety Measures</td>
<td></td>
</tr>
<tr>
<td></td>
<td>a. Check assistive and supportive devices for safety.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>b. Uncluttered, non-skid walking surfaces, good lighting.</td>
<td></td>
</tr>
</tbody>
</table>
The understanding and cooperation of the family of stroke patients is vital in the overall care. Families can negate improvements which he may potentially achieve if they do not understand the multiplicity of problems involved in stroke.

It is the responsibility of all professional personnel (nurses, physical therapists, physicians, speech therapists and occupational therapists) to counsel with family members and involve them as early as possible in care of the patient.

Stroke usually is a sudden onset resulting in varied, often marked, disability. It has a traumatic effect on the patient and family members. Families differ in their emotional ability to cope with such situations but often family members can be very helpful in all stages of care of the patient if they understand the problem.

In early discussions, much can be learned about the home (location, steps, bathroom facilities, etc.), about the patient (kind of work, general disposition and emotional make-up, education) that will be basic in approaching treatment and planning.

Following are some general guidelines for family teaching:

1. Discuss with the family members early (within the first 24 hours), the mechanism of stroke in terms they understand. (Possible speech involvement, emotional changes, motor sensory and balance deficit.)

2. Teach simple positioning and passive exercise AND EXPLAIN THE REASONS FOR SAME. The family can be most helpful during hospitalization in some aspects of care. You must give them specific instructions.

3. Help the family to understand the necessity for having the patient "do for himself". They must recognize needs for assistance and how much to assist.

4. Teach how to get patient up; into a chair; walking. BALANCE AND SAFETY MUST BE PRIMARY FACTORS for patients when ambulation is a goal.
5. Family must learn to give the patient responsibilities at home.

6. Planning for social and recreational involvement for the patient (going to church, movies, visiting; group recreational activities at local YMCA, recreational centres or churches).

7. It is desirable to include one session for family members in the in-service training programme in the communities. At this time review of exercises to maintain range of motion, use of pulley for shoulder exercise, ambulation and home safety measures may be reviewed.

Professional personnel must transmit to the family a positive attitude (NOT A FALSE ONE) that the patient has much functional ability which we help him to regain. Our goal is not return to normal but to achieve the highest functional level possible for that person.

Various booklets may be referred to for information (Aphasia and The Family; Range of Motion Exercise; mimeographed materials) but SHOULD NOT SUBSTITUTE for the personal contact, explanation, and discussion with by professional personnel with the family. Each of us has a responsibility to increase our knowledge about the basic anatomy, neurology, and symptomatology of stroke and about the general patterns and time limits of improvement.

Any booklet material given to families should be discussed and explained with them. Family teaching and education is a personal relationship between professional staff and the family.
WHO publications may be obtained, direct or through booksellers, from:

<table>
<thead>
<tr>
<th>Country</th>
<th>Address</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALGERIA</td>
<td>Société nationale d’Edition et de Diffusion, 3 bd Zirout Youcef, ALGIERS</td>
</tr>
<tr>
<td>ARGENTINA</td>
<td>Librería de las Naciones, Cooperativa Ltda., Alvia 500, BUENOS AIRES</td>
</tr>
<tr>
<td>AUSTRALIA</td>
<td>Mail Order Sales, Australian Government Publishing Service, P.O. Box 84, CANBERRA, A.C.T. 2600; or over the counter from Australian Government Publications and Inquiry Centres at: 113 London Circuit, Canberra City; 247 Swanston Street, MELBOURNE; 309 Pitt Street, Sydney; Mr. Newman House, 200 St. George’s Terrace, PERTH; Industry House, 12 Pirie Street, ADELAIDE; 156-162 Macquarie Street, HOBART — Hunter Publications, 38A Gipps Street, COLLINGWOOD, Vic. 3066.</td>
</tr>
<tr>
<td>BANGLADESH</td>
<td>The WHO Representative, G.P.O. Box 250, DACCA 5.</td>
</tr>
<tr>
<td>BELGIUM</td>
<td>Office international de Librairie, 30 avenue Marnix, BRUSSELS.</td>
</tr>
<tr>
<td>BRAZIL</td>
<td>Biblioteca Regional de Medicina OMS/OPS, Unidad de Venta de Publicaciones, Caixa Postal 20.361, Vila Clementino, 01000 São Paulo — SP.</td>
</tr>
<tr>
<td>CANADA</td>
<td>see India, WHO Regional Office.</td>
</tr>
<tr>
<td>CHINA</td>
<td>China National Publications Import Corporation, P.O. Box 88, PEKING.</td>
</tr>
<tr>
<td>COLOMBIA</td>
<td>Distribuidos Ltd, Pio Alfonso Garcia, Carrera 4a, Nos 36-119, CARTAGENA.</td>
</tr>
<tr>
<td>COSTA RICA</td>
<td>yey Santa Fe, Apartado 1313, SAN JOSÉ.</td>
</tr>
<tr>
<td>CYPRUS</td>
<td>MAM, P.O. Box 1674, NICOSIA.</td>
</tr>
<tr>
<td>CZECHOSLOVAKIA</td>
<td>Artia, Smeky 30, 111 27 PRAGUE 1.</td>
</tr>
<tr>
<td>DENMARK</td>
<td>Einar Munkszaard, Ltd, Nørregade 6, COPENHAGEN.</td>
</tr>
<tr>
<td>ECUADOR</td>
<td>Libreria Cientifica S.A., P.O. Box 362, LUQUE 223, GUAYAQUIL.</td>
</tr>
<tr>
<td>EGYPT</td>
<td>Nabaa El Fikr Bookshop, 55 Saad Zaehiol Street, ALEXANDRIA — Anglo Egyptian Bookshop, 165 Mohamed Farid Street, CAIRO.</td>
</tr>
<tr>
<td>EL SALVADOR</td>
<td>Libreria Estudiantil, Edificio Comercial B No 3, Avenida Libertad, SAN SALVADOR.</td>
</tr>
<tr>
<td>FIJI</td>
<td>The WHO Representative, P.O. Box 113, SUVA.</td>
</tr>
<tr>
<td>FINLAND</td>
<td>Akateeminen Kirjakauppa, Keskuskatu 2, HELSINKI 10.</td>
</tr>
<tr>
<td>FRANCE</td>
<td>Librairie Arnette, 2 rue Casimir-Delavigne, PARIS 6e.</td>
</tr>
<tr>
<td>GERMANY</td>
<td>Buchhaus Leidzig, Postfach 140, 701 LEIPZIG.</td>
</tr>
<tr>
<td>DEMOCRATIC</td>
<td>The WHO Representative, P.O. Box 5360, 6236 ESCHBORN — W. E. Saarbach, Postfach 150, Unterslattstrasse 2, 5 COLOGNE 1 — Amsel Horn, Spiezelsasse 9, Postfach 3340, 62 Wiesbaden.</td>
</tr>
<tr>
<td>GREECE</td>
<td>Max Bouchereau, Librairie “A la Caravelle”, Boîte postale 111-B, PORT-AU-PRINCE.</td>
</tr>
<tr>
<td>HAITI</td>
<td>Kultura, P.O.B. 149, BUDAPEST 62 — Akadémiai Könyvvesbolt, Váci utca 22, BUDAPEST V.</td>
</tr>
<tr>
<td>HUNGARY</td>
<td>WHO Regional Office for South-East Asia, World Health House, Indraprastha Estate, Ring Road, NEW DELHI 1 — Oxford Book &amp; Stationery Co., Scindia House, NEW DELHI; 17 Park Street, CALCUTTA 16 (Sub-agent).</td>
</tr>
<tr>
<td>INDONESIA</td>
<td>see India, WHO Regional Office.</td>
</tr>
<tr>
<td>IRAN</td>
<td>Iranian Amalikannat Distribution Agency, 151 Khiabon Soraya, TEHERAN.</td>
</tr>
<tr>
<td>IRELAND</td>
<td>The Stationery Office, DUBLIN.</td>
</tr>
<tr>
<td>ISRAEL</td>
<td>Heiliger &amp; Co., 3 Nathan Strauss Street, JERUSALEM.</td>
</tr>
<tr>
<td>ITALY</td>
<td>Edizioni Minerva Medica, Corso Bramante 83-85, TURIN; Via Lamarosa 3, MILAN.</td>
</tr>
<tr>
<td>JAPAN</td>
<td>Maruzen Co. Ltd, P.O. Box 5050, Tokyo International, 100-31.</td>
</tr>
<tr>
<td>KENYA</td>
<td>The Caxton Press Ltd, Head Office: Gathani House, Huddersfield Road, PO Box 1742, NAIROBI.</td>
</tr>
<tr>
<td>KUWAIT</td>
<td>The Kuwait Bookshops Co. Ltd, Thunayan Al-Ghanem Bldg, P.O. Box 2942, KUWAIT.</td>
</tr>
<tr>
<td>LAO PEOPLE'S</td>
<td>The WHO Representative, P.O. Box 343, VIENTIANE.</td>
</tr>
<tr>
<td>DEMOCRATIC</td>
<td>Documenta Scientifica/Redico, P.O. Box 5641, BEIRUT.</td>
</tr>
<tr>
<td>REPUBLIC</td>
<td>Librairie du Centre, 49 bd Royal, LUXEMBOURG.</td>
</tr>
<tr>
<td>LEBANON</td>
<td>The WHO Representative, Room 100, Fitzpatrick Building, Jalan Raja Chulan, KUALA LUMPUR 05-02 — Jubilee (Book) Store Ltd, 97 Jalan Tunang Abdul Rahman, P.O. Box 629, KUALA LUMPUR — Parry’s Book Center, K.L. Hilton Hotel, KUALA LUMPUR.</td>
</tr>
<tr>
<td>LUXEMBOURG</td>
<td>La Presse Médica Mexicana, Ediciones Científicas, Pasco de las Facultades 26, MEXICO CITY 20, D.F.</td>
</tr>
<tr>
<td>MALAYSIA</td>
<td>Libraria de la Unidade, 49 bd Royal, LUXEMBOURG.</td>
</tr>
<tr>
<td>MEXICO</td>
<td>W. E. Saarbach, Spiezelsasse 9, Postfach 3340, 62 Wiesbaden.</td>
</tr>
<tr>
<td>NIGERIA</td>
<td>WHO Publications Office, 3 bd Zirout Youcef, ALGIERS.</td>
</tr>
<tr>
<td>PAKISTAN</td>
<td>Libreria de las Naciones, Cooperativa Ltda., Alvia 500, BUENOS AIRES.</td>
</tr>
<tr>
<td>POLAND</td>
<td>Société nationale d’Edition et de Diffusion, 3 bd Zirout Youcef, ALGIERS.</td>
</tr>
<tr>
<td>PORTUGAL</td>
<td>The WHO Representative, P.O. Box 113, SUVA.</td>
</tr>
<tr>
<td>PORTUGUESE</td>
<td>Libreria de las Naciones, Cooperativa Ltda., Alvia 500, BUENOS AIRES.</td>
</tr>
<tr>
<td>ROMANIA</td>
<td>The WHO Representative, P.O. Box 113, SUVA.</td>
</tr>
<tr>
<td>SOUTH AFRICA</td>
<td>The WHO Representative, P.O. Box 113, SUVA.</td>
</tr>
<tr>
<td>SWITZERLAND</td>
<td>The WHO Representative, P.O. Box 113, SUVA.</td>
</tr>
<tr>
<td>TURKEY</td>
<td>The WHO Representative, P.O. Box 113, SUVA.</td>
</tr>
<tr>
<td>UNITED KINGDOM</td>
<td>The WHO Representative, P.O. Box 113, SUVA.</td>
</tr>
<tr>
<td>UNITED STATES</td>
<td>The WHO Representative, P.O. Box 113, SUVA.</td>
</tr>
<tr>
<td>VENEZUELA</td>
<td>The WHO Representative, P.O. Box 113, SUVA.</td>
</tr>
<tr>
<td>VIET NAM</td>
<td>The WHO Representative, P.O. Box 113, SUVA.</td>
</tr>
<tr>
<td>YUGOSLAVIA</td>
<td>The WHO Representative, P.O. Box 113, SUVA.</td>
</tr>
<tr>
<td>ZAMBIA</td>
<td>The WHO Representative, P.O. Box 113, SUVA.</td>
</tr>
<tr>
<td>ZIMBABWE</td>
<td>The WHO Representative, P.O. Box 113, SUVA.</td>
</tr>
</tbody>
</table>

*Note: The list is not exhaustive and may be updated regularly.*
WHO publications may be obtained, direct or through booksellers, from:

<table>
<thead>
<tr>
<th>Country</th>
<th>Address</th>
</tr>
</thead>
<tbody>
<tr>
<td>MONGOLIA</td>
<td>see India, WHO Regional Office.</td>
</tr>
<tr>
<td>MOROCCO</td>
<td>Editions La Porte, 281 avenue Mohammed V, RABAT.</td>
</tr>
<tr>
<td>NEPAL</td>
<td>see India, WHO Regional Office.</td>
</tr>
<tr>
<td>NETHERLANDS</td>
<td>N V. Martinus Nijhoff's Boekhandel en Uitgevers Maatschappij, Lange Voorhout 9, THE HAGUE.</td>
</tr>
<tr>
<td>NEW ZEALAND</td>
<td>Government Printing Office, Government Bookshops at: Rutland Street, P.O. Box 5344, AUCKLAND; 130 Oxford Terrace, P.O. Box 1721, CHRISTCHURCH; Alma Street, P.O. Box 857, HAMILTON; Princes Street, P.O. Box 1104, DUNEDIN; Mulgrave Street, PRIVATE Bag. WELINGTON — R. Hill &amp; Son Ltd, Ideal House, Chr. GILLES Avenue &amp; Eden Street, Newmarket, AUCKLAND S.E. 1.</td>
</tr>
<tr>
<td>NIGERIA</td>
<td>University Bookshop Nigeria Ltd., University of Ibadan, IBADAN.</td>
</tr>
<tr>
<td>NORWAY</td>
<td>Johan Grundt Tanum Bokhandel, Karl Johansgt, 43, OSLO 1.</td>
</tr>
<tr>
<td>PAKISTAN</td>
<td>Mirza Book Agency, 65 Shahrah Quaid-E. Azam, P.O. Box 729, LAHORE 3.</td>
</tr>
<tr>
<td>PARAGUAY</td>
<td>Agencia de Librerihas Nizza S.A., Estrella No. 721, ASUNCION.</td>
</tr>
<tr>
<td>PERU</td>
<td>Distribuidora Inca S.A., Apartado 3115, Emilio Althaus 470, LIMA.</td>
</tr>
<tr>
<td>PHILIPPINES</td>
<td>World Health Organization, Regional Office for the Western Pacific, P.O. Box 2932, MANILA — The Modern Book Company Inc., P.O. Box 632, 926 Rizal Avenue, MANILA.</td>
</tr>
<tr>
<td>POLAND</td>
<td>Skladnica Ksi¹garska, ul. Mazowiecka 9, WARSAW (except periodicals) — BKWZ Ruch, ul. Wronia 23, WARSAW (periodicals only).</td>
</tr>
<tr>
<td>PORTUGAL</td>
<td>The WHO Representative, Central P.O. Box 540, SEOUL.</td>
</tr>
<tr>
<td>REPUBLIC OF KOREA</td>
<td>The WHO Representative, 144 Moulmein Road, G.P.O. Box 3457, SINGAPORE 1.</td>
</tr>
<tr>
<td>SINGAPORE</td>
<td>University of Ibadan, IBADAN.</td>
</tr>
<tr>
<td>SOUTH AFRICA</td>
<td>Van Schaik's Bookstore (Pry) Ltd, P.O. Box 724, PRETORIA.</td>
</tr>
<tr>
<td>SRI LANKA</td>
<td>see India, WHO Regional Office.</td>
</tr>
<tr>
<td>SWEDEN</td>
<td>Aktiebolaget C.E. Fritzes Kunig. Hovbokhandel, Fredsgatan 2, STOCKHOLM 16.</td>
</tr>
<tr>
<td>SWITZERLAND</td>
<td>Medizinischer Verlag Hans Huber, Länggasse Strasse 76, 3012 BERN 9.</td>
</tr>
<tr>
<td>THAILAND</td>
<td>see India, WHO Regional Office.</td>
</tr>
<tr>
<td>TUNISIA</td>
<td>Société Tunisienne de Diffusion, 5 avenue de Carthage, TUNIS.</td>
</tr>
<tr>
<td>TURKEY</td>
<td>Librairie Hachette, 469 avenue de l'Indépendence, ISTANBUL.</td>
</tr>
<tr>
<td>UGANDA</td>
<td>see address under KENYA.</td>
</tr>
<tr>
<td>UNITED KINGDOM</td>
<td>H.M. Stationary Office; 49 High Holborn, LONDON WC1V 6HB; 13a Castle Street, EDINBURGH EH2 3AR; 109 St Mary Street, CARDIFF CF1 1JW; 80 Chichester Street, BELFAST BT1 4JY; Brazenose Street, MANCHESTER M60 8AS; 258 Broad Street, BIRMINGHAM B1 2HE; 50 Fairfax Street, BRISTOL BS1 3DE. All mail orders should be sent to P.O. Box 569, London SE1 9NH.</td>
</tr>
<tr>
<td>UNITED REP. OF TANZANIA</td>
<td>see address under KENYA.</td>
</tr>
<tr>
<td>UNITED STATES OF AMERICA</td>
<td>Single and bulk copies of individual publications (not subscriptions) : Q Corporation, 49 Sheridan Avenue, ALBANY, NY 12210. Subscriptions : Subscription orders, accompanied by check made out to the Chemical Bank, New York, Account World Health Organization, should be sent to the World Health Organization, P.O. Box 5284, Church Street Station, NEW YORK, NY 10014. Correspondence concerning subscriptions should be forwarded to the World Health Organization, Distribution and Sales Service, 1211 Geneva 27, Switzerland. Publications are also available from the United Nations Bookshop, NEW YORK, NY 10017 (retail only).</td>
</tr>
<tr>
<td>USSR</td>
<td>For readers in the USSR requiring Russian editions : Komsomol'skij prospekt 18, Medicinskaja Knija, MOSCOW — For readers outside the USSR requiring Russian editions : Komunzky most 18, Medzunarodnaja Knija, MOSCOW G-200.</td>
</tr>
<tr>
<td>VENEZUELA</td>
<td>Editorial Interamericana de Venezuela C.A., Apartado 50785, CARACAS — Libreria del AV. Francisco de Miranda 52, Edificio Galipán, CARACAS.</td>
</tr>
<tr>
<td>YUGOSLAVIA</td>
<td>Jugoslovenska Kniga, Terazije 27/11, BELGRADE.</td>
</tr>
</tbody>
</table>

Orders from countries where sales agents have not yet been appointed may be addressed to: World Health Organization, Distribution and Sales Service, 1211 Geneva 27, Switzerland, but must be paid for in pounds sterling, US dollars, or Swiss francs.

Price: Sw. fr. 30.–

Prices are subject to change without notice.