CHAPTER 16

TECHNICAL GUIDELINES FOR THE PREVENTION, DIAGNOSIS, TREATMENT, AND CONTROL OF ARI AT THE PRIMARY CARE LEVEL

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I. INTRODUCTION

Acute respiratory infections (ARIs) are among the most disturbing problems that health professionals face in their attempts to improve children's health. These diseases cause enormous harm each year, and yet effective means of controlling them are available.

II. THE TOLL OF ARI AMONG CHILDREN

ARIs are considered among "the big three" fatal illnesses of early childhood. Together with diarrhea and protein-calorie malnutrition, pneumonia, which causes more than 85% of all ARI mortality, is responsible for between 10% and 30% of deaths in children under 5 in most of the developing countries of the Americas (*1-4*).

The available data present a clear panorama of the impact of the annual harm that ARI causes in children (*5*).

- More than 100,000 deaths of children under 1 in the Region are due to pneumonia; that is, 300 deaths daily, of which 99% occur in countries of Central America, South America, and the Caribbean.
- The number of pneumonia deaths among children under 1 in the United States and Canada is lower than in most countries of Latin America and the Caribbean and up to 20 times lower than in Peru and Mexico.

- Another 40,000 children die of pneumonia before reaching the age of 5 (more than 100 additional deaths a day). Once again, most of them occur in the countries of Latin America and the Caribbean.
- Pneumonia death rates have remained constant or registered only slight decreases in most developing countries of the Region, whereas in the developed countries the rates have fallen by 10% to 12% a year.
- ARIs account for 30% to 60% of all health service visits and 20% to 40% of all pediatric hospitalizations, many of which are associated with subsequent complications that affect the child's health and social relationships.

ARIs are also the leading reason for administration of antibiotics and other drugs to children under 5. In most cases these medications are unnecessary and inappropriate, since they do not help to alleviate the symptoms or cure the disease. They do, however, have potential toxic side effects, and their use may contribute to bacterial resistance (*6*).

The Region of the Americas has been one of the pioneers in echoing the concerns expressed at the global level about the problem of ARIs in children and their role in high pneumonia mortality rates.

Since the problem began to be a focus of attention and concern, considerable progress has been made in implementing activities at the country level to control it and thereby improve the health and wellbeing of children.

The Pan American Health Organization (PAHO) has participated actively in the development of these activities through the support provided by its ARI control program and through direct technical assistance and promotion of the strategy for standard case management (SCM) of ARI, whose effectiveness in controlling the problem has been demonstrated.

The countries of the Region have developed control programs—generally in the framework of their other maternal and child health activities—which recognize the importance of the problem and define steps for implementing control activities to reduce mortality from ARIs, especially pneumonia.

These action plans, which are being developed in most countries of the Region, are expected to contribute soon to an increase in the positive results observed in some areas. These areas are mainly the reductions in pneumonia deaths but also improvements in several important factors in the overall solution to the problem, particularly the reduction in the indiscriminate use of antibiotics and other drugs to treat and reduce the serious sequelae of upper respiratory infections (e.g., deafness and hearing loss due to otitis media).

Despite these efforts, the ARI-related situation of children in the Region is far from ideal. Estimates for the 1990s indicate that ARIs are responsible for more than 100,000 deaths a year among children under 1 in the Americas. Almost 90% of these deaths are due to pneumonia and 99% or more occur in the developing countries of Latin America and the Caribbean.

This situation is a reflection of the existing inequality between countries. One of the most acute manifestations of this inequality is the fact that five countries account for 85% of the aforementioned deaths: Brazil (40%, mainly in the northeast region), Mexico (20%), Peru (14%), Bolivia (7%), and Haiti (5%).

At the same time, an analysis of the situation within this group of countries reveals significant differences in the mortality rates and therefore the health conditions in different areas of each country.

At the hemispheric level, there are countries that have substantially lower mortality rates—including both infant mortality and overall pneumonia and influenza death rates—than the five countries mentioned above and than others with high mortality. For example, Argentina, Costa Rica, Cuba, and Uruguay are among the countries that have relatively low mortality from pneumonia and influenza among children under 1, with rates ranging between 90 and 100 per 100,000 live births. The second group includes, in addition to the countries mentioned, almost all the countries of Central America (El Salvador, Guatemala, Honduras, Nicaragua), which have even higher rates than some of the first group of countries, as well as other countries of South America, such as Ecuador and Paraguay.

ARIs are not only a leading cause of mortality but an important cause of morbidity as well. However, of the huge number of outpatient pediatric visits, serious illnesses such as pneumonia and bronchiolitis in young children account for only a small proportion. The majority of children with ARI seen in health services are suffering from relatively minor illnesses, such as self-limited viral infections of the upper respiratory tract that will generally resolve spontaneously with home care and without the need for drugs.

Nevertheless, the reality in the countries of the Region is that excessive use of antibiotics to treat ARIs is widespread. Recent studies have shown that 50-60% of all ARI cases receive antibiotics.

In response to a problem of such magnitude, the countries of the Region have launched major efforts to implement ARI control activities. Some of these efforts can be seen in concrete activities aimed at making standard case management more available to the population.

This strategy consists of detection of severe cases of ARI based on simple, highly specific, and sensitive signs that are predictors of pneumonia and a basis for immediate hospital referral of these cases. Standard case management makes it possible to detect pneumonia cases that can be treated at home with antibiotics; it helps to identify cases of mild illness that do not require antibiotic treatment; and it includes community education on the signs that indicate serious illness in a child.

The standard case management strategy was devised by PAHO/World Health Organization (WHO) on the basis of studies that were supported, promoted, and conducted to define and optimize. PAHO has encouraged its member countries to apply the strategy in their health services, and the vast majority of them now include standard ARI case management among their medical care guidelines.

The dissemination and application of this strategy, along with detailed, realistic activities planning, make it possible to set achievable goals for the improvement of child health. The proposed goals are expressed in terms of the reduction of pneumonia deaths among children under 5. Despite their potential difficulties, these goals are entirely feasible.

III. Control measures

The studies conducted with regard to developing appropriate control strategies found specific actions that, carried out within the available health care infrastructure, help to improve care for ARI cases and reduce ARI mortality and complications and the inappropriate use in treatment of antibiotics and other drugs (*7*).

In recent years, both WHO and PAHO have undertaken a major effort for research and action to ensure that ARI control strategies are effectively applied at the national level and that appropriate case management is accessible to the entire population (*8*).

Additional efforts have been directed toward strategies to introduce ARI control that will be integrated into existing development policies and to strengthen local health care and foster community participation in the management and execution of control activities (*9*).

The results of these efforts have gradually become apparent, and the impact of ARI control activities is well documented (*10-12*).

IV. ARI control strategies

The policies of the WHO Global ARI Control Programme, within the framework of integrated child health care, recommend two basic strategies at the national level:

- Immunization against measles and whooping cough to prevent some cases of pneumonia, and
- Standard ARI case management. This includes:
- Treatment of pneumonia cases at the primary care level (responsibility for which in some countries may rest with community health workers);
- Treatment of severe pneumonia and other cases of serious disease in hospitals;
- Treatment in hospitals of severe pneumonia and other serious disease in infants;
- Treatment of (non-pneumonia) cases of cough or cold;
- Treatment of wheezing;
- Treatment of ear infections;
- Treatment of throat infections;
- Education of the mother (or other caretaker) on danger signs and home care (*13*).

In addition to these specific ARI control strategies, PAHO has emphasized a plan of action within the general framework of the strategic orientations adopted by the XXIII Pan American Sanitary Conference in June 1991. The plan is aimed at contributing to:

- Reorganization of the health sector through strengthening and development of health care capabilities at the local level, possible incorporation of social security institutions, and channeling of external financing toward sector reorganization;
- Targeting of high-risk groups;
- Health promotion;
- Use of mass communications for health;
- Involvement of women in health and development;
- Information management;
- Resource mobilization;
- Cooperation among countries.

Thus, lines of action that complement and are consistent with the general strategies of PAHO programs have been developed, resulting in greater efficiency and effectiveness in the activities (*13, 14*).

V. Diagnostic criteria

The guidelines for case management and antibiotic use recommended by the PAHO/WHO ARI Programme are appropriate for developing countries with limited resources and an infant mortality rate of more than 40 per 1,000 live births. They are predicated on the assumption that the incidence of bacterial pneumonia among children seen in primary health care establishments is high and that the risk factors for pneumonia (e.g., malnutrition and low birthweight) are relatively common, leading to high pneumonia death rates (*15*).

The main objective of ARI control at the level of primary care establishments is the identification of pneumonia cases among all the children suffering from acute respiratory infections and ensuring that appropriate treatment is provided. To simplify and facilitate instruction, the least possible number of criteria is used for the diagnosis and classification of cases. The process comprises three essential steps:

- Identification of children who should be examined for possible pneumonia (case investigation based on "entry criteria").
- Identification of pneumonia cases (case diagnosis).
- Commencement of proper treatment (at home or by referral).

a) Entry criteria

Cough and difficult breathing are the two entry criteria for assessing children for pneumonia. These two signs were selected because they are present in almost all children under 5 with respiratory tract problems.

Fever is not considered a good sign for use as an entry criterion, because it is found in many children with other diseases, such as urinary tract infections (*16-18*).

b) Identification of pneumonia cases

To identify pneumonia in children among the many children assessed presenting with cough or difficult breathing, respiratory frequency and chest indrawing were selected as the two signs most predictive of pneumonia. Respiratory frequency is assessed according to age, bearing in mind that the normal rate decreases as the child grows older. In children under 2 months of age, fast respiration (60 or more breaths per minute) and chest indrawing are considered highly predictive of severe pneumonia.

In children aged 2 months to 4 years, children are considered to have pneumonia if their respiratory rate is 50 or more breaths per minute in children 2 to 11 months old and 40 or more in children of 1 to 4 years. Subcostal indrawing is considered a sign of severe pneumonia in children aged 2 to 4 years.

In all cases, it is recommended that children with wheezing be reassessed after administration of a bronchodilator to determine whether the elevated respiratory rate or chest indrawing is caused by asthma (*19, 20*).

c) Home care

Because pneumonia can lead to death within 3 to 5 days, rapid and easy access to antimicrobial therapy is a crucial factor in reducing mortality from this cause. Many pneumonia deaths occur because sick children are not taken in time, if at all, to be seen by a health care provider. For a case management program to be effective, mothers must be able to recognize the signs of pneumonia and they must be encouraged to seek proper care outside the home and to administer the full course of antimicrobial treatment. Mothers must be told that antimicrobial treatment will not result in an immediate cure and that they must return to the health service if the child's condition fails to improve or worsens.

Experience has shown that it is possible to teach family members to observe the respiration of young children, and it has also been shown that the qualitative impression of rapid respiration serves as a predictor of pneumonia (*28-30*). Some languages contain specific words to express the ideas of fast breathing and difficult breathing, so cultural recognition of these signs is widespread.

Effective health education must be based on an accurate understanding of prevalent knowledge, beliefs, and practices in a community. Communication efforts intended to encourage mothers to look for the signs of pneumonia must be based on thorough ethnographic study that reports how mothers perceive pneumonia and identifies the obstacles that deter them from seeking attention from a qualified health care provider.

VI. Treatment

In children over 2 months of age, chest indrawing (in the absence of wheezing) indicates severe pneumonia and the need for hospital referral. The standard antimicrobial for treatment

of severe pneumonia is crystalline penicillin administered intramuscularly, but if the child is very seriously ill (e.g., cyanotic or unable to drink) injectable chloramphenicol and oxygen are indicated. Chloramphenicol is recommended for these cases because it is effective against a broad spectrum of organisms, including *Staphylococcus aureus* and Gram-negative bacteria. It may cause serious side-effects, such as agranulocytosis, but the occurrence of such toxic effects is infrequent and is an acceptable risk if the drug is used only for very severe cases. Oxygen is indicated because in children with pneumonia the lungs cannot transfer sufficient oxygen from the air to the bloodstream and consequently blood oxygen falls to dangerously low levels (*21, 22*).

Children over 2 months of age who have rapid respiration without chest indrawing are considered to have pneumonia but may be treated at home. The standard antimicrobial outpatient treatment must be effective against the two most common agents of pneumonia: *Streptococcus pneumoniae* and *Haemophilus influenzae*. The options include injectable penicillin procaine and two oral antibiotics: cotrimoxazole and amoxicillin. Amoxicillin is preferred to ampicillin because it is more readily absorbed, it is administered three times a day rather than four, and it has fewer gastrointestinal side-effects. Owing to its efficacy, broad spectrum, low cost, ease of administration, and relatively low rate of harmful side effects, cotrimoxazole is the drug of choice in most cases. Oral penicillin and penicillin benzathine should not be used to treat pneumonia in children because they do not reach sufficiently high serum levels to be effective against *H. influenzae* or *S. pneumoniae* strains with reduced penicillin susceptibility, which are increasingly common in some countries (for example, Papua New Guinea and the Philippines).

All children with pneumonia should be reassessed by a health worker after two days of home antimicrobial treatment. The procedures described in the protocol are important to reduce mortality from inappropriate treatment or antimicrobial resistance.

All infants under 2 months of age with any sign of pneumonia or sepsis should be referred to a hospital for treatment with crystalline penicillin and gentamicin to cover both Gram-positive and Gram-negative organisms. Chloramphenicol, recommended for older children, should not be used during the neonatal period due to the high risk of fatal circulatory collapse (gray syndrome). Antimicrobials are only part of the treatment of pneumonia in the newborn. Support measures are also of utmost importance: oxygen if the child is cyanotic or agitated, or if the child has severe chest indrawing; frequent nursing; monitoring of temperature; and, especially, protection from possible chills.

PAHO/WHO has proposed very selective guidelines for the use of antimicrobials in the treatment of ARIs. In many places, the amount of antimicrobials required for the treatment of suspected pneumonia cases is limited compared to the current, generally inappropriate, use of antibiotics (often in improper doses) for the majority of respiratory infections (*19*).

Most children with cough do not require antimicrobials. Nevertheless, it is important to teach mothers to pay special attention in the home to children with cough and common cold and to watch for signs of pneumonia or other complications that might be life-threatening. The key components of home care are liquids and nutritional support: adequate intake of fluids, con-

tinued nursing, and frequent small meals. The parent can also help the child by reducing a high fever, removing nasal secretions, and avoiding exposure to excess heat or cold (*23*).

Most cough medications are expensive and of little or no value in treating children with cough. Some may even be harmful because they contain ingredients such as alcohol or codeine, which are toxic for infants and young children. Others are of questionable usefulness because they combine ingredients that are supposedly expectorants with others that suppress the cough; in other words, ingredients with diametrically opposed purposes. Generally speaking, a productive cough should not be suppressed and support measures should be aimed at mobilizing secretions. Good hydration is the most beneficial approach. Simple and safe home remedies can also help to soothe the throat and calm the cough reflex (*20-22*).

VII. Importance of bacterial pneumonia

Available data indicate that in developing countries bacteria are much more important as causes of pneumonia in children than in developed countries. This finding is based on two types of data: etiologic studies of pneumonia and information on the prevalence of nasopharyngeal carriers of pathogenic bacteria.

The etiologic diagnosis of pneumonia in infants and young children is very difficult to establish because sputum is generally unavailable (*24*). Rapid immunologic techniques such as counter-immunoelectrophoresis, ELISA, latex agglutination, or coagglutination are not totally satisfactory for determining the role of bacteria in the etiology of pneumonia in children (*25*). Only cultures of blood and matter aspirated from the lungs can yield a reliable bacteriologic diagnosis (*26*).

Lung puncture is the most sensitive method for recovering and identifying the bacterial agents of pneumonia in children. Cultures of pulmonary aspirates produce a very low false positive rate (a positive result is a concrete demonstration of bacterial infection, excluding microorganisms commonly found on the skin, such as *Staphylococcus epidermidis*).

In thirteen studies conducted in the 1970s and the early 1980s, pulmonary aspirates from children with pneumonia who had not received any prior antimicrobial treatment were examined (*27-30*). When the results of these studies were combined, it was found that bacteria had been isolated in 456 (55%) of the 835 aspirates examined. Bacteria were found in at least 50% of the children examined in all these studies, with the exception of three.

Moreover, a large proportion of the negative results were probably false negatives due to a number of factors that may obscure the presence of bacteria; for example, the affected part of the lung may not be reached with the needle, the material recovered may be insufficient, or the laboratory methods may not be appropriate for isolating all bacterial pathogens. The studies may also have included children who had received prior antibiotic treatment, since it is not always possible to accurately determine what treatment has been administered to young children. Hence, the actual proportion of positive bacterial cultures was probably higher than reported.

Published studies of pulmonary aspirates conducted before the era of antibiotics indicate that the bacteriology of pneumonia in the developed countries at that time was similar to that observed currently in many developing countries (*27*). Nevertheless, it is accepted that the majority of pneumonia episodes in children in the developing countries are of viral origin, the most important viruses being respiratory syncytial virus, parainfluenza, influenza, and adenovirus.

In a study of pulmonary aspirates carried out in Newark, New Jersey (United States of America), bacterial etiology was demonstrated in only 11% of untreated community-acquired cases of pneumonia (*31*). However, recent studies using antigen detection techniques have led to the conclusion that bacterial infections may be more common in developed countries than has generally been recognized (*24, 32, 33*).

VIII. Limitations of antibiotic treatment of ARIs

The common cold, in the absence of complications, generally produces thick, opaque nasal secretions of a color that many observers would characterize as "purulent." Thick yellow secretions during a common cold may simply be thick mucus (containing epithelial cells desquamated as a result of intense viral infection) or they may be purulent or mucopurulent secretions (containing leukocytes). This is solely the result of a viral infection in the vast majority of common colds. It is estimated that bacterial sinusitis occurs as a complication in only 0.5% of colds in children and adults.

In children, this infectious inflammatory syndrome differs from the syndrome in adults in that it is more extensive and frequently affects the paranasal sinuses, the middle ear, and the nasopharynx. Acute nasopharyngitis is the most common infectious ailment of children.

With regard to pathological anatomy, the first manifestations are edema and vasodilation of the submucosa, followed by infiltration of mononuclear cells, which become polymorphonuclear within 1-2 days. The superficial epithelial cells detach and may desquamate, leading to the production of profuse mucus discharge, first clear, then becoming thicker and purulent.

In older children, the characteristic initial symptoms are dryness and irritation of the nose and sometimes the pharynx, followed within a few hours by sneezing, chills, muscular pain, clear nasal secretions, and sometimes cough. The symptoms may also include headache, general malaise, anorexia, and a slight fever. The secretions generally become thicker within a day and ultimately become purulent. The secretion is irritating, especially during the purulent phase. Blockage of the nasal passages necessitates mouth-breathing, which dries out the mucous membranes of the throat and increases the feeling of discomfort, sometimes to the point of pain. The acute phase lasts 4-10 days. A descriptive study on nasal secretions concluded that there was no correlation between the color of the secretions and the results of bacterial culture.

Among the suppurative complications of the common cold, bacterial sinusitis is more frequent in adults and adolescents than in young children, among whom otitis media is most common.

It is not known how often bacterial sinusitis is preceded by viral sinusitis. Rhinovirus has been isolated from the maxillary sinuses in some adults with sinusitis. Bacterial sinusitis can be

suspected if the symptoms persist and are accompanied by other physical symptoms observable on physical examination. Greenish nasal secretions in a child with an upper respiratory infection that continues for 2-3 weeks without noticeable improvement may indicate bacterial sinusitis, particularly if the child also has pain in the nasal sinuses, bad breath, and a low-grade fever. In such cases, the child may have bacterial sinusitis as a complication and may improve with antibiotic treatment. This occurs in a very small percentage of children with purulent nasal secretions, especially in those younger than 5 years of age.

Clinicians in Papua New Guinea and other developing countries have reported that chronic purulent nasal secretions are an almost universal symptom in young children, but there is no clear relationship between this symptom and a progressive bacterial infection. No study has determined the proportion of children with chronic purulent nasal secretions who show signs of sinusitis on transillumination or X-ray.

Even if such a relationship could be demonstrated, antibiotic treatment of all cases of chronic purulent nasal secretions would probably not be justified, given the risks inherent in long-term administration of antibiotics. Moreover, it has not been shown that antibiotic treatment is any more effective or cost-efficient than repeated cleaning of the nose to clear out secretions. In addition, some of the commonly used antibiotics do not reach adequate concentrations in nasal mucus.

Some studies consider tracheobronchitis a common acute infection of the lower airways. Denny, in an 11-year study in North Carolina, defined tracheobronchitis as cough and hoarseness without laryngeal obstruction or wheezing. It occurs most frequently during the first two years of life (5-7% annually), although it also occurs in schoolchildren. Tracheobronchitis in children is normally associated with acute upper respiratory infections such as nasopharyngitis and is generally of viral origin, although it may also occur as a secondary bacterial infection. As with the common cold, infection of the bronchial mucosa may produce thick sputum with a purulent appearance, without this necessarily indicating a bacterial infection.

Acute bronchitis is generally preceded by a viral infection of the upper respiratory tract; it may develop as a secondary bacterial infection caused by *S. pneumoniae* or *H. influenzae*. In typical cases, 3-4 days after the onset of the rhinitis, the child develops a dry, hacking, unproductive cough, which begins gradually and is often accompanied by low retrosternal discomfort or burning pain in the chest, which intensifies when the child coughs. As the disease progresses, the patient develops wheezy breathing (probably snoring), thoracic pain, and sometimes dyspnea. The paroxysmal cough and the obstruction produced by the secretions may be accompanied by vomiting. After several days, the cough becomes productive and the sputum purulent. Within 5-10 days more, the mucus secretions diminish and the cough gradually disappears. The intense discomfort often associated with the illness may last for a week or more after the acute symptoms have resolved.

Complications are rare in healthy children, but in children who are malnourished or whose health is delicate, otitis, sinusitis, and pneumonia are frequent. There is no specific treatment, and most patients recover satisfactorily without treatment. Antibiotics do not shorten the dura-

tion of a viral illness, nor do they reduce the incidence of bacterial complications. The fact that some patients with recurrent episodes do occasionally improve with this treatment suggests the existence of a bacterial infection.

Children with clinically severe malnutrition and tracheobronchitis, who are at greater risk of developing bacterial pneumonia or another serious infection, should be hospitalized to ensure appropriate nutritional support. Many hospitals and feeding programs treat these children during the initial phase of nutritional therapy with antibiotics, even though they do not meet the criteria for bacterial pneumonia. This procedure may be justified in this small group of malnourished children, who are at particularly high risk and who may not show clinical signs of pneumonia as quickly as well-nourished children. However, antibiotic treatment is not warranted in children who are only slightly to moderately malnourished, based on height and weight criteria, or in the larger group of children classified as malnourished on the basis of lack of growth.

IX. "PREVENTIVE" ANTIBIOTIC TREATMENT

There is no proof to support the formulation of control actions that would seek to reduce pneumonia incidence or mortality by treating upper respiratory infections with antibiotics, even in suppurative cases.

Treating the common cold with antibiotics has not shortened the course of the disease or reduced the percentage of bacterial complications, despite many tests and the fact that many clinical physicians frequently prescribe antibiotics against viral upper respiratory infections. It has been demonstrated that doctors with experience in infectious disease do not prescribe antibiotics against common respiratory infections as frequently as family doctors. Other authors have analyzed the "non-bacteriological determinants of antibiotic use."

Antibiotics have been shown to be effective as prophylactics only for a limited number of conditions. For example, routine antibiotic treatment of ARIs has reduced the rate of recurrence of otitis media, and some pediatricians use this therapy for children who are particularly prone to multiple episodes of acute otitis media. Penicillin benzathine given monthly also prevents relapses of acute rheumatic fever. It was to be expected that penicillin benzathine would reduce the rate of local suppurative complications of streptococcal pharyngitis (peritonsillar abscess, retropharyngeal abscess, and otitis media), but it has not been shown to affect the frequency of bacterial pneumonia.

In addition, a program that concentrates the majority of antibiotic use on upper respiratory infections in an attempt to prevent pneumonia will not likely cover most children who eventually develop the condition. In a study conducted in Newcastle upon Tyne (England) involving 1,011 infants under 12 months of age, only 12 of 47 pneumonia cases were preceded by a severe cold (during the study the infants suffered a total of 1,417 colds, 270 of which were classified as "severe"). The findings of studies of ARI treatment in Jumla (Nepal) and Bagamoyo (Tanzania) also suggest that very severe pneumonia may develop and lead to death within a few days. Control actions should therefore focus on early detection and treatment of pneumonia

cases, given that the objective is to reduce mortality. ARI intervention studies support this approach.

Not only is there no proof to support a strategy of extensive antibiotic use for ARI to prevent pneumonia, but there is considerable evidence demonstrating that this practice is dangerous.

The risk of superinfection must be carefully considered. Antibiotics administered at the beginning of a viral infection may alter the flora or lead to a superinfection that may make the individual more prone to bacterial complications in a later phase of the disease. A higher rate of complications has been reported in children with measles who had been given antibiotics previously in the home than in those who were not treated in this way.

The risks of toxic effects of antibiotics are small compared to the risk of dying or suffering permanent harm due to a severe bacterial infection; but the adverse effects outweigh the benefits when antibiotics are administered more often to prevent, rather than treat, a severe infection. Moreover, large doses of antibiotics can lead to resistance and render the chosen antibiotic useless (*34*).

X. Use of cotrimoxazole in control activities

Advantages:

- Only two doses a day needed;
- Less costly than penicillin benzathine;
- Appropriate treatment for *H. influenzae* (fewer treatment failures can be expected), penicillin-resistant pneumococci, and other pathogenic germs such as *S. aureus*.

Disadvantages:

- Broad-spectrum activity: cotrimoxazole is a useful drug for other infections, and the resistance induced by its widespread use may limit options for treating important organisms such as *Shigella*;
- Requires strict compliance with dosage;
- Several countries have reported resistance;
- Side effects.

Pathogenic germs that affect the respiratory tract may develop resistance to cotrimoxazole if it is not used judiciously and in accordance with appropriate protocols. A recent report from Australia indicates a 37.5% prevalence of cotrimoxazole resistance in the case of *S. pneumoniae*, as a result of which the drug ceases to be useful for empiric treatment of respiratory infections. This resistance is believed to reflect excessive use of antibiotics in the community.

With regard to cotrimoxazole toxicity, an analysis of nine studies of the drug in children found no fatal reactions associated with a 7- to 10-day course of treatment with cotrimoxazole. According to the data compiled, only 8 of 2,061 children had to stop taking the drug due to

dermatological or hematological reactions. In all cases, these reactions disappeared once the treatment was suspended.

All the serious side effects of short-term treatment of children with sulfonamide are rare and are generally reversible; the treatment should be suspended if a rash appears in order to avoid serious dermatological problems. If red blood count is systematically monitored (which is necessary), slight hematological reactions are observed relatively often, but only serious neutropenia or thrombocytopenia are important, and these reactions are rare.

Gutman also summarizes a study of cotrimoxazole carried out in Sweden between 1965 and 1975. The estimated incidence of fatal reactions was less than 1 per 100,000 cases. A similar rate was observed in Great Britain. The frequency of adverse reactions increases with age, but severe reactions are seemingly rare.

Sulfamethoxazole, one of the components of cotrimoxazole, is a fast-acting sulfonamide. Most serious reactions to sulfonamides (Stevens-Johnson syndrome, for example) have been caused by long-acting sulfonamides (such as sulfadoxine). Nevertheless, intense reactions may occur and it is therefore necessary to establish prudent guidelines for the use of antibiotics in acute respiratory infections. The Committee on Drug Safety in Great Britain published a report comparing the mortality associated with cotrimoxazole, ampicillin, and trimethoprim. The committee estimated that there were 1.42 deaths per 1,000,000 prescriptions of cotrimoxazole, compared with 0.18 per 1,000,000 for ampicillin. Most of these deaths occurred in older persons, not children.

The Malaria Division of the Centers for Disease Control and Prevention of the United States recently analyzed the adverse reaction rate for cotrimoxazole. The data were on adults, and it was to be expected that the allergic reaction rates for children would be lower still, especially during the first exposure to the drug.

Another concern relating to the use of cotrimoxazole is its prescription for infants younger than 2 months. Much of this concern stems from repeated warnings by pharmaceutical companies that the drug should not be used to treat children younger than 2-6 months of age. The main worry is the possible risk of kernicterus, resulting from displacement of bilirubin from albumin by sulfonamides, in newborns. Sulfamethoxazole, the sulfonamide in cotrimoxazole, is one of the weakest displacers of bilirubin. In a study of newborns, no displacement of bilirubin from albumin was found, even at sulfamethoxazole concentrations of up to 300 mg/ml (much higher than maximum values or therapeutic serum concentrations). In this study, no other side effects were observed. The current edition of *The Use of Antibiotics* by Kucers condones the occasional use of cotrimoxazole for the treatment of serious infections in neonates aged 2-3 weeks. It is recommended that the drug not be used in premature infants or during the first week of life (*35, 36*).

XI. Integrated management of childhood illness (IMCI)

ARIs, acute diarrheal diseases (ADDs), and malnutrition continue to rank among the five leading causes of death in the majority of developing countries. In some of these countries, or in regions therein, malaria also remains an important cause of death. Measles, the incidence and mortality of which has declined markedly as a result of mass vaccination campaigns, will continue to figure among these prevalent diseases until the eradication plan is completed.

There is a clear need to sustain and increase the efforts undertaken up to now in order to achieve the goals for reduction of child mortality proposed by the countries for the year 2000 (*37*).

For this reason, PAHO/WHO and the United Nations Children's Fund (UNICEF) have jointly developed in recent years a strategy for integrated child health care. This approach makes it possible to assess, classify, and treat diarrheal diseases, malnutrition, and malaria, as well as ARI.

Implementation of this strategy will enhance the activities already under way to control these problems in the developing countries. The activities will also complement one another and thus have a greater impact on mortality and morbidity (*8*).

PAHO/WHO intends to disseminate this strategy over the next few years to encourage its progressive implementation. The integrated and specific actions aimed at improving health care for children are expected to mutually reinforce one another and lead to better child health.

a) Objectives of IMCI

The proposal for IMCI is aimed at contributing to the achievement of three major objectives of the utmost importance:

- Strengthening the concept of integrated child health care in health services, shifting the focus from treatment of illness to the comprehensive care of child health, thus providing opportunities for detecting the main health problems that affect children.
- Strengthening the planning and problem-solving capability of the first level of care, giving health workers the tools they need to properly manage the problems that most frequently affect child health and prompt health service visits.
- Achieving greater equity of access to adequate health care for children, making appropriate diagnostic and treatment technologies available to the population for the most frequent health problems.

The IMCI strategy will also contribute to the achievement of the following specific objectives:

- Reduction of mortality in children under 5 in particular from ARI, ADD, malnutrition, malaria, and measles.
- Reduction of the occurrence and severity of cases of ARI, ADD, and measles.
- Improvement of the quality of care for children in health services, reducing the inappropriate and excessive use of diagnostic and treatment technologies.

b) Rationale

Implementation of the IMCI strategy will help to prevent a large number of deaths of under-5 children from pneumonia, diarrhea, malnutrition, malaria, and measles.

Implementation of the strategy will also make it possible to prevent many cases of these illnesses from getting worse and even prevent them from occurring in the first place through application of the recommended home care measures.

In addition to these significant benefits for child health, implementation of the strategy is also expected to help improve the quality of child health care in the following ways:

- Extension of the coverage of care for the major childhood illnesses through personnel training, not only at the health service level, but also in the community.
- Improvement of the quality of care currently being provided by health services through enhancement of the capacity for detection and identification of problems and the possibilities for providing appropriate treatment. Application of the strategy will also help to reduce the indiscriminate use of diagnostic and therapeutic technologies.
- Strengthening of the technical and management capacity of health service personnel at the primary care level. This will be accomplished through training, not only in the application of the strategy in the care of children seen by the service, but also in matters relating to planning and organization of activities. These activities will help to focus attention on at-risk groups to ensure their access to the strategy.

The implementation of this strategy will strengthen and complement the ARI/ADD control activities already under way. PAHO/WHO propose to proceed with the implementation of the IMCI strategy in three phases.

- Phase 1: Analysis of the epidemiological situation and the status of efforts to control the principal health problems of children.
  This phase will include a review of the information available at the national and subnational levels on the magnitude and trends of the principal child health problem. Special emphasis will be placed in this phase on identifying the areas with high morbidity and mortality from pneumonia, dehydration, malnutrition, and malaria. Areas with high morbidity from these causes, based on records of medical consultations and hospitalization, will also be identified. Special attention will be given to several factors that impede the population's access to child health care, such as geographic or cultural barriers, lack of professional health personnel, or difficulties with referrals to higher levels of care.
- Phase 2: Analysis of the strategy of integrated management of childhood illness and organization of its implementation in the country.
  This phase will include presentation of the rationale for the IMCI strategy and its characteristics to make national officials aware of the benefits of its application. In this phase, spe-

cific control strategies will also be analyzed to determine what adjustments are needed to bring them in line with the integrated strategy.

- Phase 3: Development and implementation of plans of operation.
  The focus of this phase will be the development of a specific plan of operation detailing the activities to be carried out to control the prevalent childhood illnesses. The plan will also provide for monitoring and evaluation of the activities undertaken and assessment of progress in relation to expected results, with emphasis on the process of training health personnel in the application of the IMCI strategy. Other components of this plan will be:
  - Provision of supplies for the implementation of the strategy;
  - Supervision of the health personnel involved in control activities;
  - Health communication and education to familiarize the population with the strategy;
  - Monitoring and evaluation of activities and results;
  - Operations research on the several components of IMCI to measure the impact and cost/benefit of its implementation at the local level (*38*).

c) Conclusions and future prospects

Over the past few years, there has been growing awareness of the need to take concrete action to reduce the social burden that child deaths represent. This has helped to accelerate the process of design and implementation of increasingly effective strategies for saving millions of children under 5 in developing countries from sickness and death.

Every year many children benefit from the application of these strategies. Through vaccination, use of oral rehydration, antibiotic treatment of pneumonia, and the use of other effective treatment, prevention, and health care measures, the risk that these children will get sick and die is being reduced.

Numerous lives are saved each year thanks to the efforts of the many people who are working to make these strategies accessible to the population. This provides an impetus for continued effort to increase the coverage achieved to benefit a larger number of children who are at risk for these diseases.

The IMCI strategy combines a set of specific strategies that are already available, thus contributing more efficiently to the prevention, early detection, and treatment of the principal health problems of children and helping to achieve the goals for reduction of child morbidity and mortality by the year 2000 (*38*).

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