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Viral respiratory diseases

Report of a
WHO Scientific Group

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Geneva, 2–6 April 1979

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VIRAL RESPIRATORY DISEASES

Report of a WHO Scientific Group

A WHO Scientific Group on Viral Respiratory Diseases met in Geneva from 2 to 6 April 1979. Dr I. D. Ladnyi, Assistant Director-General, opened the meeting on behalf of the Director-General.

1. INTRODUCTION

In 1977 the World Health Organization embarked on an acute respiratory diseases programme within the context of technical cooperation with and among developing countries. The continuing massive morbidity from acute respiratory infections, with the attendant economic losses in all countries and the high premature mortality from viral and bacterial pneumonia in many of the developing countries, poses a real challenge to WHO. This challenge is to initiate and promote national programmes in which appropriate health technology is applied on a community basis as part of a community health care scheme.

The control of acute respiratory infections is more complex than that of many other diseases. Numerous pathogenic agents are involved, often acting synergistically and in various combinations. In view of this complexity, future control programmes are likely to differ from those for the control of other communicable diseases. The control of acute respiratory infections is not an easy task, and the World Health Organization will have to tackle this socially relevant problem with increasing efforts and resources.

Viruses have been blamed for the majority of acute respiratory diseases. Several studies have shown that they are the cause of severe and not infrequently fatal diseases, especially at the two extremes of age.

The aims of this Scientific Group were to advise the Organization on the role viruses play, give an up-to-date perspective of their contribution to the total picture of respiratory diseases, and study ways and means of containing viral respiratory diseases, particularly in the underserved populations in the developing world. The need for a multidisciplinary approach cannot be overstressed, not only because of the need to take into account respiratory diseases of nonviral origin (e.g., whooping cough, pneumonia) but also because of the necessity to integrate the control of these diseases with, for instance, maternal and child health care services and primary health care services.

2. THE WHO ACUTE RESPIRATORY DISEASES PROGRAMME IN THE CONTEXT OF TECHNICAL COOPERATION WITH AND AMONG DEVELOPING COUNTRIES

The control of communicable diseases accounts for a great proportion of the expenditure within national health budgets and will continue to be a drain on resources for health for many years to come. The continuing serious health problems created by communicable diseases in terms of mortality and morbidity reflect the relationship between health and socioeconomic development. To use the available resources to the best advantage, the surveillance and control of these diseases must be formulated as part of the countries' total health effort. Therefore, in formulating control programmes, cognizance should be taken of their inextricable interrelationships with, on the one hand, developmental efforts in the other major areas of primary health care, health services delivery systems, environmental health, health manpower, and biomedical and health services research, and, on the other hand, the development and application of efficient managerial, information, and evaluation systems for the total health programme.

The adaptation and application of technology for the control of communicable diseases often meet with constraints: inadequate community understanding and involvement; weakness of the health infrastructure and supporting services, and inadequacy of epidemiological surveillance and of managerial capability to identify problems and develop the most suitable approaches to control programmes at all levels of the national health services. Accordingly, countries may first put promising techniques for the control of communicable diseases to the test within the framework of their operational and health services research programmes. The purpose should be to develop the most efficient means of applying the most effective tools both at the community level and within a supporting health structure. For example, acute respiratory diseases are likely to be controlled most effectively by national health services as part of primary health care.

In the communicable diseases field, WHO has at its disposal a highly competent panel of experts—epidemiologists, virologists, bacteriologists, and others. In addition, there is a network of over 170 WHO collaborating centres in communicable diseases. This expertise for advisory services to countries and to WHO plays a pertinent role in the development of control programmes, e.g., by reporting, on behalf of WHO, on the epidemiological situation as regards communicable diseases; organiz-

ing training courses; and participating in WHO consultantships and in the WHO Emergency Relief Operations scheme. Collaborating centres also play a useful and rewarding role in the coordination of research. At present WHO is studying ways of making better use of the centres. Thus, in addition to research and reference functions, they might provide advisory services to countries and to WHO. The more these centres participate in national disease control activities, the greater will be their involvement in technical cooperation with and among developing countries and the better they will serve the needs of the countries in which they are located.

3. PUBLIC HEALTH IMPORTANCE OF ACUTE RESPIRATORY DISEASE

Communicable diseases of the respiratory tract are a major cause of morbidity and mortality all over the world. For this reason, the Twenty-ninth World Health Assembly (1976) decided that WHO, during its Sixth General Programme of Work, beginning in January 1978, should expand its activities to include the control of these diseases.

To this end, WHO has endeavoured to provide more precise and complete information on the magnitude of the problem.

Unfortunately, since morbidity data on acute respiratory diseases are available from very few countries, it is not possible to present a comprehensive picture of morbidity from respiratory diseases in the world. Data on mortality are available from 88 Member States: 9 in Africa, 29 in the Americas, 14 in Asia, 28 in Europe, and 8 in Oceania. These 88 countries have a total population of nearly 1200 million—a little more than one-quarter of the world's population. However, because of the large numbers involved, the aggregate data have an important message to convey, although a true assessment of the global situation is difficult, since acute respiratory diseases may constitute an even more serious public health challenge in countries from which no reports are available.

Thus, although the material available is restricted and superficial in its coverage of certain aspects, it may serve as a basis for a critical appraisal of what is known so far about the problem of acute respiratory diseases in the world.

The aggregate information presented in Table 1 indicates that the total number of deaths from acute respiratory diseases reported for the above-mentioned 88 countries was 666 726 in one year for the reference period 1970–1973.

Table 1. Mortality from respiratory diseases in the world : latest available reference years, 1970–1973 (all ages)
Percentages in parentheses

Continent and number of reporting countries	Population in thousands	Acute respiratory diseases				Chronic respiratory diseases			Acute
		Acute upper respiratory tract infections	Influenza	Viral and bacterial pneumonia	Total	Tuberculosis of the respiratory system	Chronic bronchitis, asthma, emphysema	Total	acute+chronic (%)
Africa (9)	77 420	51 095 (64.0)	332 (0.4)	28 460 (35.6)	79 887 (100.0)	4 974 (11.4)	38 663 (88.6)	43 637 (100.0)	64.7
America (29)	401 573	17 775 (7.3)	29 624 (12.1)	197 527 (80.6)	244 926 (100.0)	28 118 (28.4)	71 032 (71.6)	99 150 (100.0)	71.2
Asia	227 310	23 097 (18.1)	5 117 (4.0)	99 633 (77.9)	127 847 (100.0)	50 473 (65.8)	26 214 (34.2)	76 687 (100.0)	62.5
Europe (28)	462 936	12 062 (5.8)	24 074 (11.5)	173 518 (82.7)	209 654 (100.0)	32 893 (16.7)	163 977 (83.3)	196 870 (100.0)	51.6
Oceania (8)	16 895	272 (6.1)	232 (5.3)	3 908 (88.6)	4 412 (100.0)	5 202 (54.1)	4 412 (45.9)	9 614 (100.0)	31.5
Total (88)	1 186 134	104 301 (15.6)	59 379 (8.9)	503 046 (75.5)	666 726 (100.0)	121 660 (28.6)	304 298 (71.4)	425 958 (100.0)	61.0

Source : Bulla, A. & Hitze, K. L. *Bulletin of the World Health Organization*, **56** (3) : 481 (1978).

On the crude assumption that the mortality in non-reporting countries is similar, it may be estimated that about 2.2 million deaths from acute respiratory diseases occur throughout the world every year.

While 666 726 deaths were related to acute respiratory diseases, the same 88 countries reported 304 298 deaths from chronic respiratory diseases other than tuberculosis (this group including chronic bronchitis, asthma, and emphysema). The mortality from respiratory tuberculosis, reported separately by these countries, was 121 660. Thus, the reported data indicate that acute respiratory diseases accounted for 61% of the deaths associated with respiratory disease. If all causes of deaths are considered, then acute respiratory diseases account for 6% of the total number reported.

Analysis of the distribution of the various clinical categories of acute respiratory disease shows that bacterial and viral pneumonia are by far the most important causes of death, together accounting for 75% of all deaths from acute respiratory diseases (46% if all respiratory diseases are considered). If all causes of death reported in the world are taken into account, pneumonia accounts for about 5%.

As may be seen from Table 2, considerable differences in mortality exist between and within continents. For example, while the average mortality from acute respiratory diseases in the Americas accounts for 7% of all causes of death (and is thus rather close to the world average of 6%), the proportion is 3% in North America, 10% in South America, and 14% in Middle America. In Asia, there is a similar range—i.e., from 4% (Israel, Japan) to 13% in the developing countries. In Oceania, mortality from acute respiratory diseases as a proportion of all causes of death ranges from 3% (Australia, New Zealand) to 8% in the developing countries. In Africa, acute respiratory diseases account for 12% of all deaths, but in Europe they account for only 4%.

The proportion of deaths from acute respiratory diseases, compared with that from "all causes of death", differs considerably from the above-mentioned (regional) averages when the mortality data are analysed separately according to age group. Such an analysis provides important information for the planning of priority action in community health programmes. It appears that mortality from acute respiratory diseases is highest in infants, declining in late childhood and early adult life; it then rises progressively through middle and old age, as shown in Tables 3 and 4.

If the child population (i.e., children aged 0–14 years) is considered, acute respiratory diseases account for 20% (range: 9–27%) of all deaths.

Table 2. Mortality from acute respiratory diseases in the world : latest available reference years, 1970–1973 (all ages)

	Number of countries	Mortality		Excess mortality due to influenza (%)	Mortality from acute respiratory diseases as a percentage of all causes of death	
		Absolute number	Per 100 000 population		Excluding influenza	Including influenza
Africa	9	79 887	103.2	0.4	12.9	12.9
America	29	244 926	61.0	13.8	5.9	6.7
North	3	70 277	30.5	8.8	3.0	3.3
Middle	18	103 523	115.5	16.8	11.7	13.6
South	8	71 126	87.5	14.5	8.3	9.5
Asia	14	127 847	56.2	4.2	8.5	8.9
Israel and Japan	2	28 960	26.3	3.0	4.0	4.1
Developing countries	12	98 887	84.3	4.5	12.8	13.4
Europe	28	209 654	45.3	13.0	3.9	4.4
Oceania	8	4 412	26.1	5.6	3.0	3.2
Australia and New Zealand	2	4 076	25.7	5.8	2.9	3.0
Developing countries	6	336	32.6	4.0	7.6	7.9
Total	88	666 726	56.2	9.8	5.7	6.3

Source : Bulla, A. & Hitze, K. L. *Bulletin of the World Health Organization*, **56** (3) : 481 (1978).

Table 3. Mortality from acute respiratory diseases in the world: latest available reference years, 1970–1973

	Number of reporting countries		0—14 years				55—75+ years			
	0–14 years	55–75 + years	Absolute number	Per 100 000 population	Percentage of all causes of death	Excess mortality due to influenza (%)	Absolute number	Per 100 000 population	Percentage of all causes of death	Excess mortality due to influenza (%)
Africa	6	2	67 075	251.8	23.2	0.2	2 781	93.1	1.8	1.6
America	23	21	125 120	89.8	18.0	13.4	93 910	157.6	4.2	13.1
Asia	11	7	80 960	111.2	27.2	2.9	32 522	139.8	4.4	5.3
Europe	28	28	34 545	30.7	15.1	3.2	163 143	145.1	4.1	15.0
Oceania	3	2	775	15.9	9.4	2.1	3 089	114.2	2.9	6.2
Total	71	60	309 475	86.6	20.3	6.3	295 445	147.0	4.1	13.0

Source: Bulla, A. & Hitze, K. L. *Bulletin of the World Health Organization*, **56** (3): 481–498 (1978).

However, the highest mortality for that group of diseases is reported for infants below 1 year of age, the death rate in some countries exceeding 2000 per 100 000 live births (Table 4).

In the age group 55–75+ the reported proportion of deaths from acute respiratory diseases does not exceed 13%.

Even in developed countries, morbidity from respiratory diseases is less easy to measure than mortality, and most information has been derived from surveys of particular populations. Military groups have proved convenient for this purpose, but do not reflect the pattern in the general population. In industrially developed countries, long-term investigations into respiratory diseases in children have provided considerable information on minor illness as well as on the incidence of more severe illnesses and their outcome, the findings being related to the socioeconomic conditions.

In studies of respiratory diseases seen by general physicians in the United Kingdom, it was found that these diseases accounted for about one-quarter of all consultations, and one-half of all patients. Nearly one-third of the patients had colds, one-third had upper respiratory disease, pharyngitis, or tonsillitis, and the rest had influenza, bronchitis, or pneumonia. Upper-respiratory-tract infections decreased with age, whereas lower-respiratory-tract infections such as pneumonia and bronchitis were particularly frequent in both the young and the old. Absenteeism in the working population through illness has also been monitored in the United Kingdom. About one-third of all absences from

Table 4. Age-specific mortality rates (per 100 000) from all causes and from pneumonia and influenza in seven countries or areas in the WHO Western Pacific Region (pneumonia–influenza mortality rate in parentheses)

Age group (years)	Australia 1974	Fiji 1975	Hong Kong 1975	Japan 1975	New Zealand 1974	Philippines 1974	Singapore 1975
0–1	1615.5 (66.5)	4259.2 (466.9)	1500.0 (200.8)	1004.7 (84.9)	1558.9 (173.6)	5889.7 (1562.2)	1389.3 (255.3)
1–4	83.8 (4.1)	314.8 (49.4)	77.6 (15.6)	84.7 (7.1)	83.3 (5.7)	745.7 (290.8)	85.7 (20.9)
5–14	36.2 (0.7)	112.9 (9.6)	33.5 (2.9)	30.7 (1.7)	40.5 (1.3)	151.2 (36.3)	35.8 (4.1)
15–24	111.7 (1.6)	205.7 (7.3)	57.1 (3.8)	71.6 (1.9)	111.1 (0.8)	174.1 (17.6)	77.8 (5.1)
25–34	107.0 (2.6)	277.1 (3.4)	104.2 (1.7)	93.2 (2.1)	108.6 (1.6)	242.2 (18.0)	126.2 (5.1)
35–44	226.9 (5.9)	516.6 (10.2)	233.7 (14.0)	196.9 (3.7)	234.3 (3.8)	449.2 (28.8)	253.7 (8.1)
45–54	634.2 (13.2)	1233.3 (15.6)	552.9 (33.9)	422.7 (8.0)	608.4 (5.7)	760.4 (48.2)	709.5 (27.6)
55–64	1593.6 (28.0)	2314.6 (37.9)	1394.5 (98.5)	1043.3 (27.4)	1521.7 (18.2)	1375.1 (91.6)	1754.9 (86.7)
65–74	3771.9 (76.9)	4591.0 (51.0)	297.77 (278.6)	2960.5 (125.1)	3586.1 (54.0)	5829.8 (380.0)	3492.1 (252.3)
75 and above	11 723.1 (455.8)	7890.0 (171.4)	7216.1 (1256.2)	9947.4 (600.6)	11 194.9 (601.3)		
All ages	868.4 (24.7)	689.0 (29.5)	485.3 (50.3)	631.1 (28.7)	829.6 (29.1)	685.0 (117.8)	508.8 (42.1)

Source: *World health statistics annual 1977*, and Fiji Health Statistics Division.

work were found to be caused by respiratory disease, with higher figures in influenza epidemic years. The consequent economic loss is enormous, both in lack of productivity and in the cost of medical care. It has been calculated that about 10% of schoolchildren are absent at any one time, respiratory infections being responsible for about one-third of the diseases keeping them at home.

A long-term family study in the late 1940s in Newcastle, England, is relevant. Of 1000 babies, 90 had episodes of acute respiratory disease and 9% of these died. Current figures in the United Kingdom are much lower, but these figures from 30 years ago may be a guide for developing countries where—as in Newcastle—socioeconomic conditions are important. A significant new factor is the rural-to-urban shift of population, with overcrowding and other conditions leading to respiratory tract infection at an early age.

Precise information is difficult to obtain in the developing countries, but the available data indicate that acute respiratory diseases are among the commonest illnesses of infancy and childhood.

A study conducted in Santiago, Chile, in a population of 500 000, showed that respiratory diseases, excluding influenza and chronic lung disorders, are the leading reason for seeking medical advice in hospitals and outpatient clinics, accounting for about 15% of all cases. However, the study showed a higher proportion among adults than among children. A subsequent study in the same area and in other regions of the country confirmed the previous findings, showing that the proportion of diagnoses relating to any respiratory disease ranged seasonally from 21% in autumn to 11% in summer.

A survey of illness among 877 children under 5 years of age in a rural area near Jakarta, Indonesia, showed that, of a total of 3000 episodes in one year, 45% were due to acute respiratory diseases. Similarly, in a household survey in other localities over a 5-year period, 24–42% of the diseases observed were respiratory. In Indonesia, health centre data indicate that, of 6 500 000 patients attending outpatient clinics in 1977, about 44% were suffering from influenza-like illnesses.

In China, in 1976, a survey in the outpatients' departments of 18 large city hospitals revealed that the incidence of acute respiratory diseases among children ranged from 39% to 60%. In hospitalized patients, including newborn babies, it was 25–56%.

In countries where surveys have been carried out, acute respiratory diseases appear to be the commonest cause of death in children. A comparison of age-specific mortality rates, including the mortality rates

from pneumonia and influenza, between 7 countries in the WHO Western Pacific Region is shown in Table 4.

3.1 Factors influencing morbidity and mortality from acute respiratory diseases

3.1.1 *Climatic and seasonal factors*

In developed countries, respiratory infections usually occur more frequently in the cold winter months than in summer. In developing countries, many of which are in the tropics, differences in incidence have also been demonstrated, respiratory infections being twice or three times as common in colder weather. In Upper Volta, where there are three seasons (one dry and temperate, one dry and hot, and one wet), respiratory diseases are more common in both the temperate and the wet seasons, while laryngeal infections are particularly noticeable in the dry hot season.

3.1.2 *Overcrowding*

In the United Kingdom, infections with respiratory syncytial virus (RSV) have been shown to be more frequent in children with siblings than in those without, and appear to be related to the density of room occupancy.

3.1.3 *Sex and age*

Although, in the case of most viruses, both sexes are equally infected, a predominance of boys over girls has been noted in RSV infections (ratio of 1.7 : 1 in infections of the lower respiratory tract).

The incidence of all respiratory disease is highest in the first years of life, with a maximum incidence of RSV infections in babies between 1 and 3 months of age.

3.1.4 *Nutritional state of the child*

Acute respiratory diseases are a particularly common cause of morbidity in areas where malnutrition is a major problem, although the exact relationship between these two problems is not clear. Breast-feeding seems to offer some protection against such infections.

4. VIRUSES, RICKETTSIAE, AND MYCOPLASMAS AS ETIOLOGICAL AGENTS OF ACUTE RESPIRATORY DISEASE

4.1 Viruses

Infectious agents other than bacteria have been estimated to be responsible for 95% of cases of acute disease of the upper respiratory tract and a considerable, if lesser, proportion of cases of disease of the lower respiratory tract. Viruses—the most frequent—belong to several families. All have been found in infections of both the upper and the lower respiratory tracts, but some viruses show a characteristic prevalence in certain disease syndromes in various age groups.

4.1.1 *Influenza A virus*

Because of its antigenic lability, which invalidates antibody induced by previous infection, this virus affects all age groups, causing a generalized febrile illness with respiratory-tract involvement. Recovery usually occurs in a few days in uncomplicated cases. Influenza A virus is an important cause of febrile convulsions in infants, and may cause pneumonia and death in the very young. In older age groups, lower-respiratory-tract involvement is common, and most deaths from influenza occur in persons over 70 years of age. The seasonal incidence is striking, epidemics usually occurring in the winter months in the Northern Hemisphere and in the winter or rainy season in the Southern Hemisphere.

4.1.2 *Influenza B virus*

This virus affects predominantly the younger age groups, spreading particularly among schoolchildren. It causes a characteristic influenza-like illness, often accompanied by abdominal pain. Recovery, usually uneventful, occurs in a few days, but in infants and in older age groups pneumonia and death may ensue. Significant epidemics occur every few years, with irregular periodicity. The seasonal incidence is similar to that of influenza A, with outbreaks in the winter months, the two viruses often circulating concurrently in the same outbreak.

4.1.3 *Influenza C virus*

This virus, of unknown significance, is probably responsible for mild disease of the upper respiratory tract, from which it is only infrequently isolated.

4.1.4 *Parainfluenza viruses*

At present, four immunotypes are known to be associated with illness in man. Type 4 appears to be of relatively little importance as a human pathogen, but the remaining three types are of consequence because of the high morbidity from disease of the lower respiratory tract that they produce in young children. Overt infections with parainfluenza viruses types 1 and 2 are characterized by croup, and type 3 produces pneumonia and bronchiolitis in infants under 6 months of age (in this respect, type 3 approximates RSV in importance as a cause of morbidity and serious disease in this age group). The parainfluenza viruses are cosmopolitan in distribution, but show differences in their epidemiological manifestations. Parainfluenza 2 virus characteristically appears in epidemic form, with varying intervals between outbreaks. Type 1 virus produces epidemics at intervals of several years, but may entrench itself in an area and become endemic. Type 3 virus has an endemic pattern: cases may occur at any time of the year. The available morbidity and mortality data give only a rough idea of the importance of the parainfluenza viruses, but seroepidemiological surveys point to widespread infection with type 1 and type 2 viruses in early childhood, and virtually universal infection of young children (by 5 years of age) with type 3 virus. Reinfections with these viruses are common.

Infection with parainfluenza viruses types 1 and 2 does not occur in the early months of infancy—apparently because of the presence of maternal antibody. As maternally conferred immunity dissipates, overt illness begins to appear in older infants (4–5 months) and a high prevalence continues until school age, diminishing thereafter. In contrast, infections with parainfluenza virus type 3 occur in very early infancy despite the presence of maternal antibody, and the mortality associated with this virus mainly reflects lower respiratory disease in this age group. Reinfection in older individuals is common and mild, and does not involve the lower respiratory tract.

4.1.5 *Respiratory syncytial virus*

RSV is unquestionably the most important respiratory disease pathogen of infants and young children because of the severe bronchiolitis and pneumonia that it may cause. In temperate climates, epidemics occur in every season except the summer, and cases occur during several months.

Serological surveys have shown that newborn infants who possess maternal antibodies lose these in the first few months of age and then

acquire antibody through infection, so that approximately 25% of infants have antibody by 1 year of age, 50% by 2 years of age, and nearly all by the age of 4 or 5 years. Most infections appear to be clinically mild. The incidence of RSV disease attains a peak at about 2 months of age and declines thereafter. Such an age distribution is not in keeping with that observed with other viral respiratory pathogens and makes RSV a unique pathogen in its predilection for very young infants. Reinfection in subsequent years occurs relatively frequently.

4.1.6 *Adenoviruses*

The "endemic" serotypes (1, 2, 5) circulate widely among young children, whereas the "epidemic" serotypes (3, 4, 7) are found more frequently in older children and in adults. The commonest clinical syndrome is acute febrile pharyngitis, but in infants the lower respiratory tract may become involved and death may follow the development of pneumonia.

The "endemic" adenoviruses are isolated continuously, with no clear-cut seasonal distribution. The "epidemic" adenoviruses appear with an irregular periodicity.

4.1.7 *Rhinoviruses*

The existence of multiple serotypes explains the frequency of infection in all age groups. Rhinoviruses are the commonest viruses isolated from persons with common colds, but are also found in a small proportion of more serious illnesses in children, such as croup, laryngitis, and bronchitis. Rhinoviruses have been isolated from infants' lungs post mortem, but their significance is still uncertain. There is little seasonal variation, except possibly some increased frequency in winter and spring.

4.1.8 *Enteroviruses*

Echoviruses and coxsackieviruses are isolated fairly often from respiratory secretions from persons of any age and with any degree of respiratory tract infection, from a common-cold-like syndrome to influenza. These viruses are more frequently found in the summer months, various serotypes becoming prevalent with an irregular periodicity.

4.2 Other pathogens

The following three groups of respiratory tract pathogens are mentioned because, although they are classifiable with the bacteria, their isolation, growth, and identification requirements formerly grouped them with the true viruses.

4.2.1 *Rickettsiae*

The only important respiratory pathogen among the rickettsiae is *Rickettsia burnetii*, which may cause pneumonia in half the patients infected. Infection is usually acquired from the products of conception of sheep, cattle, or goats. It is thus an occupational hazard and is largely restricted to persons exposed to the pathogen—predominantly adults.

4.2.2 *Chlamydia B*

Psittacosis and ornithosis are acquired by the inhalation of dust or aerosols from infected birds. Clinically, they present as an influenza-type illness, which may proceed to severe pneumonia. A history of exposure to birds is usual, the disease being an occupational hazard in pet shops and among bird fanciers.

4.2.3 *Mycoplasmas*

Of the 8 or 9 species of human mycoplasma, *Mycoplasma pneumoniae* is the only one that is unequivocally a pathogen, causing a febrile bronchitis or "atypical pneumonia" of insidious onset. The disease is endemic, with peak prevalence at 3–5-year intervals, without any seasonal variation. The age group 5–15 years is predominantly affected, with spread in families and institutions.

4.3 Global overview

In 1963, WHO established a system for collecting and distributing information on viral infections, and by the end of 1976 laboratories in 49 countries had joined the WHO Virus Reporting System. During the period 1967–1976, a total of 135 702 reports on respiratory disease associated with virus infections had been entered into the computer data bank. Table 5 gives a breakdown of these reports.

Influenza A, adenovirus, RSV, parainfluenza, and *M. pneumoniae* infections accounted for almost three-quarters (100 966 of 135 702, or 74%) of the total number of reports; enterovirus infections were responsible for an additional 8%.

Table 5. Reports on viral respiratory diseases, according to year of collection or receipt of specimens for viral examination, 1967–1976

Virus	Year										Total
	1967	1968	1969	1970	1971	1972	1973	1974	1975	1976	
Adenoviruses	1 462	1 325	1 549	1 713	1 591	1 737	2 291	2 508	1 883	1 712	17 771
Influenza virus A	670	2 676	5 174	3 745	3 144	4 365	3 856	2 612	5 066	6 484	37 792
Influenza virus B	96	413	508	441	933	147	591	1 551	299	1 284	6 263
Influenza virus C	24	38	29	17	22	24	29	29	12	11	235
Parainfluenza virus	1 029	1 406	1 191	1 650	1 284	1 521	1 610	1 608	1 435	1 495	14 229
Respiratory syncytial virus	1 149	1 166	1 240	1 262	1 348	1 938	2 123	2 514	2 114	2 106	16 960
Rhinovirus	355	265	277	296	251	350	410	395	429	367	3 395
Measles virus	72	116	218	525	278	371	457	405	347	227	3 016
Enteroviruses	1 077	902	804	857	1 169	1 133	1 375	1 425	1 317	1 001	11 060
Herpetoviruses	424	538	510	584	620	802	1 123	1 104	1 176	1 200	8 081
Mycoplasma pneumoniae	407	357	350	537	1 536	1 997	1 198	2 196	3 565	2 071	14 214
Other viruses	73	64	86	182	201	285	303	266	490	736	2 686
Total	6 838	9 266	11 936	11 809	12 377	14 670	15 366	16 613	18 133	18 694	135 702

4.4 Seasonal distribution

As might be expected, the highest frequency of viral respiratory infections in the Northern Hemisphere is in the autumn and winter—the peak being usually in January. However, a considerable number of cases are reported also during the summer months. The complete picture is in fact a composite one representing the summing-up of a number of discrete viral seasonal patterns (Fig. 1). The winter months are dominated by influenza A and B, parainfluenza, and RSV infections.

Influenza A virus infections are most frequently reported during the months of December, January, and February, with the peak usually in January. In epidemic years, such infections are reported far more often than any other virus infection. The peak number of reports of influenza B virus infections has been in March, whereas that for parainfluenza virus infections has been in October. RSV infections are most common in December, January, and February, as are infections with influenza A viruses, but they extend into March, with the peak—which is much less marked than that for influenza A—in February. In the summer months the enterovirus-associated respiratory diseases dominate, reaching their peak in July. No clear seasonal variation is apparent for adenoviruses. In the case of rhinoviruses and mycoplasmas, there is some indication of a seasonal pattern, with a preponderance of reports in the autumn.

Only about 10% of the reports on viral respiratory disease were from the Southern Hemisphere, but they showed a general picture more or less similar to that seen in the Northern Hemisphere—i.e., a high frequency of respiratory disease associated with influenza A and RSV in winter, with the peak in July, and parainfluenza infections dominating in the autumn. The differences among the various viral infections are less marked.

4.5 Age distribution

The age was given in 126 089 reports, and 77 972 (i.e., over 60%) of the reports were on children below 15 years of age. Of these, 56 731 concerned children below the age of 5 years and 23 666 related to infants in the first year of life—i.e., 45% and 19%, respectively, of the total number of reports on viral respiratory infections (Table 6).

Viral respiratory diseases in children below 1 year of age were associated with RSV in almost 40% of cases (Fig. 2). In children aged 1–4 years, RSV had to some extent given way to parainfluenza and adenovirus, each of which accounted for 20% of the cases of respiratory

Fig. 1. Respiratory diseases associated with influenza viruses A and B, parainfluenza virus, and RSV, by month, in the Northern Hemisphere

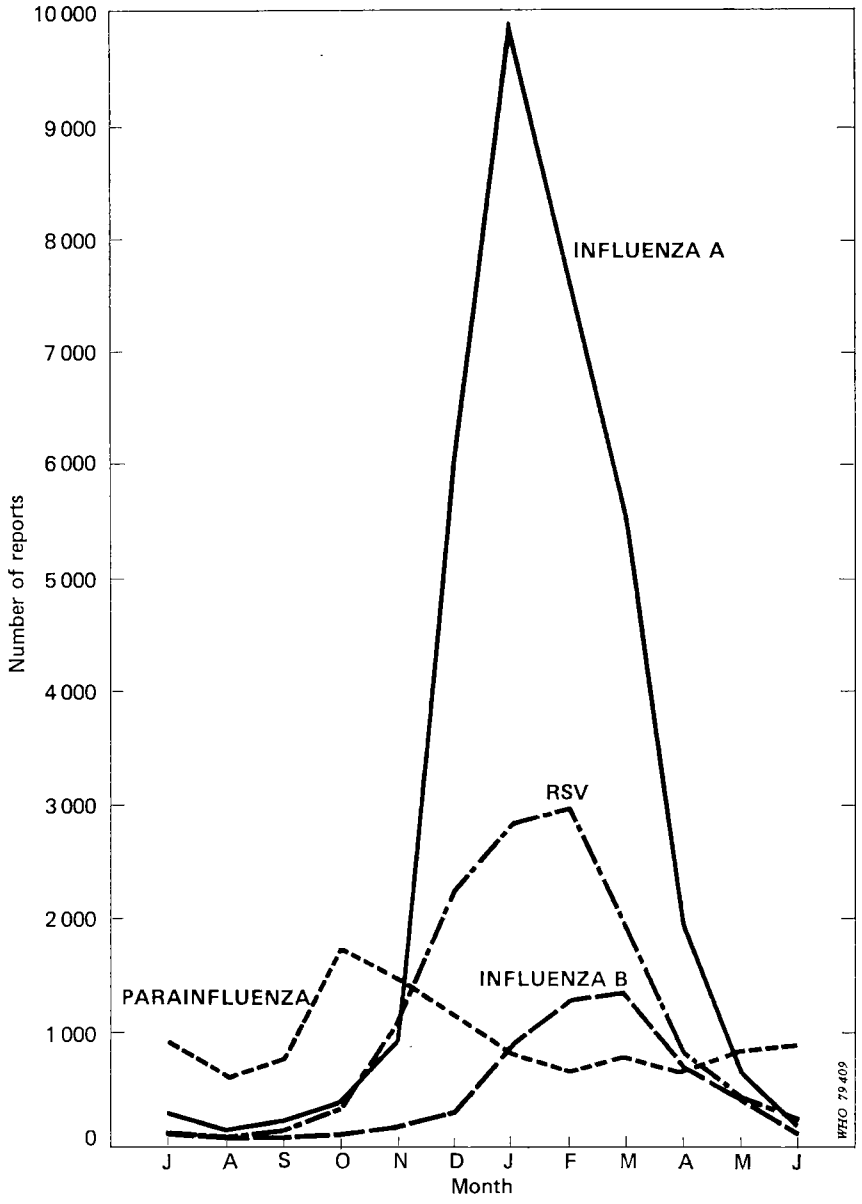
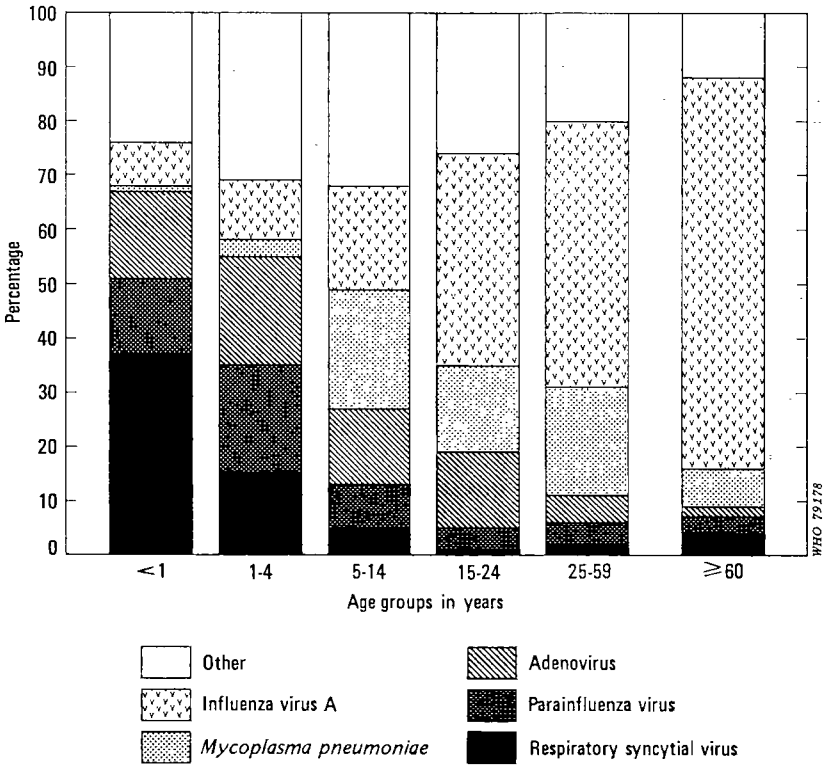


Table 6. Reports on viral respiratory diseases, according to age (in years), 1967–1976

Virus	<1	1–4	5–14	0–14		15–24	25–59	⩾60	⩾15		Total
				No.	%				No.	%	
Adenoviruses	3 859	6 706	3 027	13 592	81.3	1 800	1 117	215	3 132	18.7	16 724
Influenza virus A	1 891	3 632	3 964	9 487	27.2	5 217	10 609	9 506	25 332	72.8	34 819
Influenza virus B	284	734	1 774	2 792	48.2	990	1 275	730	2 995	51.8	5 787
Influenza virus C	18	43	33	94	44.5	31	55	31	117	55.5	211
Parainfluenza virus	3 401	6 760	1 663	11 824	88.3	458	772	343	1 573	11.7	13 397
Respiratory syncytial virus	8 813	4 866	1 015	14 694	92.7	181	457	527	1 165	7.3	15 859
Rhinovirus	697	768	535	2 000	68.3	372	473	83	928	31.7	2 928
Measles virus	290	1 240	994	2 524	87.2	218	133	18	369	12.8	2 893
Enteroviruses	3 039	4 250	1 811	9 100	90.3	386	514	74	974	9.7	10 074
Herpesviruses	908	2 481	1 174	4 563	61.9	820	1 275	715	2 810	38.1	7 373
Mycoplasma pneumoniae	320	1 086	4 597	6 003	44.6	2 127	4 365	970	7 462	55.4	13 465
Other viruses	146	499	654	1 299	50.8	647	546	67	1 260	49.2	2 559
Total	23 666	33 065	21 241	77 972	61.8	13 247	21 591	13 279	48 117	38.2	126 089

Note : The difference between the grand totals of this table and of Table 5 is due to the fact that the age was unknown in 9613 cases.

Fig. 2. Relative frequency of virus association with acute respiratory diseases, by age



diseases reported in this age group. Respiratory disease in the age group 5–14 years already showed a more adult-like pattern in that *M. pneumoniae* and influenza A virus were the dominating agents, accounting for 21% and 19% of the reported cases, respectively.

Among adolescents and young adults (15–24 years), influenza A virus accounted for almost 40% of all reported cases of respiratory diseases, *M. pneumoniae* being responsible for 16%. In the older age groups the pattern was maintained, but was more marked, influenza A virus accounting for 49% and *M. pneumoniae* for 20% of all cases reported. Finally, in the age group 60 years and over, 72% of all reported cases of respiratory diseases were associated with influenza A virus, while *M. pneumoniae* had dropped in importance — to 7% of all cases reported.

5. LABORATORY INVESTIGATION OF VIRAL RESPIRATORY DISEASE

To set up a laboratory simply to establish the etiological agent in acute respiratory disease might seem difficult and hard to justify in most countries, and it must be accepted that the information gained would be used for epidemiological purposes rather than in the care of patients.

However, these epidemiological data are of considerable interest and importance and, until they are available, preventive measures to control acute respiratory diseases cannot reasonably be contemplated.

5.1 Standard methods

Viral diagnosis and epidemiology are closely linked, and the use of simple techniques—either for the isolation of viruses or for serology—is well within the compass of any hospital laboratory in which microbiological work is performed.

A simple procedure for investigating specimens from patients is set out in Annex 1.

5.2 Rapid methods

In recent years other techniques have been developed, which allow the demonstration of viral antigen directly in respiratory secretions. Such rapid diagnostic methods offer certain advantages, notably: (*a*) the early recognition of a viral disease may allow for the prevention of the spread of virus in the home or hospital, and (*b*) the demonstration of a viral etiology may prevent the unnecessary administration of antibiotics.

Methods of rapid diagnosis are now numerous and need to be evaluated as to their general usefulness in the diagnosis of respiratory virus infections in two situations: in the sophisticated central laboratory and under field conditions in the small laboratory in a developing country. Rapid diagnostic methods currently available are: electron microscopy, immunofluorescence, various enzyme techniques, radioimmunoassay, haemagglutination and haemadsorption (usually in a solid phase), and techniques for the detection of specific IgM. Of these, only immunofluorescence has been widely used and compared with standard procedures, and it is probably the method most appropriate for the small laboratory. The requirements and method are shown in Annex 2.

In this context it is necessary to consider what viruses cause serious illness and bring children into hospital. In the United Kingdom and the United States of America these are: RSV, three parainfluenza viruses, influenza A and B, adenoviruses, and measles virus. All these viruses are amenable to rapid diagnosis. Other respiratory viruses, especially rhinoviruses, do not appear to cause serious illness in normal persons and therefore do not constitute a problem. Because of the multitude of antigenic types, rapid diagnosis of rhinoviruses would be difficult.

6. SURVEILLANCE OF VIRAL RESPIRATORY DISEASE AT THE COUNTRY LEVEL

In all countries acute respiratory diseases are a leading cause of hospitalization and of death. In spite of this widely acknowledged fact, there is often inadequate information about:

(1) which groups of the population are suffering from which types of acute respiratory infection;

(2) which pathogenic agents are most often involved;

(3) which controllable factors can be shown to discourage the transmission and/or the effects of these pathogens.

Viruses are often isolated from patients with acute respiratory diseases but it is often undetermined whether bacteria are also involved in these illnesses, what the patients' past medical history has been, how their social and environmental characteristics differ from those of other patients, how severe the disease is, and how the clinical course is affected by treatment. Coordinated information of this kind is required from at least a sample of the population if one is to understand and tackle the problem.

A team approach is required, in which data about the patient from epidemiologists, clinicians, microbiologists, immunologists, and social scientists are pooled in an endeavour to improve clinical results and to apply the most appropriate preventive measures.

6.1 Acute respiratory disease surveillance units

WHO is assisting in the development of a methodology whereby countries could undertake the necessary multidisciplinary collection and analysis of data on acute respiratory diseases. The meeting-point for the various disciplines involved in the monitoring, care, and investigation of

cases of such diseases would be the acute respiratory disease surveillance unit. There is a need for operational research into the management and control of acute respiratory diseases and for the development of appropriate control measures.

It is hoped that countries in which these diseases are rated as a high priority health problem will consider the establishment or designation of at least one surveillance unit, on either a national or a regional basis. Its functions might include the following:

(1) to monitor mortality and morbidity attributable to acute respiratory diseases in defined populations;

(2) to define population groups at special risk;

(3) to monitor the agents responsible for acute respiratory diseases;

(4) to define the environmental conditions (including physical, cultural, and social conditions) that influence the incidence and severity of these diseases;

(5) to investigate host factors (including immunological, behavioural, nutritional, and genetic factors) that might determine susceptibility to acute respiratory diseases;

(6) to assemble, analyse, evaluate, and disseminate the information in (1)–(5);

(7) to evaluate and monitor control measures;

(8) to train personnel concerned with surveillance and control of acute respiratory diseases;

(9) to investigate methods of improving the effectiveness of control measures; and

(10) to formulate recommendations to administrative authorities.

The use of standard terminology, methods, and data collection systems in surveillance efforts in which WHO would participate will permit an accurate local statement of the problem and enable epidemiological comparisons to be made between populations and regions.

Through a global network of surveillance units it is hoped that a clearer picture of the world problem will emerge. These units might also become involved in the testing of new preventive measures and treatment regimens that are locally relevant and applicable to the country or region concerned.

It is expected that the organizational and administrative relationships between surveillance units and the national health structure will vary.

Such units would benefit from the support of existing national influenza surveillance laboratories and national institutes of communicable disease. These institutions can often provide the virological and epidemiological expertise required for the tasks described above. The activities of a surveillance unit should blend into the existing health care system so as to strengthen and streamline the clinical management and prevention of acute respiratory diseases.

6.2 Type of population to be observed by surveillance units

The population chosen for surveillance should be easily definable and should be in relatively close proximity to the laboratory that is to provide the microbiological services.

The number of population groups to be brought under surveillance in a particular country will depend on the availability of resources and on the priority accorded to the control of acute respiratory diseases in that country. As a general principle, quality should take precedence over quantity, and countries with limited resources should ensure that at least one unit is collecting information of high quality and reliability from a defined population. In the first instance, surveillance should be established in a community group in which acute respiratory diseases are believed to be a significant problem. As further resources permit, new populations may be brought under surveillance, and it may be desirable, for comparative purposes, to add a population believed to have low morbidity and mortality from respiratory infections.

6.3 Data to be collected from population under surveillance

Four principal types of data should be collected:

(1) *Population identification data*. These include information about the social, environmental, and demographic characteristics of the individuals who make up the population under surveillance. In some surveillance units, additional identifying information will relate to certain biological characteristics of the individuals.

(2) *Clinical data*. When patients in the surveillance area make use of health services for acute respiratory disease, all clinical findings and information on treatment should be entered on standard data forms. A system of death notification needs to be established in the study area and, whenever death occurs, every effort should be made to ascertain and confirm the likely cause.

(3) *Intervention data*. These refer to anything done to or for individuals, either in an endeavour to change the respiratory infection pattern—e.g., by means of immunization programmes or new methods of clinical management—or through social or environmental change.

(4) *Laboratory data*. These include information about microorganisms recovered or serum specimens collected from patients suffering from acute respiratory diseases. Serological surveys on healthy people, where feasible, will help to provide background information.

A guide detailing methods of collecting data is being prepared for use by surveillance units and will be kept up to date as part of the acute respiratory disease control programme. These data will be entered on computer tapes to permit intraunit analysis and interunit comparisons.

6.4 Use of surveillance unit data for programme planning

Acute respiratory disease is not simply a viral problem, nor is it a merely bacterial, social, or environmental problem. In different populations and at different times many factors interact in various ways. Control measures must be tailored to local needs and national health service resources. Data collection is necessary to determine the most appropriate control strategy. The form in which data are collected from a population under surveillance must permit their immediate use locally in defining and monitoring control strategies. At the same time, local data should be comparable with those collected from other populations under surveillance.

Control measures devised against acute respiratory diseases should first be applied in a population under surveillance. Methods and results should be described, so that successful control measures may be duplicated elsewhere in the country or in other countries with similar patterns of acute respiratory diseases. It would, of course, be easier to duplicate control measures if all surveillance units used the same clinical and laboratory terms and methods.

6.5 Staffing and organization of surveillance units

Each surveillance unit should offer:

(1) *Epidemiological surveillance* that will detect changes in the population at risk, morbidity and mortality patterns within that population, and the occurrence of acute respiratory diseases and the microorganisms responsible for them.

(2) *Treatment services*. The clinical care available to patients with acute respiratory disease among the population under surveillance should be appropriate for the country concerned and within its resources. In countries with a very low health budget, the first population to be placed under surveillance should be that of an area provided with primary care services that could be duplicated throughout the country. Research in that population would lead to a national approach to primary care for acute respiratory diseases, to be constantly reviewed and modified in the light of detailed epidemiological information.

(3) *Laboratory investigation services*. A standard set of bacteriological and virological techniques should be available to assist in identifying the role of the common viral and bacterial pathogens in the community. These pathogens might include influenza viruses, RSV, adenoviruses, parainfluenza viruses, and *M. pneumoniae*, as well as pneumococci, haemolytic streptococci, *Haemophilus influenzae*, *Klebsiella pneumoniae*, *Bordetella pertussis*, and *Staphylococcus aureus*.

(4) *Data collection and analysis*. It is vital for the success of these units that the information system should serve the needs of the units rather than vice versa. In order to coordinate demographic, social, clinical, and microbiological data and to review the effects of intervention, each unit should be served by a worker acquainted with modern techniques of data collection and analysis.

In a multidisciplinary unit of this kind, coordination of the activities of the various disciplines represented is crucial to success.

6.6 Cooperation between surveillance units

In the early stages, some surveillance units may be unable to undertake all the core-data collection. In that case, they should try to collaborate with a unit that is better staffed and equipped.

6.7 Virology in surveillance units

As an absolute minimum, units should be able to identify influenza and RSV infections. Where national surveillance units are not linked to the WHO influenza network (see below) and are unable to type influenza viruses, they should establish contact with the nearest WHO collaborating centre or other laboratory able to undertake this function. It is also desirable that techniques for the identification of parainfluenza viruses and adenoviruses should be available. The identification of rhinoviruses,

reoviruses, and enteroviruses has a low priority, but some surveillance units should be able to define the role of these viruses in clinical respiratory disease.

6.8 Possible extension of the WHO global influenza surveillance system

Since its inception, the World Health Organization has been collecting and disseminating information on current influenza trends and on the characteristics of influenza virus. This work has been carried out in collaboration with the health authorities of Member States, and has been maintained through the efforts of 101 national influenza centres in 72 countries and 2 WHO Collaborating Centres for Reference and Research on Influenza (Atlanta, GA, USA, and London, England). The network of national influenza centres, which is the basis of the system, covers nearly all parts of the world: 48 laboratories are located in 40 developing countries and 53 laboratories are in 32 developed countries. These centres are nominated by national health authorities and brought into the WHO programme through formal recognition by WHO.

More than one laboratory may be recognized as a national influenza centre in a country. The number depends in general on the size of the country, the density of the population, and the number of competent virus laboratories. It is hoped that, in time, every country will have at least one designated national influenza centre.

It would be desirable for surveillance units on acute respiratory diseases to make use of established WHO national influenza laboratories for their viral investigations.

7. MANAGEMENT AT THE PRIMARY HEALTH LEVEL

7.1 Simplified categories of acute respiratory disease

International communication between health workers on acute respiratory diseases is often confused by ambiguity in the use of clinical diagnostic terms. This problem is compounded, for epidemiologists and health administrators trying to come to grips with the problem, by the fact that, even if clinical terms were used uniformly by doctors, many patients suffering from acute respiratory diseases are not examined by an experienced clinician.

For purposes of clinical management at the primary care level and for notification and epidemiological surveillance there is a need for

simplified clinical categories of acute respiratory diseases, based on symptomatology and applicable by relatively inexperienced health workers. The system of categorization shown in Fig. 3 is suggested for these purposes. It has the advantage that it can be elaborated to a more precise diagnosis by more highly trained clinicians for their own needs. For the purpose of calculating the incidence of acute respiratory diseases in defined populations, it is felt that the use of two simple categories —mild and severe—will be more useful than current practices. This approach needs to be tested and evaluated before it can be recommended for wider use.

7.2 Clinical management of viral respiratory disease

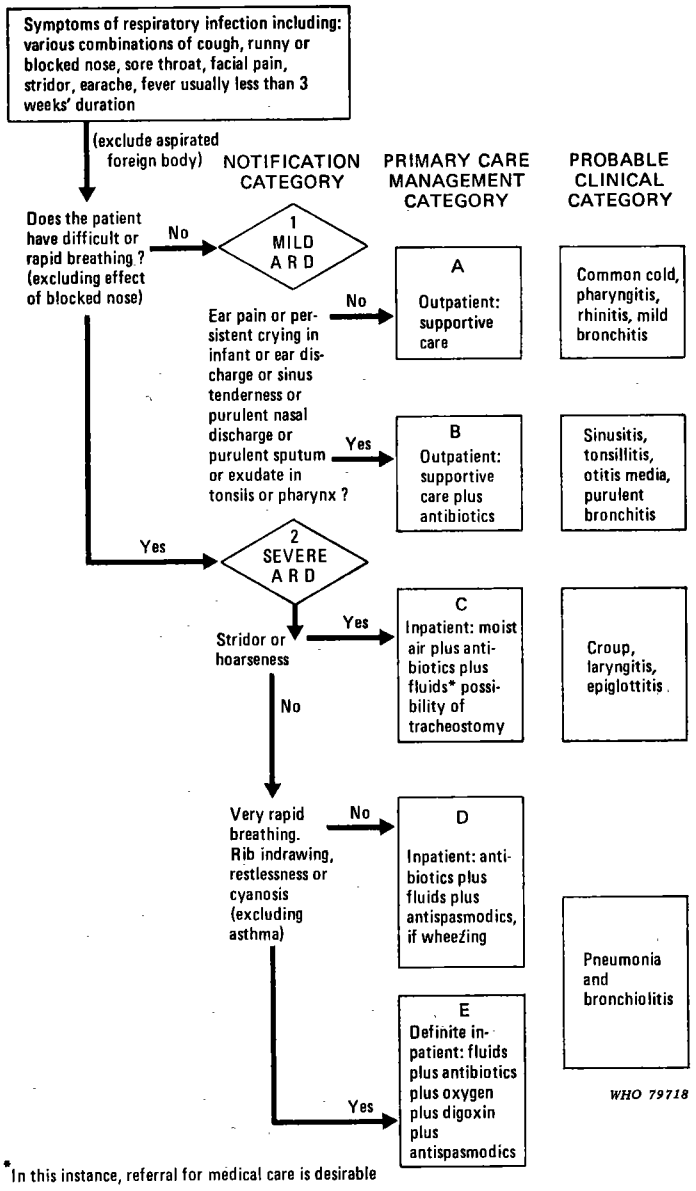
Although there is widespread agreement that viruses are the principal cause of acute respiratory diseases, there is also evidence that certain bacteria may superinfect the virus-damaged respiratory tract or cause clinical infection on their own.

It is difficult, even for experienced clinicians, to distinguish confidently patients whose symptoms are due exclusively to virus infection from those whose respiratory tracts are already invaded or at serious risk of invasion by bacteria. Without laboratory support, health workers tend to err on the side of caution, and antibiotics are widely overprescribed. The consequences of this widespread abuse of antibiotics cannot be accurately forecast, but there are disturbing signs that a number of the commoner respiratory bacteria, including pneumococci, streptococci, and *H. influenzae*, are becoming increasingly resistant to commonly used antibiotics. The primary care management categories shown in Fig. 3 would provide the best available estimates of the likelihood of a bacterial etiology or of the risk of bacterial superinfection. In general, therefore, it would seem that antibiotics should not be used for patients who have mild acute respiratory disease but show no evidence of sinusitis, exudative tonsillitis, exudative pharyngitis, or middle-ear infection.

For most people in developing countries, sophisticated laboratory and radiological investigations of acute respiratory diseases are not available, clinical diagnostic capabilities being limited to the categorization of symptoms.

Viruses, bacteria, mycoplasmas, and rickettsiae can all cause mild and severe acute respiratory diseases, and the contribution made by each group to the clinical spectrum of such diseases is impossible to

Fig. 3. Simplified categories of acute respiratory disease



*In this instance, referral for medical care is desirable

determine in any country without careful laboratory studies. One exception is measles, which may be recognized by the characteristic rash and Koplik's spots. Though such studies are best undertaken in the surveillance units described above, it is at present quite unrealistic to consider laboratory investigation as a prerequisite to clinical management in the vast majority of episodes of acute respiratory disease. Three serious bacterial diseases that may present as acute respiratory diseases are: whooping-cough, diphtheria, and tuberculosis. Primary health care workers must be alert to the possibility that these conditions may show symptoms indistinguishable from those of acute respiratory diseases.

The choice of antibiotics for routine clinical management will vary from one country to another depending on local drug supplies and on information about the susceptibility to drugs of common bacterial pathogens. Among the drugs that may be available to primary care workers, penicillin, sulfonamides, chloramphenicol, and co-trimoxazole (5 parts of sulfamethoxazole + 1 part of trimethoprim) are relatively inexpensive and still act efficiently against many bacterial respiratory pathogens. Surveillance units are needed to monitor this drug susceptibility and to undertake viral and bacteriological examinations of patients suffering from various acute respiratory diseases. Such information may well lead to local modifications in the framework of clinical management outlined in Fig. 3. As a starting-point for the instruction of primary health care workers, a simple training guide, which elaborates the principles enumerated above, is given in Annex 3.

In the diagnostic and clinical management categories, use of the term "bronchiolitis" has been intentionally avoided. RSV often causes a pathophysiological syndrome in infancy characterized by air trapping and hyperinflation of the lungs, but its differentiation by clinicians has little relevance either to the clinical management or to the epidemiological reporting of acute respiratory diseases, and it is expected that these cases will simply be reported as severe.

Oxygen administration has been shown repeatedly to be a major life-saving measure in young children with severe acute viral respiratory disease and evidence of rib indrawing, restlessness, cyanosis, and very rapid breathing. But it is an expensive form of management and the logistics of maintaining supplies to the peripheral health services of many of the developing countries are enormously difficult. Wherever possible, oxygen should be made available to rural hospitals and health centres, and health personnel must be taught the indications for and methods of its administration, so as to ensure that it will reach these young children, whose

lives it is most likely to save. There is an urgent need for the development of simple methods of administration and for data on the desirable duration of administration.

In early infancy, heart failure is a common and often unrecognized cause of death from severe acute respiratory disease. Similarly, severe bronchospasm may complicate some cases of such disease and require special management in hospital.

At the present time, and for the immediately foreseeable future, there is little prospect of cheap or widely available antiviral agents. Although huge research endeavours are proceeding in this field, and although there are promising reports of attenuation of symptoms in influenza by amantadine and rimantadine, the specificity and expense of these agents make their administration impracticable except in very limited circumstances. Studies of the clinical usefulness of interferon are limited by its expense and scarcity, and more research is needed into methods of producing it on a larger scale.

The vast majority of episodes of acute respiratory disease are mild and self-limiting. The challenge for health workers is to help people in the community to recognize when the disease is progressive and requires health service intervention. This challenge is particularly serious in rural communities of developing countries, in which therapeutic resources are scarce and children are dying for lack of treatment because of ignorance about when intervention is necessary. But the same challenge faces the more highly developed countries, in which sophisticated resources are widely available and expensive health services are being seriously strained by community-wide expectations that health workers will provide a cure for acute viral respiratory disease when none is possible.

A guide has been prepared to help to fill a lack that is present the world over—i.e., a lack of simple instructions that primary care workers can teach to parents and that will ensure that patients with such diseases who need modern medical intervention receive it, and that those who do not need it make use of their own considerable resources to minimize symptoms and complications.

These simple measures, which are grouped as "supportive measures", include the use of steam and moist cloths in hot climates to produce a therapeutic environment for the respiratory tract; clearance of the nasal airways, especially in very young children whose sucking ability is often impeded by nasal secretions; and the use of nonpharmacological symptomatic preparations, such as hot lemon drinks and syrup for people with cough. Dependence on pharmacological remedies for the symptomatic relief of mild acute viral respiration diseases should not be

encouraged, particularly since their use may instil a false sense of security into parents whose children really require antibiotic therapy.

Experience in China and other countries suggests that what is often referred to as "traditional therapy" may be at least as effective in the management of acute respiratory diseases as modern pharmacological preparations for symptomatic relief.

In building resistance to viral infections, physical exercise, the cessation of smoking, and an improvement in the physical environment are believed by some workers to be important. Minimization of droplet transmission might well be an important factor, and isolating at home those who are suffering from acute viral respiratory disease is believed to be a useful method of containing the spread of infection.

There are unpublished reports that radix astragalus, used in traditional Chinese medicine, may play a role in enhancing the nonspecific immunity of the host, and it has been suggested that oral or aerosol administration of this medicine produces increased interferon and secretory IgA, which may have some preventive activity against respiratory infections.

The possible usefulness of these measures in the clinical management and prevention of viral respiratory diseases needs further investigation.

8. ANTIVIRAL DRUGS IN THE TREATMENT OF ACUTE RESPIRATORY DISEASE

So far, the use of antiviral drugs against acute respiratory disease has been limited, owing to their relative ineffectiveness, occasional toxicity, and high cost.

Amantadine, a stable synthetic amine, possesses antiviral activity *in vivo* against influenza A viruses, but has no effect against influenza B, measles, or other RNA viruses.

Rimantadine, a synthetic analogue of amantadine, is somewhat more active than amantadine against influenza A, but a monoalkyl derivative of rimantadine is active against influenza B as well as influenza A virus infections. This drug and its derivatives have not been recommended for use in children, however.

Ribavirin, a synthetic analogue of guanosine, has given conflicting results against influenza viruses in clinical trials, and its therapeutic efficacy has yet to be determined.

In the USSR, immunoglobulin derived from vaccinated persons has been used in the treatment of influenza in children. Double-blind studies

have shown that, if given very early, immunoglobulin shortened the period of fever and reduced the frequency of complications four-fold. The frequency and duration of catarrh were unaffected.

In China, traditional herbal and Western medicines are both used. Herbal therapy is used in patients with upper respiratory tract disease or mild disease of the lower respiratory tract. Hospitalized patients receive a combination of herbal therapy and Western therapeutic measures. Current investigations in China suggest that the ingestion of radix astragalus induces interferon production and stimulates IgA secretion; the latter effect appears to correlate with a protective effect of radix astragalus against the common cold.

9. THE ROLE OF IMMUNIZATION IN THE CONTROL OF ACUTE RESPIRATORY DISEASE

The rational and logical approach to the control of acute respiratory diseases is immunoprophylaxis aimed specifically at each given etiological agent. In recent years much time and effort have been devoted to the development of specific vaccines.

9.1 Influenza vaccines

Influenza is the main example of a respiratory disease for which effective vaccines have been produced and are currently available. In theory, at least, mass immunization against influenza should prevent epidemics or halt their spread. Immunization on such a scale has never been achieved: the nearest approach to this objective was the campaign in 1976 against swine influenza virus in the USA. The more or less continuous process of antigenic drift, which is the gradual alteration in the antigenic constitution of a viral strain, and the occasional appearance, through antigenic shift, of a mutant constituting an essentially new virus, make it necessary to keep influenza vaccines up to date through the incorporation of currently active viruses. A number of field trials have shown that vaccines so constituted are highly effective (70–90%) in protecting against disease. Continuous monitoring is required to keep public health authorities informed of the antigenic nature of the virus or viruses currently circulating in a population, as well as the qualitative and quantitative changes that have occurred or the appearance of a new strain.

So far, influenza vaccines have been used primarily in certain selected population groups—e.g., in industry to reduce absenteeism and in

public services to prevent disruption of critical public services, such as the police, fire protection, transport, and medical care. Also, certain groups—e.g., the elderly and individuals in any age group who have a known underlying chronic or debilitating disease—are selectively immunized because of the high risk of severe complications and even fatal infection in such persons.

9.2 Vaccines under development

On the premise, based on immunological considerations—i.e., the induction of local secretory (IgA) antibodies—that an attenuated live influenza virus administered nasally should constitute a more potent and concomitantly a less reactogenic vaccine, studies are in progress to produce mutant viral strains that are adequately attenuated but still capable of eliciting the requisite immune responses. Temperature-sensitive, cold-adapted, and inhibitor-resistant mutants have been produced in recent years and found in exploratory tests to be relatively avirulent for man. Recombination techniques may serve to produce similarly attenuated strains through hybridization of a new virus with a laboratory virus of known characteristics and properties.

Because of the severity of the illness (disease of the lower respiratory tract) produced by the parainfluenza viruses in infants and very young children, efforts to develop suitable vaccines have been under way for some years. So far, several inactivated virus preparations from chick-embryo-derived virus, have been tested for protective efficacy, and the results have consistently shown that such vaccines, although they elicit a good antibody response, give no protection. On the other hand, evidence that protection may be linked to local immunity (secretory nasal antibody) rather than to humoral antibody suggests that protective immunity might be achieved through the use of live attenuated virus administered intranasally. Studies are under way to develop temperature-sensitive mutants of parainfluenza virus types 1 and 3—the two types most frequently associated with severe lower respiratory disease. Vaccines containing these modified viruses would have to be administered in early infancy (under 6 months of age).

Although the severity of primary infection with RSV and the early age at which it occurs have not yet been explained, these characteristics demonstrate the need for an effective vaccine. Therefore research on methods of producing RSV vaccine must continue to be given high priority. The first vaccines, prepared according to traditional methods, consisted of virus grown in monkey kidney cell cultures, concentrated by

centrifugation, inactivated with formalin, and adsorbed to alum as an adjuvant. The vaccine elicited humoral antibody and cell-mediated immune response, but failed in the crucial test: protection against infection. More important, failure of protection was compounded by a heightened response to subsequent natural infection, characterized by bronchiolitis or pneumonia, sufficiently severe in many cases to require hospitalization. Moreover, since naturally acquired infection with RSV confers protection against significant disease on reinfection, producing inapparent infection or mild disease of the upper respiratory tract, a live attenuated virus that would bring about the initial infection without the severe disease caused by the natural virus would appear to be the logical and rational choice as an immunogen. To this end, attempts are being made to develop a temperature-sensitive, genetically stable mutant for intranasal administration. It is reasonably sure that this can be achieved.

In the adenovirus group, some 34 antigenically distinct serotypes have been associated with human infections. On the basis of haemagglutination characteristics, these serotypes are divisible into three groups. Group III constitutes the serotypes (types 1, 2, 4, 5, 6, 12, 18, and 31) most commonly recovered from human infections, and Group I includes the types (3, 7, 14, and 21) responsible for more severe respiratory disease; Group II is more rarely encountered.

Acute respiratory disease of adenoviral origin is of major importance among military recruits, who, for unclear reasons, appear to be at special risk. On the other hand, in college students—a counterpart age group—such disease is relatively infrequent. It is also unusual in the general population, in which it accounts for about 3% of all respiratory disease. It has been estimated that perhaps only 5% of all acute respiratory disease occurring under the age of 5 years is of adenoviral etiology. This low incidence, and the infrequency of severe disease in this age group, raises the question (as it does for the general population) of the practical value, on a cost/health-benefit basis, of immunization against the offending serotypes.

The earliest vaccines, directed at the protection of military recruits against the three most commonly encountered immunotypes—types 3, 4, and 7—consisted of viruses grown in monkey kidney cell cultures and inactivated with formalin. While vaccines that met the minimum potency requirements were shown to confer immunity, the consistent inability to produce lots or batches of vaccine that would meet potency requirements, together with the occasional presence of a contaminating monkey virus (SV40) and the demonstrated oncogenicity of certain

adenovirus immunotypes in animals, suggested the need for other approaches. At the present time, adenoviral immunotypes to be used as vaccines are cultivated in human cells (WI-38 line) and administered orally in enteric-coated gelatin capsules. An oncogenic potential of adenoviruses for man has not been demonstrated. However, since oral–oral and fecal–oral transmission is frequent among children, and since natural infection results in colonization of the intestinal tract by the virus, oral administration would mimic this phenomenon and also induce a presumably higher degree of protection than would parenteral inoculation of inactivated virus. Live virus vaccines orally administered have been shown to be highly effective in lowering the incidence of acute respiratory diseases caused by the immunotypes against which the vaccines are devised.

Protection against adenoviral respiratory disease caused in military personnel by an immunotype represented in the vaccine may, indeed, be so effective that the strain is replaced in the population by another not represented in the vaccine.

In sum, because of the above-mentioned considerations, adenovirus vaccines are currently used primarily in military populations; should these problems eventually be solved, the vaccines may find a broader utilization in other population groups.

Rhinovirus infections (common colds) are the most common acute infections of man, as well as being the most common acute respiratory diseases. This high morbidity, together with the associated economic loss, makes these infections of considerable importance. Preventive measures are thus desirable, but it is doubtful, judging from the information currently available, whether specific prophylaxis can be achieved in the near future, if at all. There is, to begin with, the multiplicity of rhinovirus immunotypes: at present, there are some 110 distinct immunotypes that may give rise to the common cold syndrome of rhinorrhoea, obstruction of the nasal passages, sneezing, pharyngeal discomfort, and cough. The problems involved in preparing a vaccine containing all known immunotypes seem virtually insurmontable, since data derived from virus isolation and serological studies indicate that rhinoviruses have a cosmopolitan distribution. To help solve the problem of specific prophylaxis it has been assumed that certain immunotypes may be present, or may circulate, within given geographical areas. These would be candidates for incorporation into a vaccine. However, there is no firm basis on which to distinguish rhinovirus types of high prevalence from those of low prevalence. Reports of the existence of antigenic relationships between some of the rhinoviruses offer a glimmer of hope

that these relationships might be exploited in the formulation of a vaccine.

Clinical trials with inactivated monovalent rhinovirus vaccines administrated parenterally have shown that such vaccines may ameliorate illness and reduce shedding of virus, but not prevent infection. Hence, since secretory nasal antibody appears to play an important role in resistance to infection, and since parenteral inoculation of virus is not very effective in eliciting such antibody, the development of a vaccine will have to be based on the use of a live, suitably attenuated virus for intranasal administration.

10. RESEARCH NEEDS

The first research need for a community control programme is a precise specification of the nature and magnitude of the problem. This specification is largely lacking in all countries. Coordinated multidisciplinary research is needed on a global scale, as well as at a local community level, to ascertain the extent to which respiratory viruses contribute to illness and to premature death. Specification of the problem in operational terms also requires an estimate of the resources that are currently being devoted to the control of acute respiratory diseases. If the necessary resources are to be allocated for this purpose, national inventories are needed of the time lost from work and school as a result of acute respiratory diseases, the time spent by hospital and primary care workers in caring for patients with these diseases, the money spent on chemotherapy, and the cost to the community of premature loss of life as a result of acute respiratory diseases. Arriving at reliable estimates of such variables is no easy task and requires a high order of methodological rigour. Research of this kind is fundamental to the planning of a community control programme and will assist in the rational allocation of resources to the various elements of the programme.

10.1 Delineation of people at greatest risk

There is a need to define the social, biological, and environmental characteristics of individuals who are at the greatest risk from acute viral respiratory diseases. Respiratory viruses are ubiquitous, but it would seem that some groups of individuals are more likely to suffer from their effects than others.

Characterization of the factors associated with high and low risk might assist in the formulation of rational control measures and would certainly help to define the target groups for such control measures.

10.2 Defining the role of viral pathogens in various syndromes of acute respiratory disease

Much information has been accumulated around the world in recent years as a result of hospital and community-based studies of patients suffering from acute respiratory diseases. The emerging pattern enables broad generalizations to be made (e.g., RSV is a major factor in acute respiratory infections of the lower respiratory tract in infancy), but such generalizations are too imprecise to form a basis for local preventive action. Regional variations and seasonal fluctuations in the activity of various organisms make it desirable to base local control programmes on local information and to monitor the effects of intervention by continuing operational research into the roles played by the specific micro-organisms.

10.3 Research into methods of clinical management

There is a need to strengthen the capacity of mothers to care effectively for their children suffering from acute respiratory diseases. Simple guidelines should be prepared for training in the clinical management of such diseases. The development of decision trees based on local knowledge of the role of various pathogenic organisms is a significant need for countries that must depend on primary health care workers with relatively unsophisticated backgrounds. To train such workers in differentiating viral respiratory disease syndromes that should not receive antibacterial therapy from syndromes that should be treated with antibiotics at the time of clinical presentation poses an educational problem that must be based on well planned operational research. There is a need for research on the effects of introducing decision trees into health services, and on methods of instructing primary health care workers in the use of such decision trees.

Oxygen has been shown to be life-saving in serious RSV infections of the lower respiratory tract. However, the provision of oxygen in developing countries may be prohibitively expensive. Simple guidelines for its optimum use should be developed and new systems devised for ensuring that it is available to those who need it and that it is not squandered on those who do not.

Cough medicines, which are widely used and prescribed, may provide symptomatic relief. But there is a belief in some developing countries that the use of such medicines may instil a false sense of security in the patient or his family and might be the cause of late presentation for treatment of some children with terminal pneumonia. Research into this issue might result in educational programmes that might appreciably change the mortality rate in some areas.

10.4 Access to clinical care

Deaths from acute respiratory disease may result from difficulty of access to life-saving care, or they may be due to parents failing to bring their children to a readily accessible health centre until too late.

One method of determining the significance of these factors is to undertake retrospective studies of children who have died following late presentation for treatment and to trace the history of the illness from there, discussing with relatives the reasons for late presentation. Research of this kind may uncover problems in community attitudes or deficiencies in the location of treatment facilities.

10.5 Nutritional factors

There appears to be a relationship between malnutrition, on the one hand, and morbidity and mortality from acute respiratory diseases, on the other hand. The specific nutritional deficiencies that may be presumed to predispose to acute respiratory diseases need further investigation. Where optimum nutrition is difficult to attain, essential nutrient supplements to staple foods might save lives.

10.6 Developing suitable social and environmental indices

If comparative studies of incidence and of viral ecology are to be undertaken in the search for effective control techniques, there is a need to develop reliable indicators of social development, community participation, social organization, and environmental factors. The indices chosen must be simple and cross-cultural in concept. They should be capable of being defined at the family level by the people themselves and by workers with relatively unsophisticated knowledge of these illnesses and should relate to factors that have been shown to be, or are believed to be, relevant to acute respiratory diseases. In the first instance, their relevance should be tested in various surveillance units. A suggested list of indices is shown below.

Household size
Bedroom occupancy
Years of completed full-time education
Hours spent weekly in paid employment
Body weight
Home-buiding materials
Bedding
Clothing
Diet
Water supply
Attitude to traditional and Western medicine
Housing ventilation
Material possessions
Household fuel
Climatic exposure
Access to primary health care
Air quality
Drug-taking habits
Interpersonal contacts
Household hygiene
Personal hygiene
Domestic animals

Category labels for each of these variables will need to be carefully chosen and investigations undertaken into their validity and the consistency with which they can be measured in diverse cultures and communities.

10.7 Vaccine development

Although vaccines provide the logical and most obvious means of preventing viral respiratory disease, they have, with the exception of those against influenza and acute respiratory disease of adenoviral origin, generally proved to be disappointing or unacceptable. There is a need for more effective vaccines that are free from adverse reactions and produce measurable protective immunity against infection and, as far as possible, resistance to reinfection. To develop such vaccines will require research into the antigenic composition of viruses and the determination of true immunogens and their separation from irrelevant viral antigens and toxic components, as well as research into the pathogenesis of the major viral respiratory diseases. For example, much more needs to be known about the immunological phenomena involved in establishing a resistant state and the immunopathological and perhaps genetic mechanisms involved in the exaggerated responses seen in naturally infected individuals previously inoculated with killed RSV vaccines.

Influenza illustrates one of the problems associated with the development of vaccines and their application. Although inactivated virus vaccines have been available for more than a quarter of a century, during which their protective capacity has been evaluated in various populations and under varying conditions, and has been found to be highly acceptable, such vaccines have not been used sufficiently widely to prevent epidemics

or to halt them once they have broken out. In view of the changing antigenic characteristics of the virus (antigenic drift and antigenic shift), new vaccines are constantly required, and they should, if possible, give better and longer-lasting protection as well as less severe side-effects.

Several research approaches might be applied to the development of better influenza vaccines and also, to some extent, vaccines against other viral respiratory viruses, the selection of an approach depending on the ultrastructure of the virus, the nature of surface antigens, and other factors. Advantage may be taken of genetic technique—i.e., recombination to produce antigenically hybrid viruses containing the desired antigens and giving a high yield of virions. With the envisaged future development of recombinant RNA techniques, more direct manipulation of the viral genome should prove feasible for the production of vaccine strains containing the desired antigenic constituents. Vaccines made with virus disrupted by ether or by *n*-butyl-phosphate (so-called "split virus vaccines") are antigenic and lack the disconcerting high reactogenicity rate of whole-virus vaccines. Another approach is the preparation in pure form of the antigens responsible for protection and the attendant removal of toxic and adventitious materials, and also irrelevant viral materials. There is now a simple procedure by means of which viral glycoproteins (haemagglutinin and neuraminidase), the antigens associated with protection, may be separated in pure form. This technique is applicable not only to the orthomyxoviruses (influenza viruses), but also to the paramyxoviruses (parainfluenza viruses) and to other enveloped RNA viruses.

In summary, with respect to killed virus vaccines, a number of approaches derived as a spin-off from studies on influenza virus might be profitably explored in devising vaccines against other viral respiratory diseases.

10.8 Antiviral drugs

It is likely that, in the foreseeable future, prophylactic and therapeutic drugs will be developed in addition to the promising ones currently available.

Amantadine has been shown to be highly effective prophylactically against influenza A, reducing the incidence of disease by as much as one-half. It is also effective therapeutically, but not to the same degree as prophylactically. Drugs with similar activity and without adverse effects should be sought, for use not only against influenza virus but also against other viral agents causing acute respiratory diseases.

Interferon shows promise in the treatment of influenza, and may be found useful in other acute viral respiratory disease syndromes, but requires extensive research.

11. RECOMMENDATIONS

11.1 Surveillance

1. In many countries, little is known about the importance of acute respiratory diseases as a cause of morbidity or mortality, and especially of infant deaths. Health authorities should be encouraged to collect and analyse the relevant data.

2. Countries should consider establishing surveillance for acute respiratory diseases in defined communities. Surveillance should be an integral part of the health services and WHO should assist in developing a uniform simplified methodology.

3. In many countries where acute respiratory diseases are recognized as an important problem the etiology remains unknown. Attempts should be made to demonstrate the etiological agents responsible for such diseases in each country. Use should be made of existing WHO national influenza centres to extend the diagnostic work to cover other viral etiological agents. Wherever possible, studies on viruses and mycoplasmas should be coordinated with studies on bacteria, to permit greater understanding of the interactions between these organisms and the role they play.

4. More use should be made of rapid fluorescent antibody techniques for the investigation of virus infections. Other, simpler diagnostic methods should be developed.

5. High-quality reagents need to be made available for virus investigations.

6. Effective training and teaching programmes are necessary to solve the problem of the scarcity of laboratory workers and to ensure that uniform methods are used.

11.2 Clinical management of acute respiratory diseases

1. Simple clinical criteria that can be used at health centres need to be established.

2. Research needs to be done on the best management of cases.

3. Methods for the care of infants with severe acute respiratory diseases should be made more readily available. Particular efforts should be made to ensure a supply of oxygen by simplifying technology and equipment.

11.3 Community programmes

1. The participation of the community in the control of acute respiratory diseases should be secured through village committees, community leaders, and schools.

2. Methods are needed to increase awareness of these diseases in parents and children, by means of broad-based health education, directed towards the appropriate family management of minor illness and recognition of more serious illness requiring help from the health services.

3. WHO should prepare a simple booklet appropriate for the primary health worker caring for children with acute respiratory disease. This needs to be well illustrated and easily translatable into local languages.

4. Use should be made of social scientists, social workers, and communications experts in establishing successful programmes.

11.4 Vaccines and therapeutic agents

1. Inactivated influenza virus vaccines are widely available, and have proved to be highly effective in protection against disease. Immunization programmes should be maintained. Any such programme should include those segments of the population that are at special risk.

2. The use of live influenza virus vaccines could be considered when these become available.

3. Research efforts need to be continued to develop and evaluate vaccines against respiratory syncytial and parainfluenza viruses. In view of the inadequacy of the killed virus vaccines so far developed, research efforts should be focused to a greater degree on the development of live attenuated virus vaccines.

4. Research into antiviral and antibacterial agents presenting no danger to children (e.g., chemical compounds, specific immunoglobulin, and interferon) should be pursued more actively.

5. The efficacy of local traditional remedies should be explored further.

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Annex 1

DIAGNOSIS BY VIRUS ISOLATION AND SEROLOGY

Specimens

1. Throat or nose swabs taken into virus transport medium (Hanks' balanced salt solution with 0.2% bovine serum albumin).

2. Nasopharyngeal aspirates taken with a mucus extractor.

3. Sera, acute and convalescent.

Storage of specimens

Keep specimens at 4 °C until they are inoculated, which should be done as soon as possible.

Inoculation

Inoculate 0.1-ml amounts of specimens into:

— the amnion of 4 fertile hen's eggs 10–12 days old,

— 2 tubes containing cultures of monkey kidney monolayers,

— 2 tubes containing cultures of HeLa or Hep 2 cells,

— 2 tubes containing cultures of human lung fibroblasts (e.g., MRC 5).

Incubate all the cultures at 33–35 °C for 48–72 hours.

Identification of virus

1. Harvest the allantoic and ammiotic fluids separately from the eggs. Perform a spot test for haemagglutinin and, if this is positive, identify the influenza type. If the spot test is negative, passage once in egg.

2. Examine the monkey kidney cultures daily for a cytopathic effect. Carry out haemadsorption test with guinea-pig or human erythrocytes on the fifth day (or earlier if indicated) by the cytopathic effect. If the test is positive, passage through 8 monkey-kidney cultures and identify the virus by haemadsorption-inhibition tests with specific antisera to influenza A, B, parainfluenza viruses, mumps virus, and SV-5, all of which antisera have been treated with receptor-destroying enzyme. If the haemadsorption test is negative, determine whether the agent is an enterovirus, rhinovirus, or some other virus.

3. Examine HeLa or Hep 2 daily for cytopathic effect. Identify respiratory syncytial virus or adenovirus.

4. Examine human lung fibroblasts daily for cytopathic effect of herpesvirus, enterovirus, or rhinovirus.

Serological diagnosis

Perform the complement-fixation, haemagglutination inhibition, and radial haemolysis tests.

Note: Since bacteria play an important role in tonsillitis and otitis media, the specimens sent for virological examination should also be used for bacterial culture.

Annex 2

RAPID DIAGNOSIS BY IMMUNOFLUORESCENCE

Reagents required for immunofluorescence

Most rapid viral diagnostic techniques require two pure reagents: specific virus antiserum and anti-species globulin. In the indirect test the anti-species globulin usually carries the label appropriate to the method, while in the less frequently used direct test the specific antiserum may be labelled. Viral antisera are made by inoculating the appropriate virus into an animal, usually the rabbit. The basic principle is to conjugate a fluorescent dye, such as fluorescein isothiocyanate, to an antibody (direct) or to an anti-species globulin (indirect).

Clinical material

The success of all techniques depends on the quality of the specimen received by the laboratory. For the investigation of infections of the respiratory tract, secretions removed from the nasopharynx are by far the best. This is done by passing a fine catheter through the nose into the nasopharynx and applying suction. In this way, secretions may be collected in a mucus trap. Other materials are less effective, since they contain fewer respiratory cells and hence less virus and viral antigen. Cough swabs, sputa, and nasal and throat washings fall into this class, although a reasonable number of the correct type of cells may be collected with an efficient nasal wash. All materials taken at the bedside must be transported as quickly as possible to the laboratory for processing by the appropriate rapid technique as well as for routine virus isolation, since most respiratory viruses are highly labile.

Preparation of slides

On arrival in the laboratory, the cells in the specimen are separated by slow centrifugation, washed free of mucus, resuspended in phosphate-buffered saline, placed in squares on prepared slides, air-dried, and fixed in acetone. The specimens are then ready for staining. Specific antisera are applied to the fixed cells for 1 h, and then washed thoroughly. The conjugated anti-species globulin is applied for a further hour. After a final, thorough washing, the slides are ready for examination under the fluorescence microscope.

Annex 3

A GUIDE FOR TRAINING HEALTH WORKERS AT THE COMMUNITY LEVEL IN THE CARE OF CHILDREN WITH ACUTE RESPIRATORY DISEASES *

Children with acute respiratory diseases have cough as the most important sign. Infection of the lower respiratory tract causes several other signs, such as stridor (noise on breathing in) and fast breathing. All mothers can recognize a cough, but they are not always aware of the other signs and the danger that they represent.

The life of the child may be saved if the mother knows what treatment she herself can give and when the child should be brought to the health worker for treatment. The health worker must be able to recognize and understand the clinical significance of signs in a child suffering from respiratory disease in order to treat the child and teach its mother. In this, the health worker may be helped by an understanding of the anatomy of the respiratory tract (airways).

The health worker should keep the following general principles in mind when discussing cough and respiratory diseases with mothers.

(1) He should find out from the mothers what they know about cough: how they recognize it, what they think is causing it, whether they do anything to treat it, and, if so, what treatment they give. In this way, the health worker can find out what is generally thought about cough and the practices applied, and can build his teaching on this knowledge.

(2) In explaining the signs and symptoms and their relation to the diseases and anatomy of the respiratory system, drawings may be used. These may be supplemented by the demonstration of cases from real life, so that the health worker can teach the mother, e.g., to distinguish a normal throat from one that shows signs of disease. Such real-life examples leave a more lasting impression.

(3) The health worker must be able to know from the signs and symptoms what action is needed, and instruct the mother accordingly.

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* In many respects, this guide was inspired by the book *Primary child care: a manual for health workers* by Maurice King, Felicity King, and Soebagyo Martodipoero, which was published on behalf of WHO by Oxford University Press in 1978. Indeed, the passage in smaller print and all the figures were reproduced directly from it by permission of the publishers, whose kind cooperation is acknowledged.

It is particularly important to detect respiratory distress. In the management of an acute respiratory disease, existing good practices should be applied—if necessary, supplemented with others applicable in the local situation.

The following rules should be kept in mind when discussing respiratory diseases with mothers:

— ask simple questions and listen carefully to the answers;

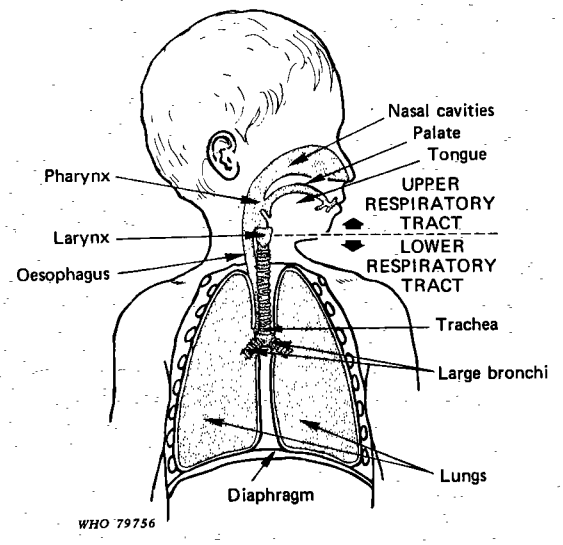
— build on existing knowledge and practices; and

— use real-life situations in demonstrations.

How a child breathes

When a child breathes, air goes from his nose (Fig. 1) into spaces inside his head called his nasal cavities. These make the air warm and

Fig. 1. The respiratory system



wet. The air then goes into his pharynx, which is the back part of his mouth. If you ask an older child to open his mouth and say "Ah", you can see his pharynx. Below his pharynx is his larynx. This is a narrow space filled with air. It is at the top of the front of his neck.

There is a large tube below the larynx. This tube has strong walls and is called the trachea (windpipe). It takes air to the lungs. The lungs are two organs filled with air, one on each side of the chest. In the middle of the chest the trachea joins two short thick tubes called the right and left main bronchi. One of the main bronchi goes to each lung and joins many smaller tubes called the smaller bronchi. The smaller bronchi join on to very small tubes called the bronchioles. The bronchioles take air to millions of small bags called alveoli, which are covered with capillaries (small blood vessels).

The tubes of the respiratory system, usually called collectively "air passages", are covered inside by thin wet tissue called mucosa. Another kind of mucosa covers the inside of the mouth and the nose. The mucosa keeps itself wet by making mucus.

The heart and lungs lie in a cage made of many curved bones called the ribs. Across the bottom of this cage there is a thin flat muscle called the diaphragm. The diaphragm is fixed to the inside of the lower ribs. It makes a wall across the body between the thorax (chest) and the abdomen.

Every time a child breathes, his ribs and diaphragm move. This brings air into his lungs. The oxygen in the air passes into his blood. The blood carries the oxygen to all parts of the body. All parts of the body need this oxygen to live.

The village health worker and mother must be able to recognize certain major signs if they are to prevent death from serious respiratory infections.

Signs of serious breathing problems, and how to recognize them

Rapid breathing. A healthy child breathes slowly when he is quiet or asleep. When he is angry or moving about, he breathes faster. He also breathes faster when he has disease of the lungs, especially pneumonia. You must be able to recognize the signs of rapid breathing.

Insuction. Notice the speed of breathing and the way the lower part of the chest is drawn in (insuction). Emphasize this last point and tell mothers that it is particularly important in babies. This movement of the lower chest shows that the baby is ill. He may have pneumonia and need urgent treatment (Fig. 2).

In an older child, insuction may not be quite as easy to see, but by putting your fingers on either side of the child's chest (as shown in Fig. 3) you will see that the fingers move in as the child breathes. With a healthy child, your fingers move out.

Fig. 2. Severe insuction in a young child

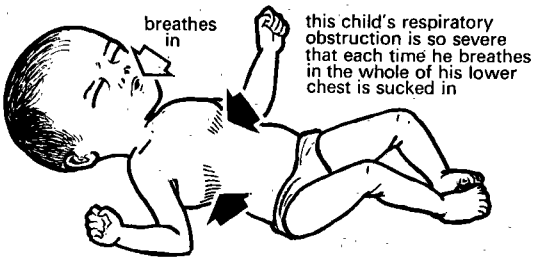
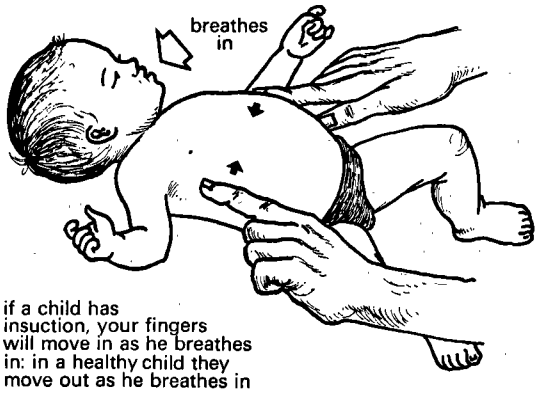
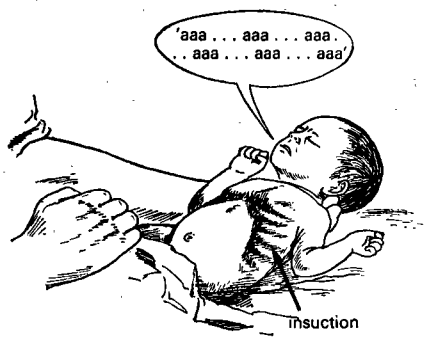


Fig. 3. Insuction in an older child



Stridor. Along with insuction of the lower chest, the child may make a noise as he breathes. This is called "stridor" (Fig. 4).

Fig. 4. Stridor and insuction in a young child



Stridor may come from the larynx. If you press your fingers on your own larynx, you will see that, as you breathe, it makes a noise. The noise may also come from the smaller tubes in the lungs. These tubes may contract or their walls may be thickened and produce mucus which the child coughs up as sputum. It is because these smaller tubes in the lungs are so tiny and easily blocked in a baby that pneumonia is so dangerous.

Cyanosis. When a baby has pneumonia, the oxygen from the air is not absorbed so well into its blood and its face turns blue.

Blocked nose. A child over 1 year of age can breathe easily through the mouth. A newborn baby usually cannot breathe through the mouth. If the nose is partly blocked, it is difficult for a baby to suck from the breast. For this reason, it is important that the mother should be aware of the problem and be shown how a blocked nose may be treated as described on page 62.

Fever. Fever is a common finding in sick children and is usually well recognized by the mother. If you do not have a thermometer and want to check whether a child has fever, feel his forehead with the back of one of your hands, at the same time feeling your own forehead with the back of your other hand. This will allow you to feel whether his temperature is greater than yours. If a child feels very hot indeed, look to see how many clothes he has on. To overwrap him when he has fever may be dangerous: his temperature may go up higher and he may get fits and brain damage. A feverish child should be undressed and sponged with warm water, which should then be allowed to evaporate. On the other hand, when a child with fever is shivering, he should be kept warm with a blanket or other covering.

The mouth and throat

The mouth and throat of a child must always be examined. Children do not like this and may get upset, so this examination should always be left to the last. Get the mother to sit with the child on her knees and to hold his head and hands firmly (Fig. 5). Then press the child's lower lip with the handle of a spoon and the child will open his mouth. Hold his lower lip away from the teeth and quickly look around the mouth and at the throat. Try not to make him gag, and avoid upsetting

him. The normal throat (Fig. 6) should be the same colour everywhere and there should be no white matter on it.

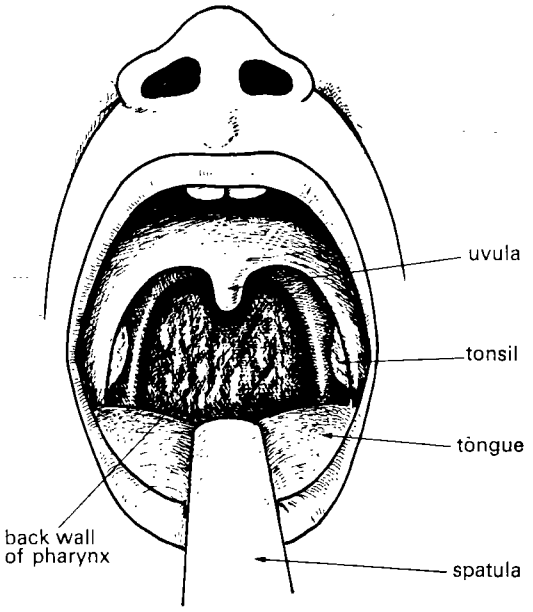
Fig. 5. Examining a child's mouth and throat

Infections of the respiratory system and what to do about them

Fig. 7 shows where an infection may occur, e.g., in the nose or throat. Let us now discuss some of these infections.

The common cold. This is a common infection that every child may have from time to time. It is not important except in a small baby, in which it may cause blocking of the nose and certain difficulties in feeding. However, the common cold may also develop into a more severe illness or involve complications. Every child with a common cold, particularly if newborn or an infant, should therefore be kept under close observation by his mother. Mothers should be instructed that a significant rise in body temperature lasting more than one day and signs of a worsening general condition (loss of appetite, dehydration, listlessness, etc.) call for consultation with the nearest health worker.

Fig. 6. The normal throat



Throat inflammation. If the throat is inflamed and sore, it will be red and there may be some white matter on either side of the tonsils (Fig. 8). If this white matter is present, give penicillin as described later on.

Note particularly if there is a white skin on the throat, for this is a sign of diphtheria. It is very serious when such a white skin is accompanied by stridor, since this means that the infection has gone down to the larynx (Fig. 9). Get the child to hospital quickly.

Ear infections. In many cases, throat infections may be associated with earache. Mothers should be instructed that, if the child has pain when the skin flap of the ear (tragus) is pressed, they should seek the advice of the health worker.

Laryngitis. The larynx is between the upper and lower respiratory tracts. When it is inflamed, there may be hoarseness or stridor. If there are signs of drawing in of the lower chest, it means that the disease is more severe and that prompt treatment should be given.

Bronchitis. This is when the tubes of the lungs are swollen. But as long as the child is not breathing fast, has no fever, and shows no signs of difficulty in breathing, he does not need any special treatment.

Fig. 7. Infections of the respiratory system

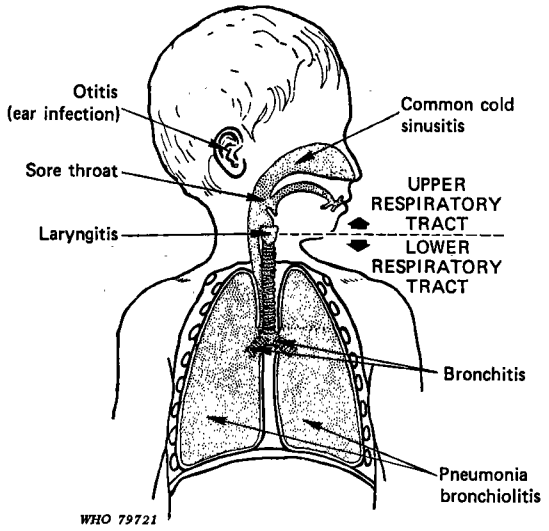
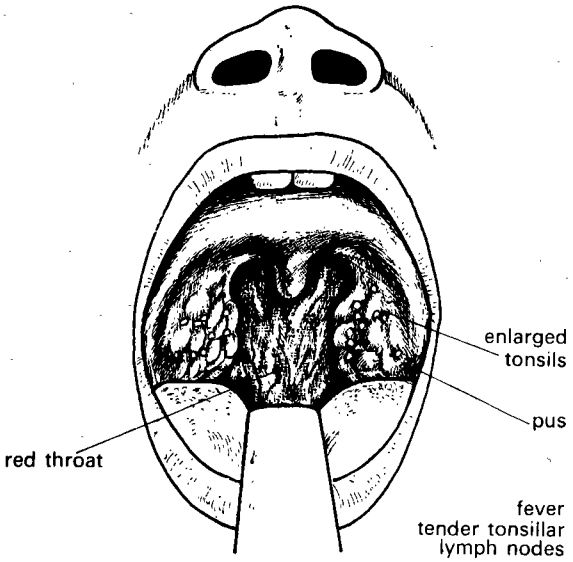
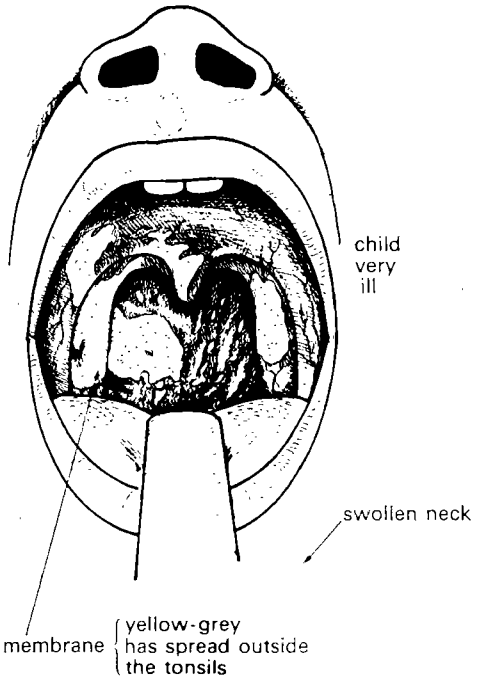


Fig. 8. Tonsillitis



Pneumonia. If the general condition of the child worsens, if he has a high fever that remains, and if he begins to have difficulty in breathing, it means that there is a serious infection of the lungs. The mother should take the child to the health facility for proper diagnosis and treatment.

Fig. 9. Diphtheria



Measles and whooping-cough. These diseases are mentioned here only because they may be associated with complications of pneumonia.

Management of the above-mentioned conditions

The common cold. When a child has a running nose, he must not be exposed to sudden changes in environmental temperature. The running nose also makes mucus drip back down into the larynx, which will cause cough. Many types of soothing cough mixture are made locally and, although they will not stop the cough, they may be helpful.

A cold in a baby. You will have noticed that, when one has a cold, the nose is often blocked. A blocked nose in a baby is serious because

a baby does not breathe through its mouth. It is important, therefore, to clear the nose, leaving the passage as free as possible. This may be tried by putting 2 or 3 drops of a salt solution in the baby's nose with a dropper or small spoon. The salt solution is prepared by putting 4 pinches of salt (or 2 level spoonfuls if you have a special small spoon for making up such mixtures) into a cup of water. The secretion may also be sucked out with a plastic syringe without the needle.

The difficulty in caring for children with colds is that parents often demand treatment—perhaps with injections—for them. It is necessary to explain that injections are not needed and may even be dangerous. However, if a child with a cold has a red throat with white matter oozing from it, inflamed tonsils or pharynx, or persistent earache, he may need an antibiotic.

Pneumonia. The child with pneumonia is in a serious condition (look at Fig. 7 to see where the infection is). Pneumonia must be treated correctly, if possible in a hospital. Preferably, the mother should stay there with her child, particularly if he is less than 2 years old. The child with pneumonia needs penicillin or a sulfonamide. If the mother cannot, or does not want to, send her child to hospital, she should watch carefully when you give the child the first dose of tablets. You should explain to the mother what to do and you must watch her giving her child the medicine the first time. Then explain when the next dose should be given and make sure to impress on her how important it is for the child to take the medicine regularly until the medicine is finished. If the child is treated at home, he should be visited within 24 hours after the treatment started.

Fluids and food. In taking care of an acute respiratory infection it is most important to give the child plenty to drink. While it is good if he drinks water, this may not be enough. He should also drink water containing sugar and salt. Make this up with 2 three-finger pinches of salt and a fistful of sugar in a cupful of water. Remember to give him a cup of plain water between cups of sugar and salt mixture. In the case of the breast-fed child under 6 months of age who is in good condition, water may be given, particularly if the baby has fever. An older child should be encouraged to eat as soon as he can. This will help him to get strong again quickly.

Keeping the room moist. While a child has a respiratory disease it helps to keep the air moist. One way to do this is to have some cloths soaked in water hung around the child's bed. The water will evaporate

and the mother should then wet the cloths again. Giving the child enough to drink and keeping the air moist will do much to help him. If he has stridor, a continuous source of moisture should be provided, especially if the atmosphere is dry or dusty. A few children, however, do not improve. They may show cyanosis (blue lips and fingernails) or breathlessness. This is a sign that they need oxygen, and if this is available it should be given. However, most children, if you look after them well as described above, will get better without oxygen. Oxygen must be reserved for the severely ill child.

Pneumonia in older children and adults. The description so far has concentrated on small children, since these are particularly liable to have pneumonia. Older children and adults will need larger doses of penicillin or sulfonamide.

Preventing chest disease. Children will get more respiratory diseases if they are living in an atmosphere polluted by smoke—either from a fire or, even worse, from cigarette smoking. Since cigarette smoking is harmful to both the smoker and those around him, try to discourage everyone from this habit.

Immunization. Vaccination against diphtheria, whooping-cough, measles, and tuberculosis is all-important in preventing diseases of the respiratory tract. Encourage all mothers to have their children immunized.

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