

PREVENTION IN CHILDHOOD OF HEALTH PROBLEMS IN ADULT LIFE

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Foreword

"The childhood shows the man,
As morning shows the day."

John Milton—
Paradise Regained

That health is essential to socioeconomic development has gained increasing recognition, but it is perhaps not so widely appreciated that, in the final analysis, human health and wellbeing are the ultimate goal of development. To focus on children's health is thus to contribute directly to socioeconomic development, since the health of the child is the key to the health of the adult.

The remarkable progress achieved in recent decades in means for the prevention and treatment of childhood diseases has unfortunately benefited only a relatively small proportion of the world's children. There has certainly been an overall reduction in infant and child mortality, but in most parts of the world—in the developing countries, particularly—the rates remain disturbingly high, with striking disparities both between countries and between areas or populations within countries. Of some 122 million children born annually, 12 million die before they reach their first birthday. Yet this figure, disquieting though it is, tells nothing of the sad reality awaiting the many millions who survive to become the victims of ill health brought about by a host of adverse socioeconomic factors, most commonly associated with malnutrition, infection and closely spaced pregnancies, or who fail to develop to their full potential.

The most important challenges today are to bridge the gap between the existing scientific knowledge and technology and their application, and, in line with the objectives of the International Year of the Child, 1979, to stimulate sustained programmes that benefit children as a part of broader efforts to accelerate economic and social development. This book is intended as a contribution to meeting those challenges. It had its origin and gradually took shape as part of the World Health Organization's efforts in support of the International Year of the Child. Another activity connected with that Year was WHO's promulgation in all countries of the 1979 World Health Day theme: "A Healthy Child, A Sure Future". That theme is subsumed in every page of the present book, which addresses itself to many important aspects of the very wide issue denoted by its title.

Much of what is said reflects the increasingly general acceptance in recent decades of the view that preconceptional factors and conditions during fetal life and early infancy profoundly influence the physical and psychosocial development of the child and ultimately the health of the adult. Among the most important early influences is the environment of the family, the basic social unit.

Three years ago the Member States of the World Health Organization, concerned at the totally unacceptable health status of so many millions of people in the world—children being the most obvious victims—decided that the main social target of governments and of WHO should be “the attainment by all citizens of the world by the year 2000 of a level of health that will permit them to lead a socially and economically productive life”. The International Conference on Primary Health Care, in 1978, and the Declaration of Alma-Ata adopted then, unanimously endorsed primary health care as the key to attaining that target. This book highlights numerous areas in which practical preventive and curative action can be taken today to improve maternal and child health and the health of the family as a whole in the spirit of primary health care.

It also draws attention to areas where further knowledge is needed and to those where differing opinions prevail. That there should be differences is not surprising; indeed, the airing of differences is part of the usual mechanism for gaining new knowledge and for unravelling the “mysteries” of nature, including the ever-astonishing process of the development of the human being from the fetus to adulthood. In view of the long span of that development and of the innumerable favourable and unfavourable events that affect the individual during that process, it is not always easy to demonstrate clear causes and effects. Among the many complex or debated issues that urgently need clarification is under what conditions and to what extent the nutritionally or psychosocially deprived child can make good its deficit and realize its full potential. We also need to know more about the antecedents in childhood of some disabling diseases prevalent among adults in order to devise appropriate means of timely prevention.

This last problem is one of the three main threads that runs throughout this book. The others may be stated as a concern with the promotion of health through the application of known measures for the prevention or treatment of disease in the first, crucial years of life in order to prevent long-term sequelae; and a concern with the impact of a person's health during the early years (including the prenatal period) upon his or her later health as a parent and family member, and thus upon future generations.

Whatever can be done to ensure the health and wellbeing of children helps to lay the foundations of health in adult life and of health for those children's children. The importance of healthy children—for their own sake, for the realization of overall development goals, and for the welfare of mankind as a whole—is such that every year should be treated as a Year of the Child. It is hoped that this book may serve as a fitting epilogue to WHO's activities for the International Year of the Child, not only leading to the necessary research, but also, and more important, stimulating positive action for better health.

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Introduction

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Ideally, the aim of human reproduction is to create children who will reach adulthood happy and healthy and who will remain so during a long life. It is clear, alas, that in many countries this aim may be unachievable for a number of years. It is at last becoming evident that the foundations for healthy maturity are laid in the earliest stages of human life and that, if it is to be attained, the curve of a child's growth and development—usually genetically targeted—must be carefully followed. For some variables, we may be satisfied with the achievement of milestones along the way within acceptable limits; deflections from the curve are a warning to take action. All too often, however, it is too late, for the deflection is irreversible, and a critical period of growth has been allowed to pass when the factors necessary for its successful passage were absent or deficient.

While it is accepted that many specific adult health problems have their origins in childhood, the environmental and genetic factors involved must be identified so that effective preventive measures can be taken. Specialization in the professions has tended to divide those with expertise in adult health from those with expertise in child health. And since a highly complex continuum is involved, there is a pressing need not only for a multidisciplinary approach, but also for the elimination of that division.

Running through the whole of the subject-matter of this publication is an all-important thread: education, e.g., education on the optimum nutritional needs of the infant, education on the long-term effects of childhood smoking. These over-simple examples mask the complexity of the word "education", but since education is so often a key to success, its complexity must never cause us to shy away. It is tempting to confine ourselves to the more simple, though still important, subject of how to prevent or deal with childhood antecedents of adult health problems, but

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having covered it we need to consider some broad areas in which family health and family planning and formation are vitally involved.

Specific health problems arise from family disruption and dispersal; they also arise from adolescent disruption and lack of schooling—the “drop-out” phenomenon. And, particularly when thinking of the adolescent, we should consider the adult sequelae of violence, criminality, abuse of drugs (including alcohol), and venereal disease. Two other areas are intimately linked with family health: child abuse, and adaptation to handicap and chronic illness.

It may be said that these problems, which are closely bound up with the family as a unit are too broad to be grouped under the heading of prevention in childhood of specific adult health problems. Broad as they are, they nevertheless demand consideration in any discussion of family health and planning and their complex, multidisciplinary nature must not be allowed to stand in the way.

There is another side to the main theme of this book—childhood antecedents of adult sequelae, yes; but we also need to consider and, we hope, eventually solve the problems of the children around us now. Instead of being concerned just with, say, the specific antecedents of later obesity, we should be concerned about the unhappy obese children themselves.

The entire field covered by the title of this book is vast and complex, and priority choices had therefore to be made. In consequence there are some gaps—for instance, the adult sequelae of nonfatal accidents in childhood—and some diseases or conditions have not been discussed in great detail; we are aware of these defects and hope they may be remedied in time.

Human biology

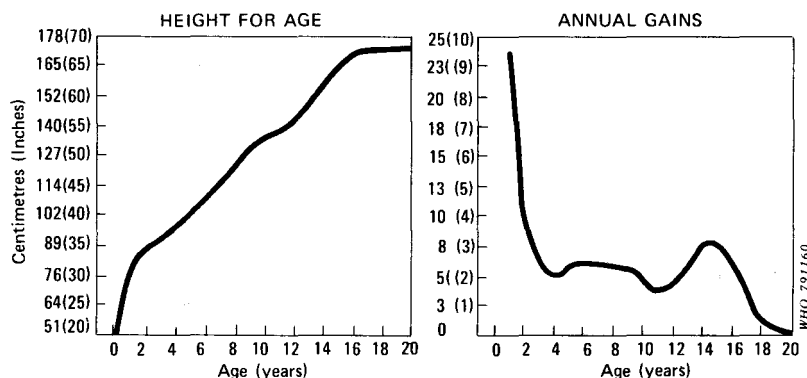
Growth is a part of biology and thus human growth a part of human biology; the study of growth is the study of change in an organism as it reaches towards maturity. Differential growth creates external form through growth rates varying from one part of the body to another, and internal form through a series of events occurring over time in which cells are endowed with special complexities related to particular functions. There is, then, at bottom no real distinction between growth and development, and it is only in recent years that those concerned with child health, and the child's ultimate outcome as an adult, have accepted that growth is the basic science peculiar to their specialty.

Fundamental to the prevention in childhood of problems likely to have adverse repercussions on health later on is a knowledge of the normal growth patterns of the healthy child. These patterns can then be screened for and monitored with advantage.

Those concerned with child health tend to think of human growth in terms of size attained in relation to age. The measurement of this and its distribution among a sample population is valuable, since it indicates progress along a standard curve—ideally obtained from the measurement

of large numbers of healthy children at specific ages. These curves, useful as they are, hide the fact that growth is not a steady, regular process, particularly when one considers growth velocity. Fig. 1 illustrates this.

Fig. 1. Growth velocity



Left: Distance curve showing height of boy at various ages. Right: Velocity curve showing annual gains, plotted from first curve.

The concept of growth velocity, or incremental growth, is not easy to grasp. Its assessment gives information on change over periods of time. Height has been chosen as an indicator of growth in the example, since it is a stable measure as opposed to, say, body weight. The right-hand curve in Fig. 1 is based on the data in the left-hand curve and simply shows how fast the boy is growing at different points over the whole period of postnatal growth. There is a rather dramatic difference between the forms of the two curves.

The velocity curve shows that, in infancy, growth is more rapid than at any other time in life, although it has, in fact, been decelerating from about the thirty-second week of gestation, when the peak velocity of fetal growth was reached. From about 3 years of age until the onset of puberty the annual growth rate is fairly steady. With the sudden growth spurt of adolescence, the rate accelerates rapidly—for the only time in postnatal life. The peak velocity is reached in the middle of puberty and deceleration occurs until growth—in this case, in stature—ceases.

A healthy infant's growth seems destined to seek an individual velocity curve. Once growth is progressing along this curve, it is not likely to be deflected permanently unless the environment becomes and remains inadequate. Various impairments to growth may cause the velocity to fall below the level of the curve, but with the impairment removed and suitable intervention, catch-up growth can occur during which the velocity will rise

above the level of the curve to compensate for the earlier slowing down or cessation. If the impairment is severe enough, or operates over a lengthy period, catch-up growth will not occur. This is of crucial importance when certain organs and systems are going through critical periods of development. For example, for the brain, this is from about the thirty-second week of fetal life to about the second postnatal year. Lack of appropriate environmental factors, or impairments, during this period may then cause reduced or defective growth of the brain, with no catch-up and hence an irreversible arrest, ultimately resulting in a greater or lesser deficiency in the mental performance of the adult.

It must be borne in mind that growth is a continuum starting at conception, and many of the secrets and foundations of later health are to be found in the all-important first 40 weeks of life—not postnatal weeks but those after growth has begun.

Prenatal growth

No completely reliable measure of gestational age is available, so, as a compromise, fetal growth is estimated from measurements taken at birth and shortly thereafter. Since fetal growth curves are thus mainly derived from data on fetuses born either too soon or too small, there is a need for curves based on data on normal fetuses that will be born at full term. This now seems feasible with certain noninvasive techniques, such as ultrasound. The resultant standards would be of great help in perinatology.

Fetal growth is extremely rapid in early pregnancy, the rate accelerating to a peak about the fifth month of gestation. The period of deceleration that follows into postnatal life has already been described. So fetal growth, too, varies greatly in velocity over time.

It is agreed that an infant born with a weight of 2500 g or less is one of low birth weight. There are, however, at least two kinds of infant of low birth weight: those born too soon—i.e., preterm infants—and those born too small for their gestational age. The latter are in fact often born at or near 40 weeks of gestation. The distinction between the two kinds of infant of low birth weight is important because of outcome. But first, all such infants face a whole host of risks in being born so small and/or immature. They are disadvantaged from birth. They contribute greatly to perinatal mortality rates and to immediate and long-term health problems. And female infants of low birth weight may well become mothers of such infants themselves. Prevention of low birth weight is therefore of vital importance.

Provided the preterm infant is immediately given first-class modern neonatal care (which is hardly available globally), is free of serious congenital defect, and survives intact, he or she will exhibit catch-up growth and by 2–3 years of age will be of normal destined size and performance. While this is being achieved, however, the risks are very great.

With infants that are too small for their gestational age, even given the

same care and survival, catch-up growth usually does not occur for sufficiently long, and irreversible stunting and less than normal mental performance can result (3).

The causation of preterm births is multiple and in part unknown. But it is often preventable by such measures as good prenatal screening and care, the discouragement of adolescent pregnancy, and treatment of hypertension.

Infants too small for their gestational age are clearly the result of retarded intrauterine fetal growth. A major factor here is probably maternofetal malnutrition, which is of course reversible. The growing brain is one of the body systems with a critical period of development; in humans, this is from late fetal life until the first or second year of postnatal life. Hence growth retardation in this period is likely to result in irreversible failure of brain development with some degree of permanent defect.

There now appear to be at least two groups of infants who are too small for their gestational age; their nature is probably related to the length of the period of intrauterine impairment malnutrition, and the timing of this period. One group appears to exhibit sufficient catch-up growth and the other does not (1, 5). It is therefore important to see that an individual is placed in the correct category, when the later outcome is being predicted.

Table 1 presents some striking statistics on infants of low birth weight. It shows the very much greater number of infants of low birth weight born in the developing world (E) compared with the developed world (F). It also shows that, in the developing world, 75 % of these infants are small for gestational age (G) compared with 33 % in the developed countries (I). Since many of the factors causing smallness for gestational age are reversible, a very great improvement in outcome and subsequent health for the neonate could be achieved by mandatory intervention.

Genetics and growth

The nature versus nurture debate—the weighing of genetic against environmental influences—is an old and complex one. A recent study of the growth and development of one pair of twins shows the multifactorial nature of prenatal influences on growth and brings out important points in the nature-nurture conflict (4).

Monozygous twins are theoretically identical phenotypically—i.e., from the point of view of genetic influences on growth, they both should grow identically. The twins described in the study were both born near term. The first-born twin (A) weighed 1460 g at birth and the second-born (B) 2806 g—or almost twice as much. It was possible to determine which part of the placenta “supplied” each twin (in the particular type of placentation applicable to these twins), and it was found that the mass of the part of the placenta supplying the smaller twin was about half that of the part supplying the larger twin. It may be that there is a “critical level” of size for a placenta, or part of a placenta, below which there is a growth deficit that

Table 1. Infants of low birth weight born in developing and developed countries, 1975^a

A.	World total of live births	137 000 000	
B.	World total of births of infants of low birth weight B as a percentage of A (range of percentage according to countries' populations)	22 000 000	16% 4-45%
C.	Total births in developing world C as a percentage of A	116 500 000	85%
D.	Total births in developed world D as a percentage of A	20 500 000	15%
E.	Total births of infants of low birth weight in developing countries E as a percentage of C	20 900 000	18%
F.	Total births of infants of low birth weight in developed countries F as a percentage of D	1 100 000	5.5%
G.	Total births of infants too small for gestational age in developing countries G as a percentage of E	15 600 000	75%
H.	Total births of preterm infants in developing countries H as a percentage of E	5 200 000	25%
I.	Total births of infants too small for gestational age in developed countries I as a percentage of F	365 000	33%
J.	Total births of preterm infants in developed countries J as a percentage of F	725 000	66%

^a Based on WHO estimates.

may be irreversible—and of particular significance, perhaps, in maternal and fetal malnutrition.

Both twins were born at term, so that twin A was not only of low birth weight, but also too small for gestational age. This pair of twins has now been followed up for 16 years. In the first 9 months, twin A grew significantly faster than twin B—in an effort, as it were, to make up for the deficit in size at birth. But, after about 1 year, twin A went on to grow at the *same* rate as twin B so that his growth did not continue sufficiently rapidly for him to catch up with his brother. While, at 16 years of age, both twins are healthy, of similar maturity and mental performance, twin B is nearly 8 kg heavier and over 5 cm taller than twin A. It may be asked whether this matters. The answer is no, since both are healthy and apparently happy. But by the age of 2½ years the twins should have been virtually free of perinatal influences and installed in their genetic growth curves. A more important biological question is whether, at 16 years, when their adolescent growth spurt is approaching its end, there is now an irreversible difference in their size due to the factors already discussed. Presumably twin A is following the growth pattern of an infant who is too small for his gestational age, and the illustration of the pair is significant because of the constancy of the genetic growth factor for both twins.

This example shows the need for greater emphasis on perinatal research and the need to pay special attention to the complex genetic influences

involved when considering the relationship of child health to health in later years.

As Scriver (6) has written, each child is born with a unique set of genes. Through life, these operate in a host of different environments and place each child, during growth and development, at different levels of risk for any condition or health problem that has any genetic component whatever. Thus, it simply is not practicable, nor desirable, to expose every individual to the same preventive programme for a particular serious, multifactorial condition or disease. Genetic screening may reveal those at risk, yet "there has been some indication"—in some countries at least—"that health care planners believe that the diseases of life-style such as lung cancer and coronary heart disease could be reduced in prevalence among middle-aged citizens by initiating a change in life-style of all younger citizens. A good idea in theory, we might agree; but in practice, reminiscent of treating all infants with thyroid therapy to prevent cretinism in childhood. It would seem better to find the persons carrying the genes which place them at special risk in the environment of the society in question, and to recommend a change in their life-style" (6). And, where we can, to intervene early with that goal in mind. This may seem over-idealistic, and the problems standing in the way are many; but the goals must be formulated and then aimed at.

Sir Francis Crick (2), referring to some of the most profound problems of human biology, wrote: "Which problems are likely to be solved by AD 2000 depends on whether they can be attacked by isolating a small part of the biological system or whether one is mainly concerned with its behaviour as a whole. In the long run, problems involving complex interaction can hardly be avoided." This philosophy is at the root of the prevention in childhood of adult health problems.

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Perinatal diseases and injuries

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Nothing has a greater impact on the eventual quality of life as an adult than the diseases and injuries of the perinatal period. This period of life is characterized by more perils to human survival and health than any other. Newborn infants may suffer from genetic disorders affecting vital systems or from disease acquired *in utero*; they may suffer from injuries incurred during intrauterine life or during the process of birth; they may suffer from deprivation of vital nutrients while *in utero* or from inability, due to disease or malformation, to be adequately nourished after the transition to extrauterine life; they may be extremely susceptible to neonatal diseases owing to prematurity or deficiencies of their immune systems. The purpose of this chapter is to analyse the diseases and injuries of the fetus and the newborn that can seriously influence health in adult life and to examine how best to prevent them. Although there is a correlation—varying from disease to disease—between perinatal mortality and the incidence of permanent sequelae in survivors, the perinatal, infant, and childhood mortality rates will be peripheral to this analysis. Thus, we shall disregard one of the prime yardsticks in the consideration of perinatal disease and concentrate on the survivors and the outcome for them in adult life.

The prevention in childhood of adult health problems can be achieved in two ways: (1) by the prevention of disease itself, and (2) by complete cure of the disease that poses a threat. Both approaches are applicable to perinatal diseases and injuries. As regards diseases diagnosed during fetal life, a third approach becomes possible—namely, interruption of pregnancy before viability of the fetus. Although this approach is being used increasingly, it is so far practised only in countries with very highly developed health care technology and it is not universally acceptable, for ethical or religious reasons.

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Congenital disorders of known genetic etiology

Strictly speaking, genetic disorders do not belong under the heading "perinatal diseases" since they are present, though not necessarily manifest, from the time of conception. But they do contribute in considerable measure to the health problems of adult life and, since many genetic disorders can now be diagnosed in mid-pregnancy, permitting preventive measures to be taken, it seems appropriate to include them.

The congenital disorders with genetic etiology include chromosomal abnormalities and inborn errors of metabolism. In addition, the blood group isoimmunization syndromes may be considered as of genetic etiology. Although they are not always listed as genetic disorders, they do depend on genetically determined blood group constellations in mother and fetus.

Amniocentesis for antenatal diagnosis of genetic disorders

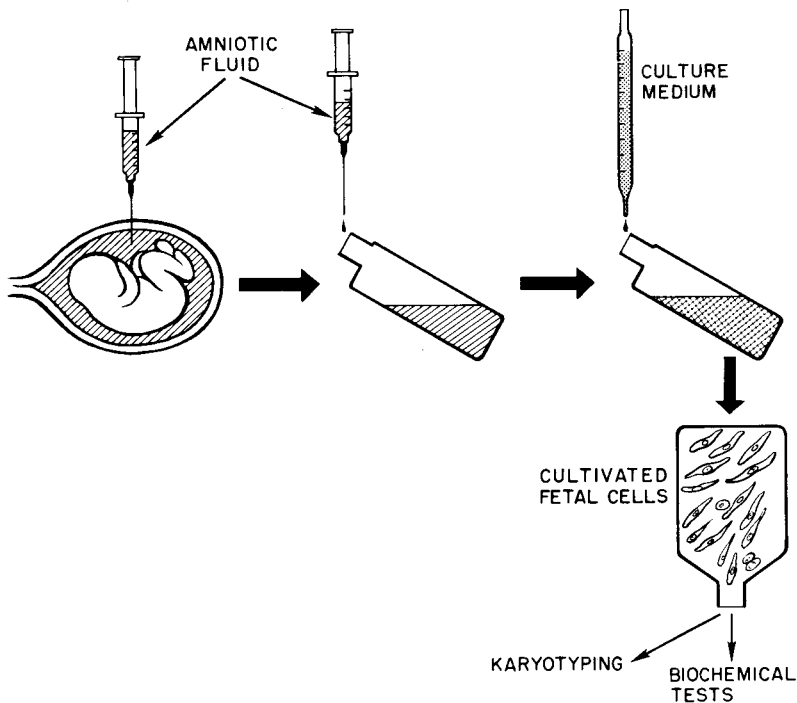
Prenatal diagnosis of fetal disorders on the basis of examination of amniotic fluid was introduced in 1952 by Bevis (6), who examined the concentration of bile pigments in cases of erythroblastosis fetalis due to Rh-isoimmunization of the mother. Some years later, it was demonstrated that examination of the cells suspended in the amniotic fluid could reveal the sex of the fetus (13, 24, 32, 33) and the fetal blood group (14), features which both could be used as genetic markers. Riis & Fuchs (31) were the first to use antenatal sex determination for the prevention of sex-linked hereditary disorders such as haemophilia and one of the forms of muscular dystrophy. Technological advances in cytogenetics soon led to attempts to culture amniotic fluid cells for karyotype studies (12), but the first reports of success did not appear until 1966 (36, 37). It was predicted as early as 1956 (15) that inborn errors of metabolism could be diagnosed by biochemical examination of amniotic fluid constituents, but it took some time for the relevant research to develop. Nevertheless, in 1973 some 50 different inborn errors of metabolism could be detected (10), and the number has grown since then.

The advantages of antenatal diagnosis of genetic disorders are quite obvious. Many of these disorders lead to severe debilitating disease, and others are associated with mental retardation, precluding a normal life. For most of these disorders no treatment exists as yet, but if they can be diagnosed early in gestation, the birth of afflicted individuals can be prevented by interruption of the pregnancy. Treatment *in utero* is so far only applicable to Rh-isoimmunization, but in a few disorders in which treatment from birth can materially alter the prognosis, such as the adrenogenital syndrome and galactosaemia, antenatal diagnosis permits the immediate institution of therapy without waiting for the disease to manifest itself.

Chromosomal abnormalities

At 16 weeks' gestation, the average volume of amniotic fluid is 175 ml (38). This permits the insertion of a long, slim needle through the uterine wall into the amniotic cavity (Fig. 1) and the withdrawal of 10–20 ml of fluid without risk. At this stage of gestation, the fluid contains enough viable cells to establish a cell culture of fetal cells. Karyotype studies are usually possible within 2–4 weeks. With modern banding techniques, abnormal karyotypes can be identified with great accuracy.

Fig. 1. Culture procedure for amniotic fluid cells



Amniocentesis, which is done transabdominally, is greatly facilitated by simultaneous real-time sonography, which often permits the avoidance of transplacental puncture and needle lesions of the fetus. Of the aspirated fluid, 5–15 ml is immediately transferred to a 250 Falcon plastic tissue culture flask for incubation with a tissue culture medium (7). Enough cells can sometimes be found as early as the fifth day, and the average time of the karyotyping is 2½ weeks.

Mothers-to-be risk carrying fetuses with chromosomal abnormalities when one of the parents is known to have chromosome translocations or

when a sibling or a close relative has chromosomal abnormalities. In addition, there are older women with an age-related risk; these constitute by far the largest group of candidates for amniocentesis.

Very few countries have so far been able to develop sufficient facilities to cover those at risk in their populations, and this is likely to be the case for the foreseeable future. For a more detailed discussion of indications, risks, and organization of services the reader is referred to the rapidly growing literature on the subject.

Inborn errors of metabolism

A large group of genetic diseases due to enzyme deficiencies can be grouped together as *inborn errors of metabolism*. The cells in the amniotic fluid, after cultivation *in vitro*, manifest these enzyme deficiencies which can be determined by biochemical techniques, often of a very demanding nature. This group includes a number of disorders of lipid metabolism, of which Tay-Sachs disease is the best known; a number of disorders of mucopolysaccharide metabolism with Hurler's and Hunter's syndromes as the most frequent; a series of disorders of amino acid metabolism, such as maple syrup urine disease and cystinosis; disorders of carbohydrate metabolism, exemplified by Pompe's disease and galactosaemia; and finally a mixed group of diseases including the Lesch-Nyhan syndrome, the adrenogenital syndrome and lysosomal acid phosphatase deficiency. With few exceptions, these diseases are extremely debilitating or associated with mental retardation. Each of them has already been diagnosed *in utero* or is potentially detectable. All are very rare, however, and general screening of the population for them is neither justified nor technically possible. In families where such diseases are known to occur, on the other hand, attempts at antenatal diagnosis are highly justified. They are complicated, though, by the fact that few laboratories in the world have mastered the techniques for all the enzyme studies involved. A simple and globally more applicable approach to the prevention of these diseases is to advise those who risk having offspring with such defects to avoid parenthood altogether.

Blood group isoimmunization diseases

This group of diseases can be considered as having a genetic etiology, because they are due to differences in blood group constitution between mother and fetus. The only one of practical importance is Rh-isoimmunization, which can occur when an Rh-negative mother is carrying an Rh-positive fetus. The incidence of Rh disease is dependent on the ratio of Rh-negative to Rh-positive individuals, which varies in different racial groups. The disease is manifested in the form of erythroblastosis fetalis, which can lead to fetal or neonatal death, or to brain damage due to

kernicterus (see below, page 27). Amniocentesis is helpful in diagnosis and management during pregnancy. Mortality from the disease is high if it is not treated, but modern management of the pregnancy and treatment of the newborn have reduced both mortality and permanent damage substantially. Furthermore, the disease can be almost totally prevented by the use of specific immunoglobulin after deliveries, abortions, and amniocentesis in women at risk.

Congenital disorders with probable or possible genetic etiology

Congenital malformations

Major anatomical defects and deformations can cause lifelong handicaps, unless corrective measures are taken. Special training, surgical procedures, the provision of artificial limbs, etc., can overcome many of these handicaps. Similarly, congenital defects of vision and hearing can greatly influence the quality of adult life. The availability of corrective measures depends on the degree of development of the health system, but it is important to stress that certain congenital defects are simple and inexpensive to treat if the correct diagnosis is made at, or shortly after, birth. This applies, for instance, to congenital dislocation of the hip and club-foot. Midwives and other categories of auxiliary personnel can be taught both to diagnose and to treat these deformities which, if left untreated, can cause severe health problems in adult life.

Every organ in the body can exhibit congenital abnormalities, ranging from those incompatible with life to the most trivial which cause no impairment at all. Detection of the major ones *in utero* is sometimes possible by radiography or sonography, but except where the mode of inheritance is known or the risk can be estimated, or where special features such as polyhydramnios raise suspicion, antenatal diagnosis is rare. Much depends on the ability of the birth attendant to diagnose the nature of congenital abnormalities at birth and on the ability of the health care system to provide adequate corrective measures.

Neural tube defects

A recent advance in antenatal diagnosis of congenital defects is the detection of neural tube defects by measurement of a specific protein of fetal origin, called alpha-fetoprotein, which can be demonstrated in maternal blood and in amniotic fluid during pregnancy. The group of abnormalities of the brain and spinal cord includes anencephaly, meningo-myelocele, and spina bifida. In neural tube defects the levels of alpha-fetoprotein are elevated. It is accordingly possible to diagnose neural tube defects by amniocentesis in the sixteenth week of pregnancy—i.e., the same stage at which amniocentesis is performed for detection of chromosomal

anomalies. The screening of pregnant women, based on determination of alpha-fetoproteins in maternal blood serum, makes it possible to ascertain in which instances amniocentesis, which is required to confirm the diagnosis, should be carried out. The advisability of such screening programmes is still debated, but amniocentesis is advocated in mothers who have previously given birth to infants with neural tube defects, and assays for alpha-fetoprotein are advocated in all mid-trimester amniotic fluid specimens, regardless of the primary purpose of the amniocentesis. Neural tube defects occur with approximately the same frequency as chromosomal abnormalities and, even when combined with inborn errors of metabolism, they are numerically rather insignificant, as compared with the main problems in maternal and child health care. When priorities are considered on a global basis, the antenatal diagnosis of genetic disorders must come rather low on the list (10).

Congenital disorders due to maternal diseases complicated by pregnancy

Diabetes mellitus and pregnancy

It is a well-established fact that maternal diabetes mellitus is associated with an increased incidence of congenital malformations, and it is generally assumed that this is due to an altered carbohydrate metabolism. The exact mechanism of the teratological effect of diabetes is not clear, but it seems that meticulous control of maternal blood sugar throughout gestation will reduce not only the perinatal mortality but also the incidence of congenital malformations associated with the disease.

It has been demonstrated that not only congenital malformations but also reduced intelligence may be found in the offspring of diabetic mothers. The results of a large-scale collaborative study of cerebral palsy (8) show that the intelligence of children whose mothers have had acetonuria during pregnancy is lower than that of control infants of the same weight groups. If the blood sugar is maintained in the normal range by meticulous control, episodes of acetonuria should be avoidable, but at the moment few diabetics in the world are given such optimum management.

Cardiac disease and pregnancy

Pregnancy imposes an increased load on the heart, the maximum increase (some 50 %) being reached by about the thirty-second week of gestation. The normal heart has enough reserve capacity to cope with this extra load, but in the presence of severe heart disease, whether congenital or acquired, there may not be any reserve and heart failure will develop. If failure occurs early in pregnancy, the fetus may be subject to hypoxia, which can result in fetal malformation. If it happens late in pregnancy, the outcome may be premature birth, whose consequences for adult life will be

discussed later. Congenital heart disease associated with a 50 % risk of premature labour (5), and even women without manifest heart disease, but with hearts that are small relative to their body size, are at increased risk of giving birth prematurely (30).

The prevention of damage to the fetus from maternal heart disease is contingent on the correction of congenital heart defects before pregnancy whenever possible, and on management of the pregnancy in such a way that cyanosis and heart failure are avoided. This can be very difficult, even with the best provision for antenatal care and, where such care is lacking, the life of the mother and both the life and the health of her offspring are in jeopardy.

Mental disease and pregnancy

The literature on the outcome of pregnancy in mothers with chronic mental disease is very limited. Patients with major psychoses such as schizophrenia and manic-depressive psychosis were formerly placed in institutions where the sexes were segregated. Modern management has reduced the need for institutional care and also broken down sex barriers in institutions. As a result several problems have arisen: (1) an increased incidence of pregnancy in women with mental disease; (2) increased exposure of fetuses to psychotropic drugs used therapeutically; and (3) increased exposure of infants and children to mothers with mental disease. The question has been raised whether pregnancy and delivery in patients with schizophrenia are associated with an abnormal amount of complications; This would not be surprising, since adequate pregnancy care is dependent on the mother's ability and willingness to follow instructions. In a Danish study, in which one of the present authors was involved (26), however, there was a difference in the incidence of complications only with regard to primigravidae. The possible teratogenic effects of the psychotropic drugs used in the long-term treatment of the major psychoses are not yet clear. Even if the incidence of anatomical malformations is unchanged, the possibility of long-term behavioural effects after exposure of the central nervous system of the fetus to potent psychotropic drugs cannot be excluded. What is clear, however, is that there is an increased incidence of mental disease in the offspring of schizophrenic mothers, as demonstrated by a long-term follow-up of data in the study cited above (F. Schulsinger, personal communication).

Epilepsy and pregnancy

Seizure disorders in pregnant women can affect the offspring in two ways:

1. The seizures are associated with hypoxia, which usually is of relatively short duration but which nevertheless deprives the fetus of oxygen for a

time; at certain developmental stages such hypoxic states can lead to fetal malformations.

2. The anticonvulsive agents used to prevent seizures can be teratogenic. It has been shown that barbiturates and hydantoin are associated with certain, rather typical, malformations (18, 25, 34). In addition, the mother with epilepsy may have seizures while handling a newborn infant and this can result in injuries to the infant which may or may not leave permanent damage. It is recommended that epileptic women requiring medication to control seizures should remain on medication during pregnancy and lactation, at the lowest possible dosage level.

Malnutrition and outcome of pregnancy

Malnutrition of the mother and the newborn constitutes the single most important cause of health problems carried through to adult life. Whether it is chronic, being due to extreme poverty, or temporary, being due, for example, to famines caused by drought or other natural calamities, the fetus and the newborn are particularly vulnerable to it. Some figures from the north-eastern region of Brazil amply illustrate this well-known fact. A survey in the state of Ceará revealed that for every 100 babies conceived in the study area 17 will die *in utero* and 13 of those born alive will die within one year. Given similar conditions in all developing areas of the world, perinatal and infant mortality would account for the loss of some 30 million children in these areas every year. One of the principal causes of this catastrophic situation is hunger. Low birth weight due to maternal malnutrition is one of the factors increasing perinatal and infant mortality. Those who survive will feel the pressure of poverty and other extrinsic factors that will tend to increase their physical handicaps and reduce their mental capacity. In the survey in the state of Ceará, it was found that 60% of the families earn, at best, one regional minimum wage, a wage that does not permit the purchase of milk, eggs, meat, or vegetables, leaving as the only option starchy and farinaceous foods that fill the stomach but do not provide the necessary nutrients. Winick et al. (42) and Zamenhoff et al. (43) have shown in experimental studies that starvation in animals leads to deficiencies in DNA, RNA, and proteins in the placenta and the fetal brain. However, laboratory evidence is not necessary to prove that chronically deficient nutrition is harmful during pregnancy and in the neonatal period; living proof of it is frightfully abundant in today's world.

There is a real paucity of specific data on maternofetal nutrition in both developed and developing countries. Since this has such a vital bearing on the outcome for the fetus and infant, it is essential to make up this gap in knowledge.

Congenital disorders due to diseases and abnormalities of pregnancy

Toxaemia of pregnancy

The specific toxaemias of pregnancy, the classic toxaemia with the triad of proteinuria, hypertension, and oedema, monosymptomatic hypertension of pregnancy, and perhaps also prolonged severe hyperemesis of pregnancy, are usually associated with retardation of fetal growth. If the outcome is a live infant it is rare for the intrauterine deprivation to have sequelae lasting into adult life.

Premature delivery

Prematurity is the most important cause of perinatal mortality, the dominant cause of neonatal morbidity, and an important cause of health problems in adult life. Premature birth accounts for more than 75 % of perinatal mortality, although only about 8 % of all births occur prematurely. The prevention of premature birth would have an enormous effect, but so far this has not proved possible in spite of the development of various pharmacological agents that can arrest uterine activity. In fact, the incidence of premature birth appears to be rising, probably mainly as a result of increasing urbanization both in the developed and in the developing world (10). A large number of predisposing factors have been identified (Table 1), but knowledge of these statistical factors is of little use in the prevention of prematurity. The dominant factors, being socio-economic, cannot be eliminated medically, but certain obstetric and medical causes can and should be dealt with.

For the rational treatment of a pathological condition, a thorough understanding of its pathophysiology is needed. Unfortunately, the physiology of human parturition is not yet fully clarified, nor is it known whether the mechanism of premature labour is identical with the mechanism of full-term labour, even though the clinical features are quite similar, apart from timing. There is now considerable evidence to support the view, which can be traced back to Hippocrates, that the primary signal for parturition comes from the central nervous system of the fetus. It would appear that a whole series of events is precipitated, but under normal circumstances this will not happen until the systems involved have reached a certain degree of maturity. Under abnormal circumstances, the train of events can be set in motion prematurely, but fortunately it can be stopped again in many cases by pharmacological intervention. A review of the physiological factors involved in the mechanism of human parturition makes it possible to pinpoint the following areas of possible pharmacological interference in threatened premature labour.

1. Although the myometrium has the capacity to contract at any time during gestation, it is essentially at rest until the onset of labour. It has been assumed that progesterone is necessary for keeping the myometrium at

Table 1. Factors frequently associated with premature labour

Maternal factors

Age below 20 or over 35 years at first delivery
 Primiparity
 Small stature
 Low socioeconomic status
 Cigarette smoking
 Small heart volume
 Congenital cardiac disease
 Chronic debilitating diseases
 Anatomical defects of the uterus
 Congenital uterine malformations
 Uterine synechia
 Fibromyomas
 Incompetent cervix
 Pregnancy complications
 Urinary tract infection
 Intercurrent febrile infections
 Accidental traumas

Placental factors

Abruptio placentae
 Placenta praevia
 Placental insufficiency

Fetal factors

Multiple gestation
 Anencephaly
 Adrenal hyperplasia
 Anomalies associated with hydramnios

Iatrogenic factors

Induction of labour for pregnancy complications
 Pre-eclampsia
 Rhesus-isoimmunization
 Diabetes mellitus
 Elective induction of labour
 Intrauterine contraceptive device *in utero*

rest, as is certainly the case in many animal species. This has led to the use of progestins to prevent premature birth. Although there are specific progesterone receptors in the myometrium and progesterone binds very rapidly, it requires 12–24 hours for the effect on myometrial motility to develop. It is too late, therefore, to try to reinforce the progesterone level once the uterus has begun to contract. In cases involving a high risk of premature onset of labour, the prophylactic treatment of patients with synthetic progestin has shown promising results, but there has been some concern about the long-term effect on the fetus.

2. Like other smooth muscle systems, the myometrium contains alpha- and beta-receptors. Stimulation of the beta-receptors causes relaxation and, although the physiological role of these sympathetic receptors is poorly understood, one of the best approaches to the pharmacological control of uterine contractions has been made possible by their presence. The beta-receptors are divided into beta₁-receptors, found in the heart, and beta₂-receptors, found in other smooth muscles, including the myometrium. During the last decade, a number of beta-agonists have been developed and widely used outside the USA for the treatment of threatened premature labour (28, 39).

3. There is considerable evidence to support the assumption that uterine contractions do not develop "spontaneously" but require active stimulation of the myometrium. Inhibition of the secretion or formation of activating agents should accordingly inhibit uterine activity. The most powerful uterine stimulant is oxytocin, and there is now incontrovertible evidence for the presence of oxytocin in the maternal and fetal blood during parturition. The secretion of oxytocin from the neurohypophysis can be inhibited by the administration of ethanol, and this approach is widely used in threatened premature labour (16). Another group of uterine stimulants is that of the prostaglandins, which are formed in the decidua, membranes, and myometrium during parturition. The formation of prostaglandins can be inhibited by prostaglandin synthetase inhibitors, and it has been shown that these agents are capable of arresting premature labour (44).

4. Calcium ions play an important role in the cellular mechanisms of muscular contraction and relaxation. Magnesium sulfate and a number of pharmacological agents interfere with the availability of calcium ions. Both magnesium sulfate and drugs such as diazoxide have accordingly been used to inhibit uterine contractions in premature labour.

5. It has recently been shown that the myometrium in rabbits and rats contains receptors for oxytocin, and preliminary studies indicate that this also applies to humans. For some 20 years several groups have tried to develop oxytocin analogues that would be devoid of oxytocic properties but would bind to the same receptors. By saturating the receptors with the analogue, the binding of oxytocin, which is necessary for its action, would be prevented.

If dangerous side-effects, particularly on the fetus, can be excluded, the availability of several approaches to the pharmacological control of premature labour may provide a partial solution to preterm birth. However, a major problem remains. In many instances, the threat of premature labour begins with premature rupture of the membranes. This opens the way for ascending infections and often creates a dilemma: should the baby be born as soon as possible after the rupture of the membranes and be subject to the perils of prematurity, or should the fetus be kept in the uterus, even if it requires tocolytic drugs, and be subject to the risk of intrauterine infections? The solution depends on the circumstances, and notably on the availability of supervision and care.

The care of premature infants has greatly progressed in recent years, but the more advanced methods demand manpower and sophisticated equipment on a scale as yet unthinkable for the developing world. Better education of birth attendants and the development of simple, inexpensive aids for resuscitation could improve the situation considerably, but prematurity *per se* will remain a major maternal and child health problem for a long time.

It is interesting to note that a preterm newborn infant who survives, has no serious defect, and receives optimum modern care will usually exhibit catch-up growth in the early years and indeed reach the size that he or she would have reached if full-term. This is in contrast to the small-for-dates

infant of comparable newborn size who, under the same conditions, does not in general appear to exhibit sufficient catch-up growth. For both groups catch-up intellectually is surely more important, and there is some evidence of increased impairment of mental development (9). The whole question of outcome for infants of low birth weight needs careful study.

Prematurity *per se* and the diseases of neonatal and infant life associated with prematurity are responsible for a wide spectrum of mental and physical handicaps in adult life. The prevention of these handicaps depends on the prevention of premature birth by eliminating the predisposing factors and by the pharmacological control of premature labour. This has yet to be achieved in countries with the very best health care facilities, and for the world as a whole it will remain one of the principal public health problems for generations.

Multiple gestation

Multiple gestation is associated with a number of risk factors leading to increases in both perinatal mortality and neonatal morbidity with possible consequences for health in adulthood. The risk factors become greater the higher the number of fetuses, but are otherwise the same. The risks include intrauterine growth retardation, premature birth, umbilical cord prolapse, and difficult deliveries, particularly of the second of twins. Early diagnosis is important to reduce the risk of premature birth because prevention depends on reducing the mother's workload. To avoid complications at delivery, hospital confinement is preferable whenever possible.

Congenital disorders due to the abuse of drugs by pregnant women

Abuse of drugs has taken on epidemic proportions during the last quarter of a century, and it is not limited to affluent societies. It is also found alongside poverty and deprivation, and tends to aggravate their effects. When drug abuse is continued into pregnancy, it can have serious consequences for the offspring. In recent years it has become clear that alcohol and tobacco are drugs that present health hazards for unborn children.

Heroin addiction and pregnancy

In the USA, the epidemic of heroin abuse of the 1960s and 1970s has drawn particular attention to the abuse by pregnant women of heroin and its therapeutic substitute methadone. Before the widespread use of methadone as a treatment adjunct, few alternatives were available for the treatment of narcotic-dependent expectant mothers; thus little attention was paid to prenatal care and there was a high incidence of complications.

Heroin-dependent gravidae are at high risk for anaemia, infectious hepatitis, toxemia of pregnancy, and venereal disease. Persons dependent on heroin often also abuse central nervous system depressants or stimulants, such as cocaine. A high incidence of obstetric complications, such as premature rupture of membranes, fetal growth retardation, and breech presentation occurs in the absence of treatment. The neonatal complications include a high death rate, particularly when mothers fail to reveal their addiction and thereby inhibit the early diagnosis of neonatal withdrawal. The neonates are further endangered by low birth weight due to prematurity or retardation of intrauterine growth. The neonatal withdrawal syndrome occurs in the majority of the infants of untreated mothers, and those who survive are at high risk for developmental and behavioural disorders (27, 41).

The use of methadone and intensive interdisciplinary antenatal care can lower the incidence of illicit narcotic use and help to bring mothers through pregnancy and delivery with fewer complications. Venereal diseases can be treated to prevent infection of the newborn, dietary habits can be regulated to prevent anaemia and toxemia, and other problems can be identified and treated. Detoxification during pregnancy is not desirable, because it may result in fetal distress, overstimulation of the fetal adrenal and sympathetic nervous system, or intrauterine death. The infants of mothers who can be maintained on less than 20 mg of methadone daily have withdrawal symptoms that require treatment much less frequently than the infants of mothers on higher doses of methadone.

Cytogenetic studies of dependent mothers and their infants have shown chromosomal aberrations in some 10 % of the examined cells. The most prevalent type of damage is chromatid breaks, but aneuploidy and other aberrations are found as well. The incidence of abnormalities in maternal and infant cell samples is about the same (1), but the correlation is poor. The implications of these findings for the future life of the newborn infants are not known. Thus, the identifiable risks for health in adulthood are the developmental and behavioural risks mentioned above and the risks associated with the increased incidence of complications of pregnancy and delivery in general.

Abuse of other psychotropic drugs

The abuse of other drugs presents problems of a similar nature when they occur in pregnancy. The drugs can be grouped in 4 main categories: nonheroin opiates, psychedelic drugs, amphetamines, and barbiturates. Withdrawal symptoms may occur in all categories and if they can occur in the drug-abuser, it must always be anticipated that they can occur in the neonate, too. To prevent such problems, it is important to identify drug-abusers and get reliable histories about the type and degree of abuse. This is notoriously difficult, and the risks are therefore considerable.

Alcohol and pregnancy

The abuse of alcohol has a very long history and it complicates all aspects of life, including pregnancy. It is astounding that the effects on the offspring were not observed many years ago but were first described in French medical literature in 1968 (22), and in English medical literature in 1973 (19). The teratogenic effects of ethanol consist of pre- and postnatal growth deficiency, an unusual facial pattern typified by short palebral fissures and maxillary hypoplasia, anomalies of joint position and function, cardiac defects, microcephaly, and mental deficiency. The last two features are thought to be due to diminished growth of the brain. There are some indications that lesser alterations of growth and morphogenesis, suggestive of the fetal alcohol syndrome, may be caused by the prolonged intake of relatively modest daily amounts of ethanol (17).

Abuse of alcohol is a worldwide problem and both prevention and treatment are known to be difficult. Its effects on offspring are probably compounded by nutritional deficiencies, but remain to be assessed on a worldwide scale. Judging from the recent literature, the fetal alcohol syndrome may well be one of the major threats to health in adulthood.

Tobacco and pregnancy

The last quarter of a century has brought incontrovertible evidence of many different perils to health arising from smoking, particularly cigarette-smoking. In pregnancy, the main dangers from smoking are retardation of fetal growth and an increase in the prematurity rate. An increased concentration of carbon monoxide in the air inhaled, with a high affinity to maternal and, in particular, fetal haemoglobin, reducing its oxygen-carrying capacity, is thought to be the main cause of the retardation of fetal growth, but other factors may be involved. Abstinence from smoking is the best way of preventing this particular outcome.

Birth injuries and traumas

The transition from the shielded life *in utero* to the independent extrauterine life is the most dangerous event in the human life cycle. To list all the perils associated with birth is not possible, but they can be divided into two main groups: physical injuries due to hypoxia during and immediately after birth, and physical traumas.

Hypoxia

During labour, the maternal blood flow is impeded by the uterine contractions. Mild contractions which exceed the venous pressure will interrupt the venous outflow during each contraction. When the con-

tractions develop, with uterine tension exceeding the arterial pressure, the inflow will be blocked as well. Under normal conditions, the fetus is able to tolerate such temporary reductions in oxygen supply quite well, but if the contractions get too frequent or last too long, or if the fetus is already partially at risk, such hypoxia can cause damage to the brain. The same can happen if the cord is prolapsed or compressed, or if the oxygenation of the maternal blood is deficient as a result of maternal heart failure. The first indication of hypoxia is a change in the fetal heart rate, usually beginning with tachycardia, followed by bradycardia. This can be detected by frequent monitoring with a stethoscope, or with electronic monitors. The result of hypoxia is fetal acidosis, which can be determined by fetal scalp blood sampling or by continuous monitoring of the fetal pH by scalp electrodes.

Fetal hypoxia is treated by removal of the causes or, if that is not possible, early delivery is induced.

After birth, the newborn infant must begin to breathe to maintain the oxygenation of the blood. To help establish breathing the airways should be cleared. With a healthy baby, this can be done by positioning the body with the head low. The process can be assisted by gentle suction to remove mucus and amniotic fluid. If the newborn infant has already been subject to hypoxia during labour and delivery, resuscitation may require more active measures, such as repeated suction, application of an oxygen mask, intubation, and assisted respiration. The performance of such interventions requires knowledge and skill and is usually only possible in a hospital setting. It would be useful to develop a better aid for suction than the traditional rubber balloon—i.e., one that would be independent of running water or suction pumps, easy to keep clean under difficult sanitary and climatic conditions, and easy to handle. It should also be cheap and of unbreakable material.

Physical injuries

A relative disproportion between the bony pelvis and the size of the fetus can make the passage through the birth canal traumatic for the baby. Likewise, the use of forceps or other instruments to complete delivery can inflict injuries on the fetus. Many of these injuries, such as cephalhaematoma and fracture of the clavicle, are relatively minor and leave no permanent damage. Others are more serious, such as depressed cranial fractures, intracranial haemorrhage, and Erb's paralysis.

The prevention of birth traumas of both types depends on the quality of the obstetrics. Fetal distress, cephalopelvic disproportion, prolapse of the cord, abnormal positions, and similar abnormalities can be diagnosed during labour and appropriate measures taken. Electronic monitoring of fetal heart rate and uterine activity, fetal scalp blood sampling, and the rapidly increasing use of caesarean section are of much greater benefit in preventing birth traumas than in reducing perinatal mortality. Since birth

traumas may cause minimal brain damage which is difficult to assess at birth but which may have fairly severe long-term consequences, the benefit is hard to quantify.

When birth traumas cannot be prevented because the birth attendant lacks the necessary equipment, their recognition after birth is important so that the long-term effects may be minimized by corrective measures.

Neonatal disorders

The moment of birth is a dramatic transition that requires a rapid adaptation of a number of vital functions. Instead of receiving oxygen and delivering carbon dioxide through placental exchange between the maternal and fetal bloods, neonates are dependent on their lungs for gas exchange. The blood circulation must be altered from a single-loop system to a double-loop system to bring the gases to and from the lungs. The gastrointestinal system must begin its digestive and resorptive functions in place of the transference of nutrients through the placenta, and the kidneys must likewise take over the excretion of waste products which were also taken care of by the placenta. The heat exchange which previously took place between fetus and mother through the placenta and the amniotic fluid, is now entirely dependent on skin exchange with air and on respiration, requiring a system of thermoregulation. In short, every system must undergo a profound change, and for this a veritable shock is necessary, a shock provided by the process of birth itself. To immerse the newborn infant in a bath of warm water does not make much sense, since the stimulus of the air against the skin helps to promote respiration. Although nature has adapted the human being for a successful transition from intra- to extrauterine life, a large number of pathological conditions can develop in the process and some of them can leave permanent damage.

Respiratory distress syndrome

The establishment of respiratory function at birth is dependent on expansion of the alveoli, clearance of lung fluids, and provision of adequate pulmonary perfusion. In many premature infants and others at high risk, developmental deficiencies or unfavourable perinatal events often hamper neonatal respiratory adaptation. If the production and release of surfactant into the alveoli is compromised, the result is the respiratory distress syndrome (RDS). This is the most common cause of death in premature infants. During the past decade, however, major progress has been made in both prevention and treatment of this condition.

It was the report of Avery & Mead (3) demonstrating a high surface tension in extracts of lungs of infants dying from RDS that led to current knowledge of the role of surfactant in the pathogenesis of RDS. Klaus et al. (20) demonstrated that the main constituent of surfactant is dipalmitoyl

lecithin. It is now clear that surface-active phospholipids are produced and stored in pulmonary cells in membrane-bound secretory granules called lamellar bodies. Late in pregnancy, under the influence of corticosteroids, these bodies migrate to the cell surface and discharge their lipid material into the alveoli, where it decreases the surface tension at the gas-fluid interface. The phospholipids are necessary for maintaining the stability of the alveoli during respiration. If they are lacking, pulmonary atelectasis will develop, leading to hypoventilation. Lack of oxygen and retention of carbon dioxide will lead to acidosis, which will further reduce the production of surfactant and pulmonary perfusion. Progressive epithelial damage will follow with oedema and fibrin deposits, finally resulting in the classic hyaline membrane disease.

Clinically, the premature infant developing RDS will show the associated signs and symptoms during the first 24 hours, with progression during the next 48 hours. The clinical management of the condition requires specially trained personnel to give intensive care and sophisticated equipment for the maintenance of body temperature and adequate oxygenation and for the monitoring of vital functions, including blood gases. A number of complications of the condition and problems in its treatment can occur, and the mortality remains high, even if it has been materially reduced in the best-equipped facilities. With improved survival, a higher incidence of long-term sequelae must be anticipated. In most series the incidence of significant developmental problems is 10–20%, but a higher incidence of deficits has been noted in some studies. Obviously, a condition that can cause prolonged hypoxia during a critical neonatal period can be expected to leave permanent damage, and every step must therefore be taken to prevent it.

The single most important measure for avoiding RDS is the prevention of preterm birth. As mentioned above, several types of pharmacological agent that can arrest premature labour are now available, but so far they have had very little effect on the incidence of preterm births, not even enough to counteract the increase due to demographic factors.

Another advance is the treatment of the mother, when premature labour is threatened, with corticosteroids and tocolytic agents such as ethanol or salbutamol (23). If delivery can be postponed for 48–72 hours, the incidence of RDS in infants having a gestational age of between 28 and 34 weeks is reported to be considerably lower than when the mothers have not been treated. Although this prophylactic treatment is still at the trial stage, there is rapidly mounting evidence in favour of corticoid treatment. The treatment of pregnant women with other steroid hormones has, however, led to undesirable side-effects in the offspring, in some instances after a latent period of many years. Data from long-term follow-up studies are therefore urgently needed.

Meconium aspiration

Infants who aspirate meconium are usually full-term, or postmature, and frequently have a history of fetal distress and meconium-stained amniotic fluid. The clinical picture is dominated by respiratory symptoms beginning shortly after birth with tachypnoea, intercostal retractions, and occasional cyanosis. Pneumothorax and pneumomediastinum are frequent radiographic findings. Many newborn infants with this syndrome require mechanical ventilation. Secondary bacterial infection is a dreaded complication.

Because the infant usually has been subject to hypoxia *in utero*, neonatal asphyxia often accentuates lesions of the central nervous system already incurred. The long-term outcome is more dependent on the damage to the central nervous system than on the pulmonary, circulatory, and metabolic involvement (4). Prevention is difficult, because meconium staining of the amniotic fluid can occur before the onset of labour. Amnioscopy in post-date pregnancies can be helpful. Conduct of labour in such a way that hypoxia of the fetus is avoided is the only preventive measure, but prompt recognition at birth and immediate treatment can reduce the long-term consequences.

Neonatal infections

A baby born at term, breast fed, and reared under sanitary conditions is relatively well protected against infectious disease. In contrast, the premature infant with respiratory problems, too sick and too small to be nursed, and born into a family living in insanitary, overcrowded conditions and beset by disease, malnutrition, and general deprivation, is frequently a prey to infectious diseases, particularly of the respiratory and gastrointestinal tracts. Apart from the high susceptibility to, and high mortality from, these diseases in the neonatal period, they are not essentially different from the infections in early childhood described in more detail in Chapter 7.

Haematological diseases

A number of haematological diseases are found in the neonatal period, notably anaemia, hyperbilirubinaemia, and erythroblastosis fetalis, which combines the features of both anaemia and hyperbilirubinaemia.

Occasionally, an infant is born with severe anaemia due to exsanguination from rupture of a fetal vessel, for instance in vasa praevia, or from vascular anastomosis with a twin. Such events are rare. Following birth, both premature and full-term infants experience a fall in haemoglobin. In premature infants, this tends to be more severe, so that these infants, while beginning extrauterine life with a high cord haemoglobin, gradually

become anaemic. The reason for this is not known, but its recognition is important because anaemia may compound the other problems associated with prematurity.

Unconjugated hyperbilirubinaemia is another haematological condition that occurs in the neonatal period and is particularly dangerous in infants of low birth weight. Virtually all neonates experience an increase in unconjugated bilirubin during the first week of life; this physiological jaundice is thought to be due to a complex interaction of increased bilirubin production, diminished uptake of bilirubin in the hepatic cells, and deficient hepatic conjugation (21). Unconjugated bilirubin is toxic to the brain cells, causing bilirubin-staining and necrosis of neurons (kernicterus), particularly in the basal ganglia, hippocampal cortex, and subthalamic nuclei. The clinical picture is characterized by lethargy, rigidity, opisthotonos, high-pitched cry, fever, or convulsions. Survivors of symptomatic or asymptomatic bilirubin encephalopathy often develop variable degrees of neurobehavioural dysfunction later, ranging from severe forms of cerebral palsy, mental retardation, and deafness to mild lack of motor coordination and subtle abnormalities in cognitive function. While in full-term infants brain damage is practically unheard of at serum bilirubin concentrations below 20 mg/100 ml, infants of very low birth weight are much more susceptible and can develop brain damage at half that concentration, particularly if they have also been subject to hypoxia.

A number of drugs are capable of inducing or stimulating the hepatic glucuronide conjugating system, including ethanol, barbiturates, antihistamines, and heroin. Ethanol and barbiturates exert this effect when given to the mother and thus the use of ethanol to prevent premature birth (16) can have a beneficial effect, even if the birth is postponed only for a short period. Pharmacological treatment of the newborn with barbiturates and other drugs has been widespread, but unfortunately phenobarbital is not effective in infants with gestational ages of less than 32 weeks. Phototherapy with exposure to high-intensity visible light has become the most frequent method of treatment in recent years, and it can often eliminate the need for exchange transfusion, now the standard method of treatment. First introduced in the management of erythroblastosis fetalis, exchange transfusion consists of replacing plasma with a high level of bilirubin by plasma containing a normal level of bilirubin, until the liver can deal with the bilirubin produced in the newborn infant.

The prevention of the dire consequences of kernicterus depends on early recognition of jaundice in the newborn and the establishment of effective treatment before the serum bilirubin reaches critical levels.

Erythroblastosis fetalis, due to blood group isoimmunization of the mother, has already been mentioned. Treatment of the newborn infant has a dual aim: (1) to remove circulating antibodies transferred from the mother during intrauterine life, and (2) to remove the high concentration of bilirubin caused by the haemolysis of the antibody-covered erythrocytes. If kernicterus can be prevented, the prognosis for the surviving infants is good.

Neonatal malnutrition

For the full-term infant and for infants in the high range of low birth weight, human milk provides the most complete source of nutrition. Infants of very low birth weight have a number of problems that preclude breastfeeding, such as inability to suck or swallow or inability to digest breast milk in undiluted form. Breastfeeding has been declining in many parts of the world—particularly, but not exclusively, in the developed countries, although the reverse is now true in some areas. The rapidly increasing industrialization and urbanization of the developing countries has been an important factor in the decline of breastfeeding in those countries. While there are substitutes for human milk that can provide the same nutrients and calories, they do not contain maternal antibodies. In the absence of clean water and good sanitary conditions, milk substitutes are much inferior to breast milk.

Malnutrition in the neonatal period may be due to a large variety of causes, both medical and socioeconomic. Prematurity, neonatal diseases of different kinds, congenital malformations and diseases—all these are often compounded by lack of ability of the neonate to obtain adequate nutrition. Hunger, disability, illness, lack of interest, and neglect on the part of the mother may jeopardize the nutrition of the newborn infant. Malnutrition *in utero* and/or in the newborn period are often just the first of many deprivations that characterize life in numerous parts of the world and that have a marked effect on the physical and mental health of adults in areas where life must be maintained without access to clean water, adequate food, adequate housing, or even a minimum of health care. Malnutrition of the newborn is, like malnutrition in general, preventable, and the consequences for health in adult life are preventable with it.

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The task of the authors of the present chapter has been to review the prevention of disorders of the perinatal period that affect the health in adult life. To keep within the allotted space, the topic—which could easily be the subject of a whole book—has had to be treated in a rather general way, leaving out a number of disorders worthy of discussion and perhaps emphasizing disorders with less important consequences.

An additional task was to attempt to take a global point of view. In spite of the different vantage points of the two authors, this has been far from easy. In trying to describe what can be done, under optimum conditions, during the perinatal period to prevent lifelong handicaps, we have been painfully aware that, almost in every single instance, the recommended preventive and therapeutic measures are beyond the reach of large segments of the world's population.

Considering, as one should in the recent context of the International

Year of the Child, that those who as adults will determine the quality of life in the next century are going to be born in the remaining part of this century, it is shocking to note the enormous gap between the have and have-not countries in regard to maternal and child health care. We cannot conclude this chapter without endorsing the principle of primary health care as proposed by UNICEF and WHO (29). The application of this principle in maternal and child health care in north-eastern Brazil has fully confirmed its value (35). But the mobilization of local forces will not be enough, unless a more equal distribution of global resources is achieved and brought to bear on the alleviation of hunger and provision of clean water, sanitation, adequate housing, and education about prevention of illness, unwanted pregnancies, and nutrition. Damage from perinatal disorders can result in lifelong suffering, and an improvement in perinatal care would therefore yield the greatest returns.

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The problem of malnutrition

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While socioeconomic variables largely determine the incidence of childhood malnutrition in a country, childhood malnutrition in turn has a crucial role to play in the country's economy. In India the incidence of severe protein-energy malnutrition in preschool children is 1–2% and that of mild to moderate malnutrition nearly 80%. As there are at present 90–100 million preschool children in India, the number of malnourished children there is simply staggering. However, whether this widespread childhood malnutrition affects health during adulthood—the productive years of life—is largely unknown. One reason for this lack of knowledge on the subject is that most of those who suffer from undernutrition during childhood in developing countries continue to exist in a state of undernutrition even in later life. It thus becomes difficult to distinguish between the effects of current undernutrition and the consequences of early malnutrition.

In this chapter, the effects of childhood malnutrition on some important variables that may affect the development of a country will be discussed. These variables are: demography, physical stature, mental function, work capacity, and fertility and reproduction.

Demographic implications

Developing countries have a high infant mortality rate. In India, it stands at 140 per 1000. Apart from such variables as a high incidence of infectious disease and poor perinatal care, maternal nutrition is an important determinant of infant mortality. One direct consequence of maternal malnutrition during pregnancy is the birth of infants who are too small for their gestational age. About 25–30% of infants born to

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undernourished mothers weigh less than 2.5 kg, and about 4–10% weigh less than 2 kg (24, 26). Where mothers are adequately nourished, the corresponding figures are 14–16% and 1–2%. Morbidity and mortality rates are much higher among children who are small for gestational age than among those who are not.

The mortality rate among preschool children in the developing countries is just as dramatic as the infant mortality rate. In India these children constitute 12% of the total population, but 13% of all deaths occur among them (71), the mortality rate for the group being about 18 per 1000. One of the two important factors contributing to this figure is protein-energy malnutrition, the other is infectious disease.

Because of the high mortality among infants and preschool children, life expectancy at birth in India stands at less than 50 years and the young and dependent form a high proportion of the population. Even if 15-year-olds may be considered as economically independent, nearly half the population still constitutes a dependent group. Moreover, since the true working force is only 33% of the population (12) and since many of them are underemployed, the actual dependency ratio is much higher than the estimated one.

The high child mortality rate generally leads to a high birth rate. A minimum of 4–5 surviving children can be expected to include at least one male (77). A high premium is placed on a male child for both economic and sociocultural reasons. This preference for males may help to explain the sex ratios characteristic of developing countries, in which the number of males usually exceeds the number of females, in contrast to the developed countries, in which the reverse is normally found. While there are more male births than female births in all populations, the male excess tends to diminish with advancing age and eventually disappears, owing to the fact that age-specific mortality rates are generally higher for males than for females. This is not the case in some developing countries, however. For example, in Middle South Asia the ratio of females to males is lower at ages 25–50 years than in childhood, mainly because of high maternal mortality. A disturbing feature in India, which has not received due attention, is the steady decline in the sex ratio from the turn of the century to the present day (27). This has been interpreted to indicate that health risks to males declined more than those to females over the years (41).

Physical growth and development

The classic studies of McCance & Widdowson (37) have shown that some animals malnourished *in utero* remain stunted for life. Important determinants seem to be the length of such malnutrition and its timing. Fortunately the finding does not appear to be universally applicable to humans. Some infants who are small for gestational age have been shown to exhibit a good potential for catch-up growth (50). With the existing nutritional situation in the developing countries, interpretation of the

subsequent growth pattern of such children becomes a difficult exercise. Bhargava et al. (4) observed that even at the end of their second year they lagged behind their "appropriate-for-age" controls in length and weight. This might be explained solely on the basis of feeding patterns.

Though undernourished mothers have been shown to secrete enough breast milk to sustain normal growth during the first few months of infancy (25), the amount is much less than that needed for the satisfactory growth of normal infants. Thus the available energy and nutrients do not provide for catch-up growth. This is of particular importance because of the view that energy and nutrient supplements should be provided to pregnant mothers to increase their infants' birth weights (33, 36, 61). If the mothers are not also provided with supplementary nourishment during lactation, infant mortality may actually rise because the needs of heavier infants will be greater.

In the absence of supplementary foods, the growth rate of such infants starts to fall off by the time they are 4–6 months old, when breast milk becomes inadequate (6, 25). The growth lag reported by Bhargava et al. (4) might be interpreted as a consequence of the timing and length of prenatal malnutrition, but must also be understood as the possible reflection of a continuing state of undernutrition from intrauterine life into childhood (see Chapter 1).

Birth weight, in fact, appears not to influence growth in the preschool period. Morley et al. (43) observed that all of the 35% of a study cohort who were above the 75th percentile for body weight at birth moved to below this mark later in infancy. Other studies (72) showed that birth weight had no bearing on the development of protein-energy malnutrition in later life. Thus the mere raising of birth weights will not be of much use unless parallel efforts are undertaken to improve health and diminish mortality among preschool children.

The effect of intrauterine malnutrition on adult stature was assessed in a study of the survivors of the Dutch winter famine of 1944. It was observed that there was a high incidence of infants who were too small for gestational age among those born to mothers exposed to the famine during pregnancy (59). The outcome appears to be related to the actual length of exposure, as shown in animal studies, and another follow-up study showed that intrauterine malnutrition and low birth weight had no adverse effects on adult stature and body size (64).

It is not known whether malnutrition in the preschool period can affect the subsequent growth of the child. A follow-up study of undernourished rural preschool children showed that, even in adolescence, they continued to be short in stature and underweight (45). However, it cannot be stated categorically that this is a consequence of early malnutrition. Nearly 20–50% of the households in communities like that studied subsist on diets poor in energy intake (47) and the people accordingly live in a permanent state of undernutrition. Krueger (35) has also stated that the physical stunting seen in some school-age children may not be attributable to early malnutrition.

Some workers are of the opinion that growth retardation in early life may result in permanent stunting (60, 68), but there is the classic example of the remarkable response of children with kwashiorkor to energy and protein supplementation, which seems to show that undernourished preschool children possess tremendous catch-up potential. Recent studies from India (27, 32) show that if energy intake is adequate, the weight increments of undernourished children will be as good as those of normal children; these studies, however, do not indicate whether catch-up growth occurs and, if so, whether it eliminates the earlier failure in growth. In fact, there is a need for research in this area.

Preliminary studies indicate that the adolescent growth spurt is delayed by about 2 years in undernourished children (46), thus permitting undernourished adolescents to attain their maximum possible height. Despite this, the adults in the communities concerned are also short in stature (34), which may be considered a sign of malnutrition in childhood and adolescence. Their deficits in body weight, on the other hand, are probably a reflection of current undernutrition, being greater than the deficits in height.

To sum up, there is little proof that malnutrition in infancy and early childhood leads to permanent stunting of growth, and the need to investigate prenatal factors is clear. Undernutrition during late childhood and adolescence can, however, result in adults who are short in stature.

Mental function

Once the effects of malnutrition on physical growth and development in general became known, nutritionists began to study the significance of retardation of growth. One of the first aspects to be studied was its effect on the development of the brain and mental function. There is a great deal of literature on the subject (7), which has obviously aroused much interest. It is important to eliminate the erroneous view that all individuals exposed to malnutrition in early life suffer irreparable mental damage.

Dobbing (18) suggested that the period of maximum brain growth may be the most vulnerable one. In the human this corresponds to the last trimester of intrauterine life and the first 18–24 months of postnatal life. Myelination (16) and maximum cell multiplication (75) take place during this period, though some authors warn against an unqualified acceptance of the idea of a critical period of development (19, 56). Since the “vulnerable period” of brain growth varies markedly from species to species, extrapolations from animal studies must be interpreted with caution.

Moreover, it may be important not to lump together all children who are small for gestational age as a homogeneous group (20, 29, 39, 48). Results of studies carried out in countries in which the major etiological factor for smallness for gestational age is not maternal malnutrition may or may not be applicable to infants in developing countries in which intrauterine

malnutrition is a dominant factor. In a 3-year follow-up study, Ghosh et al. (23) observed no handicap in the infants studied either in motor and adaptive development or in social behaviour, whereas other studies have suggested a different outcome (5, 21). Strong evidence that intrauterine malnutrition may not result in permanent mental retardation comes from Stein et al. (63), who studied the 19-year-old children of mothers exposed to the comparatively short Dutch winter famine while pregnant.

There are many reports to indicate that malnutrition in late postnatal life can result in severe mental changes. The classic example is the characteristic apathy and irritability of the child with kwashiorkor. On the basis of animal experiments, Platt et al. (54) concluded that brain lesions caused by protein-energy malnutrition may persist for a long time after rehabilitation. Children who had suffered severe malnutrition during infancy and the preschool period were found, on follow-up at school-going age, to have low IQs, as well as poor learning ability and intersensory integration (9, 11, 15, 42, 65). However, this appears only to be a matter of delayed development rather than a permanent condition (62). Korean orphans adopted by well-placed foster-parents were found to have no residual mental deficiencies (76).

A question that needs to be answered is to what extent environmental factors other than nutrition affect mental development. Patel et al. (53) observed in a tribal community that 45% of the children of normal nutritional status fared badly in intelligence tests, and nearly 30% of those classified as malnourished performed normally. An important factor influencing behavioural and neurological development is of course the dyadic relationship between the infant and its mother or mother-surrogate. Cravioto (14), too, is of the opinion that at least some aspects of intersensory integration are retarded because of inadequate environmental stimulation rather than malnutrition.

One of the greatest handicaps in testing mental function is often the inappropriateness of the tests to the cultural background of the child. This is a factor that deserves much more attention.

Considering, then, the various factors that can influence investigations of mental function, it may be said that there is little solidly based evidence to show that malnutrition *per se* causes mental retardation and even less to show that it causes permanent mental retardation.

Physical activity and work output

Rutishauser & Whitehead (57) observed that undernourished children spent only 15% of a given period of time on activities such as walking and running whereas normal children spent 35% of the time on such activities. This would naturally affect the exploratory behaviour of the children, thus perhaps contributing to a lack of initiative and drive in adulthood.

It has been shown that sustained physical activity and exercise can increase lean body mass and to some extent the height of normal children

(51). Torun et al. (70) observed similar effects in the case of malnourished children undergoing rehabilitation. However, in undernourished states, because of low energy intake, exercise or physical activity may have no effect either on body composition or on longitudinal growth.

Body size has been shown to be an important variable in the determination of physical activity and work output (1). Pařížková (52) is of the opinion that this does not hold good for children, since she found the work output of Tunisian boys to be as good as that of Czech boys, even though the Tunisians were lighter and shorter. Areskog et al. (2) also found that nutritional status did not influence work output. The experience of Satyanarayana et al. (58) was different, since they concluded that body weight was the most important factor related to work capacity in adolescent boys. Their study does not, however, indicate whether the reduced work capacity of the undernourished adolescents was a carry-over effect of early malnutrition or a direct consequence of current malnutrition. When adults known to have been undernourished in childhood were placed in situations that permitted adequate energy intake over a considerable period of time, their work capacity was found to be normal (73, 74). Thus, the reduction in work performance seen in undernourished adults appears to be not a permanent shortcoming but one amenable to rectification. This suggests that it is a reflection of current rather than early malnutrition. Thus, from the available evidence, it may be inferred that though undernutrition may lower work capacity in adults this is mostly a result of continuing undernutrition and not a residual deficiency carried over from childhood.

Reproduction, fertility and lactation

Human reproduction is believed to withstand the rigours of undernutrition surprisingly well (69). However, a careful scrutiny of available data indicates that malnutrition, in fact, limits fertility. It should, however, be pointed out that such data as are available are concerned with the effects on female fertility, studies of the effects on male fertility being rare, mainly because of the difficulties encountered in finding a way of assessing male fertility.

It is believed that restriction of energy intake delays the onset of puberty (67). Menarche, an easily recordable event, is a good marker of maturity and there is much evidence that this, too, is delayed by restriction of energy intake (8, 22, 30, 38, 49). Undernutrition has been shown to increase the incidence of amenorrhoea. More than half of the women of reproductive age held in an internment camp were found to have amenorrhoea (66). However, here the effects of the emotional trauma of war and internment cannot be dissociated from those of malnutrition. It is difficult to assess the incidence in chronically malnourished populations because the women are generally either pregnant or lactating for practically the whole of the reproductive period. Amenorrhoea related to lactation has been found to

be of longer duration in undernourished mothers (3). Chen et al. (13) observed that rural women in Bangladesh resumed menstruation more often in the immediate post-harvest period. Though prolonged lactational amenorrhoea has been attributed to malnutrition (10, 17), it may merely be due to an extended period of lactation and the continuous stimulus of suckling. In well-nourished groups, whose socioeconomic status is usually relatively high, the early introduction of supplementary foods is bound to decrease the stimulus of suckling, which in turn leads to early failure of lactation and early resumption of menses.

There is a reciprocal relationship between maternal malnutrition and fetal nutrition. Most of the mothers in developing countries are underweight and subsist on nutritionally inadequate diets even during pregnancy. This has very serious consequences for fertility, fetal nutrition, and growth.

There is not sufficient information on the incidence of prematurity. Thomson (69) found no correlation between energy intake and the length of gestation. Stein et al. (64) felt that, although the duration of gestation appeared to be affected by starvation during the last trimester, the changes were too small for meaningful interpretation.

The ability of undernourished mothers to breastfeed their infants successfully for 4–6 months (25) would, at the outset, indicate that lactation is probably not affected by undernutrition. It is also believed that the output of breast milk is affected only by gross undernutrition (31). However, the lactational performance of undernourished mothers is probably not optimum and seems to occur at the expense of maternal tissue. It was also observed that lactation totally ceases below a certain body weight (31), indicating that nutritional status does indeed affect lactation. The yield of breast milk is also poor in undernourished mothers (3, 25).

It is not known whether the menopause is of earlier onset in undernourished mothers and, if so, whether this effectively reduces their span of reproductive life. It is probably not affected (40, 44).

All the available evidence indicates that undernutrition considerably reduces female fertility. This is of considerable importance in the populations of the developing countries in which undernutrition is widely prevalent and in which children, contrary to what is generally thought, are economic assets to the family.

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It appears that most of the ill-effects of malnutrition seen in adults, with the exception of reduced physical stature, may be the results of current malnutrition and not necessarily permanent residual effects of childhood malnutrition. The socioeconomic implications of childhood malnutrition

in a country such as India are more far-reaching than has been appreciated. Childhood malnutrition is only one facet, albeit an extremely tangible one, of the socioeconomic and cultural structure of a society. Thus, to believe that the improvement of child nutrition will solve many of the ills of the developing countries—for instance, to assume naïvely that, if health and nutrition services are made more widely available to children, the population problem will automatically be solved (44, 55)—betrays a lack of understanding of the many-faceted nature of child nutrition. It is important to appreciate that only all-round development can solve the problem of malnutrition among children, and that, however laudable its objectives and however devoted the workers, no programme aimed solely at improving child health can achieve this. This is not to decry the real value of providing services for children but rather to emphasize that they should be part and parcel of an integrated programme.

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Social implications of early protein-energy malnutrition*

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In a book on the prevention in childhood of health problems later in life, undernutrition must clearly be a crucial issue. Since childhood undernutrition, with its causes, prevention, and sequelae in adulthood, is such a vast and complex subject and involves so many different disciplines, it was felt appropriate, in the limited space available, to concentrate on one specific aspect—protein-energy malnutrition. Special attention is paid to the developing world, where the consequences of early protein-energy malnutrition may be of particular significance in terms of public health and national development.

Early protein-energy malnutrition is defined as malnutrition suffered before birth and/or during the first 5 postnatal years. Before birth it is defined by low birth weight (i.e., equal to, or less than, 2.5 kg). During the first 5 postnatal years it is defined by weight equal to, or less than, 90 % of the standard weight for age.

Worldwide incidence

Despite the high risk of damage associated with early protein-energy malnutrition, relatively little information is available on the magnitude of the problem (1) and its economic cost.

An indicator of the world prevalence of fetal malnutrition is the huge number of babies of low birth weight. On the basis of prior estimations (14, 16) we have concluded that 21 million such babies were born in 1978 (see Table 1). If present trends continue, the annual number of such babies is expected to be 33 million by the year 2000. Data in Table 2 indicate that in

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Table 1. Estimated number of babies of low birth weight (2.5 kg) born in 1978

Region	Population (millions) ^a	Number of births (millions) ^a	Percentage of babies of low birth weight ^b	Number of babies of low birth weight (millions) ^b
Asia	2 434	73.7	21	15.48
Oceania	22	0.5	20	0.10
Africa	436	19.9	15	3.06
Latin America	343	12.3	13	1.60
Northern America	242	3.6	10	0.36
Europe	480	7.1	7	0.50
USSR	261	4.7	4	0.19
Total	4 218	121.8	17.5	21.29
Developing countries	3 235 (76.7%)	106.4 (87.4%)	19.0	20.24 (95%)
Developed countries	983 (23.3%)	15.4 (12.6%)	6.8	1.05 (4.9%)

^a Computed from unpublished United Nations document ESA/P/WP.55, and from Population Reference Bureau, Inc. (23).

^b Computed from Lechtig et al. (17).

Table 2. Estimated number of children less than 5 years of age with protein-energy malnutrition during 1978

Region	Number of children less than 5 years of age (millions) ^a	Percentage with protein-energy malnutrition ^b	Number of children with protein-energy malnutrition (millions) ^b	Number of deaths at less than 5 years of age (millions) ^a
Asia	350	84	294.0	10.4
Oceania	3	80	2.4	0.01
Africa	79	60	47.4	4.9
Latin America	55	52	28.6	1.5
Northern America	19	3	0.6	0.1
Europe	37	2	0.7	0.1
USSR	22	1	0.2	0.1
Total	565	65.8	373.9	17.1
Developing countries	487 (86.2%)	76.0	372.4 (99.6%)	16.8 (98.3%)
Developed countries	78 (13.8%)	1.9	1.5 (0.4%)	0.3 (1.7%)

^a Computed from unpublished United Nations document ESA/P/WP.55, and from Population Reference Bureau, Inc. (23).

^b Defined by weight less than 90% of the standard weight for age.

1978 an estimated total of 374 million children less than 5 years of age had protein-energy malnutrition. If the same trends continue, the figure for the year 2000 will be 573 million.

Early protein-energy malnutrition is thus the most extensive and serious public health problem affecting man. The estimated risk of early protein-energy malnutrition is 40 times lower in developed countries than in developing countries. Further analysis has indicated a clear association between two important socioeconomic variables at national level (*per capita* gross national product, and energy available *per capita* per day) and the proportion of children with early protein-energy malnutrition (16). These findings confirm prior observations in urban and rural populations on the relationship between socioeconomic factors and the incidence of early protein-energy malnutrition (12).

Cost to society

It is now beginning to be accepted by nutritionists, social scientists, and laymen that, for communities and countries, the cost of early protein-energy malnutrition in terms of development may be enormous. Yet, important as it is for planners to know the nature and extent of this cost, relatively little objective evidence exists concerning the cost to society of the sequelae of early protein-energy malnutrition.

The ultimate implications of a high incidence of early protein-energy malnutrition depend on its adverse effect on mortality, population dynamics, physical growth, morbidity, mental development, school performance, social competence, and economic productivity. In the following paragraphs, we shall try to assess these implications.

Mortality

Infants suffering from protein-energy malnutrition are less likely to survive during the first years of life than normal infants (11, 13). In addition to the human tragedy involved, there is also extensive economic waste due to a reduction in the potential labour force and a consequent loss of productive effort. Thus there is a decreased return on investments made by both individual families and society as a whole during the infant's gestation and early postnatal life. The decrease in return will vary from country to country, depending on such factors as life expectancy, future productivity, and employment opportunities. Here again, the published estimates are few. It is probable, however, that in developing countries the economic cost of infant and preschool mortality may be much greater than that of deaths produced by such major killers of adults as cancer and cardiovascular disease.

Population dynamics

The social mechanisms relating fertility to mortality and early protein-energy malnutrition are poorly understood, and it is difficult to predict what the short-term fertility outcomes might be with changes in infant mortality rates and in the incidence of early protein-energy malnutrition. Preliminary results from recent studies suggest that these may be major factors in altering fertility as well as in accepting family planning (18). Consequently, it seems convenient to integrate programmes designed to decrease the incidence of early protein-energy malnutrition with programmes in family planning.

Retardation of physical growth

Although both pre- and postnatal growth retardation are associated

with early protein-energy malnutrition, this relationship has only slight economic implications in itself (20).

However, in poor populations growth retardation is a useful indicator of economically important disabilities, such as higher morbidity in preschool children, that entail increases in the cost of medical care services.

Morbidity

Morbidity associated with the occurrence of early protein-energy malnutrition can be divided into two categories: neonatal and postnatal.

(a) *Neonatal morbidity.* At birth, the infant suffering from protein-energy malnutrition manifests suboptimum physical development, loss of subcutaneous fat, dry skin with reduced turgor, hypoglycaemia, hypothermia, frequent and severe infections and high mortality (16). Early protein-energy malnutrition is also associated with perinatal asphyxia, polycythaemia, elevated levels of erythropoietin, and an increased incidence of congenital malformations.

The lower survival associated with early protein-energy malnutrition is undoubtedly associated with impaired resistance to infection. The increased frequency of infection in the infants concerned is an established clinical observation, and in the last few years it has been shown that babies suffering from protein-energy malnutrition have decreased IgG levels at birth, a significant reduction in the number of peripheral T-lymphocytes, significantly impaired cell-mediated immunity, reduced opsonic functions of plasma because of reduced C3 levels, and severe defects in the bactericidal capacity and oxidative metabolism of polymorphonuclear cells following phagocytosis (3).

Given that an infant who has suffered protein-energy malnutrition *in utero* and is thus subject to these infirmities is also likely to be exposed to postnatal malnutrition and high levels of infection, it is hardly surprising that the infants affected are less likely to survive the first year of life (15, 21). If they do survive their first year, maturation of critical tissue such as brain cortex, neuronal cell function, and subsequent development may well be limited, and there is a poorer chance for catch-up if and when nutrition is later improved (6, 10, 15).

(b) *Postneonatal morbidity.* There are almost no data available on the relationship between early protein-energy malnutrition and postneonatal morbidity. However, it is reasonable to expect that the common diseases will be more frequent and of longer duration in the children concerned. If these children are going to experience increased morbidity as adults, this will have highly unfavourable effects on productivity. In addition, children

who have suffered greatly impaired development may, should they survive, have to be supported all their lives by the society to which they belong (17).

Mental development

Despite the large number of investigations that have been carried out in the area of malnutrition and mental development, the effects of protein-energy malnutrition on the developing intellect are still not well understood. As reviews by Brožek (2), Warren (27), and others indicate, most studies which have compared children who have suffered severe early protein-energy malnutrition with control children have reported an association between poorer performances in mental tests and malnutrition. This association has frequently been observed even several years after the reported incidence of malnutrition. Recent studies by Hoorweg & Stanfield (8) and Richardson (24) suggest that neither age nor the acuteness of the adverse nutritional condition at the time of hospitalization is associated with poorer test performances, but the degree of chronic undernutrition at admission is associated with lower test scores. Thus, wasting appears to be a better indicator of the risk of reduced mental development than stunting.

Serious problems arise in connexion with the interpretation of the associations between malnutrition and poor performance in mental tests. This is largely because malnutrition generally appears in a context of poverty, poor health, and lack of intellectual stimulation, and each of these conditions is known to affect mental development adversely. As Warren (27) has pointed out, the relationship between malnutrition and mental development should ideally be investigated through a longitudinal study in which nutrition, morbidity, and social factors are all monitored concurrently with development.

Several such studies have been undertaken during the past decade, in Colombia (19, 22), in Guatemala (9), and in Mexico (4). Although not all these studies are as yet complete, the results so far provide stronger evidence than ever before that nutritional status, in addition to such factors as health and the level of social stimulation provided by the child's environment, does indeed influence mental development.

Although discussions of the effects of malnutrition on mental development aimed at laymen, notably in the media, have frequently suggested that malnutrition causes profound mental retardation, it is important to note that studies like those reviewed here do not show this to be the case. The effects recorded in these studies, including the longitudinal studies described above, are typically modest in size, although statistically significant. Nevertheless, these studies do suggest that children who have suffered from chronic protein-energy malnutrition, even in a mild to moderate degree, are likely to fail to reach their true intellectual potential.

Performance in formal and informal learning

Although educational wastage is an ever-present problem for schools in less developed countries, there have been no studies specifically relating school drop-out or year repetition to early protein-energy malnutrition. A number of authors have identified family factors associated with school failure, including parental background and income (7). But in none of these studies have data concerning early protein-energy malnutrition been presented. This is unfortunate, since such data are often available, particularly in developed countries in which they are routinely collected.

It is apparent, however, that children from families of low socioeconomic status have a relatively poor chance of success at school, a higher incidence of early protein-energy malnutrition, and a generally less stimulating social environment. An unsatisfactory level of learning at school, the repetition of the first school year by an unduly high proportion of children, and high drop-out rates can thus be considered as possible consequences of impaired development. In such conditions, the return on educational expenditure is appreciably diminished, and the resultant economic wastage can involve a substantial proportion of the budget for education.

The likelihood that the incidence of early protein-energy malnutrition is an important determinant of poor school attendance and performance has significant implications for both nutritional and educational planning. In the less developed countries, educational wastage is enormous, high drop-out rates, repetition, and school failure being endemic. Under such conditions, it is generally the poorer children who are most likely to suffer. If early protein-energy malnutrition is, at least in part, a factor in poor performance, there is little sense in investing large sums on the improvement of educational systems in isolation from other systems; if children of low socioeconomic status are to benefit from increased government investments in education, their chances of school success must be improved by attacking such basic problems as early protein-energy malnutrition.

Competence for social development and economic productivity

The relationship of early protein-energy malnutrition to economic activities and general competence in adults is not well understood. Only a limited number of studies investigating the relationship between nutritional status and the work productivity of adults have been performed (25, 26). In particular, the relationship of early protein-energy malnutrition to level of participation in the domestic economy, the acquisition of skills and information both in and out of school, and the development of abilities beyond those demanded and displayed at home and school has been practically unexplored.

The association between early protein-energy malnutrition and sub-optimum learning during childhood and adolescence, especially when the

family is of low socioeconomic status, may contribute to inequity in employment opportunities, lower productivity, lower income, and poor quality of life. It is very difficult to estimate to what extent early protein-energy malnutrition is a determinant of this chain of unfavourable events and what the whole vicious circle costs society. However, it seems clear that human resources, or human capital, are the main determinants of technological development and economic growth. As development proceeds, such characteristics as initiative and receptivity to, and understanding of, technological innovation become critical determinants of productivity in both urban and rural populations. Thus, human quality becomes more important than physical work for social and economic development.

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Although it is very difficult to disentangle early protein-energy malnutrition *per se* from interrelated cultural, familial, and institutional influences, the available evidence suggests that it has a negative effect on intellectual, physical, and social development. A high incidence of the condition may entail a heavy economic burden and be a serious obstacle to development in many countries.

From this it may be inferred that investment in programmes designed to decrease the incidence of early protein-energy malnutrition will yield an economic return important enough to stimulate social and economic development. Such an investment is justified not only because the ultimate goal of development is to improve the quality of human existence but also because human quality is a key to development. It seems particularly warranted in view of the fact that investment in other sectors, such as education, has traditionally been made without consideration of the complex interrelationships between the factors involved in development. Thus, for example, international agencies have encouraged the expansion of formal educational systems in less developed countries although it is known that many children in such countries never attend school, or attend for a short time only, or fail their examinations. It is probable that an increase in educational opportunities alone will not raise educational attainment, although investment in programmes designed to decrease early protein-energy malnutrition, combined with investments in education, may do so. Finally, a clear need exists for evaluation to be carried out in conjunction with such programmes, since only by this means can the cost-benefits of programmes containing educational, health and nutrition components in various combinations be accurately determined.

The negative impact of early protein-energy malnutrition on physical, intellectual and social development has been well documented in recent years. Although the implications for national development have yet to be systematically explored, it is likely to contribute largely to continued

underdevelopment, through inequality in employment opportunities, lower productivity, lower income, and poorer quality of life. Investment in programmes aimed at decreasing the incidence of early protein-energy malnutrition will thus operate synergistically, by helping not only individuals but also poorer countries to reach their true potential for development.

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Overnutrition and obesity

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Overnutrition leading to obesity is common in the developed countries. In the developing countries it is already common in the more privileged sections and is becoming a problem amongst the less affluent social groups. Although the exact relationship of obesity to health and disease cannot be clearly defined (44), there is agreement that in adult life overweight is associated with increased mortality rates, and that there is an association between obesity and ischaemic heart disease, hypertension, and diabetes mellitus (39). Obesity also causes disability and reduces the quality of life by reducing physical fitness, work capacity, and respiratory function, by exacerbating osteoarthritis, by increasing liability to postoperative complications and poor obstetric performance, and by causing emotional and social disability, especially in women (39). Because about one-third of adult obesity originates in childhood or adolescence and obesity in children tends to persist into adult life, prevention during childhood is of major importance.

Before discussing preventive measures, it is necessary to define terminology, review methods of measurement, and discuss prevalence and prognosis by age group, and the etiological factors involved.

Terminology and measurement

Strictly defined, obesity is a condition in which the whole adipose tissue mass (adipose organ) is enlarged out of proportion to other body tissues (83). This definition is, however, of limited practical value because of the difficulty of assessing the size of the adipose organ. Thus obesity is usually defined in terms of relative body weight or of skinfold thickness. Both

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methods have their technical limitations, but whatever procedure is used there is a lack of agreed ideal values. Data on patients are compared with data obtained from populations of healthy children, but within the range of values recorded in such populations there are no criteria by which to judge what is desirable in health terms. In presenting revised standards for skinfold measurements in British children, Tanner & Whitehouse (74) emphasize that the standards represent "what is, not what ought to be". If paediatricians and other health workers are to play a more active role in the prevention and early detection of obesity, some agreement must be reached on definitions and standards. There are well-known ethnic differences in the rate and pattern of growth; some of these are genetically controlled whereas others depend upon environmental differences of which nutrition and infection are probably the most important. Thus standard charts based on the growth of the best-nourished local group should be used wherever possible (71), although it must be remembered that there is a great potential for better growth among children in the developing countries; for example, Americans of African descent mature faster and end up taller than those of European descent (25).

The methods of measurement chosen to define obesity in a given population not only should provide a reliable index of body fatness but also should be sufficiently simple and quick to be of use in the community as well as in hospital clinics. Some of these methods, with their advantages and disadvantages, are discussed below.

Inspection

Inspection, the easiest and least expensive of all methods, still has a place in the assessment of obesity. Visual assessment has long been used for the appraisal of carcass traits in animals and correlates well with measurements of body composition (58). An experienced doctor is seldom in doubt about diagnosing obesity when he sees a child undressed. Crawford et al. (17), in a study designed to determine the most useful indices for the definition of obesity in babies, used the visual appraisal of 3 paediatricians as the reference standard. Rauh & Schumsky (60) found visual ratings by highly trained observers to be of value in the assessment of schoolchildren, and noted a strong positive relationship between the visual rating of fatness, on the one hand, and body weight, estimates of body fat, and triceps skinfold measurements, on the other. Visual assessment should not be ignored; a child who looks too fat probably is too fat, and conversely the adipose tissue mass of a child who looks lean is unlikely to be significantly enlarged. Inspection is of particular value in recognizing children in whom an unusual degree of muscular development results in above-average weight-for-height.

Weight

Marked overweight usually indicates some degree of obesity, and the statement that children whose weight exceeds the standard for their height, age, and sex by 20 % are likely to be obese, provided they are not oedematous (82), has long furnished a working basis for the definition of obesity. Reviewing 3 methods of deriving weight-for-height standards, Newens & Goldstein (54) conclude that neither a power-type index nor a relative weight index should be used in place of centile standards of weight-for-height, and that, in calculating standards of weight-for-height in children, age should be taken into account. Recently the US National Center for Health Statistics provided such standards (51), but these are not widely available and in practice centile charts that give height and weight separately are used. These have limitations when used for assessing overweight; weight centiles are skewed upwards, especially in the case of girls at puberty, and the gain in height of many obese children has been accelerated by overnutrition.

Further difficulties arise in situations where accurate height measurements may be difficult to obtain. Under such circumstances the weight-for-age Harvard tables (67) are widely used as a standard of growth against which to assess the nutrition of children. The errors that arise in the use of these tables for assessing nutritional status have been well defined by Sykes (69), and it is to be hoped that the standards of the US National Center for Health Statistics will now be used. Growth charts for use in developing countries, based on standards suggested by a WHO working party (84) and adapted to be applicable to boys and girls (for practical reasons), have been described by Morley (49). It is probable that, especially in the case of adolescents, weights above the 97th centile on such charts would indicate obesity, but the degree of fatness cannot be readily quantified.

Skinfold thickness

Skinfold measurements are a means of estimating the amount of fat in the subcutaneous compartment and give a useful index of obesity. It is essential to measure at standard sites, and centile charts for triceps and subscapular skinfolds are available (74). For babies aged 6 months a single triceps skinfold measurement was found to correlate better with the clinical assessment of fatness than the more traditional weight-for-length ratios (17). A committee on nutrition of the American Academy of Pediatrics recommended in 1968 that triceps skinfold measurements should be used in conjunction with height and weight standards in the assessment of body fatness. We agree that skinfold calipers should become part of the standard measuring equipment in paediatric clinics and that their use should be extended into the community wherever possible. When, however, obesity is extreme it may not be possible to apply the calipers.

Skinfold measurements can also be used to estimate the total amount of body fat. Durnin & Rahaman (22) correlated body density (estimated by underwater weighing) with the sum of skinfold measurements taken over the biceps, triceps, subscapular, and suprailiac sites in adolescent boys and girls and produced regression equations that enable body fat to be calculated. Brook (6) showed that similar skinfold measurements can be used to estimate total body fat in children over the age of 1 year, and, for infants during the first year of life, Dauncey et al. (18) have described a formula using triceps and subscapular skinfold measurements only.

Upper arm circumference

Arm circumference, measured at the midpoint of the upper arm, was proposed as an index of undernutrition by Jelliffe & Jelliffe (40) and has subsequently been extensively used for this purpose. The method is cheap and easy to use and could probably be more widely employed for the quantification of obesity.

Combined measurements

For 6-month-old babies Crawford et al. (17) have evaluated a large number of anthropometric measurements and have found that a linear equation using 3 variables—weight gain since birth, waist circumference, and suprailiac skinfold—gives the most discriminating measurement of obesity. Similar combined indices for older children (apart from multiple skinfold measurements) have not been elaborated.

Body fat

In addition to skinfold measurements, 3 well-established and more accurate measurements are used for the estimation of body fat. These are measurements of total body water, of total body potassium and of body density. The techniques involved are all relatively complex, require specialized laboratory facilities, and cannot be used for routine clinical purposes or for epidemiological studies. They are, however, useful for validating simpler methods. "Normal" values for body fat in children have not been established but from the limited data available it seems likely that total body fat in excess of 25 % of body weight is "abnormal".

Prevalence and prognosis

Studies of prevalence and prognosis in respect of obesity in developed countries indicate differences between the various age groups.

Infancy

During the past decade there has been considerable concern over the high prevalence of obesity in babies under 1 year of age in industrialized countries such as Sweden and the United Kingdom. Thus Hutchinson-Smith (38) found that 70 out of 200 babies followed throughout their first year exceeded their expected weight-for-length by 20 % or more; Taitz (70) in a study of 240 babies during the first 6 weeks of life found that 59 % had exceeded the 90th centile for weight; and Shukla et al. (62), in a cross-sectional study of 300 infants up to 1 year old, found 16 % to be "obese" (20 % above standard weight-for-length) and a further 27 % to be "overweight" (10–20 % above standard weight). The difference in the prevalence of obesity between the babies in the studies of Hutchinson-Smith and Shukla et al. may be due in part to the fact that Hutchinson-Smith used the 1959 standards of Tanner & Whitehouse (72) whereas Shukla et al. used the 1966 standards of Tanner et al. (75). Recently, Tanner & Whitehouse (74) produced revised standards for skinfold measurements which showed that the infants of their later study were fatter than those of 12 years earlier. It was in the first 6 months of life that the most marked increase in the incidence of fatness, as judged by triceps skinfolds, occurred so that the 90th centile measurement became the 50th centile measurement.

More recent studies, however, indicate a fall in prevalence, possibly because of a change in attitude towards fat babies. Sveger et al. (68), using the same definition and standards as Shukla et al., reported a prevalence of only 6 % in Sweden, and Whitelaw (78) indicated that a downward trend in prevalence had also occurred in the United Kingdom.

Some of the concern regarding the long-term effects of obesity in infancy has proved to be unjustified. The view that fat babies are destined to become fat children and fat adults and that obesity is inevitably determined in the first year of life has been too widely and too easily accepted. It is therefore important to review the more recent evidence, much of it obtained from prospective studies, on which current concepts about the prognosis of obesity in infants is based.

Probably the earliest study of the prognosis of obesity in the first year of life was made by Asher (1), who showed that at least 20 % of obese infants would remain obese at 5 years of age. Similar observations were made by Eid (24), and the more recent study of Poskitt & Cole (59) found between 11 % and 17 % (depending upon the method of defining obesity) of obese babies to be still obese at 5 years. That weight gain in early infancy is not a strong indicator of obesity at school entry is also shown by the large and careful longitudinal study of Mellbin & Vuille (46) in Sweden. They found only a weak correlation between velocity of weight gain in infancy and weight at 7 years; only 10 % of the overweight schoolchildren had been obese as babies. The age at which most obese babies lose their excess fat is not known.

It has been suggested that fat babies are more likely to become fat again in adolescence. A retrospective study of a group of obese adolescent girls in

the USA (36) supports this hypothesis, showing that the girls in the group had gained weight more rapidly during the first year of life and had been heavier at the age of 1 year than their nonobese peers. A prospective study of children in Switzerland showed little correlation between skinfold measurements at 1 year of age and at puberty (37). The conclusions of these two studies are not necessarily at variance because the Swiss workers studied an unselected population of children and their findings may not apply to obese children. The relationship between weight in infancy and obesity some 20–30 years later has been studied in the USA by Charney et al. (11), who found that infant weight correlates strongly with adult weight independently of other factors such as education and social class. In terms of actual risk, 14 % of heavy babies (greater than the 90th centile) were found to be “obese” in adult life (more than 20 % above standard weight) and a further 22 % were “overweight” (10–20 % above standard); the comparable figures for babies of average weight (25th–75th centile) were 5 % and 11 % respectively.

From these studies it may be concluded that in only a minority of fat babies (less than 20 %) will obesity persist after the first year or two of life. Nevertheless the risk of obesity is not negligible and is greater than that for thin babies. Furthermore, retrospective studies of obese children show that about half of such children will have been obese by the age of 1 year (1, 8, 16, 81). Thus, although the dangers of obesity in infancy have been exaggerated, prevention remains important. The results of a current coordinated analysis of data from 4 longitudinal studies in the USA are awaited with interest.

Childhood and adolescence

The prevalence of obesity in most of the industrialized countries is of the order of 2–6 % during the early school years and rises during adolescence. In a recent longitudinal study in the United Kingdom (66), based on a cohort of 12 368 children born in 1946 (21), the prevalence of overweight (defined as weight in excess of 20 % of the standard for age, sex, and height) at the age of 7 years was 2 % in boys and 4 % in girls; by the age of 14 it had risen to 7 % and 10 % respectively and by the age of 26 it was 12 % and 11 %. Colley (13) also found the prevalence of obesity to increase during the second decade of life and to be higher in females than males. At present, there are no reports to indicate whether, in the individual boy or girl, the development of obesity during the second decade tends to coincide with a particular stage of pubertal development, which is of course accompanied by a growth spurt on the part of the adipose organ. Colley (13), comparing his findings in a group of 6–14-year-old children with those of Scott (61), concludes that in the United Kingdom obesity had become more common in the older girls during the period spanned by the two studies.

Studies of the effects of social class on the prevalence of obesity show that in adults in industrialized countries it is more common in the lower

socioeconomic groups (47, 63, O. Stark & E. Atkins, personal communication), and similar findings have been reported for children (77, 81). In the cohort studied by Stark & Atkins, however, the difference was not present during the first decade. In females it was noted during the second and third decades whereas in males it became obvious only during the third decade.

Studies are needed on the prevalence of obesity among children and adolescents in developing countries, particularly in relation to social class. Clinical impressions suggest that, in childhood, adolescence, and adult life, obesity is not uncommon even in parts of the world where undernutrition during infancy and the early years of childhood is the main nutritional problem.

Studies of the prognosis for children referred to hospital clinics on account of obesity have indicated that about 80 % will remain obese as adults (33, 35, 42). Such studies may not, however, reflect the natural history of obesity in the community (41). In a community study in the north of England (81) only one-third of the people had been given professional dietary advice. In the longitudinal study by Stark & Atkins (66), about 40 % of the children obese at the age of 7 years were still obese at the age of 26; for the more obese girls (more than 30 % overweight) the prognosis was worse, 70 % remaining fat in adult life.

The observation that obesity in childhood frequently persists into adult life must not lead to the assumption that prevention and treatment of childhood obesity would necessarily have a great impact on the vast problem of obesity in adult life. Mullins (50), in a study of obese adults attending an outpatient clinic, found that in one-third of the patients the obesity had started in childhood. In the cohort studied by Stark & Atkins (66), there were 519 men and 467 women whose weight at the age of 26 exceeded the standard by 20 % or more. Of these overweight individuals, only 7 % of the men and 13 % of the women had been obese at the age of 7; however, 28 % of the men and 45 % of the women had been obese at the age of 14. Thus prevention and/or effective treatment of obesity during the first decade of life would have had relatively little effect in reducing the prevalence of obesity in young adults. On the other hand, during the second decade, successful prevention or treatment could theoretically have reduced its prevalence among young women by about one half and among young men by about one-third.

Etiology

The increased storage of fat in obesity is due to an energy intake in the form of food in excess of the individual's requirements, including, in the case of infants and children, requirements for growth. Many factors can disturb energy balance and they differ in their importance, not only between individuals but also in the same individual at different times. Although we shall discuss the various etiological factors separately, they

seldom occur in isolation. Furthermore, the etiology of obesity is complicated by the development of certain vicious circles. To give two examples: physical inactivity may cause obesity, which then further restricts activity; emotional disturbance may cause overeating and the resulting obesity then worsens the emotional upset. In the individual child it may be impossible to distinguish between cause and effect, and a search for the primary event may be meaningless logically and unhelpful practically.

Genetic, familial and socioeconomic factors

Although it is accepted that there is a genetic component in the etiology of obesity it is difficult to separate the effects of heredity from those of the common family environment and, therefore, to estimate the size of the genetic influence. This difficulty applies for instance to the interpretation of the classic study of Gurney (32), who found that, if both parents are obese, two-thirds of their children will be obese, whereas if one of the parents is obese only half of their children will be obese. Accurate measurements of heritability (that is, the proportion of the total variance of a characteristic in a population due to genetic causes) can be derived only from studies of twins. Such studies show a close correlation between the weights of identical twins (4, 55) even when they are reared in dissimilar environments (76). Brook et al. (9) examined the relative contributions of genetic and environmental factors in determining skinfold thicknesses in 222 pairs of like-sex twins of whom 78 were monozygotic and 144 dizygotic. The conclusions reached were that, taking all ages together, and for both sexes, genetic factors appeared more significant in determining trunk fat (estimated by subscapular skinfolds) than limb fat (estimated by triceps skinfolds). Genetic factors played a greater part in determining limb fat in girls than in boys. Heritability was found to be high for both trunk and limb fat in boys and girls above 10 years of age, but for younger children environmental influences appeared to be of greater importance, and only in the trunk fat of younger boys was the degree of heritability high. The study included only a few twins who were obese and no special investigation of these was possible; the results of the study, therefore, strictly apply only to heritability of skinfold thickness over the normal population range and could be different for individuals who are obese. Similar caution is needed in the interpretation of the other twin studies reported. The mechanisms whereby genetic factors influence fat deposition are not known.

That there are powerful family influences, apart from heredity, determining fatness is demonstrated by the extensive studies of Garn et al. (30), which have shown that, in families containing both biological and adopted children, the relationship in fat-fold thickness between parents and their children is similar, irrespective of whether the children are biological or adopted. These workers conclude that the age at which living together begins and the duration of communal eating and living are two important determinants of family fatness.

The effects of socioeconomic status on the development of fatness are complex. In general, taking the world as a whole, fatness follows the gross national product, the *per capita* income, and the average consumption of fats and animal protein. The leanest nations are the poorest nations, and the fattest nations the richest. Within more affluent countries, however, obesity is more prevalent in the lower socioeconomic groups, though even here the relationship is complex and may alter during life. Thus in a study in 10 states of the USA (29), it was observed that the poorer girls were leaner but became fatter as adult women, whereas more affluent girls were fatter in the prepubertal years but leaner thereafter. It would be important to know whether in countries such as the Netherlands and Sweden, where social inequalities are less marked than elsewhere, the difference between social classes in the prevalence of obesity has disappeared. The reason for the persistence of the social class difference in several industrialized countries, particularly those in which mass poverty has been eradicated, is another subject requiring research. In many countries the poorer socioeconomic groups tend to be less accessible to health education and thus may not yet be as aware of the deleterious effects of obesity as the more affluent groups are.

Energy intake

Energy is consumed as food. The composition of the food, the periodicity with which it is eaten, and the absolute amount of energy derived from it are all relevant to the etiology of obesity.

Few data are available on the role of individual nutrients in food in causing obesity. Carbohydrates are generally considered to be "fattening", and the increased prevalence of obesity in children of the lower socioeconomic groups has been attributed to increased consumption of these relatively cheap foods (78). Cook et al. (15) found that children from the less favoured social classes and larger families obtained a higher proportion of their energy intake from carbohydrates and added sugar; however, they also found that the heavier children in their study had a lower sugar intake than the lighter children, but considered that some of the restriction by the heavier children may have been intentional.

Periodicity of eating may be important in the regulation of energy balance, with a correlation between obesity and infrequent meals. Nibbling (the taking of small frequent meals) appears less likely to lead to obesity than gorging (the taking of large infrequent meals). Studies in adults have given discrepant findings (31); in one study of schoolchildren between 10 and 16 years, it was found that those who ate 3 meals a day were fatter than those who ate 5 or 7 meals a day (26). There is a clinical impression that many obese children do not eat breakfast; one study of schoolchildren (12) reported that 8% of children had no breakfast before going to school, and these children were more likely to be from less favoured social classes or to have mothers going out to work.

In normal individuals, at all ages and of both sexes, there is a large variation in energy intake (79), but the reasons for this wide range of nutritional requirements are not known. The concept of nutritional individuality needs to be stressed, and its neglect may result in the overfeeding of some children whose needs happen to be less than the "average standard requirement".

In infancy, babies who are breastfed tend to be less overweight than those who are bottlefed (27, 53, 62). The reasons for this difference are not fully known. One explanation is that artificially fed infants are more likely to have their nutritional individuality ignored by being urged to consume a predetermined volume of feed based on the standard "recommended intake", which may be inappropriate for the individual baby. Overconsumption of nutrients in feeds based on cow's milk can also arise because of inaccuracies in the reconstitution of the feeds (80).

The recent increase in breastfeeding in the United Kingdom (45, 65) has coincided with the more widespread use of low-solute milks, better instructions relating to the reconstitution of powdered milk feeds, and advice against the early introduction of solids. Reduction in the prevalence of obesity, therefore, cannot be simply ascribed to an increase in breastfeeding. In one study, in which infants fed solely on a cow's-milk formula during the first 6 weeks were compared with fully breastfed infants, no difference was found in weight gain, and the breastfed infants were found to have a significantly greater increase in triceps and subscapular skinfold thickness (57). The mechanisms whereby milks of different composition influence the development of adipose tissue are clearly complex and require further study.

There is some evidence in normal babies (27) and in malnourished children (3) that appetite can be adjusted to the nutritional status. It is possible that the mechanism for this adjustment fails in some individuals; for instance, studies in heavy newborn infants have suggested that they have an appetite-regulating system which is relatively insensitive to internal cues of hunger and satiety (56). Hall (34) postulated that in the newborn infant the appetite-control mechanism is sensitive to the change in the composition of breast milk which occurs during the feed. This mechanism cannot operate in babies fed on cow's-milk preparations, whose composition does not alter during the feed.

A further cause of increased energy intake in infancy is the introduction of nonmilk solids at an early age. There has been a tendency to start these foods, usually in the form of cereals, during the first 3 months and often before the age of 1 month (20). Although Hutchinson-Smith (38) found that early introduction of cereals was equally common among breastfed infants and those who were bottlefed, Neumann & Alpaugh (53) reported a much earlier introduction of solids in bottlefed infants (mean 1.9 months) than in breastfed infants (mean 3.9 months). However, the general assumption that early introduction of solids contributes to obesity is not validated; the study of Davies et al. (19) failed to demonstrate that the early introduction of solid foods had any effect on the growth of bottlefed infants

in the first 3 months of life, and Poskitt & Cole (59) also found no correlation between age at weaning and excessive weight at 5 years of age.

As regards older children there is little evidence that obese children as a group consume more energy than their nonobese peers. Population studies have shown that heavy children have a higher average daily intake than light children (10, 15), but the heavy children were not necessarily fat. In groups of 14-year-old children, Durnin et al. (23) found that, between 1964 and 1971, body fat had increased in the boys, while over the same period there had been a decrease in daily energy intake of 837–1046 kJ (200–250 kcal). Among the girls the fattest consumed consistently less energy than the thinnest. This study suggests that, at least in this age group, decreased energy output is of greater importance than excess energy intake in determining fatness.

Energy output

Reduced energy output is probably more important in the etiology of obesity than used to be thought. The finding of Durnin et al. (23) that adolescent boys in Scotland were fatter than a comparable group studied 7 years previously, despite a reduced energy consumption, suggests that children in industrialized societies are becoming less active. Bradfield et al. (5) showed that adolescent girls in the USA spent, on the average, less than 1 hour a day in moderate or strenuous physical activity and that, of the remaining 16 waking hours, 9 were spent in light activity such as sitting while being transported to school, at school, or at home watching television. A similar pattern probably applies to younger children though perhaps less to boys.

Emotional factors

The relative importance of emotional factors in the etiology of obesity may be difficult to assess in the individual child. In cases of extreme obesity, the role of such factors is usually great and often obvious. Once obesity has developed, the child's appearance—which often leads to teasing and, in adolescents, to lack of attractiveness to the opposite sex—perpetuates the emotional problems and may set up a vicious circle.

There are several psychological mechanisms whereby emotional disturbance can lead to a food intake in excess of physiological requirements. In early infancy the giving and taking of food is central to the mother/infant relationship. Normally, as the child grows older, the psychological significance of food becomes less, though even in the older child food continues to have important psychological meaning in addition to satisfying physiological needs. For obese children, eating may be a means of dealing with ungovernable or undesirable emotions, such as frustration or anxiety, because they are unable to deal with them in more mature and

realistic ways, and because their parents may be unable to help them to find more desirable means. The child may subconsciously wish to revert to babyhood, a stage of life when food was of prime importance in the mother/infant relationship. In some children, food may have the psychological significance of a "transitional object" and take the place of the more usual rag or soft toy. Overeating may be a symptom of depression in childhood, as it is in adult life.

Some adolescent girls may eat more than they need because subconsciously they believe that they will be more attractive to boys if they are not too thin. Others, who do not want to attract boys, overeat because they believe that fatness is unattractive. Possibly a disturbance of body image may play a role in the etiology of obesity similar to that which may occur in anorexia nervosa (64). Different cultures differ in their concepts of beauty and attractiveness, and within the same culture these concepts may change with time.

Family eating patterns are also relevant, and excessive eating may be part of such a pattern. In the life of some families, eating together has an unusually important place and in these families, whose members also often have a close and complex relationship, any attempt, however minor, to change the eating pattern is likely to meet deep resistance.

Psychological disturbance in the parents, and especially in the mother, is particularly likely to be present when the obesity is gross. Some mothers feel themselves most adequate in their maternal role when their children are still babies and may use food subconsciously as a means of maintaining the kind of relationship that existed when the child was an infant. Other mothers feel guilty because they believe that they do not love their child sufficiently and subconsciously give food in place of love. Whether the primary emotional disturbance is in the mother or in the child, it is bound to have secondary effects on the mother/child relationship and may also affect other members of the family.

Endocrine and metabolic causes

Although the pathways involved in the storage and release of triglyceride in the adipose cell have been extensively studied (28), in the great majority of obese patients it has not proved possible to establish a primary metabolic defect in the mechanisms responsible for triglyceride synthesis or breakdown. The various metabolic abnormalities that occur in obese individuals tend to be corrected by weight loss and are therefore likely to be results rather than causes of the obesity.

In hypothyroidism and Cushing's syndrome, obesity may occasionally be the presenting feature. These conditions are also associated with short stature, and their diagnosis should be considered when an obese child is found to be below average height or below that expected for his family. Children receiving long-term therapy with corticosteroids will usually

become obese unless preventive measures are taken. Children with growth hormone deficiency tend to be heavier than expected for their height and have increased skinfold thickness; loss of body fat occurs during their treatment with growth hormone (6).

Prevention

Obesity is a difficult and refractory condition to treat. About 80 % of treated cases relapse in the long term (42). Prevention should therefore be the aim. The adoption of certain preventive measures is suggested, even though proof of their efficacy is not yet available. Such measures may be instituted in the prenatal period, in infancy, and in later childhood and adolescence.

Prenatal period

The avoidance of excessive weight gain during pregnancy is desirable from the obstetric point of view and may reduce maternal mortality (43). It may also play a role in preventing fetal overnutrition. Antenatal care should include advice on infant feeding (20). The advantages of breastfeeding should be emphasized, notably the fact that obesity is probably less common in breastfed babies than in those artificially fed. The mother's intention to breastfeed and the encouragement of those advising her are probably the most important factors in ensuring successful breastfeeding. The disadvantages of overfeeding must be stressed and the concept of nutritional individuality explained; what is an adequate intake for one baby may be excessive for another of the same age. Other points to be made are that a baby may cry because of thirst rather than hunger, and that it is usually unnecessary to give foods other than milk before the age of 4–5 months.

Infancy

Weight records are kept by all infant clinics and many mothers; the original aim was the prevention of underfeeding, and in the developing world the weight chart is an important tool in the prevention of malnutrition (48). Because undernutrition has become uncommon in developed countries, it has been suggested that there is no longer any need there for routine weight records. We believe that the value of weight charts in the prevention of overnutrition deserves investigation. If infants are found to be gaining weight at an excessive rate, their mothers can be given appropriate advice—for example, to make up more dilute feeds or give less solid food, especially cereals.

Childhood and adolescence

The prevention of obesity in children consists mainly in establishing sensible eating habits and encouraging regular physical activity (52). When nutritional advice is given, cultural and social differences in eating patterns must be respected, and the expense and time involved in the provision and preparation of meals remembered. In the prevention of obesity, broad guidelines can be suggested for all children and indeed for the rest of the family. Meals should be spaced throughout the day, and excess consumption of carbohydrates, especially in refined products such as sweets, biscuits, and the various proprietary sweetened drinks should be avoided. Children in families with a high incidence of obesity and those who are beginning to become too fat might also be advised to avoid snacks between meals and satisfy hunger with vegetables and fruit rather than with fried and starchy foods.

During adolescence, prevention becomes particularly important because of the increasing prevalence of obesity at that age, because adult obesity frequently has its onset in adolescence, and because for teenagers, especially girls, obesity may present a very distressing problem. Unfortunately adolescents, even more than children, tend to resist advice regarding their eating and exercise habits. There is also the danger that too much emphasis on the disadvantages of obesity and the desirability of a slim figure may precipitate the development of anorexia nervosa. Especial sensitivity is needed in giving advice to adolescents.

Prevention of obesity is particularly important for children with a disorder that interferes with physical activity, such as meningomyelocele, myopathy, or cerebral palsy other than the athetoid variety. Children with severe emotional disorders and mental retardation also carry a special risk for the development of obesity. Another group at risk consists of those introduced to normal feeding after a long period of undernutrition (3) or restrictive diet. Preventive measures should be instituted routinely for children on long-term corticosteroid treatment.

Regular weight checks are indicated for all children at special risk, including those with a family history of obesity. The role of school medical examinations in the prevention and early detection of obesity in the community needs to be evaluated.

Nutrition education

Health education should include the important subject of nutrition; and because obesity is such a common nutritional disorder a discussion of its prevention is appropriate. Such education should start in childhood and continue through adolescence into adult life. During the antenatal period and when their children are young, parents are likely to be particularly receptive to advice aimed at ensuring the good health of their children.

At present, doctors and nurses often find themselves ill-prepared to give

either specific dietary advice to patients or education on nutrition in the community. The subject of nutrition deserves much greater emphasis in undergraduate and postgraduate training. Dietitians, in addition to their involvement with individual patients, contribute to the education in nutrition of other health workers, as well as of the community, including teachers. Many communities and hospitals lack adequate dietetic services, especially for children.

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Prevention in childhood of major cardiovascular diseases of adults

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According to the *Fifth Report on the World Health Situation* (45), cardiovascular diseases were the first cause of mortality in the American and European, second in the Eastern Mediterranean, and third in the Western Pacific Regions of WHO in 1974. The *Sixth Report on the World Health Situation* (51) states that cardiovascular diseases remain the leading cause of death in the industrial countries, and are emerging as a major problem in the developing countries as communicable diseases are better controlled.

A small proportion of all deaths from cardiovascular diseases occur in childhood, mainly as a result of congenital heart disease. The vast bulk of such deaths occur in adulthood, going on into old age; in fact, cardiovascular mortality increases with age on a logarithmic scale. If a conjecture on future world morbidity and mortality trends may be made, the coming decades will witness a considerable further increase in cardiovascular diseases (31) unless a major effort is devoted to their prevention.

It will be shown that the prevention of a great proportion of the major cardiovascular diseases is far from being a utopian expectation, provided—and this is the point—it is started early in life. The following sections will present a review of the possibilities—or, more categorically, of the necessity—of preventing cardiovascular diseases of the adult and the elderly while the potential victims are still children.

Rheumatic fever and rheumatic heart disease

Rheumatic heart disease—the crippling and often fatal sequel of rheumatic fever—is vanishing from developed countries, but is still the major cardiovascular problem in the developing world. Considered in the context of history, rheumatic fever is a function of socioeconomic

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development (30, 32). It would be false, however, to wait for rheumatic fever to disappear spontaneously as socioeconomic development progresses in the countries of the developing world; the vicious circle of poverty – disease – poverty (28) has to be broken also, with the aid of preventive medicine. Rheumatic heart disease furnishes an example of what can be done to prevent heart disease even under unsophisticated conditions.

Rheumatic fever is a delayed complication of upper respiratory infections due to any of the various types of group A haemolytic streptococci. Streptococcal infections are very common, especially in children living in underprivileged conditions, and rheumatic fever occurs in 1–3 % of those infections. In temperate countries rheumatic fever used to occur mostly around the age of 8–10 years, but in tropical and subtropical countries it often occurs in much younger children and severe rheumatic heart disease around the age of 4–5 years is not rare in developing countries. While the prognosis in such cases is very poor, children with less severe rheumatic heart disease may well reach adulthood and middle age but, owing to frequent reinfections and recurrences (unless there is secondary prophylaxis), their heart condition constantly deteriorates, leading to gradual incapacity, invalidism, heart failure and death. Exact data on the incidence of rheumatic fever and the prevalence of rheumatic heart disease are difficult to obtain. Despite the voluminous literature on the subject, most data reported from developing countries are based on hospital admission statistics, which are difficult to extrapolate to entire populations (30); nevertheless, they give a fairly good idea of the seriousness of the problem as illustrated by the concentration in hospitals of teenage and adult patients with extremely severe valvular heart disease, necessitating long-term medical treatment and often costly surgery involving valvotomies and the insertion of valve prostheses. Rheumatic heart disease is of particular importance in young pregnant women (35), since asymptomatic mitral valve disease often produces its first severe manifestations in pregnancy, notably round the time of delivery, endangering the life of both mother and child.

Pathogenesis

Advances in knowledge of the pathogenesis, bacteriology, clinical aspects, prevention, and control of rheumatic fever were recently reviewed (9). As regards pathogenesis, the most prevalent concept is the toxic-immunological hypothesis. According to this theory, group A streptococcal products have certain toxic properties and components of the streptococcus and of host tissues have an antigenic cross-relationship, leading to immunological processes that result in an attack of rheumatic fever. Of the streptococci it is the group A streptococcus that is rheumatogenic, but its pathogenicity greatly depends on type-specific antibodies and there are more than 50 types with little cross-immunity

among them. Hence the frequently deleterious effects of throat reinfections.

Carriers of group A streptococci are frequent and may be of the transient, convalescent, or chronic type. Many chronic carriers are beyond the risk period for the development of complications and are not likely to spread infection. Transient and convalescent carriers, however, may cause epidemics in closed communities such as school classes.

Methods of prevention (9, 42)

Primary prevention of rheumatic fever is based on the timely detection and treatment of streptococcus group A throat infections with the aim of preventing the first attack of rheumatic fever that may arise as a complication. Secondary prevention protects children and young adults with a history of acute rheumatic fever, as well as those having rheumatic heart disease, from streptococcal reinfections that would inevitably result in the development of rheumatic heart disease or, if the valves have already suffered, in deterioration of the heart condition.

Primary prevention of rheumatic fever should no doubt be the preferred approach. Streptococci are sensitive to penicillin, and a single injection of benzathine penicillin is usually most effective in eradicating the bacteria from the patient's throat, putting an end to the acute infection, and preventing the possible occurrence of rheumatic fever. Penicillin is the drug of choice as no group A streptococci have been found to be resistant to penicillin *in vitro*. Individuals allergic to penicillin should be given erythromycin. Sulfonamides are unsuitable for the treatment of acute streptococcal infections since they do not eradicate the streptococcus from the throat; they may be used, however, in continuing secondary prophylaxis (see below). Broad-spectrum antibiotics (tetracyclines) should not be used because many strains of streptococci are resistant to this group of antibiotics and also because their indiscriminate use may further augment the resistance of various microorganisms. Tetracyclines may also damage the developing teeth in children.

While theoretically simple, the practice of wide-scale primary prevention of rheumatic fever is difficult, since it implies the diagnosis of all cases of acute sore throat due to streptococcal infection in a community. This is extremely difficult, because many infections are unapparent or, if apparent, are not brought to the attention of the health services; even if they are reported, quick and reliable laboratory services are needed in order to identify the pathogenic microorganism, since streptococcal infections account for only some 20 % of all acute sore throats. If laboratory services are not available, an alternative solution would be to administer penicillin to all children with any acute throat infection; this, however, is clearly far from being the ideal solution.

A feasible approach to the primary prevention of rheumatic fever is through bacteriological or, simply, clinical surveillance of school classes or

the other closed communities of children and adolescents. When a cluster of cases of acute sore throat is found in a class, school health services or other appropriate bodies should be alerted in order to stop a potential epidemic of streptococcal infection. This is the ideal situation in which to prevent an increase in the number of rheumatic fever cases by means of primary prophylaxis. Motivated laymen—in particular, schoolteachers—can play a crucial role in detecting potential epidemics of rheumatic fever. This, however, presupposes the existence of adequate information and training programmes for schoolteachers or other lay personnel and also of health care structures that will respond efficiently to any alarm that is raised.

Prevention of recurrences (secondary prevention) should be simpler than primary prevention, because the high-risk individuals can be defined and the prophylactic agents are effective and of low toxicity. Monthly intramuscular injection of benzathine penicillin is the method of choice, although oral penicillin or sulfadiazine is also effective when taken regularly each day. Erythromycin may be given to individuals who are allergic to penicillin or sulfadiazine. Oral medication, however, raises important problems of compliance, and mainly for this reason the parenteral administration of penicillin is recommended as the surest way of secondary prophylaxis.

Secondary prophylaxis should continue over long periods, certainly during the whole of childhood and adolescence, and it should not be stopped, even in young adults, until several years after the last recurrence. The main problem in long-term secondary prophylaxis of rheumatic fever is patient compliance. Nevertheless, all too often the patient alone is blamed for noncompliance, although the blame may lie mainly with the physician or other health worker responsible for regular long-term prophylaxis, whose enthusiasm for the task may decline with time, thus encouraging patient drop-out.

Community control of rheumatic heart disease

One approach to the systematic prevention of rheumatic fever and rheumatic heart disease in entire communities or populations consists in establishing community control programmes. The feasibility of such programmes in various socioeconomic settings, notably in developing countries, has been assessed by WHO (33, 47).

It was assumed that most impediments to the successful community-wide prevention of rheumatic fever could be abolished or mitigated by an organized, systematic approach to rheumatic fever control. A model was designed based on case-finding, follow-up (including noncompliers), the regular administration of penicillin for secondary prophylaxis and, where possible, also primary preventive measures. The operational backbone of the model was a register permitting all identified patients to be followed up. The general model was adapted to the actual situations in various centres,

taking local resources and sociocultural characteristics into account. Thus, in some communities the programme was based on the local hospital, while in others school health services were also utilized. An important part of the project was education of the health personnel in the community as well as volunteers and the general population.

Although limited programmes for the community control of rheumatic fever proved to be feasible, strategies for their active extension to a whole population or country have still to be developed and implemented. Rheumatic fever control should become part of primary health care in developing countries so that programmes may be maintained and extended to the whole population.

There are some encouraging signs that active immunization against group A streptococci may be feasible, but it will be a long time before organized long-term penicillin prophylaxis can be replaced by immunization campaigns. Rheumatic fever is preventable at the present time, however, even before immunization is perfected. By relatively simple measures and with a high cost-benefit ratio much ill health and suffering among children, adolescents and adults can be prevented.

Hypertension

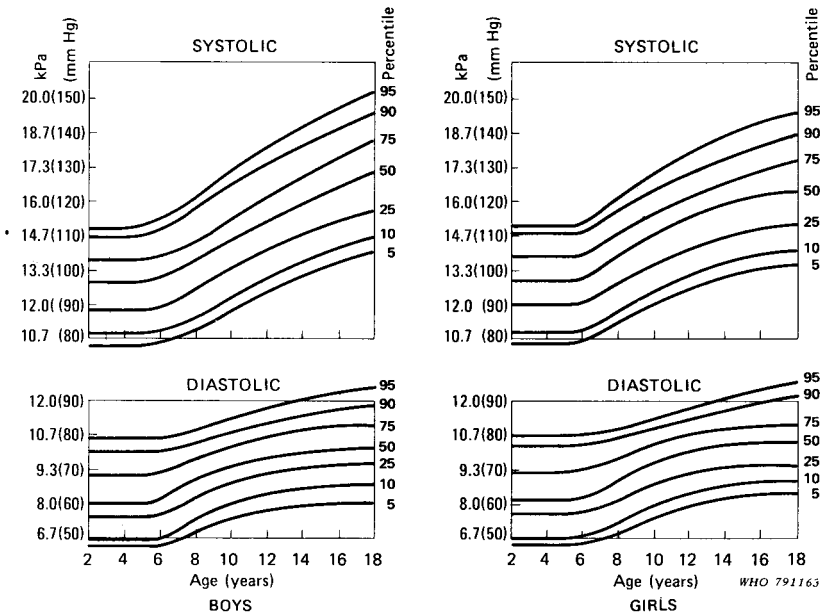
Blood pressure in children and adult hypertension

High blood pressure is a major factor in atherosclerosis, coronary heart disease, and stroke. Some 10–20 % of most middle-aged populations are considered to be hypertensive. The term “hypertension” is a simplification since it tacitly implies a clear distinction between abnormal pressures and “normotension”. There is, however, no natural dividing line between “high” and “normal” pressure; blood pressure elevation is a continuous, though curvilinear, function of the blood pressure values. In most populations (though not in all) blood pressure rises with age; this rise starts as far back as childhood (4, 19), as shown in Fig. 1.

If the definition of hypertension is arbitrary and difficult in respect of adults, it is even more so in respect of children. In fact, little is known of the association between blood pressure in childhood and blood pressure levels later in life. However, correlations between blood pressure values in parents and children indicate that children tend to fall into the same segments of the age-specific blood pressure distribution curves in the population as their parents do (15, 21). These correlations are moderately close; they may be due both to genetic influences and to the sharing of common environmental factors such as food (e.g., salt) by members of the same family. Within-family aggregations have also been found in a number of other studies—for example, the recent review by Lauer et al. (18).

Another important, more recent observation is the “tracking” of blood pressure—i.e., the tendency of children whose blood pressure is being followed up over a period of years to fall repeatedly into similar segments of

Fig. 1. Percentiles of blood pressure measurement (right arm, seated)



Source: Blumenthal et al. (4).

the blood pressure distribution curve, despite considerable individual variations and age-related changes. In other words, young children at the upper end of the blood pressure distribution of their age group tend to have, after years of observation, still relatively high values, and *vice versa*. An analogy might be made with the "horse-racing" effect in adults (34), whereby blood pressure tends to increase in time as a function of the initial pressure—i.e., subjects with higher initial pressures experience a higher increase. There are, however, no data to support this conjecture.

Prevention in children of adult hypertension

Essential hypertension accounts for by far the greatest part of the public health problem of high blood pressure in adults. The various types of secondary hypertension are responsible for no more than a small percentage of all hypertension in adults. Since, however, some causes of secondary hypertension are already accessible and responsive to treatment in childhood, this aspect of preventing hypertension must not be neglected.

The value of timely surgical treatment of coarctation of the aorta need

not be re-emphasized. Chronic urinary infections, potentially leading to renal impairment, and adolescent and adult hypertension demand early detection and treatment. Relatively little is known of the childhood determinants of adult nephrolithiasis, another area in which it might be possible to prevent potential disease, including hypertension as a complication of renal impairment. Cases of endocrine disorders causing hypertension are too rare to be a public health issue of any importance.

The key to the problem of high blood pressure is the primary prevention of *essential* hypertension. The treatment of high blood pressure effectively prevents complications and reduces the risk of atherosclerosis of the coronary arteries, and of stroke. However, there are huge numbers of hypertensive subjects in most countries, so that as many as 15–20 % of the middle-aged in the population might have to be given long-term drug treatment—a task shown to be feasible in the context of community-based hypertension control programmes. Nevertheless, drugs are only a partial and temporary solution, since it is undesirable to have a sizeable portion of the population ingesting medicaments, even of low toxicity.

A few leads for the primary prevention of essential hypertension are slowly emerging from epidemiological investigations. Since hypertension tends to cluster in families, the family history of hypertension may be used to identify individuals at risk among children or adolescents and apply some measures of possible preventive value. The measures are those applicable, in principle, also at the community level: control of obesity and reduction of sodium intake.

Epidemiological observations have identified obesity as a risk factor for hypertension (27, 36), and it is thus plausible to assume that the control of body weight by balanced nutrition and physical activity should become part of hypertension prevention. Prospective studies to document the impact of body-weight control on blood pressure and hypertension are in progress; however, as will be shown below, there is no reason for *not* fighting overweight, in children as well as adults, when no possible harm can come from such a measure (see Chapter 4).

The role of sodium ingestion in hypertension is still a controversial point, but there is an increasing body of information to the effect that a high salt intake contributes to the development of hypertension (13). Several prospective intervention studies on the effect of reducing the salt intake of children are now in the planning or early operational stage; such action should of course take in the whole family.

The drug treatment of hypertension in childhood should be undertaken with great circumspection (4) and reserved for selected cases. However, children found to be at the upper end of their age-specific blood pressure distribution (Fig. 1) should be advised about salt intake and body-weight control (including physical activity) and should be followed up periodically throughout their teens and young adulthood. This should help to ensure that potential cases of hypertension do not remain undetected and untreated and should contribute to the prevention of coronary and cerebrovascular disease.

Ischaemic heart disease and stroke: the end-points of atherosclerosis

Extent of the problem

The incidence of acute ischaemic heart disease in males aged 50–54 years in selected European population groups was shown by the WHO cooperative study of acute ischaemic heart disease registration to be between 2 and 14 per 1000 (52). While myocardial infarction is rare in developing countries, the incidence of stroke was found to be about 3–9 per 1000 in men aged 55–64 years in a variety of populations, including some African and Asian communities (6). Ischaemic heart disease and cerebrovascular disease are primarily due to atherosclerotic changes in the coronary or cerebral arteries as the case may be. Coronary atherosclerosis is very common in technically developed societies: a WHO cooperative morphological study has shown that, among autopsied cases (at an autopsy rate of 85 %), 90 % of men and 70 % of women aged 40–44 years had raised atherosclerotic lesions in their coronary arteries (16).

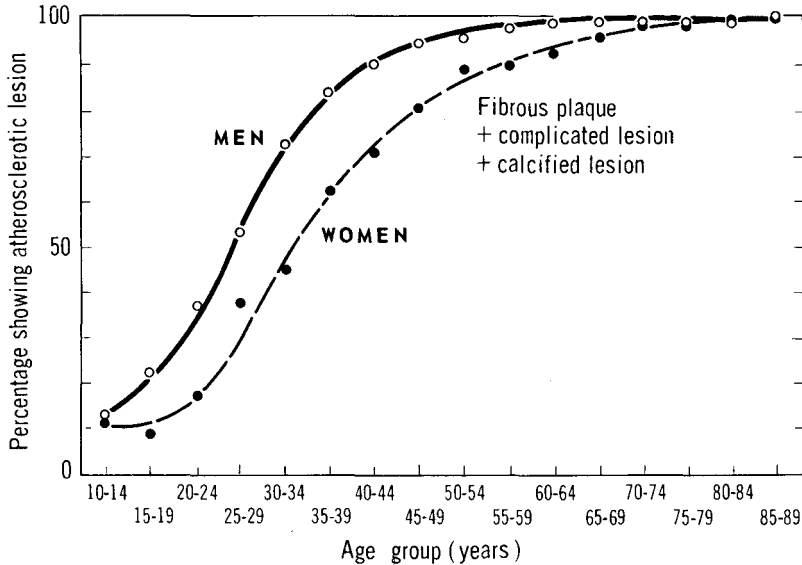
Pathogenesis

As shown in Fig. 2, some 10 % of autopsied subjects aged 10–15 years already had raised atherosclerotic lesions (plaques) in the coronary intima (12, 43). Despite much research on the subject, the morphology of atherosclerotic lesions in the very early stages is still unclear (41). Thickening of the intima has been described in very young children, and even in the newborn, and it has been thought that changes of this kind might predispose to atherosclerosis (24). There are a number of indications that an atherosclerotic lesion may start as a microthrombus, as a localized oedema of the intima (insudation), or as a yellow fatty streak (14). The relationship of fatty streaks to raised lesions has still to be elucidated. The factors that cause fatty streaks seem to be only partly the same as those that convert streaks into raised lesions, and plaques may develop also independently of the fatty streaks (37).

The well-known theories of atherogenesis—i.e., the blood-clotting and infiltration theories—seem slowly to be converging, as the cellular mechanisms of the atherosclerotic process begin to be understood. The endothelial cell of the intima seems to be the key element, its integrity and its active metabolism being easily impaired by hyperlipidaemia, hypertension, or smoking. Platelets adhering to sites on the endothelium thus damaged secrete substances that may induce changes in the smooth muscle cells of the media, creating an early atherosclerotic lesion, which then evolves further under the influence of the risk factors for atherosclerosis.

There is no doubt that atherosclerosis is a condition with multiple causes and that its prevention accordingly demands a multifactorial approach.

Fig. 2. Age distribution of atherosclerotic lesions in left anterior descending coronary artery among 17 455 autopsy specimens examined in a WHO collaborative study in Czechoslovakia, Sweden, and the USSR



Sources: Fejfar (17); World Health Organization (43).

Approaches to prevention

Although there is some evidence that a regression of existing atherosclerotic changes may be achieved in experimental animals and perhaps also in man (38), it is obvious that primary prevention—if feasible—should have priority, from the public health point of view, over the treatment of atherosclerosis and its complications. Despite some rather emotional controversy over the nutritional aspects, there is a firm epidemiological basis for the prevention of coronary heart disease (20). The role of the major risk factors is now well established; over half the incidence of coronary heart disease may be “explained” by hyperlipidaemia, hypertension, and smoking (11), and, while the primary prevention of hypertension is still being studied, both smoking and hyperlipidaemia due to faulty nutrition should be entirely preventable—especially if adequate behavioural patterns are acquired early in life.

What does an “adequate” behavioural pattern imply? Avoidance of overeating, low fat and moderate salt intake, rigorous physical activity, and abstaining from smoking seem to be matters of simple common sense; yet they cannot be expected to come about spontaneously, since they run

counter to present societal trends. If healthy habits are to be acquired in childhood, the images children hold have to be changed accordingly—here, more often than not, the key persons may well be the parents and teachers.

How early should prevention start? Personality is already being shaped in early childhood, and thus the propensity for the later acquisition of faulty habits might begin to develop as early as the preschool years. Regardless of these as yet speculative considerations, the possible biological effects of risk factors when a child is still very young must not be dismissed. There is electron-microscopic evidence of the effect of the mother's smoking on the arteries of the fetus (see below). On the other hand, cordblood seems to be low in lipids; the lipid composition of human milk has been found to be remarkably similar in well-nourished mothers from various parts of the world, such as Denmark, Tanzania, Uganda, and the United Kingdom (7). Breastfeeding clearly has many advantages over bottlefeeding and is likely to be advantageous also as regards the avoidance of atherosclerosis risk factors. The adipose tissue of obese and nonobese children differs significantly in fatty-acid composition (5), owing to differences in food intake. In a study comparing serum-cholesterol levels of East African infants with those of European infants, no differences were found; but children aged 7–8 years had clearly distinct serum-cholesterol levels (8). Whether, and how early in life, it is possible to detect structural changes in the arterial intima associated with nutritional characteristics are questions to be examined in a cooperative morphological study planned by WHO (49).

Should measures for the prevention of atherosclerosis risk factors in childhood be aimed at *all* children, or should they focus on children whose parents are known to be at high risk? Obviously, the two approaches are not mutually exclusive; the children in the community as a whole need to be educated and motivated appropriately, but children of high-risk parents, together with their parents, might benefit from more intensive action designed to correct or prevent harmful habits.

How to go about shaping children's behaviour regarding atherosclerosis risk factors is an open question, calling for intensive research. One possible approach has been formulated in the "Know Your Body Program" (39, 40), but the practicability of such an approach definitely depends on the sociocultural setting.

Research: the future

The childhood precursors of atherosclerosis and coronary heart disease, as well as current studies on the subject, have been repeatedly reviewed (17, 25, 26, 44, 48) at various conferences and symposia in recent years. A considerable number of descriptive epidemiological studies are under way in various parts of the world; most of them were reported on at the meetings just mentioned. The overall conclusion is that, in affluent societies, childhood obesity, relatively high serum-lipid levels and early teenage

smoking are common phenomena. Little has as yet been published to show *how* the necessary prevention should be practised in childhood and youth; therefore, intervention studies for assessing the most suitable and effective methods are very much needed.

Is intervention to influence children's behaviour so that they avoid atherosclerosis risk factors justified? It could be objected that the positive effects of such intervention have not been demonstrated in children or, for that matter, in adults, and that any such intervention would be based only on circumstantial but not on direct evidence. However, these and similar objections—and they are made rather often when the primary prevention of atherosclerosis and coronary heart disease is discussed—do not hold good, because there is a strong probability that the avoidance or, better, prevention of the above risk factors would not only help to prevent arterial disease but be beneficial in a number of other ways, and because the proposed intervention consists of wholly innocuous measures: encouraging adherence to a balanced diet and avoidance of obesity, promoting physical activity, and preventing the "smoking disease". If a proposed health measure is harmless, cheap, and very probably useful, controversy about whether it is justified or not can only be counterproductive (29), all the more so when the accumulation of direct evidence—if at all feasible—would probably take 30–50 years. The reply to the question "Wait or act now?" is clear (10).

Society does "intervene" in countless ways in the development of its children, by shaping their intellect, character, and physique. What is proposed by the early childhood prevention of the precursors of atherosclerosis is simply the conscious and systematic addition of a few commonsense health measures to the wide array of societal influences on children and youth. The problem is that all too often such measures tend to run counter to the actual trends in society.

The "smoking disease"

Historically the cigarette-smoking pandemic is relatively recent, as the spread of the cigarette habit started to gather momentum in the first half of this century and, in fact, is still in full swing, extending to the developing countries and to adolescent girls and young women. The term "pandemic" seems to be entirely appropriate, since smoking is an unnatural form of behaviour, resulting in impaired wellbeing and often in severe illness, and is spread throughout the world by a process of psychological contamination. The ravages of smoking, especially of cigarettes, are enormous: the main consequences are bronchial carcinoma, chronic bronchitis, and coronary heart disease. Electron-microscope studies have demonstrated important alterations in the umbilical and placental vessels of mothers who smoke, suggesting that similar changes may be present in the vessels of the newborn child (1, 2). The deleterious effects on the fetus of smoking in pregnancy, already demonstrated by the reduced birth weights of the

offspring of mothers who smoke, is thus documented by direct evidence of vascular damage. If the term "passive smoking" is applied to adults (or, for that matter, to children) who inhale tobacco smoke by being in a closed space where other people are smoking, the unborn child of a mother who smokes is a truly innocent victim of "coercive smoking". Combating smoking is one of today's major public health tasks and as such a matter of concern to WHO (46, 50).

Cigarette-smoking habits are formed early in life. For example, some 40 % of primary schoolchildren in Derbyshire, England, had smoked their first cigarette before the age of 9 (3). In primary schools in Belgrade, Yugoslavia, (children up to 14 years), some 33 % were found to be smokers and 20 % regular smokers (48). Repeated surveys have shown that children are starting to smoke earlier and earlier (22).

Smoking is a very complicated behavioural and psychosocial phenomenon. The typical psychosocial influences affecting the decision of a child or adolescent to take up or refrain from smoking were recently reviewed (22). These influences include changing sex roles, parents' smoking habits, parental acceptance of smoking by their children, the influence of siblings who smoke, rebellion against family authority, peer pressures, school environment, the mass media (advertising, television, cinema), and—on the positive side—educational influences promoting awareness of the dangers of smoking. However, as pointed out in a recent report (23):

"It is futile to continue to tell teenagers that smoking is harmful and that they shouldn't do it. They know it is harmful. Most do not *want* to do it. The most effective thing we can do is to help them to understand the benefits of smoking as compared with the costs and dangers so that they will have the facts they need in order to make a thoughtful decision as to whether to smoke or not to smoke."

Apart from the fact that this proposal may be overtaxing the intellectual strength of many young children—and, perhaps, of many adults as well—merely informing the potential victims of smoking on the dangers of taking up the cigarette habit may not be an effective approach. The numerous factors contributing to the habit ought to be better understood; prospective studies of children (3) may be helpful in this connexion.

The very extensive literature on smoking and its prevention will not be reviewed in this chapter. Suffice it to state that, while the smoking habit is usually formed in childhood and adolescence, by the same token, the *non-smoking* attitude is established early in life, too. A Swedish experiment in which it is sought to raise a smoking-free generation by intensive counselling of newly wed couples to give up smoking for their children's sake—even before their first child is conceived—thus merits full attention.

The key to combating the smoking pandemic—and thus, to a great extent, cardiovascular disease in adults—lies in intervention among children and parents. Such intervention, however, can succeed only if the tremendous, often insidious, social pressure on children to take up smoking is abolished, an undertaking that by far transcends the limits of medicine. WHO has contributed to its realization by participating in international antismoking programmes, by putting forward recommendations to na-

tional authorities (46, 50), and by consecrating World Health Day 1980 to the antismoking struggle.

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Infections affecting the fetus

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Since Gregg's classic work in Australia (7) which demonstrated fetal malformations due to maternal infection with rubella during pregnancy, it has become evident that several prenatal infections can cause severe damage to the fetus. Since the fetal lesions are specific for each disease, it must be assumed that they are caused by the infectious agent itself, be it a virus, a bacterium, some other microorganism, or a toxin produced by the agent. Fetal damage can also, however, be caused by hyperthermia. There is an abundance of data to show that these infections of the mother during pregnancy may seriously affect the fetus, leading to *in utero* fatality and abortion, illness apparent at, or soon after, birth, or disease that may not be recognized for months or years after birth. Attention will be directed here to the intrauterine infections that persist through fetal life, infancy, and childhood with residual sequelae that may have some impact on the adult. These include infections caused by rubella virus, cytomegalovirus, *Toxoplasma gondii* and *Treponema pallidum*. To these may be added, on the basis of less substantial data, transplacental infection from enteroviruses, the viruses of mumps, measles, varicella-zoster, herpes simplex, hepatitis, smallpox, and Western equine encephalitis, as well as *Mycobacterium tuberculosis*, *Listeria monocytogenes*, *Leptospira*, *Staphylococcus aureus*, *Bacillus anthracis*, malaria, and trypanosomiasis (16). Although herpes simplex (*Herpesvirus hominis*) infection is mainly acquired from the vaginal canal, rather than transplacentally, this infection will be considered here because of its similarity to other infections affecting the fetus.

In a collaborative research study of 30 059 pregnancies, 5.2 % were found to be complicated by one or more viral infections other than the common cold (18). In a separate report the prevalence of fetal infection was found to be 3 % when elevated IgM levels in cord sera were used as indicators of

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intrauterine infection (1). Of 7500 infants delivered, 1 in 400 had prenatal infection from cytomegalovirus, 1 in 682 had toxoplasmosis, 1 in 938 had rubella, and 1 in 1250 had syphilis.

Rubella

Acquired rubella is an acute infection while congenital rubella is a chronic one. Acute maternal rubella has an associated transient viraemia chronically infecting the placenta and fetus. The fetus remains infected throughout gestation and for months and sometimes years postnatally. The gestational age at which maternal infection occurs is a major determinant for the extent of fetal infection as well as the magnitude of effects on the fetus. With maternal infections occurring during the first 2 months of gestation 54 % of fetuses become infected; with those occurring during the third month 34 % are infected; and with those occurring during the fourth to sixth months only 10 % are infected. Thereafter chronic infection of the fetus is rare (14).

Of infants infected during the first 2 months of gestation, 85 % have detectable defects during the first 4 years of life; such defects are also found in 52 % of those infected during the third month and in 16 % of those infected in the fourth and fifth months, but not in those exposed to infection after the fifth month (14).

Despite the host of abnormalities congenital rubella inflicts on infants, the outcome for those reaching adulthood is not entirely a dismal one, although certain defects are conspicuous. In a 25-year follow-up of 50 patients originally described by Gregg (7) and others, most had achieved reasonably good socioeconomic adjustment although 48 had hearing loss, 26 had cataracts or retinopathy, 11 had cardiac defects, and 5 were considered mentally deficient (12). It must be pointed out that this population was selected with the relatively limited concept of the congenital syndrome of cataracts, deafness, and cardiac lesions in view. Prospective studies have shown that 20–30 % of all infants born after maternal rubella are deaf (3, 9). In a more recent study of 118 children with congenital rubella who failed to respond to sound, 30 were found to have central auditory imperception as the only cause and an additional 20 children had central auditory imperception in association with peripheral hearing loss and blindness (2).

In the past it was assumed that congenital rubella was commonly associated with mental retardation and microcephaly. In a recent study, 92 children surviving the infection were tested at 4–6 years of age and found to have normal intellectual potential. Any apparent microcephaly was found to be an effect of small stature—i.e., they were small children with proportionately small heads, rather than children of average size with unduly small heads (11).

The neurological course of congenital rubella has been followed in non-retarded children from 9 to 12 years of age. Out of 29 children, 25 had

residual defects, which included learning deficiencies in 52 %, behavioural disturbances in 48 %, poor balance in 61 %, muscular weakness in 54 %, deficiencies of tactile perception in 41 %, and hearing loss in 93 % (4).

Such sequelae of congenital rubella as gross cardiac lesions, hepatitis, meningoencephalitis, and interstitial pneumonitis are often fatal to infants. Others such as pancytopenia, retinopathy, hepatosplenomegaly, lymphadenopathy, and bone lesions are usually self-limited and seem to pose no long-term risks. Thus, in adults who have survived congenital rubella, hearing defects will be the major handicap, with psychomotor, perceptual, and corrected cardiac abnormalities as less common complications.

The currently available rubella vaccines, first licensed in the USA in 1969, have been shown to be effective in the prevention of congenital rubella (8). After licensing, a total of 53.6 million doses of vaccine were distributed in the USA alone. The development of a safe vaccine has made rubella a preventable disease. Vaccination should be carried out before young women start a family, though the optimum age for such immunization has not been established. The incidence of congenital rubella has been shown to fall drastically when inoculation is carried out on a broad basis. The lesson is clear.

Cytomegalovirus infection

The incidence of congenital cytomegalovirus infection acquired prenatally varies from 0.5 % to 2.0 % of all live births, and over 95 % of the infants affected appear normal at birth. Acquisition of the infection at the time of delivery from the vaginal canal accounts for an additional 5 % (17). With cytomegalic inclusion cell disease of the neonate, the less common form, there are severe generalized manifestations of hepatomegaly, thrombocytopenia, jaundice, purpura, central nervous system involvement with cerebral calcification, microcephaly, chorioretinitis, deafness, and psychomotor retardation, resembling the effects of congenital rubella. The excretion of the virus by the infants infected continues for much longer than it does in the case of rubella infections. By 3–4 years of age most children with congenital cytomegalovirus infection are still excreting the virus, which may be recovered from urine, saliva, tears, etc. Obviously, this is a significant factor in the transmission of the virus to susceptible individuals. Data on the prevalence of cytomegalovirus antibody in child populations are given in Table 1 (16).

The sequelae of symptomatic cytomegalovirus infection for the infants who survive include microcephaly, cerebral palsy, hemiplegia, epilepsy, blindness, deafness, and mental retardation. Recent studies indicate that sensorineural hearing loss is perhaps the most frequent residual damage resulting from symptomatic and asymptomatic congenital cytomegalovirus infection, occurring in 17–20 % of cases (10, 19). It has been estimated that 1 infant out of every 750 born alive will experience hearing

Table 1. Prevalence of cytomegalovirus antibody in child populations^a

Country or area	Age range	Number tested	Percentage positive
Canada	6 months to 15 years	225	13.3
England	6 months to 15 years	447	16.3
France	6 months to 14 years	281	18.6
Hungary	4 to 14 years	120	27.5
Japan	10 months to 13 years	238	65.5
Puerto Rico	1 to 11 years	99	20.2
Sweden	7 months to 15 years	108	25.0
Switzerland	6 months to 14 years	1 212	28.6
United Republic of Tanzania	6 months to 14 years	66	90.9
USA (5 cities)	Birth to 17 years	763	15.72

^a Modified from Remington & Klein (16).

impairment as a result of cytomegalovirus infection. At least half of those so affected will be significantly handicapped by their particular defect.

Long-term studies of infants who have had congenital cytomegalovirus infection and survived into adulthood are not available, but from the above-mentioned defects recognized in children, some idea of the type of sequelae can be gained, although it is difficult to estimate their relative importance. A cytomegalovirus vaccine is being developed but has not yet reached the stage at which an evaluation of its effectiveness in the prevention of intrauterine infection would be feasible.

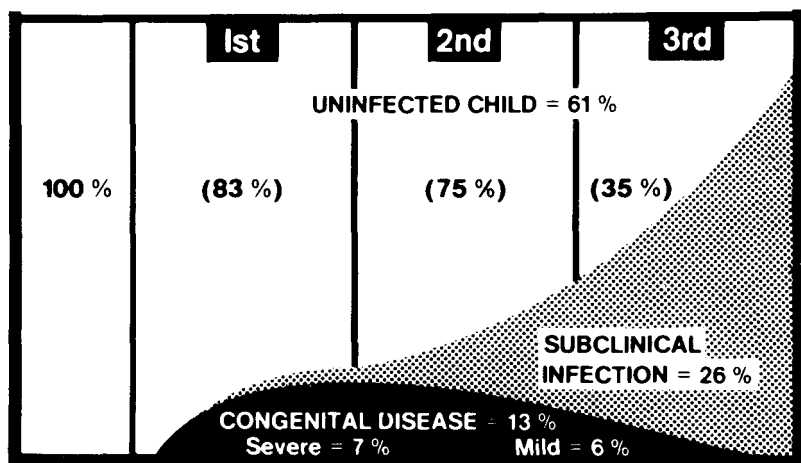
In most populations studied in Western Europe and the USA, antibodies gradually appear with increasing age. By contrast, in populations in Africa, Asia, and Eastern Europe there is a high prevalence of cytomegalovirus antibodies even among children; young adults are almost universally antibody-positive, so that childbearing women are largely protected against primary infections. Chemotherapy of the cytomegalovirus infections has been disappointing and, in view of the high prevalence of intrauterine infection, the development of immunoprophylaxis would be highly desirable, particularly for populations in which antibodies are acquired late.

Toxoplasmosis

The incidence of congenital toxoplasmosis has been roughly determined as 5–7 cases per 1000 births in Göttingen (Federal Republic of Germany), the Netherlands, and Vienna, and 1.3–3.0 per 1000 births in Mexico, Paris, and the USA (16). Thus, congenital toxoplasmosis is less frequent than cytomegalovirus infection, though more damaging to the fetus and infant. Residual damage varies considerably, but chorioretinitis has been found in 94 % of cases, intracerebral calcification in 59 %, psychomotor retardation in 45 %, convulsions in 39 %, microphthalmia in 36 %, and hydrocephalus in 22 % (5). The cost of health care and special education for infants infected congenitally with *Toxoplasma gondii* in the USA is estimated to be between US\$30 and US\$40 million each year (6).

The outcome of pregnancy depends to some extent on the stage of gestation at which the mother acquired the disease (Fig. 1), but since the maternal infection is often subclinical, this time factor can only be determined by serial antibody determinations, which is highly impracticable. Fetal infection has many manifestations, and subclinical congenital infections may result in sequelae much later, even in adult life, when the origin is difficult to trace. It is therefore of great importance to screen mothers in early pregnancy and identify sero-converters. Treatment with chemotherapeutic agents (pyrimethamine and sulfadiazine) is possible; it is rarely used during pregnancy and few data exist on its effectiveness. But if congenital toxoplasmosis is diagnosed at birth, by serological tests or demonstration of *Toxoplasma gondii* in cord or neonatal blood, both therapeutic and prophylactic treatment may be considered. The incidence of congenital toxoplasmosis certainly would justify exploration of the possibilities of immunoprophylaxis. No effective vaccine is available.

Fig. 1. Outcome of pregnancies in which toxoplasmosis was acquired, by trimester. Frequency of deliveries of infants with clinical congenital toxoplasmosis (darkly shaded area), with subclinical infection (lightly shaded area), and with no infection (unshaded area), following maternal acquisition either before or during the three trimesters of pregnancy



Herpes simplex

Neonatal infection with herpes simplex virus was first described in 1934 by Batignani in Italy. There has been a definite increase in the numbers of cases reported in recent years, and neonatal herpes is worldwide in distribution though data on the incidence or prevalence of congenital herpes simplex infection are scanty. The disease is transmitted at birth from mothers with active lesions in the genital area. Since there is no treatment

that will reliably cure the disease, the only prophylactic measure is to deliver the infant by caesarian section to prevent the neonate from coming into contact with the mother's herpetic lesions. It has been estimated that approximately 1 clinically apparent case occurs with each 7500 deliveries (13). The mortality rate is relatively high. Out of 180 patients with disseminated infection 82 % died, while among 86 infants with localized infection only those with central nervous system involvement died. Of a total of 266 infants with congenital herpes simplex infection who were studied 46 (17 %) survived with sequelae and 55 (21 %) survived without apparent sequelae (16). Thus, because of the relatively low incidence and high mortality rate, survivors into adulthood following the more serious infections can be expected to be rare.

An antiviral agent, adenine arabinoside, is being evaluated in collaborative studies to determine its efficacy in the treatment of systemic herpes simplex infection but conclusive data are not yet available.

Bacterial infections

Of the bacterial infections that are transmissible from mother to fetus and neonate, syphilis appears to be the only one that can be transmitted in early pregnancy. Amnionitis, developing after premature rupture of the membranes, leads to fetal infection and to pneumonia in newborn infants. Treatment of the infection *in utero* is not effective; early delivery and appropriate therapy for this dangerous complication after birth constitute the method of choice. Streptococcal infections and gram-negative bacterial infections are usually transmitted at, or after, birth, and the same is usually the case with tuberculous infections.

Congenital syphilis

Congenital syphilis has long been recognized as a severe form of the disease. Although syphilis in women is curable and although prophylactic programmes with mandatory serological screening of all pregnant women have existed in many countries for years, the recent increase in the incidence of infectious syphilis in the adult population has also resulted in an increase in the incidence of congenital syphilis. To improve the situation, therefore, there must be serological testing for syphilis in both early and late pregnancy. The offspring of mothers treated for syphilis during pregnancy should be carefully examined after birth and, if the mother has been treated in the second half of pregnancy, the baby should be re-treated.

If syphilis is contracted during pregnancy, about 95 % of fetuses will become infected during the latter half of gestation. The most severely affected infants will be stillborn. Most of the liveborn infants will have no visible lesion at birth, yet over 90 % will develop skin and osseous lesions. Infection of the nasal cartilage results in a saddle-nose deformity, while

skeletal lesions of the long bones, though frequent, are self-limited and rarely cause permanent damage. Involvement of the liver, lungs, kidneys, spleen, and lymph nodes are less common, though invasion of the central nervous system occurs frequently with early congenital syphilis.

With late congenital syphilis the more permanent sequelae include dental deformities, rhagades, interstitial keratitis, eighth nerve deafness, and Clutton's joint. A more important form is the meningovascular involvement of the central nervous system leading to paresis.

Congenital syphilis is preventable by treatment of the maternal infection with penicillin.

Congenital malaria

Transplacental passage of malaria parasites rarely occurs, but more than 150 cases of congenital malaria have been reported, mainly in nonimmune populations (e.g., 15). In endemic areas the congenital infection has been estimated to occur in about 0.3 % of the offspring of infected mothers (e.g., 20). The clinical features of congenital malaria and of malaria acquired after birth are similar. The effects of congenital malaria on survivors who might reach adulthood are unknown.

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The sequelae of infectious diseases of childhood

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A factor basic to the understanding of current problems arising from infectious diseases, and especially to future expectations in this domain, is the constantly changing pattern presented by these diseases in a population over several generations. The importance of this factor has become apparent only during the last few decades. Although the earth has been populated by microbes for many millions of years and by mankind for more than a million years, scientific knowledge of microbiology and infections has developed only since the Pasteur era, a mere century ago. The etiologies and modular patterns of the devastating plagues that occurred before that time are largely a matter of reasonable speculation. Within the present century, remarkable changes have taken place. Smallpox, familiar to senior physicians living today, is now extinct. In developed countries, hospital beds once filled with patients suffering from scarlet fever, diphtheria, tetanus, and tuberculosis are now occupied by sufferers from other maladies, such as cancer, heart disease, stroke, mental disease, and accidental injury. In turn new problems have emerged—namely, nosocomial and opportunistic infections of which the causative agents are organisms previously considered avirulent and nonpathogenic, but which are now responsible for disease in 1 in every 20 hospitalized patients.

Advances in the treatment of several noninfectious diseases, including the use of immunosuppressive irradiation and chemotherapy, organ transplantation, prosthetic devices, indwelling catheter lines, and mechanical units for respiratory and cardiac assistance, have made patients vulnerable to opportunistic microbes of their normal environment and flora, thus contracting infections from which they may die even though the primary disease has been cured.

In most developed countries, poliomyelitis has virtually been eradicated and the majority of young physicians have never seen a case. However, new

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diseases continue to arise, such as legionnaire's disease, Lassa fever, rotavirus gastroenteritis, *Pneumocystis carinii* pneumonitis, and Kawasaki's disease. Rheumatic fever following group A beta-haemolytic streptococcal infection is mysteriously subsiding, while group B beta-haemolytic streptococcal infection in the neonate is on the increase for equally mysterious reasons. Effective vaccines, while successfully reducing infection rates, are shifting the "common childhood" exanthemata of measles and rubella from the child to the young adult. The past hundred years have witnessed a series of similar changes, first from the Pasteur-Koch-Lister era to the early 20th century with its vaccines against smallpox, tetanus, diphtheria, and pertussis, then to the antibiotic era of the 1940s, to the emergence of antibiotic-resistant bacteria in the 1950s, to the advent of the viral vaccines against poliomyelitis, measles, rubella, and mumps in the 1960s, and to the opportunistic infections of the 1970s with their attendant problems. There is every reason to believe that such changes will continue and, on reaching adulthood round about the year 2000, the infant of today can expect to be confronted with problems due to microbial disease that are quite different from those facing adults now.

In some developing countries, tuberculosis, malaria, poliomyelitis, tetanus, typhoid fever, measles, and parasitic diseases—to take only a few examples—continue to be serious problems. Even if the most intensive effort to control these diseases were started now, infants in those countries would still be likely to have rather different problems on reaching adulthood in the year 2000 than those reared in industrialized societies.

Greater consideration should be given from now on to the prevention and limitation of *morbidity* from infectious diseases. The general measure of successful health action in the past was the reduction in mortality rates, and efforts in this direction must be continued. Nevertheless, there is a growing reservoir of patients who have survived infectious disease with either temporary or permanent sequelae, ranging from minor defects to severely incapacitating ones. It is with this subject that we are concerned here and more specifically with infections in infancy and childhood, the survivors of which are left with impairments that persist into adulthood.

Infections affecting the respiratory tract

Since the lung continues to develop during the first 6 years of life at a rate of 50 million new alveoli annually, it is not surprising that respiratory tract infections can inflict permanent damage by interfering with the normal development of the lung (22).

Bronchiolitis is a common viral infection of the lower respiratory tract occurring almost exclusively in infants and small children and caused in most instances by respiratory syncytial virus. The acute episode is usually self-limited, with apparent clinical recovery within a week or so. Recent studies indicate that this seemingly mild infection affects the small airways

during a time of rapid growth and may account to some extent for chronic obstructive lung diseases in adulthood.

In Toronto, Canada, children who had bronchiolitis before the age of 18 months were evaluated 10 years later for abnormalities of pulmonary function (17). The majority of these children showed evidence of hyperinflation, abnormal gas exchange and/or small airway disease. In 31 % of the children affected, the arterial oxygen tension and volume of isoflow, as well as the residual volume to total lung capacity ratio, were abnormal. The study showed the presence of residual parenchymal or airways lesions a decade after the initial episode of bronchiolitis.

In a similar study, children in Arizona, USA, with bronchiolitis and croup were examined prospectively for residual effects of these infections on pulmonary function and compared with age-matched controls who had not experienced either infection. By 4–7 years of age—i.e., 3–6 years after the initial illness—baseline abnormalities in maximal flows at functional residual capacity were demonstrated in 46 % of children who had had bronchiolitis and croup. Such abnormalities were not demonstrated in the controls, suggesting residual airway obstruction in the children who had suffered the illnesses (1).

It is not known whether or not these abnormalities in pulmonary function are eventually reversible. However, since lung growth is almost complete by 6–10 years of age, it seems likely that they are permanent defects and may well increase the susceptibility of the adult to chronic obstructive lung disease upon exposure to exogenous factors such as smoking.

In primitive tribes from the highlands of Papua New Guinea, 50 % of the adults over 40 years of age have chronic cough and impaired pulmonary function. Cigarette-smoking is uncommon in this society, but serious respiratory tract infection, including bronchiolitis, is present in childhood (43).

Adequate data on the incidence of bronchiolitis are available from few countries. Prospective studies in North Carolina, USA, of between 6000 and 7000 children over a period of 10 years showed that 6–7 cases of the infection occurred per 100 children per year in the population under 2 years of age. Respiratory syncytial virus accounted for the majority of cases (6). It is important to note that the infection was markedly predominant in males.

Chronic infections with acute episodes of bronchitis and pneumonitis characterize children with cystic fibrosis. These infections are caused uniquely by *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Cystic fibrosis was exclusively a disease of children, but advances in its management have now increased the patients' period of survival to the point that a sizeable proportion of them reach adulthood. The national 50 % survival rate in the USA is now 16 years. It is expected that, of the patients now detected and treated while the pulmonary involvement is still reversible, more than 96 % will survive beyond 18 years of age (42). Thus, the control in childhood of the infections associated with cystic fibrosis is crucial.

The incidence of cystic fibrosis is highest in white populations, ranging from 1:620 in Namibia (persons of Dutch descent) to 1:15 000 in Italy (42). Successful management of the disease has now been achieved through effective antimicrobial therapy and supportive regimens of nutritional and physical therapy. It is not known why the infectious complications remain almost exclusively localized in the lungs or why *P. aeruginosa* in mucoid form colonizes the respiratory tract.

Infections affecting the central nervous system

Gram-negative bacillary meningitis is predominantly a disease of infants and small children. *Haemophilus influenzae*, the most frequent cause of bacterial meningitis in children, occurs almost exclusively in those less than 5 years of age. *Escherichia coli*, together with group B beta-haemolytic streptococcus, accounts for the majority of cases of neonatal meningitis.

The impact of childhood meningitis on those surviving to adulthood is considerable. With currently available antibiotics, the mortality rate for bacterial meningitis has been reduced to remarkably low levels. With increased survival rates, growing numbers of patients are reaching adulthood with permanent sequelae.

The current mortality rate for *H. influenzae* meningitis is approximately 8% with appropriate antibiotic therapy (24) and even lower in some paediatric centres. Thus, over 90% of children with the infection can be expected to survive, and the majority will live to adulthood. Estimates of the incidence of residual handicaps in these individuals vary to some extent, but the general pattern is apparent. Even now, *H. influenzae* meningitis is the leading cause of acquired mental retardation in the USA (32). Longitudinal appraisals of survivors have revealed such complications as hydrocephalus, spastic hemiplegia, paresis, ataxia, vestibular damage, blindness, deafness, convulsions, psychosis, learning disabilities, and behavioural disorders (9, 14, 20, 33, 35). In one careful study, it was found that 30% of infants and children with the infection experienced serious sequelae (IQ less than 70, convulsions, severe hearing loss, motor deficits, or partial blindness) (33). An additional 14% had residual conditions probably related to the infection. Of the children with *H. influenzae* meningitis, 43% recovered with no apparent sequelae. On the other hand, another study revealed that only 8% had serious sequelae and 28% milder abnormalities, while 64% of patients survived without any detectable sequelae (9).

The incidence of *H. influenzae* meningitis is estimated at 4.5 cases per 100 000 population in the USA and 2.7 per 100 000 in Finland (27). The incidence in Sweden is in a similar range (20). The global annual attack rate in those aged 5 years or less is about 1 case per 2000; however, in poor socioeconomic communities the incidence is about 3.6 per 1000 (11). There is also evidence to suggest that children with sickle-cell anaemia are at higher risk than others. On the assumption that at least one-third of those

infected will survive with some permanent sequelae and that the attack rate is 1 per 2000 per year (which is on the low side), approximately 1 in every 6000 individuals can be expected to reach adulthood each year damaged by *H. influenzae* meningitis.

A recently developed *H. influenzae* type b polysaccharide vaccine has been extensively evaluated and found to be ineffective in protecting individuals below 18 months of age against *H. influenzae* infection, while protecting those above that age (27). Unfortunately, about half the episodes of bacteraemia, meningitis, or both, caused by the infection occur in the younger age group.

With current therapy, over 95 % of children with pneumococcal meningitis can be expected to survive it. Sequelae recorded in survivors include deafness (11 %), hydrocephalus (11 %), convulsions (7 %), mental retardation (7 %), strabismus (4 %), and behavioural problems (4 %) (19).

In neonatal bacterial meningitis, caused predominantly by *Escherichia coli* or group B beta-haemolytic streptococcus, the long-term sequelae are estimated to affect between 40 % and 60 % of the survivors (3, 4, 7, 10, 26, 33, 41, 46, 47). Fortunately, meningitis is relatively rare in neonates, affecting approximately 0.4 per 1000 live births. However, the mortality rate is remarkably high, even with current treatment procedures. Roughly, 40 % of the infants infected will die from the infection (10). Thus, with its relatively low attack rate and high mortality rate, neonatal meningitis accounts for a relatively small proportion of the adults with sequelae of meningitis.

Encephalitis due to measles virus occurs in approximately 1 in every 1000 cases of measles. Roughly 70 % of the cases of encephalitis recover without sequelae, 20 % recover with neurological sequelae, and 10 % die. Subacute sclerosing panencephalitis, probably etiologically related to measles virus, is estimated to occur at a rate of 5.2–9.7 cases per million cases of measles. The incidence in those vaccinated against measles is reported as 0.5–1.1 cases per million (23). The data in Table 1 show that 1.85 million cases of measles are reported annually (44).

Mumps virus is probably the most common cause of viral meningoencephalitis. Pleocytosis is found in 30–50 % of cases of mumps. Fatalities are rare and recovery is usually complete without residual effects, deafness being probably the most frequent permanent sequela. The mumps vaccine is highly effective in providing complete immunity against infection (see Table 1).

Though attack rates are relatively low even on a global basis, poliomyelitis is of considerable significance when viewed from the standpoint of serious residual sequelae after survival to adulthood (see Table 1). This preventable disease still demands attention in view of the unnecessary disablement and dependence it continues to impose on potentially productive individuals, mainly in the early years of life.

Encephalitis is less common with varicella than with measles. Furthermore, fatalities are rare and recovery is usually complete, although mental defects and spastic paralysis have occurred in some rare instances.

Table 1. Number of cases of infectious diseases considered preventable reported each year

Disease	Number of cases per year						Percentage of patients less than 15 years of age
	Africa	Americas	Asia	Europe	Oceania	Total	
Measles	916 411	103 255	164 986	300 181	366 270	1 851 103	91.0
Mumps	46 673	75 877	61 781	545 745	728	730 804	-
Poliomyelitis	5 691	3 065	4 894	293	131	13 874	97.0
Tetanus	1 377	827	7 723	403	-	10 330	-
Pertussis	216 142	121 230	74 837	30 166	15 070	457 445	94.5
Diphtheria	2 181	5 319	8 897	594	200	17 191	91.0
Tuberculosis	254 867	116 929	350 289	235 579	2 044	959 708	7.9
Total = 4 040 455							

Source: *World Health Statistics Annual 1977 (44)*.

Perhaps the greatest effect of childhood varicella on subsequent adulthood is its legacy of herpes zoster. The varicella-zoster virus appears to persist in latent form following varicella. In older adults, activation of the virus may occur along peripheral nerves resulting in an eruption of zoster. Zoster rarely, if ever, occurs in individuals who have not had varicella previously.

A live attenuated varicella-zoster virus vaccine has been developed in Japan and tested in patients with reduced resistance. Although early studies suggest that it is effective in preventing varicella, its safety and its role in the prevention of zoster have not been established.

Infections affecting hearing

Acute otitis media is a highly prevalent infection in children. At least 90 % of children in some studies have at least one episode in the first 6 years of life (2, 28). Recurrent infections are more frequent in those in whom the first infection occurred during the first year of life and when the causative agent is *Streptococcus pneumoniae* (15).

The incidence of purulent otitis media varies from one population to another. An unusually high incidence is reported in Alaskan Eskimos, American Indians, the aborigines of Australia, and the Maoris of New Zealand (21, 29). In a study of 489 Alaskan Eskimo children who had been infected and were followed up for 10 years, it was found that 41 % had perforations or scars of the tympanic membrane and 16 % had significant hearing losses (16). On the other hand, in East Africa chronic purulent otitis media is uncommon even in severely malnourished infants with their susceptibility to serious infections.

There are few studies on the association between acute otitis media and permanent hearing loss. An examination of 403 British children 5–10 years after at least one episode of acute otitis media revealed that 17 % had a hearing loss of 20 dB or greater in at least two frequencies, compared with 4.5 % in a group of matched controls (12).

Mumps-associated deafness

Mumps-associated deafness is usually unilateral, often permanent, and results from a secondary labyrinthitis with retrograde demyelination of the auditory portion of the eighth cranial nerve. The incidence has been reported to be from 0.5 to 7.0 per 100 000 cases of mumps (8, 40).

Other infections

Hearing defects deriving from congenital infections have been described in Chapter 6, while those arising as a result of meningitis have been dealt with earlier in the present chapter.

Infections affecting the eye

Trachoma is one of the leading causes of preventable blindness (45). The endemic form is a chronic follicular conjunctivitis, caused by *Chlamydia trachomatis*, which results in pannus formation, scarring of the conjunctivae, and blindness. Secondary bacterial infection is responsible to a large extent for the severity and chronicity of trachoma. The disease is a major problem in North Africa, sub-Saharan Africa, the Middle East and south-eastern Asia (30). In holoendemic areas, almost everyone is infected by 2 years of age and reinfection within families perpetuates the disease. Although active infection tends to subside by adolescence, permanent residual lesions lead to blindness. Thus, visual impairment may occur 20 years or more after the active infection subsides (44). It seems that only individuals repeatedly "sensitized" to *C. trachomatis* develop severe and progressive trachoma. The endemic disease is closely associated with poverty and crowded living conditions.

The causative organism is sensitive to any of several chemotherapeutic agents, including tetracycline, rifampicin, the sulfonamides, and erythromycin. Although effective, the systemic or topical administration of these substances, even in mass campaigns, has not succeeded in suppressing trachoma to any great extent. Improvements in hygienic conditions, in the economic status of the inhabitants of the endemic areas, and in methods of drug administration are essential for the eradication of this disease. Attempts to develop an effective vaccine have failed so far (13). In fact some of those immunized have suffered more intensive infections than persons who were not immunized.

The effects on vision of congenital rubella, toxoplasmosis, syphilis and cytomegalovirus infection have been dealt with in Chapter 6, and those of meningitis and encephalitis are mentioned elsewhere in the present chapter.

Gonococcal ophthalmia of the neonate may progress from a purulent conjunctivitis to chronic conjunctivitis, corneal ulcers and scarring, or extensive panophthalmitis and blindness. Since the causative organism is acquired from the mother's vaginal canal, the incidence of the ophthalmia is related to the incidence of gonorrhoea in a given population. Although its value has yet to be confirmed in properly controlled studies, the Credé method of prophylaxis, consisting of the instillation of 1% silver nitrate drops into the newborn infant's eyes, seems to be reasonably effective.

Infections affecting the pancreas

The role of mumps virus in the provocation or development of diabetes mellitus has been a subject of speculation from time to time since the turn of the century. Episodic cases of diabetes mellitus have followed mumps infection (5) and immunization with the attenuated mumps virus vaccine (34). Some data suggest that, in a specific population, the incidence of diabetes has paralleled the incidence of mumps after a 4-year interval (37).

Infections affecting nutrition

Tuberculosis in a malnourished child may be more extensive than in a well-nourished one, because of depressed cell-mediated immunity as a result of protein deprivation.

Although urinary tract infections are common in children and chronic irreversible renal disease is frequently seen in adults, there is a remarkable lack of clear information about residual disease being carried into adulthood after infection in childhood. Variations in definitions of urinary tract infection and the absence of careful longitudinal studies account in part for this gap.

Studies in schoolgirls show that vesicoureteral reflux can be demonstrated in about 19% of those with bacteriuria, and caliectasis is associated with about one-third of those with reflux. While vesicoureteral reflux was found in 35% of girls between 5 and 9 years of age, only 11.5% of those aged 15 and over experienced it, and it is rare in adult women. This suggests that it tends to resolve with age.

* * *

In the preceding pages, attention is drawn to certain infections that occur in infancy or childhood and whose sequelae may persist into adulthood. The many infections that affect child and adult alike, such as malaria, cholera, influenza, yellow fever, and parasitic infections, have not been considered. Rheumatic fever, of great importance as regards sequelae in adulthood, is covered in Chapter 5.

It is obvious that sound data are lacking on the long-term sequelae of many of the childhood infections. The relationship of such infections as pertussis, influenza, and mycoplasma infection to chronic obstructive pulmonary disease in the adult is not known. The effect of symptomatic and asymptomatic bacteriuria on renal function later in life needs further elucidation. More extensive studies on the late effects of congenital and acquired cytomegalovirus infection are needed.

Although the polysaccharide vaccines for *Haemophilus influenzae* and the pneumococcus seem to be effective and safe for children aged 2 years and over, it is for younger children that vaccines to prevent residual effects from meningitis and otitis media are most needed. A fresh effort to provide such vaccines for infants is desirable. Infants with sickle-cell disease, who are at high risk for fatal pneumococcal infection, would benefit particularly from an effective vaccine. Vaccines against respiratory syncytial virus, cytomegalovirus, and varicella-zoster virus are in varying stages of development, and each will present its own problems and special features. For example, will the live attenuated varicella-zoster virus vaccine increase the likelihood of shingles in adulthood? Can a cytomegalovirus vaccine be given safely during pregnancy?

There is a worldwide increase in the incidence of venereal diseases among even younger age groups, affecting young adolescents in particular. The sequelae of untreated gonorrhoea and syphilis cover a wide and well-known spectrum and include—significantly—virtually irreversible sterility. Thus there is a great need for education in the early diagnosis and prevention of these diseases, with emphasis on the high infectivity of the major organisms involved, as well as for early detection and treatment, research into vaccine development, and improved therapeutic procedures.

Methods of proved efficacy are now available for the prevention of several of the major infectious diseases that plague children, including measles, rubella, mumps, poliomyelitis, tetanus, diphtheria, pertussis, and tuberculosis. Effective and relatively safe vaccines have been developed that are capable of immunizing a high proportion of children and adults against these diseases. The need for them can be appreciated from a study of Table 1. The data in this table cover the more than 4 million cases of preventable infectious disease reported to WHO each year, but reflect only a fraction of the true worldwide prevalence. The effort required to deliver the necessary vaccines to a high proportion of the populations concerned will vary considerably from community to community and from country to country and will depend to a great extent on socioeconomic and political factors.

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Oral health

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Epidemiology

Populations with a high prevalence of dental caries are a relatively modern phenomenon. From the evidence available, it is clear that the prevalence of this disease was very low in ancient and medieval times and it was only after the social and economic changes that occurred during the 18th and 19th centuries in many countries, with the progress of industrialization, that substantial increases in the disease were observed. The most dramatic increases in prevalence, sometimes to more than 95%, happened only when traditional local diets were almost completely replaced by the mass-produced, variously processed foods of urban society. On the other hand, there is evidence suggesting that the other broad category of oral diseases—periodontal diseases—has existed at about the same level from time immemorial.

To facilitate the comparison of caries levels throughout the world, 5 categories have been defined, covering the range from very low to very high, as follows:

Sum of decayed, missing and filled teeth (DMFT)

Very low	0.0–1.1
Low	1.2–2.6
Moderate	2.7–4.4
High	4.5–6.5
Very high	6.6 and over

Generally speaking, dental caries shows a pattern of high prevalence at extreme latitudes and lower prevalence in the equatorial regions (*1*), though obviously there are variations within each broad group and some

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important exceptions—for example, in nearly all southern American countries, including the tropical ones, the prevalence is high or very high.

The general picture for technically advanced nations shows that the level of dental caries ranges from moderate to very high. The actual level in a particular area may depend on many factors such as the cariogenicity of the diet, the genetic endowment of the people, and cultural attitudes to oral health and treatment. These factors, provided they remain constant, tend to produce a stable prevalence figure. That caries levels change dramatically in response to significant changes in diet or habit is well documented (22). The incidence and prevalence of caries in children fell in many countries during the deprivations of 1939–1945, but after the return to normal diets they showed a remarkable tendency to revert to the exact pre-war levels.

It has also been clearly demonstrated in countries with well-organized treatment services that curative services do not prevent the disease. In a study of dental manpower systems in relation to oral health status (23) in 6 countries, the only population that exhibited a significant decrease in caries level (about 33 %) was one in which preventive methods other than water fluoridation (though based on fluoride) and an active oral health education programme had been in progress for more than 10 years and were only reinforced by water fluoridation late in that period. This successful preventive campaign was carried out in an area where the treatment coverage of the population by professional dental care was far inferior to the almost total coverage enjoyed by other samples in the study.

The situation with regard to periodontal diseases is much less clear. The prevalence of these diseases appears to be at least moderate in all populations with well-organized dental services, and dentitions that have been preserved by preventive and curative services from loss due to dental caries suffer damage from periodontal disease during and after the third decade of life, when the period of greatest caries activity is past.

In developing countries the picture is very different and less well documented. Traditionally these populations, for the most part, enjoy and still enjoy a low or very low prevalence of caries. However, it is important to realize that within a country a very wide range of DMFT (sum of decayed, missing and filled teeth) values may be found in different groups of people. This is well illustrated in Table 1, which gives the results of a recent national pathfinder survey in Thailand. These results are now being used to formulate a national oral health plan for the country. Another example is to be found in the Sepik area of Papua New Guinea (20), where some villages have a mean DMFT of zero, while others less than 30 km away have a mean DMFT of more than 8, the environment being one in which virtually no refined foods are available.

Informed observation suggests a high or very high prevalence of periodontal diseases in most developing countries. There is a great deal of epidemiological evidence to support this, though it is obviously not comprehensive for all countries or even for all age groups. However, because of the defects of present measures to deal with periodontal

Table 1. Levels of dental caries in 12-year-old children, Thailand

Year	Area	DMFT ^a	Level
1960	All areas	0.4	Very low
1976	Bangkok	2.5	Low
"	Chiangmai	1.0	Very low
"	Chon Buri	4.7	High
"	Karikanabun	5.2	High
"	Krabi	2.9	Moderate
"	Nakhon Sawan	2.7	Moderate
"	Nakhon Si Thammarat	4.1	Moderate
"	Samut Sakhon	1.8	Low
"	Ubol Rat Thani	1.4	Low
"	Udon Thani	1.8	Low

^a Decayed, missing and filled teeth.

diseases, it is still not clear whether these diseases are more severe in the developing countries than elsewhere, especially if the final consequences—i.e., loss of dental function and of teeth—are considered. It is certainly clear that the prevalence of initial and chronic gingivitis is very high, and data indicating the presence of large amounts of oral debris, plaque and calculus support these conclusions. Nevertheless, where treatment is completely lacking, tooth loss due to periodontal disease in the age group 35–44 years appears to be rarely as much as 1 or 2 per person.

Trends in disease levels

There is relatively little evidence of the effects of large-scale community or national programmes for caries prevention in developed countries—apart from the areas in which water fluoridation has been introduced and the few in which school programmes oriented towards prevention are in operation. Data indicating downward trends in caries prevalence and severity are available for Australia, Canada, Denmark, New Zealand, Switzerland, the United Kingdom, and some areas in the USA. On the other hand, Japan shows an increase in caries levels of from 3 DMFT to approximately 8 DMFT in children aged 13–14 years over the last 20 years, and this increase has occurred at the same time as a rapid expansion of dental services. Tables 2 and 3 give data on caries prevalence in selected countries. No large-scale periodontal disease preventive programmes have been reported as showing positive results at a community level.

Table 2. Trends in prevalence of dental caries in 12-year-old children in various countries or areas

Country or area	Year	DMFT ^a	Level	Year	DMFT ^a	Level
Canada ^b	1958	8.5	Very high	1977 ^c	8.0	Very high
Japan	1957	2.8	Moderate	1975	5.9	High
France (urban)	1903	5.3	High	1973	5.6	High
French Polynesia	1963	6.4	High	1977	10.5	Very high
Italy (urban)	1966	3.0	Moderate	1977	6.9	Very high
Norway	1940	12.0	Very high	1973	12.6	Very high

^a Decayed, missing and filled teeth.

^b There is recent evidence of a decrease in Ontario Province.

^c 12–14 years.

Table 3. Levels of dental caries in 12-year-old children in Australia and Switzerland

Country	Area	Year	DMFT ^a	Level
Australia	All areas	1956	^b	Very high
	Adelaide	1974-77	4.6	High (6 years' water fluoridation)
	Brisbane	"	4.7	High (fluoride tablet programme)
	Canberra	"	2.9	Moderate (12 years' water fluoridation)
	Townsville	"	4.0	Moderate (10 years' water fluoridation)
Switzerland	All areas	1963	^b	Very high
	Basel (Stadt)	1974-75	2.3	Low (water fluoridation since 1962)
	Glarus (Canton)	"	7.0	Very high
	Lucerne (Canton)	"	4.8	High (fluoride tablet programme)
	Solothurn (Canton)	"	7.3	Very high
	Vaud (Canton)	"	5.4-4.4	High to moderate (salt fluoridation and tablets since 1969-70)
	Zurich (Canton)	"	3.9	Moderate (school-based prevention since 1964)

^a Decayed, missing and filled teeth.^b No national figure available.

Table 4. Levels of dental caries in 12-year-old children in 3 developing countries

Country	Year	DMFT ^a	Level	Year	DMFT ^a	Level
Ethiopia	1958	0.2	Very low	1975	1.5	Low
Kenya	1952	0.1	Very low	1973	1.7	Low
Nigeria (northern)	1963	1.1	Very low	1973	2.5	Low

^a Decayed, missing and filled teeth.

Table 5. Level of dental caries in 12-year-old children, Indonesia, 1973

Area	DMFT ^a	Level
Rural areas	0.7	Very low
Badung	3.5	Moderate
Cirebon	2.7	Moderate
Menado	4.9	High
Palembang	2.7	Moderate
Pontramak	4.6	High
Samarinda	5.1	High
Semarang	2.4	Low
Surabaya	2.4	Low

^a Decayed, missing and filled teeth.

The situation is more disturbing in developing countries, in which there are many cases of well-documented increases during the last 10-15 years, as shown in Table 4. Moreover, although there are several populations for which no baseline data are available, it is often possible to monitor trends by considering the figures for rural and urban areas separately. The problems arising from these trends are accentuated by rapid urbanization and the changes in diet and habits associated with adaptation to a cash economy, new education patterns, and other aspects of urban life. For

example, in Indonesia there is a mean overall caries prevalence at 12 years of age of 0.7 DMFT, but in the cities the mean is 3.5 DMFT (Table 5). One very large change in an urban population took place over a relatively short period of time in Ho Chi Minh City, Socialist Republic of Viet Nam, where the DMFT figure at 12 years of age changed from 2.0 in 1958 to 6.3 in 1970.

Basic considerations of oral health

Some basic considerations of oral health are reviewed below, with emphasis on the prevention of poor oral health in adulthood by attention to problems arising in childhood.

The deciduous teeth

An unhealthy mouth in an adult is often a direct result of neglect of the mouth and teeth in very early childhood. The mere presence of a healthy set of first teeth may well ensure the foundation of adequately developed and balanced adult jaws. If these first teeth are to be retained to perform their normal function as "foundation" teeth, they must be properly cared for throughout their existence. In order to accomplish this, proper care of the teeth should be established in infancy, for irreparable damage may be caused to the mouth of a very young child by sheer neglect before he or she has reached the age of 2. Ignorance or indifference amounting to neglect on the part of parents is the cause of the majority of the dental troubles of toddlers. Such troubles are very often preventable or capable of correction by comparatively simple methods.

Infections of the soft tissues of the mouth are rarely observed in healthy children. With systemic diseases that cause catarrhal obstruction to nasal breathing, the child may be compelled to breathe through the mouth, with the result that the oral mucosa becomes dried and fissured. The fissures provide pathways for the penetration of bacteria and fungi into the mucosa so that stomatitis, such as thrush, can develop.

Between an erupting tooth and the surrounding gum, there is a crevice into which food and bacteria can penetrate. Provided the baby is in good health and the mouth is well cared for, no trouble will develop, but should the food remain undisturbed in this crevice it will stagnate and ulceration of the gum will take place. Depending on the health of the child, the infection may spread to the mucosa or gum tissues around a tooth and produce an infection of the whole mouth that may involve the tongue as well.

From about the age of 6 months, a variety of symptoms in infants are attributed to erupting teeth. As this age, antibodies are at a minimum and the child is prone to infections that may not be very obvious. It is also the period of weaning. Many symptoms of the milder systemic diseases, such as colds, coughs, respiratory infections, and alimentary upsets, have been blamed on the teeth. Carpenter (5) reviewed the literature, which indicated

that many "teething troubles" are undiagnosed systemic conditions. He then surveyed the records of 528 well babies and found that, whereas one-third experienced no disturbances during the eruption of primary teeth, the remainder experienced one or two. He regretted the absence of virology studies to confirm the absence of systemic upsets. Parents still use a variety of methods to pacify children during teething, in the form of comforters or bottles filled with sugary fluids. These can produce rapid caries of the teeth and it is not uncommon to see a child of 3 years who, owing to gross parental neglect, has no front teeth.

A child without front teeth is often a child with decay in other teeth, and the extraction of all deciduous teeth by the age of 3 is a fairly familiar practice. The child may have to cope with a new kind of diet because of inability to chew food; later he may encounter social problems at school, for a child with no teeth is liable to be ridiculed by other children. The occasional gap in the front teeth is normal evidence of the exfoliation of deciduous teeth at the age of 6 or 7, when the permanent incisors are erupting, but a total lack of teeth at 5 is unusual. Apart from affecting ability to chew and masticate, the absence of "foundation" teeth may lead to malposition of the adult teeth.

These are some of the relatively unassessed consequences of inadequate dentition which are a subject for ridicule in the child and which also affect the adult. The foundations for a healthy adult mouth may be destroyed before the age of 3 is reached, and it is clearly important to ensure that prevention is established early in life, thus influencing the attitude of the adult to dental health.

It is well known in health education that unless a disease is perceived to be harmful, it is unlikely that the individual or the public will see any value in preventive efforts. It is easier to arouse interest in the prevention of diseases that shorten life than in the prevention of those that appear to produce only irritating minor symptoms. The general public does not seem to realize that dental disease is not a simple irritant but a group of disorders that can aggravate poor health, weaken general health, and—for a few patients—shorten life considerably. Because of the widespread distribution of dental caries and gum disease, dental disease is considered to be a normal part of life in many populations. It may therefore be of value to consider ways in which such disease can influence a person's life so that its effect and the value of its prevention can be viewed in perspective.

The value of adult teeth

Teeth are of value to the individual in several ways. First of all, they contribute to personal appearance. Children without teeth can become laughing-stocks at school, and a child with poor teeth often refuses to smile—in fact, this may be the first sign of a child's anxiety about the appearance of his or her teeth. There have been many reports (19, 21) documenting this relationship between the appearance of the teeth and people's self-esteem.

As well as contributing to personal appearance, both the front and the back teeth are of great functional importance because of their role in mastication. Degrees of dyspepsia occurring in persons with few molars have not been correlated with the number of missing teeth, but there are reports associating dyspepsia with the swallowing of an unchewed bolus of food. It is worth mentioning that dental disease can occasionally have lethal consequences—for example, infective endocarditis following the removal of teeth.

The extent of the problem of dental disease in adults has not been fully estimated. While attempts have been made to assess the consequences of untreated dental disease, it is doubtful whether suitable methods exist for doing so. There are indices to describe the extent of dental disease, whether caries or periodontal disease, but they cannot easily be expressed in terms of the effect on the quality of life of the patient.

Consequences of dental disease

One obvious consequence of dental disease is pain or severe discomfort. It has been estimated that in the United Kingdom each person may, on average, suffer as many as 3–4 days of pain of dental origin per year (16). Thus there could be as many as 200 million days of dental pain per year in the United Kingdom, so that dental disease probably can be very seriously compared with most other forms of sickness as regards its role in certified absence from work. Although it is unlikely that dental pain will cause prolonged absence, it will probably impair working skills and occasion absence from work for treatment. Children suffering from pain of dental origin can cause their parents to lose hours of sleep, with debilitating effect. Because of its frequency, toothache is sometimes accepted with resignation as a part of normal life. It is clearly, however, a major source of economic loss both to the individual and to his country.

A further disastrous economic consequence of dental disease arises from the very high cost of dental care. This is especially so in the less affluent countries, in which money that might be spent on preventing highly prevalent and dangerous infectious diseases is channelled into restorative and rehabilitative services for dental patients.

Many of the consequences of the early loss of deciduous teeth can be corrected by orthodontic treatment, but this is not available in many parts of the world; where it is available, it may be too expensive either for the patient or for the social system providing it. In skilled hands, extractions can be planned to minimize the consequences of the premature loss of deciduous teeth, but this is perhaps difficult to teach economically. Therefore the maximum should be done to prevent such a loss.

Twisted or badly placed teeth in the adult have an unfavourable effect on personal appearance and make parts of the mouth more difficult to clean, either by natural mastication or by artificial substitutes for brushing, so that gingival or periodontal troubles will develop. These may lead to loss of

support for the teeth and to loss of permanent teeth. It is the aim of preventive dentistry to help the child's mouth to develop in such a way that there will be no undue stresses on any particular tooth or group of teeth in adulthood.

Etiology and prevention of dental disease

Of the childhood dental diseases which can affect the adult, the most important in the developed countries is dental caries. There is little doubt that the prevalence of dental caries is directly associated with the intake of refined sucrose as much as with any other factor. Countries that have a very restricted intake of sugars—for example, Thailand—have a very low caries rate. Countries such as the United Kingdom, which has a high intake of sugars, have a high caries rate (10). The absence of dental caries does not necessarily ensure good dental health, for in Nigeria dental problems are associated mainly with nutrition and periodontal disease (7). One object of dentistry is to maintain the patient dentate and free from dental disease throughout adult life. It is possible to bring a child to adulthood free from dental disease and free from disfiguring irregularities of the teeth. This can be done by therapeutic methods, but often these cannot be applied because of insufficient knowledge of the patient and the patient's family. The prevention of dental disease depends to a great extent on knowledge of social or ethnic attitudes and habits of life, including eating habits. Dental caries develops from the accumulation on the teeth of deposits of plaque from saliva and from food containing sugars; in the presence of bacteria, acid is produced which erodes the teeth. Diet can influence both the initiation and the progress of dental decay in two distinct ways: (1) through its content, particularly the amount of sugars, and (2) through the frequency with which food is taken into the mouth, whether it is taken at regular mealtimes, in the form of snacks, or in the form of sweetmeats between meals.

The rate of dental plaque formation is related to the intake of sugars into the mouth (13). The rate of dissolution of the enamel of the teeth, and hence the rate of caries, is related to the retention of sugars in the plaque against the surface of the enamel (11). Thus a preventive programme should seek to persuade people to reduce both the volume and the frequency of the intake of sugars in their diet. This can be achieved more easily by encouragement than by prohibition. Much can be done through diet analysis, but eventually it will be necessary to develop some form of "sugar drill" to help children to control the intake of sugars in the same way as they are taught the dangers of traffic by means of "kerb drill". Attempts at "absolute prevention" are liable to fail when children eventually go out on their own and are tempted to indulge in sweetmeats by their friends and by what they see in the shops. Knowledge of the mechanism whereby sugar is held against teeth by plaque and of the sugar content of different foods will help people to decide which of them they would prefer to have. Bibby &

Mundorff (2) studied the destruction of dental enamel by the acids from snack foods and found that there were several contributory factors.

It is now possible to advise patients on the relative effects of some foods in causing damage to dental enamel. In addition to the fundamental task of encouraging people to steer clear of caries-producing foods, it is also necessary to see that this measure is supplemented by oral hygiene and mouth-cleansing. Ideally, teeth should be cleaned after every meal. However, although there is some doubt whether brushing can clean all the surfaces of the teeth completely, there is no doubt that brushing the gums in childhood lays the foundation for maintaining gingival health in adulthood. Pending confirmatory evidence of the efficacy of brushing the teeth, it is important to continue stressing the undoubted value of brushing the gums. It is impossible not to clean the teeth in brushing the gums.

It is apparent that a primary object in the prevention of dental caries is to reduce both the amount of sugars in the diet and also the frequency of sugar consumption. Before considering how to achieve this, it may help to consider the possible reasons why people eat "sugar" foods. Apart from habit, these foods are eaten to assuage hunger. Hunger may be satisfied by many means but in simple nutritional terms carbohydrates ("sugars") satisfy hunger for a shorter period than proteins or fats. The hunger reflex will be calmed for longer by a meal with an adequate content of protein or fats than by one based on carbohydrates. An example is provided by children going to school; if, at the beginning of the day, they have a meal containing protein and fats, their hunger reflexes will be satisfied for an hour or so. If they have no breakfast, they will be hungry and will get into the habit of having snacks at mid-morning, thus making themselves less hungry for the protein meal at midday. A vicious circle develops whereby the child comes to nibble carbohydrate snacks every hour or so throughout the day and does not receive a balanced diet with adequate protein. In addition, the habit of assuaging hunger by carbohydrates can lead to obesity in later life.

A properly balanced diet should satisfy the hunger reflex for a reasonable period and needs to be established early in life. The value of such a diet for dental health has been shown by Bradford & Crabb (3), who reported on an 80 % reduction in the caries rates among a group of children whose parents restricted their carbohydrate intake.

Fluoridation

Once the foundations have been laid, through diet control, for good eating habits that will leave a minimum of cariogenic debris in the mouth, it will probably be necessary to take some additional preventive measures. These will undoubtedly include the provision of sufficient fluoride in water supplies to ensure the minimum occurrence of caries. It was in 1892 that Sir James Crichton-Browne first asserted that fluoride would benefit the teeth and reduce caries (6). But it was not until 1933 that it was shown how the

incidence of dental caries could be influenced by the presence or absence of 1 mg of fluoride per litre in the domestic water supply.

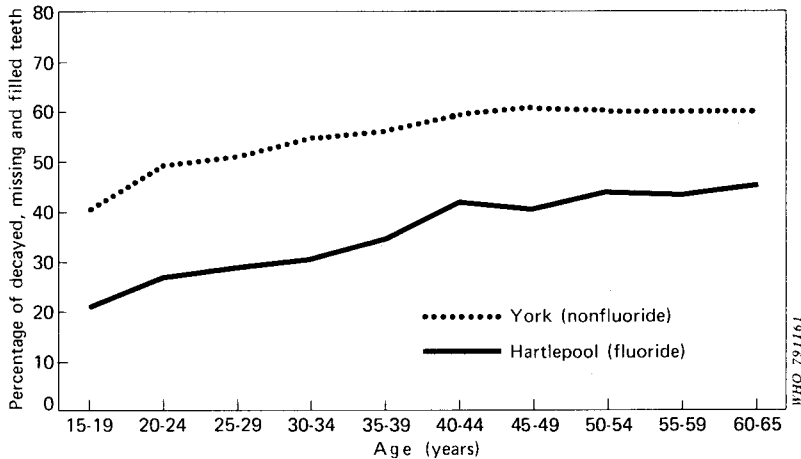
Fluoride occurs in all foods to some extent and is thus a normal part of the diet, but the level in domestic water supplies can vary. Excessive amounts in water are associated with white spots on the teeth. By adjusting the level of fluoride in the water supply to an optimum concentration of 1 mg per litre, dental caries may be reduced without any untoward effects.

Since 1892 there has been considerable research to find out whether adjustment of the fluoride content of water supplies to 1 mg per litre would lead to adverse side-effects. Since 1940, a whole series of studies (9) has failed to demonstrate any undesirable effects due to this measure. Excessive amounts of any chemical—even water—can have adverse effects on the body, but with fluoride at 1 mg per litre the safety margin is wide and the risk minimal, especially when balanced against the undoubted benefit of the fluoridation of water supplies to children. There are those who assert that people should not be deprived of the right to drink water in its “natural” state; others consider that children living in a civilized society have a right to benefit from the advantages of civilization as well as suffering the disadvantages. Fluoridation has been legally validated in some countries after demonstration that the adjustment of the water supply to contain 1 mg of fluoride per litre is beneficial and improves the wholesomeness of water. For countries not to adjust the fluoride content of a water supply, when desirable and possible, could today be properly said to be grossly negligent.

Fluoride when provided in controlled quantities in public water supplies and taken for a lifetime will benefit not only the child but also the adult. Many reports on the subject have stressed the success of fluoride for children in particular, chiefly because it was easier to assess the effects of fluoride in children. People who have lived all their lives in areas with fluoride in the water supplies have been shown to retain more teeth to the age of 65 than those in areas without fluoride in the water supply (18) (see Fig. 1). It has been shown that the cementum of the roots of teeth contains fluoride, or absorbs it, as the gums recede in the aging process. It has been observed that cavities develop rapidly in cementum that has been exposed by scaling at frequent intervals; it may be that scaling removes the protective fluoride layer from the surface of the cementum. There is little doubt that adults will benefit from fluoride in the water supply if they have retained their teeth.

It is not easy to provide a fluoridated water supply to communities that are isolated and may depend on individual sources for their water supplies. In such places it is possible to arrange for the household treatment of water but this would depend a great deal on the conscientiousness of those looking after the treatment system, and alternative methods of fluoride supplementation, might have to be considered. In schools the fluoride content of the water supply can be increased to as much as 5 mg per litre so that, during part of the day, children may have the supplementary fluoride necessary to prevent some degree of dental caries. Supervised group

Fig. 1. Effects of fluoride in water supply on retention of teeth: data from two British cities



Source: Murray (18).

application of fluorides, especially in schools, whether by tablets, rinses, or pastes (see below), are worth encouraging.

Other ways fluoride supplementation have been considered, such as the adjustment of the fluoride content of milk, but this has as yet proved to be only of moderate value and is limited to countries in which children drink milk. Another system is to add fluoride to domestic salt (15). Where such methods are not used and where fluoride is not provided in the water supply, consideration should be given to supplements in the form of lozenges that children can suck or in the form of drops to be added to their drinks. There is evidence that the fluoride is not only incorporated systemically into the structure of the tooth, but is also absorbed on to the surface of enamel from fluids passing through the mouth. If these fluids contain fluoride, they will add fluoride to the teeth; if they do not contain it, they may wash away some fluoride from the surface of the teeth. Tablets, lozenges, or drops containing fluoride can be prescribed by a dental practitioner, who will know the level of fluoride in the domestic water supply and will thus be able to prescribe accurately.

In addition to public health measures or dietary methods of increasing fluoride intake, fluoride may be applied to the teeth either by dental personnel or by children themselves in a variety of ways—i.e. as stannous fluoride or as sodium fluoride in various concentrations (4) applied to the teeth after cleaning. These have produced reasonable results but have yet to be shown to be cost-effective as a public health measure. None of the topical methods (for example, gels, mouth rinses, and varnishes) are as effective as water fluoridation, but they are useful when this measure is not

feasible. They are especially valuable in mouths where teeth have been neglected and there are particular problems that need to be corrected very rapidly. The relative merits of these various methods of topical application are still being assessed but they all appear to be of some benefit. Children (and older persons) should be encouraged to use fluoride toothpaste to reduce dental caries.

Timing of preventive care

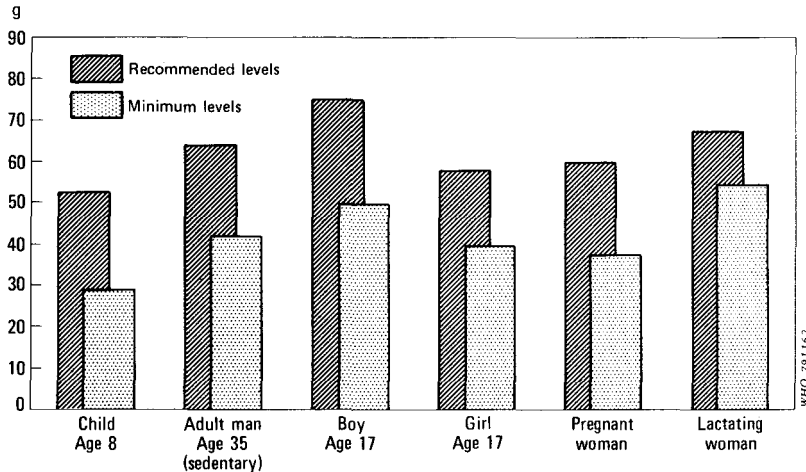
There are many views as to the ideal time at which to advise a mother on the dental care of her child. At present it is thought best to influence the mother while she is pregnant with her first child and possibly has more time to devote to herself than she will have in later pregnancies. She should be given normal dental treatment for any neglected teeth, together with advice on preventive dental care for herself and later on for her child. This will include advice on diet during pregnancy and the need for adequate nutrition, especially during lactation. There is no need to add special supplements to the diet to meet particular needs of the teeth, which will receive such substances as they require from the mother. A suitable diet for pregnancy is available from several sources; in the United Kingdom, the *Manual of Nutrition* (17) is one source:

After the expectant mother, the next major target chronologically is the child who is about to become an adult; the appropriate age will differ from one society to another. It is when children are beginning the adolescent growth spurt that one should stop treating them as children and start treating them as adults responsible for their own bodies and their own oral health, on which they should be given suitable advice. It may be necessary to tell parents that their "developing adult" needs considerably more protein than they may realize and refer them to the recommended protein levels for adolescent boys and girls (Fig. 2). From the age of 12 the adolescent will need as much energy as a sedentary adult, and from the age of 15 he or she will need as much as all but the most active adults in protein as well as in general energy. In addition to chemical needs, a greater fluid intake will be required as new cells develop during growth. These facts should be remembered when advising adolescents on eating and drinking habits. If they understand the needs, they may learn to select foods and beverages that do less harm to the body, including the teeth.

Future research needs

It was first proposed by Macphee in 1934 (14) that a vaccine might be developed to immunize children against dental caries. In recent years this idea has been studied in more detail (12) in connexion with the development of a vaccine against *Streptococcus mutans*, which is associated with many of the various lesions of enamel. At present the method is still at the

Fig. 2. Recommended dietary protein levels



Source: Ministry of Agriculture, Fisheries and Food (17).

experimental stage; it has been shown that it is possible to produce such a vaccine for use in monkeys and that it can reduce the incidence of dental caries. However, much work will have to be done before such a vaccine becomes a practical proposition, though childhood immunization unassociated with complications would clearly be of very great benefit in promoting good oral health in adulthood.

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Mental health

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The history of the child guidance movement in the USA can serve as a cautionary tale against excessive claims about preventing mental health problems in adults by intervening in childhood. This movement, from the 1920s, when it began, to the 1960s, when its results were given sober reconsideration, suggested that mental illness in adults could be prevented by the appropriate treatment of children. On the basis of the psychoanalytical theory that psychopathology in adults has its origin in arrested psychosexual development during childhood, it was assumed that, if interruptions in emotional maturation could be prevented or treated in childhood, children would grow up able to cope with stress in their adult lives, and consequently be healthy and happy adults, free from mental illness.

Treatment was to be offered by a mental health team consisting of a psychiatrist, a social worker, and a psychologist. Together they would evaluate the child and plan a programme of psychotherapy for him and his family. In practice, this plan was seldom carried out. After the battery of test results and recommendations for therapy, only about one child in four returned for treatment (1). Sometimes the acute problem had subsided by the time evaluation was complete, and sometimes the child and his family would not cooperate in the ways required. Children referred for problems of acting out (the majority of referrals) were often not good psychotherapy patients, being restless in the face of long, confessional conversations with a psychotherapist. Often a child was not accepted for treatment unless a parent was willing to be treated as well, and on a frequent schedule. Parents of acting-out patients typically had behaviour problems of their own and were poor at keeping appointments or following the social worker's suggestions about handling the child at home.

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Nor were the problems solely problems of compliance. Even in cases in which the recommended therapy actually went forward, it soon became clear that the claims for the type of treatment offered were exaggerated. When evaluation studies included control groups, so that the contribution of spontaneous improvement could be taken into account, findings were uniformly discouraging, even in the short term (13). While there undoubtedly were subgroups of children for whom treatment worked well, it was not possible to show replicable results attributable to anything more than chance, even in most carefully conducted studies. There have been very few attempts to learn whether the therapy was effective in reducing disorder in adults, but a recent evaluation (14) indicates that not only was it not helpful, but may actually have been harmful.

It may be just as well that the child guidance movement's promise that psychotherapeutic treatment in childhood would prevent disorders in adulthood was not fulfilled, because, if it had been, the attempt to provide psychotherapy for the estimated 15–25 % of children generally believed to have emotional or mental problems would have placed an enormous financial and educational burden on any government that took its obligations to the mental health of its citizens seriously.

Disillusionment with the traditional child guidance techniques for solving children's problems led to the development of a set of alternative treatments for children, some of which have shown extremely good results on a short-term basis. It has been found possible to reduce behaviour problems at school in children diagnosed as hyperactive by means of stimulant drugs, and children displaying aggressive and uncooperative behaviour in school and in institutions have been made to remain in their seats and accomplish more of their schoolwork through the use of various behaviour modification techniques. Intensive tutoring and the nursery school approach have been found to raise the IQs of preschool children from poverty-stricken homes. The fears of children who had phobias about animals have been effectively reduced by relaxation and by showing unfrightening representations of the animals concerned; the treatment of phobias about school through the rapid return of the child to school, sometimes supplemented by drug therapy, has been successful as well. While this array of up-to-date techniques makes it possible for therapists to select the one that is most appropriate for a particular child, rather than offer psychotherapy to all, we still are not sure that these techniques can prevent psychiatric disorder in adulthood. The first few efforts at following up children treated with these methods over a period of time have been disappointing. The IQ advantage attributable to preschool tutoring usually disappears within the first years of school (29). The behaviour modification techniques that quieten unruly school behaviour seem to require continual reapplication (18). Stimulant drugs, which sometimes have dramatic effects in controlling the schoolroom behaviour of hyperkinetic children, apparently do not help them to achieve a normal level of learning and do not prevent an elevated rate of adolescent delinquency and acting-out behaviour (30). The childhood fears overcome by relaxation and de-

sensitization do not reappear, but many of them would have disappeared spontaneously even without treatment, and so, even here, the value of childhood treatment in altering expectations for mental health in adulthood has not been demonstrated. A number of the newer therapies found effective in the short term have not yet been studied for their long-term impact. Early stimulation of children of mothers with low IQs from impoverished households has had particularly impressive results (11). Whether these will turn out to have beneficial effects that stretch into adulthood remains to be discovered.

Given that therapies that have proved extremely helpful to children have yet to be shown to have effects that carry over into adulthood, it may seem presumptuous to suggest that, nevertheless, there are certain types of attention to children that seem likely to be of some success in preventing mental health problems in later life. What we know about the association between the events of childhood and mental health in adulthood suggests some preventive strategies, encompassing activities other than those usually conceived of as treatment for disturbed children.

Before considering these, we still need to ask whether the mental problems of adults do indeed have their roots in childhood. Here the evidence seems overwhelmingly positive. Many psychiatric disorders run in families in ways that suggest the influence of common genes and common childhood environments. Others virtually always begin with childhood symptoms, and yet others are associated with perinatal problems and childhood disease. If childhood is defined as the period from conception up to the age of 16–18 years, then there are a variety of ways of reducing the risk of future disorders during childhood. Among these, in addition to treatment, are genetic counselling, prenatal and postnatal physical care, and efforts to prevent the occurrence of those childhood emotional and behavioural disorders often known to continue into adulthood.

Prevention through prenatal services and general health measures

In the last 30 years, many psychiatric disorders have been shown to have a genetic element. Virtually every study of the family histories of psychiatric patients has shown a higher than average rate for the same psychiatric disorder among their relatives (26). By itself, this does not prove that genetic factors are involved, since families provide their offspring with environments as well as genes. However, studies taking advantage of the “natural experiments” of twinning and adoption have shown that there almost certainly is a genetic component in most psychiatric disorders. Mental retardation and schizophrenia have both been shown to have a higher incidence in the remaining twin when a monozygotic rather than a dizygotic twin is the one affected, and a child adopted at an early age who has a schizophrenic natural parent is more liable to have schizophrenia than an otherwise comparable adoptee with no schizophrenic natural parent. There appears to be a genetic component even in disorders

that have traditionally been interpreted as reactions to environmental stress, such as depression and alcoholism, or to economic and cultural deprivation, such as antisocial personality. Even disorders of sexual identity, which almost by definition rarely come to the child through his parent's example, seem to have a genetic component, since concordance in this respect is higher in identical than in fraternal twins.

It was popular a few years ago to question whether mental disorders were genetic *or* environmental. It is now recognized that both types of factor almost always play a part, and the question to be asked is what environmental factors foster or suppress the expression of the genetic predisposition. This change of approach has emerged as a result of studies of identical twins, in which there are almost always discordant cases to be accounted for, even when the evidence for a genetic factor is strong. However, if the studies referred to earlier are correct in showing that a genetic predisposition often plays a role in psychiatric disorder, then it is possible, at least in principle, to prevent a proportion of cases by discouraging those affected from having children.

Unfortunately, however, genetic counselling may not be a practical way of effecting a marked reduction in rates of psychiatric illness in the population, even though it can help prospective parents in deciding whether or not they want children. The prospective parent wants to know what the risk is that the next child will have the disorder, and how long a genetically vulnerable child is likely to remain healthy, should he or she contract the disorder eventually. If both the prospective parents have the same disorder, the risk may well be high enough to justify a decision against having children. Society, on the other hand, is not so much interested in the chance that a particular parent will have a disabled child, but rather in the proportion of such children born to parents in whom a genetic risk can be shown. Society is also interested in knowing how long persons who develop a disorder are likely to survive after they fall ill, since that determines how long society will have to bear the costs of their treatment and support. The proportion of all cases in the population that are the offspring of parents with the disorder is usually rather low. The incidence of disorders that appear early enough in life to interest prospective parents in genetic counselling is particularly low, and consequently, even if all those affected refrained from having children, this would have relatively little effect on the incidence in the population, to which the principal contribution is made by offspring of parents who are not affected. Indeed, the procreation rate among persons affected during the reproductive years is often low, because they are hospitalized or socially unskilled and thus unlikely to have children. Thus, while the risk of two schizophrenic parents having a schizophrenic child is high, only a very small proportion of schizophrenics are born to parents both of whom are themselves schizophrenic. Even if all schizophrenics refrained from having children, there would be little change in the incidence of schizophrenia.

While genetic counselling cannot, then, hope to bring about any marked change in the incidence of specific psychiatric disorders suffered by one or

both of the prospective parents, counselling about having children has other potential preventive benefits. The fact that parents who are psychiatrically ill often cannot take good care of their own children and so rear them poorly, or allow them to be placed elsewhere, may make the children vulnerable to disorders other than those affecting the parents (5). Family planning may make a particularly important contribution to reducing the number of mentally ill offspring of parents who abuse alcohol and drugs and who engage in antisocial behaviour. Such people are common in many populations and notoriously poor parents. Unfortunately, they are also particularly unlikely to seek advice about family planning or to comply with such advice with the necessary regularity. Still, many of them are not eager to become parents and thus would have no objection to using methods requiring relatively little effort and forethought.

The value of family planning is not restricted to parents with mental disorder. One way in which it can presumably help to reduce mental illness in adults is to diminish the number of very large families. There is considerable evidence in the literature that children from such families have more difficulty in school and more behaviour problems than do children from smaller families, unless the family they come from has considerable economic resources (31). In addition, the outlook for adulthood is worse for children with behaviour problems from large families than for children with similar behaviour problems from smaller families (20).

Another vulnerable group whose numbers may be reduced through family planning are the offspring of very young or unusually old mothers. These mothers have higher proportions of children who are premature, and of children who are too small among those who are full-term (19); such infants appear to be at high risk for neurological disorders and mental defects. For children born to very young mothers, the risk of poor school performance is higher than for children born to less young women from similar economic backgrounds, even in the absence of obvious neurological damage (6). In addition, early childbearing, particularly in the event of multiple births, puts the mother herself at risk of psychiatric and social problems later on (2, 3, 17). Ways must be found to make family planning not only available but useful to these groups. While teenagers having their first illegitimate infant might be expected to welcome contraceptive advice, its availability in prenatal clinics has not effectively prevented further pregnancies (23). Presumably what is needed is a more continuous form of support and instruction in easily accessible locations.

While being no panacea, family planning should be seen as a potentially effective method of preventive psychiatry, since it can reduce the number of children who are not only vulnerable to inherited genetic defects, but also likely to be small at birth, to be members of very large families, and to be born to parents of the kind least able and willing to care for them.

Another useful approach to preventive psychiatry is through improvement of the physical health of the population. Many studies have shown a strong relationship between physical and mental disorder, both in child-

hood and in adulthood. Every study of the utilization of general medical services by psychiatric patients, and by others, shows that the psychiatric patients have more recourse to these services. Not only do mentally disturbed patients visit doctors more frequently, but they also have more diagnosable physical illness (10). At one time, their high utilization of services was considered only as an indication that the psychiatrically ill were complainers and hypochondriacs. But more recent health surveys suggest that this is not the whole answer. It appears that there is actually more physical illness among persons with mental problems. In some, the stress of the physical illness may have triggered off the mental disorder. Some physical illnesses affect brain function directly, along with the functioning of other organs. Finally, genetic links have been discovered between certain physical and mental disorders. One such link is between Down's syndrome and cancers of the blood. Whatever the reasons, psychiatric and physical illnesses do seem to go together, and it is by no means clear that the psychiatric illness always comes first, provoking either actual physical illness or complaints of illness.

This relationship between psychiatric and physical illness has been confirmed in studies of children (22). Children with physical illnesses, particularly congenital neurological disorders, have a strikingly high rate of psychiatric disturbance. Sometimes there is no known reason for the association, but it seems probable that any disorder affecting the brain, as neurological disorders do, is likely to have a psychiatric expression as well. One well-known example is that of encephalitis, often a consequence of infectious diseases of childhood. Thus, immunization against infections in childhood would have preventive value, as would rapid treatment of the childhood infection to avoid psychiatric sequelae. Since the encephalopathies have long-lasting and irreversible effects, such intervention should reduce the incidence of psychiatric illness in adults.

Childhood infections are definitely more devastating in malnourished children. While the relationship between children's general level of nourishment and other aspects of their early mental development is not yet completely clear (27), a good level of nutrition in early childhood would appear to be helpful in preventing the psychiatric sequelae of infections as well as obviously desirable on grounds of general health and humanity.

Ingestion of lead (usually as a result of eating paint) has also been shown to affect children's IQs and school performance (particularly by increasing distractibility), even when there is no clinical evidence of lead poisoning. Since school behaviour is predictive of adult functioning, even such a simple public health measure as prohibiting the manufacture of leaded interior paints can be expected to reduce the burden of mental handicap in adults.

The neurological conditions associated with psychiatric problems in children are also associated with prematurity and being small for gestational age at birth. Since prematurity is particularly common among the offspring of poor women, who usually get little prenatal care, it was hoped that the provision of such care might prevent them from having

premature babies. Unfortunately, recent evaluations of the relationship between the amount of prenatal care and the birth weight and health of the infant have been decisively negative (19). Nevertheless, certain preventive measures in the prenatal period should be effective. Mothers who smoke or have high blood pressure are more liable than others to have small infants. Persuading pregnant women to reduce their smoking and treating them for high blood pressure should thus improve their chances of carrying infants of normal weight to term. This in turn should improve the infants' chances of good mental health later on.

Other important preventive measures include immunizing prospective mothers against infections that, were they to contract them during pregnancy, might damage the fetus neurologically, and in warning women of childbearing age against the heavy use of both licit and illicit drugs, including alcohol, at any period during which they might become pregnant, or while nursing. Although it is not yet clear how much the increased risk of behaviour and learning problems in childhood and of subsequent addictions experienced by the offspring of drug abusers is attributable to direct exposure to the drugs consumed by the mother while the child is *in utero* or being breastfed, rather than the mother's genetic contribution and faulty child-rearing practices, there is circumstantial evidence that the higher rates of neurological abnormality in these children may be due, at least in part, to the direct effects of chemicals on the developing nervous system.

In sum, it should be possible to prevent psychiatric disorders in adults to some extent by encouraging well-baby clinics, prenatal care for mothers (particularly with an eye to discouraging smoking and the heavy use of drugs and alcohol and reducing blood pressure), the immunization of young children and prospective mothers, and any public health activity that reduces the risk of infection, including adequate nutrition. In fact, there is no conflict or competition for manpower between programmes to prevent mental illness and programmes to prevent physical illness and debilitation, since each type of programme supports and reinforces the other.

Disorders of childhood that foreshadow disability in later life

There is ample evidence that many psychiatric disorders of adult life are foreshadowed in childhood. In some cases, the disorder begins in childhood and continues into adult life, while, in others, although the disorder is not diagnosable until young adulthood, it is frequently prefigured by certain abnormalities in childhood.

The most serious of the disorders beginning in childhood are the childhood psychoses and severe mental retardation. With few exceptions, children with these disorders are sure to continue to be ill as adults. For other disorders of childhood, the chances of carry-over into adulthood may be considerable, even if not complete. Examples are children's phobias. While these usually dissipate before adulthood, phobic adults can

nevertheless usually trace the onset of their phobias to their childhood. Similarly, conduct disorders of childhood and hyperactivity frequently improve in adolescence. But many children retain these traits and grow up to become antisocial adults. Disorders of sexual orientation—homosexuality, transvestism, and transsexualism—seem, like antisocial personality, always to have their beginnings in childhood. It is not known how often these dissipate before the child becomes adult, although Green (9) has shown that the rate of recovery from marked femininity of behaviour among boys is low.

Drug addiction and alcoholism are usually thought of as adult disorders. It has been found, however, that they almost always begin with the use of the dependence-producing substances in childhood (12). Heavy drinking and drug use that start after adolescence apparently rarely result in clinical disorders. The occasional case of late onset generally occurs in the context of another psychiatric disorder, such as depression or mania, or among adults who have had no access to the dependence-producing substances in childhood because they were brought up in abstinent cultures.

The only disorder typically beginning in adulthood that has frequently been reported to have early childhood prodromata is schizophrenia. Among schizophrenic men, there is evidence that early in life they tend to display an excess of acting-out behaviour and poor performance in school; whereas, among schizophrenic women, there is sometimes an early history of excessive conformity in childhood (28). For other psychiatric disorders with adult onset, such as depressive disorders, mania, and panic disorder (anxiety neurosis), there is no clear evidence of premonitory signs in early childhood. While "neurotic" and "depressive" symptoms are often seen in early childhood, these usually dissipate without an increased risk of disorders later on (20). Only the onset of a disorder in adolescence is clearly linked with its continuation into adulthood (7). Consequently, the opportunities for preventing affective disorders and neurosis through direct intervention in childhood are not great.

Treatment of childhood disorders

Nevertheless, because many adult disorders do begin in childhood, if they could be successfully treated in children, the rate of psychiatric disorder in adults might very well be reduced, as the child guidance movement promised. Its failure to keep that promise may be attributable in part to the fact that the childhood symptoms on which the greatest effort was concentrated were just those neurotic and depressive symptoms of early childhood that have been found not to forecast disorders in adulthood. But even had it concentrated on the disorders that do involve a high risk of continuation into adult life—e.g., the childhood psychoses, mental retardation, sexual orientation problems, drug abuse, and conduct disorders—the results might not have been very different. While current treatment techniques are useful, no cure is yet available for any of these

childhood problems. In the absence of adequate treatment, the emphasis must be on the development and evaluation of therapeutic methods. The fact that many children recover "spontaneously" from these disorders probably means that they are responsive to some environmental effects. Through case-history studies, we should be able to learn under what conditions these disorders dissipate. The next step is to develop and test methods for reproducing these conditions for children not lucky enough to experience them by chance.

Perhaps the greatest challenge is to develop techniques for handling antisocial behaviour, including drug abuse, in childhood, because it is so common and because it has a comparatively poor prognosis. Although about half of those displaying severe antisocial behaviour in childhood do recover spontaneously, the costs both to the individuals themselves and to society, in the case of those who fail to recover, are enormous in terms not only of treated mental illness but also of failure to support themselves and their dependants, criminality, broken homes, and transmission of the disorder to the next generation. The development of more efficient ways of interrupting the process is thus a matter of the highest importance.

In seeking new treatments, it is important to evaluate the long-term effects of the new techniques that seem to be successful in the short term, in particular, the methods of stimulating and educating very young children that are said to be capable of preventing mild mental retardation in children of parents with low IQs (11). If these treatments are found to have long-term beneficial effects, it will then be necessary to try to determine their essential features so that it may become economically practicable to offer them on a large scale.

Prevention through a better home environment

In addition to developing better methods for the treatment of children, we need to apply what we now know about giving children home environments that will minimize the risk of their developing the psychiatric disorders that continue into adulthood. It has already been mentioned that children born to psychiatrically ill parents are at high risk for poor parental care and/or placement out of the home (4). For illegitimate and institutionalized children, adoption has been shown to be an excellent preventive strategy (24, 25). Skeels' study (25) shows that the gains in IQ experienced by children who leave institutions for adoptive homes last into adult life. While the adoptees in the Seglow study (24) have not yet become adults, their adequate school functioning promises reasonably good mental health as adults (20). In addition, studies of the offspring of criminals and alcoholics that compare those reared by their parents with those adopted by others show lower rates of adult criminality and alcoholism in the adoptees (8, 15, 16). Thus there is good reason to think that the provision of replacement homes for children who cannot be properly reared by their own parents would be helpful in reducing the rate of mental disorder in

adults, although this measure clearly raises the ethical problem of the parents' rights concerning their own child. It also involves the important responsibility of ensuring that the alternative homes provide warm and stable environments. Frequent changes of foster homes and institutions and absence of opportunity to form close relationships with foster parents or staff can also be damaging. When children are to be adopted, it is important that the decision should be made early. In many developed countries, a delayed decision means that the child is constantly moved from one foster home to another and in and out of his parents' home. While the evidence is not as comprehensive as one might wish, this seems to be a damaging experience.

There has been a recent increase in concern about child abuse. Not only can beating by parents endanger children's lives, but "battered" children have a variety of emotional and learning problems. In some cases, these problems undoubtedly precede and trigger off the parental abuse, but the abuse itself undoubtedly creates or worsens some problems. Abusive parents often have histories of being abused as children themselves and seem to be repeating the only child-rearing practices they know. This suggests that an effective preventive approach might be to make training in parenthood a standard feature of the educational curriculum. Since those most likely to have problems with child-rearing are those who bear children very early and out of wedlock, it would be important to introduce the subject of child-rearing into the school curriculum in the early stages, so that it would reach students well before they were likely to have their first child or to drop out of school. If education on child-rearing is delayed until later, those most in need of it are likely to miss it. Because child abuse frequently arises from efforts to control and discipline infants and preschool children, particular attention should be given to alternative methods of producing behavioural change in young children.

Prevention through a better school environment

Preventive opportunities within the school are of two kinds: direct teaching of facts and skills that might prevent psychiatric disorder, and the provision of more supportive, less stressful learning environments.

Direct teaching

Ordinary teaching of academic subjects can be seen as contributing to some extent to mental health, since illiteracy and a low level of education certainly contribute to poor self-esteem and possibly, therefore, to mental disorder. Attempts to teach values and give information intended to reduce deviant behaviour have been made in some schools, but with doubtful success. It had been hoped that school programmes advising adolescents of the dangers of illicit drugs, alcohol, and tobacco would reduce the number

of users and teach moderation to the others. Unfortunately, there is as yet no evidence that such educational efforts are effective. At present, the only preventive methods known to have some effect are the control of traffic in illicit drugs and the imposition of a legal age limit for access to alcohol and tobacco. Such controls do seem to reduce the use of these substances, although much illegal use continues. Research to discover effective approaches in preventive education is badly needed.

School environments conducive to mental health

Schools vary markedly in the levels of achievement and degree of delinquency of their students. Most attempts to account for these differences have found the explanation to be more in the characteristics of the student body than in the characteristics of the school itself (31). However, efforts to identify characteristics of schools that are conducive to learning and good behaviour continue to be made (27). Little has been done to design schools so as to reduce the risk of psychiatric disorder in children by counteracting the negative effects that the school experience does seem to have on some of them. It has been noted, for instance, that mild mental retardation is generally detected when a child enters school and disappears as a problem when he leaves school. The fact that schools repeatedly measure and evaluate children is stressful for those who do not compete successfully. Children who experience failure at school seem particularly likely to become resistant to school authority and engage in truancy, fighting, stealing, and other forms of antisocial behaviour, which may be carried into adult life (22). Schools frequently cannot cope with these aggressive children and expel them, adding educational handicap to the personality handicaps under which they already labour.

In developing countries, pressures to perform well in school will increase, for rising educational requirements go hand in hand with industrialization. At the same time, families' geographical mobility will increase, as job opportunities arise in industrial centres and agricultural activities become less labour-intensive. This will lead to more frequent changes of school for children, which, in turn, is likely to lead to poor adjustment in school. Thus the number of children finding themselves early school failures and in conflict with school authority is likely to increase in the developing countries.

It is not yet known to what extent early school failure is a cause of school truancy and childhood aggression with which it is associated, and to what extent it is only the symptom of an existing disorder. To the extent that it is a cause, it should be possible to prevent behavioural disorders of childhood by limiting the frequency of changes of school and by protecting children from the experience of academic failure. One simple measure would be to allow children to continue in the same school after a local move, rather than having the place of schooling strictly determined by the place of residence. Industries might be asked to concentrate the long-distance moves of their

employees within school holidays, so as to avoid the need for changes of school and the resulting readjustments in the middle of a school year or term. More diversified curricula might be devised, so that children not ready to succeed at reading or arithmetic would have the chance of succeeding at other kinds of learning until they were ready. Exploring ways of making the early school experience fit the needs and abilities of more children may well be one of the most important preventive mental health measures of all.

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This paper has reviewed what is known about the prevention of mental disorder in adults through services to children. While there are many gaps in information on the subject, it appears that there are certain activities that can be expected to reduce the mental illness rates for adults. These include the following, whose order of importance will, of course, vary according to the circumstances:

- Readily available family planning services, particularly for teenagers.
- Limitation of access by children to supplies of psychoactive drugs, both licit and illicit, through legislation and law enforcement.
- The provision of good alternative homes for children whose natural parents are inadequate.
- Early decisions about putting children up for adoption.
- Good day-care programmes for young children with working mothers or with mothers who are unable to provide them with adequate early education because of their own educational deficiencies.
- Immunization for children and for women of childbearing age.
- Supplementary diets for children in impoverished families.
- Adequate medical care for children and for pregnant women.
- Avoiding changes of school as far as possible.
- Devising alternative school curricula for children with delayed ability to read.
- Addition of nonacademic material to the school curriculum to broaden the opportunities for achievement.
- Educating young women about the dangers to the fetus of ingesting drugs when they are or might be pregnant.
- Introduction of child-rearing as a subject in the school curriculum to be taught to children before or at the age of puberty, with emphasis on methods of managing infants' and children's crying, disobedience, and food refusal, since these are factors that frequently trigger off child abuse.
- A research programme with the following goals: (a) to develop better methods of treatment for children's psychiatric disorders and learning difficulties; (b) to develop effective educational programmes to reduce the abuse of dependence-producing substances by children; (c) to

develop educational methods that will help to reduce the number of teenage pregnancies; and (d) to study ways of reducing the harmful impact on children of frequent moves by their families.

To make such a programme a reality, methods need to be worked out in each country for a regular review of progress and the establishment of policy for the next phase. Every effort should be made to utilize existing pools of professional manpower to carry out the programme. Much can be done by teachers, nurses, and general practitioners who regularly have access to the mothers, children, and young people in the population.

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By means of direct technical cooperation with its Member States, and by stimulating such cooperation among them, WHO promotes the development of comprehensive health services, the prevention and control of diseases, the improvement of environmental conditions, the development of health manpower, the coordination and development of biomedical and health services research, and the planning and implementation of health programmes.

These broad fields of endeavour encompass a wide variety of activities, such as developing systems of primary health care that reach the whole population of Member countries; promoting the health of mothers and children; combating malnutrition; controlling malaria and other communicable diseases including tuberculosis and leprosy; having achieved the eradication of smallpox, promoting mass immunization campaigns against a number of other preventable diseases; improving mental health; providing safe water supplies; and training health personnel of all categories.

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