



SECTION I

MAGNITUDE OF THE PROBLEM



CHAPTER 1

EPIDEMIOLOGY OF ACUTE RESPIRATORY INFECTIONS IN CHILDREN: REGIONAL OVERVIEW

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I. INTRODUCTION

Knowledge about the epidemiology of acute respiratory infections (ARI) has grown significantly; nevertheless, many urgent questions are still being raised about case definition, the sensitivity and specificity of diagnostic tests, the association of such factors as chronic adult diseases, direct and passive smoking, housing characteristics, crowding, the absence of natural breast-feeding, nutritional status, vaccinations, and the history of other respiratory pathologies.

This introductory chapter presents a summary of the knowledge documented up to 1993 in the countries of Latin America, in order to share the experience of Latin American institutions. This essay does not so much attempt to give a critical analysis of the epidemiological situation (which, in any case, would require essential information that remains unavailable); rather, the effort here attempts to reflect the current state of knowledge about the epidemiology of ARI in children. It is hoped that this overview would encourage members of the scientific community to quicken the pace of this knowledge acquisition more deeply.

Predictions are commonly made about changes in health policies on the basis of results expected from research that has yet to be carried out. In almost all the areas cited in this overview, broader and more in-depth basic information is needed. Currently, in several developing countries studies are under way on the effects of vitamin A supplements, malnutrition, indoor pollution, and other areas. These studies may help to define the priority of problems.

For example, we need to elucidate the relationship between HIV infections and ARI, and between low birth weight and respiratory infections. Studies sponsored by the National

Research Council in the United States have provided important new data on the etiological agents of ARI in children from developing countries, but there is too little information on pneumonia in adults and the elderly to be used for the design of effective integrated programs.

In developing countries, it would be quite useful to assess the relationship between the levels of maternal immune response (humoral and cellular) and passive immunity in infants; the causes of increased mortality among the elderly; and the relationship between air pollution and ARI, as compared to morbidity due to bronchial reaction. From the methodological standpoint, there is a need to explore the relationship between prior bouts of respiratory infections, particularly in the first year of life, and subsequent respiratory infections. If the strength of the association turned out to be high, multivariate models should then be applied.

There is a need for health services to place greater emphasis on methodological consistency in the collection of data in both developing and industrialized countries. In light of advances in this area, it should be possible to develop a survey on acute symptoms (analogous to those developed by the American Lung Association and its counterparts concerning chronic respiratory diseases) to be used in developing and industrialized countries alike. The use of daily records, despite the considerable inconvenience entailed, could be of great value under certain circumstances (1).

Epidemiological research on ARI in infancy should be geared first toward the improvement and timeliness of diagnosis and treatment at the primary care level, and second toward the study of specific preventive interventions, mainly immunizing agents. This requires progress in three separate areas, specifically:

- a) clinical, etiological, and epidemiological studies on the nature and distribution of common causative agents, including the identification, hierarchy, and stratification of such risk factors as the probabilities of becoming infected; determining the seriousness and complications of the disease and its lethality; and the characteristics and distribution of vulnerable social groups;
- b) studies on the immune response of the infant population, the effectiveness and tolerance of the most economic and effective immunizing agents and better-tolerated antimicrobial treatments; research methods (clinical and epidemiological surveys), simpler procedures for identification of microbes; and
- c) operational research to evaluate the efficacy and efficiency of such interventions as improved nutrition, health education, vaccinations, monitoring response to chemotherapy, environmental management, and development of health services and health promotion programs, particularly for the promotion of ARI control and prevention (2).

The elevated incidence of ARI in children in developing countries requires the establishment of control strategies that are politically viable and financially feasible. The Program of the Pan American Health Organization is attempting to reduce mortality from ARI through recognition of serious cases and the rational use of existing treatment (3).

To show which areas of epidemiological research have received attention in the countries of the Region and at the same time disclose the paucity of essential epidemiological information, the following review of information published prior to 1993 is offered.

II. DIAGNOSIS

In Argentina (4) the sensitivity of the complement fixation test for the serological diagnosis of acute lower respiratory infections (lower ARI) in children was evaluated and compared to direct methods such as indirect immunofluorescence (IIF) of nasopharyngeal aspirate and isolation of tissue culture. A study was conducted of 264 matched samples from children under 5 years with ARI. Thirty-nine sera turned out to be anticomplementary, and seroconversion was detected in 38% of the children with confirmed viral ARI, whereas seroconversion was detected in only 14% of those with unconfirmed diagnoses. For respiratory syncytial virus (RSV) seroconversion was observed in 39% of the cases, whereas for adenovirus it was found in 50% of the cases. Sensitivity of the complement fixation test in relation to direct methods (IIF) and/or cultures was 38.5%.

In Brazil two rapid diagnostic techniques were compared for detection of RSV in nasopharyngeal secretions: immunofluorescence (IF) and the enzyme-linked immunoadsorbent assay (ELISA), with the isolation of the virus in tissue cultures (5). The specimens were obtained from children under 5 years of age with ARI in the six months from January to June 1982. Of the 471 specimens examined, 54 (11.5%) were positive with viral isolation and 180 (38.2%) were positive with immunofluorescence. Bacterial contamination of inoculated tissue cultures inhibited the isolation of the virus in many samples. Specimens from 216 children were tested to compare ELISA and IF. Of these 60 (27.0%) were positive in ELISA and 121 (56.0%) were positive by IF. These results suggest that the high specificity of ELISA notwithstanding, its sensitivity is low. Perhaps when the tests were performed the original nasopharyngeal secretions were significantly diluted and held more suspensions of mucus than the cell suspensions used for immunofluorescence. But of the three techniques tried, IF yielded the best results. Even so, ELISA could be useful when performing IF is not feasible.

In providing care for respiratory disease the question almost inevitably arises of whether to use antibiotics. Mir del Junco, et al. (6) studied 424 children with ARI between the ages of 29 days and 14 years over a one-year period. Blood samples were taken from all the patients in order to perform hemograms, erythro sedimentation, and measurement of reactive C protein; chest x-rays were also taken of all the patients. It was concluded that positive reactive C protein is more likely to be definitive than leukocytosis, erythro sedimentation, or fever in identifying the bacterial origins of ARI, reducing the occurrence of false positives and negatives in the results. However, reactive C protein should be combined with clinical symptoms and signs and radiology when discussing the most appropriate treatment to be administered.

Viral ARI are a frequent cause of hospitalizations in the first two years of life. For a rapid diagnosis, fluorescein-conjugated antibodies to the main respiratory viruses are used. Bello Corredor, et al. (7) studied the nasopharyngeal exudates of 2-year-olds, admitted to four pediatric hospitals in Havana, who were diagnosed with ARI in the period from January 1987 to September 1988. For the diagnosis, samples were processed using direct immunofluorescence (DIF) with conjugated antibodies for RSV, adenovirus, influenza A virus, influenza B, and parainfluenza 1, 2, and 3. Forty positive samples were obtained, with RSV accounting for the highest incidence.

Larrañaga and colleagues (8) studied 78 clinical cases hospitalized for lower ARI from 1983 to 1986. In all cases, adenovirus was confirmed using viral isolation and antigen detection in nasopharyngeal aspirate or matched serology. Of the techniques used to determine the virological diagnosis, viral isolation yielded the highest positive results (66 of 78 cases). The personal characteristics of the patients were examined, as were the risk factors of acquiring serious adenovirus infection, the clinical manifestations, and the viral results obtained. Of the 78 cases studied, 69.2% were children under 1 year of age. Mixed viral infections occurred in 43.6% of the patients and were preponderant among the 1-year-olds. The most frequent risk factor was a history of respiratory pathology, treated through ambulatory and/or hospital care. Clinical evolution was prolonged and characteristic of adenovirus infections. Lab tests showed an unaltered hemogram, a tendency toward hypoxemia, and radiological alterations with frequent images of pneumonitis, condensation, and pulmonary hyperinsufflation. The lethality of the cases studied was 7.7% (6 cases).

In Brazil (9) clinical and microbiological evaluations were done for patients with bacterial pneumonia treated with tobramycin. The group of patients averaged 40 years of age. A comparison was made of the results obtained using two hemogram methods. Germ presence and changes in pathogenic flora during and after antibiotic therapy were confirmed. In five patients, bacteria remained during convalescence and the subsequent relapses caused mainly by *Streptococcus pneumoniae*. After five or more days of treatment, the flora persisted in 9 cases and were modified in 13 of the 22 cases treated. In cases in which the same flora persisted, the association of *Staphylococcus aureus* and *S. pneumoniae* was preponderant (9.1%). The most frequent changes in flora were found in cases in which *Klebsiella* sp. was isolated in the first culture (13.7%), followed by *S. aureus* (9.1%).

Lederman, et al. (10) studied the etiology of acute pneumopathy in 43 children between the ages of 1 month and 13 years (average age: 18 months). In 53.4% of these cases, viral etiology was found with marked preponderance of RSV; in 9.3%, bacterial etiology was found by pulmonary puncture; and in 4.3%, mixed etiology. In the hemogram, the absolute count of neutrophils is generally significantly greater in cases of bacterial pneumonia, although this does not occur with lymphocytes or the hourly rate of sedimentation.

In Santiago, Vicente and colleagues (11) determined what proportion of ARI were due to viral infections in nursing infants between 1980 and 1982 by using serological techniques. The authors confirmed viral presence in 58.4% of the cases, with RSV and parainfluenza virus (PI)

the main ones detected. In 14.5% of the ARI cases studied, the presence of two or more viruses was confirmed. RSV was preponderant in children under 6 months, whereas PI predominated in children 6 to 12 months, and adenovirus in children over 1 year. RSV and PI were important in acute obstructive and recurrent bronchitis, pneumonitis, and cases with mixed symptoms; RSV was preponderant in the cases of bronchopneumonia. Among children with positive and negative results, no great differences were found from the clinical, laboratory, or radiological standpoints. The importance of serology as a method of viral detection is important in those places where there is no opportunity for more thorough examination. Radiography can be quite useful in reaching a diagnosis of lower ARI in pediatric cases.

Five to seven years later in Santiago, a study was conducted of 235 nursing infants under 1 year of age who were hospitalized in 1987, 1988, or 1989 due to radiologically confirmed lower ARI (ALRI) and who had been sick for no more than 5 days and hospitalized for no more than 2. A control group of 74 healthy children was used. All of the patients had cultures taken from pharyngeal secretions, hemocultures, antigen assays in concentrated urine, serology specific for IgM with indirect immunofluorescence (IIF), direct immunofluorescence (DIF) of pharyngeal aspirates, and isolation of causative agents. Respiratory virus was detected in 57.5% of children with ALRI and in 28.3% of the control group; RSV was predominant. Of 119 patients with ALRI, *Haemophilus influenzae* was detected in 18 and *S. pneumoniae* in 2 in the urine antigen. Antigenuria was also found in 6 of the 24 control group members, which raises questions about the specificity of the method. In 80 patients, *Chlamydia trachomatis* was investigated and was found positive in 5 of them (ratio of 1:16), all of whom were under 5 months of age. In 80 patients all available methods were used, resulting in the detection of a presumed causative agent in over 70% of the cases; an undetermined respiratory virus in 57.5%; *H. influenzae* in 10%; *S. pneumoniae* in 1.2%, and *C. trachomatis* in 6.2%. When only two regular methods of bacterial study were employed (nasopharyngeal culture and hemoculture), the causative agent was not identified. However, when serology and viral isolation were added, positivity rose to 30%. When IF was done for respiratory viruses, in addition to antigenuria and determination of IgM specific for *C. trachomatis*, positivity rose to 70%. Among factor characteristics (e.g., age, presence of fever, apnea, breathing rate, obstructive bronchial syndrome, leukocytosis with count above 15,000, band neutrophils over 5,000, sedimentation rate, reactive protein C, and radiographic status) no satisfactory clinical, radiological, or etiological correspondence was found that would distinguish between a presumed viral infection and a bacterial infection—except for one child with a pleural effusion in which positive antigenuria was detected for *H. influenzae* (12).

Although the radiological findings may suggest a certain etiology, results are generally non-specific and need to be strictly correlated to the clinical history and laboratory tests. It is important to recognize different radiological patterns that can represent pediatric ALRI and thereby make better use of radiographs for etiological diagnoses and treatment. Interstitial pneumopathies for the most part have a viral origin; purely alveolar infections for the most part have a bacterial etiology. The term “pneumonitis” is often applied inappropriately; its use is inaccurate.

rate, nonspecific, and confusing. Results from chest x-rays improve considerably when antero-posterior and lateral projections are made (13).

Salas and colleagues (14) collected nasopharyngeal aspirates from 76 children hospitalized for ARI in San José, Costa Rica. To obtain these secretions, a plastic device attached to a food catheter and a mechanical vacuum were used. Secretions were divided into two portions for the viral and bacterial isolations. For the viral isolation, samples were placed in a preservative and transported quickly in an ice bath to the laboratory where they were inoculated into HFT-2, HEp-2, and LLCMK cells. Observations were made of the cytopathic effects, hemadsorption, and indirect immunofluorescence, resulting in the identification of virus in 70.5% of the bronchiolitis and in 59.4% of the bronchopneumonia and pneumonia. The most frequently isolated virus was RSV, followed by the *herpes simplex* virus and adenovirus. To isolate bacteria, samples were placed in blood agars, chocolate culture media with isovitalex, Levine, and mannitol salt. Identification was made of group A β -hemolytic streptococcus, *S. pneumoniae*, and *S. aureus*. *S. pneumoniae* was the bacterium most frequently isolated in children with bronchiolitis (13.6%), followed by *Streptococcus* sp. (12.5%) in children with bronchopneumonia-pneumonia. The diagnoses were extremely efficient, given that some etiology could be determined in 93.2% of the children with bronchiolitis and 87.5% of the children with bronchopneumonia.

González Ochoa and colleagues (15) reported on the results of serological surveys of monospecific sera from students of the "Raquel Pérez School" in Havana, Cuba, during 1980 and 1981. It became evident that the student population was highly susceptible to viral infections from strains of influenza A virus (H3N2 and H1N1), which led to a growing epidemic situation. The effort demonstrated the usefulness of this type of study through epidemiological surveillance, which allowed situations to be anticipated and control measures taken.

Martínez and colleagues (16) measured the breathing rate (BR) of 966 children while awake and 263 children while asleep, establishing normal ranges and average rates for the breathing of children from 15 days to 60 months old and finding broad differences in this ratio in relation to age and state of wakefulness or sleep. The authors performed the same procedure for 566 children with ARI whom they evaluated, using a system of clinical notation, for wakefulness or sleep, the type and seriousness of ALRI, and whether it was obstructive or mixed. The variation in the respiratory frequency in relation to the indices studied remained stable. From this, it was concluded that respiratory frequency alone is not a measure useful for rating the severity of an ALRI, even though when awake, with moderate and severe ARI, children under 2 years of age tend to present a respiratory frequency above 60 breaths per minute and over 2 years above 50 breaths per minute.

In light of the high morbidity and mortality of ARI, particularly in children under 5 years of age, and the abuse of medicine used for their treatment in Mexico (17), a management plan was proposed based on the diagnosis of syndromes. The plan includes: a) performing the diagnosis of syndromes, distinguishing between syndromes that cause breathing difficulty and those that do not; b) a decision tree for those patients that do not have respiratory insufficiency, which differentiates between syndromes that merit antimicrobial prescription from those that do not

require it and which also includes therapeutic decisions according to the course of the disease; c) a decision tree for those patients who have respiratory insufficiency; and d) indications for the drugs that should be used and their dosage. The proposed standards in this work are essentially geared toward the physician, although it is thought that they could also be applied, at least in cases of ARI where respiratory insufficiency is not present, by other properly trained and supervised personnel. There are different considerations on the usefulness of this type of plan, particularly the simpler ones which have been or are being implemented in several parts of the world, including Mexico.

III. TREATMENT

A serious problem most countries face is the excessive use of antibiotics in the treatment of ARI, which have comprised up to 50 to 60% of all infections. The situation is compounded in some countries by high mortality rates, and it has been shown time and again that the deaths result from a lack of primary health care and timely and effective treatment. To address the situation, the countries of the Region have decided to implement the strategy of standard case management for ARI in all the health services for first level care. This strategy attempts to detect serious cases on the basis of signs that are simple, but highly specific and sensitive for predicting pneumonia, so that they can be urgently referred to a hospital. The strategy also includes identification of cases of pneumonia that can be treated at the patient's home and community education on signs indicating the status of a sick child (18).

In a double-blind parallel comparative clinical study (19) of 40 pediatric patients carrying ALRI (n = 20 in each group), chloramphenicol associated with naproxen sodium and placebos were used. The naproxen sodium and the placebo were administered orally in suspension over a 10-day period, 3 times a day, at 8-hour intervals. The dose of the naproxen sodium was between approximately 11 and 16.5 mg/kg/day. Routine x-ray examinations were done before and after treatment. The medicated group showed improvement with faster relief of coughing, breathing difficulty, and fever compared to the placebo group. Tolerance to naproxen sodium was good; in only one case was there a collateral gastrointestinal effect of slight intensity with spontaneous ejection.

In another study (20) midecamycin in the form of myocamicin was used in treating 32 patients suffering from suppurative tonsillitis, acute otitis media, acute sinusitis, tonsillar abscess, lobar pneumonia, acute bacterial bronchitis bronchopneumonia, pyodermitis, erysipelas, bacterial paronychia, deep lesion, chronic cellulitis, and furunculosis. Clinical recovery occurred in 90.6% of the cases with doses ranging from 30 to 40 mg/kg/day, indicating that this medicine is a new option for treating respiratory and dermatological infections brought on by germs sensitive to the action of the drug. As for the lower respiratory tract, it was concluded that the symptomatology (coughing, breathing difficulty, and fever) evolved over time in the group that received the drug more favorably than in the control group that received the placebo.

In autumn and winter of 1981-1982 and 1982-1983, respectively, prodigiosin was tested in a trial run in preschool institutions of Tallinn as a way to protect against acute respiratory viral infections (ARVI). Primági, et al. (21) used it during an epidemic seasonal increase in ARVI and influenza in children 3 to 6 years of age. The prodigiosin was administered via the nasal passages in doses of 25 to 50 mg per child, once a week over a three-week period. The application was observed to induce formation of endogenous interferon and the concentration in the blood fluctuated between 8 and 64 IU during the first 72 hours. After the third application a statistically significant decrease in interferon levels could be observed. During the fourth and fifth weeks no interferon was found in the blood, which would indicate increased tolerance. The morbidity of ARVI demonstrated a statistically significant decrease, dropping 2.5 to 2.9 times in the time the drug was administered. After administration of prodigiosin had been completed no significant reduction in ARVI or influenza morbidity was observed.

A study of the patterns of antimicrobial prescriptions issued by doctors in rural Mexico (22) analyzed prescribed treatments in 8,002 episodes of ARI over the course of a year in 1,359 families residing in 137 rural and semirural areas throughout the country. Each locality had a medical unit of the IMSS/COPALMAR Program, which had a listing of essential drugs that regulates prescription and availability. In 87% of the cases at least one drug was prescribed; 48.6% received antibiotic treatment, 49.3% received antihistamines, and 69.8% ingested an antipyretic drug. The frequency of dosage varied with each clinical syndrome. The most frequently used antibiotics were penicillin benzathine (54.7%), erythromycin (17.1%), and ampicillin (14.8%), which was associated with the presence of the aforementioned listing. Remission occurred in 95.3% of the cases; 4.6% became chronic, and 0.1% resulted in death. Lethality due to pneumonia was 4.4%. These rates, which may be regarded as satisfactory, are mainly attributed to the timely access to medical services enjoyed by the rural population studied.

IV. INCIDENCE AND PREVALENCE

According to PAHO/WHO data (18), little information is available on the incidence and prevalence of the different respiratory diseases that make up the ARI group. Nevertheless, in 37 countries of the Region, it is agreed that ARI represents the major cause of outpatient pediatric consultations. Some studies have verified that 40 to 60% of consultations are due to ARI. It is common for children to have between four and six consultations per year, with seasonal variations, which implies quite a high demand for medical care. Only a small portion of the vast volume of consultations correspond to serious cases such as pneumonia or bronchiolitis in young children. Generally, the cases concern viral infections of the upper respiratory passages and are self-limiting and spontaneously cured with care at home. Mentioned below are some of the studies documented by Latin American researchers.

In 518 children who received outpatient treatment from Social Security in Río de Janeiro, ARI incidence was registered at 47.5%; there was 92.68% prevalence of the infections in the upper

respiratory passages, particularly in the group of children between 1 and 5 years of age; and there was an associated presence of diarrhea (10.5%), otitis (5.2%), and vulvovaginitis (3.5%) (23).

According to Campuzano de Rolón (24), ARI remain the principal cause of morbidity from acute diseases among every age in Paraguay. Different clinical and etiological aspects of the acute infectious bacterial pneumonopathies were studied with the following objectives: 1) to determine the importance of bacteria as an etiological factor and the incidence of each of them in acute infectious pneumonopathies; 2) to determine the sensitivity of isolated germs in acute infectious pneumonopathies; 3) to use a technique for rapid identification of bacterial antigens, such as the latex agglutination test; 4) to better understand such diagnostic aspects of the disease as physiopathology, clinical development, treatment, and prognosis in the national context in order to set guidelines for treatment and lower corresponding mortality and morbidity.

To determine the incidence of ARI, identify its clinical characteristics and etiology, and treat and learn about its lethality and mortality, a study was done in 1985 of 696 patients with ARI who composed a representative sample of outpatient consultations and 330 hospitalized children. Both groups were from the pediatrics department of Belén Hospital in Trujillo, Peru (25). The study included 583 of 1,000 outpatient consultations and 285 ARI cases of 1,000 hospitalized patients. There were registered 12 and 276 cases per 1,000 ARI in the upper respiratory passages, and 273 and 308 cases per 1,000 ALRI, respectively. Of those hospitalized for ALRI, 60.13% were for pneumonia, 29.1% for acute bronchiolitis, and 3.7% for laryngotracheitis. All of these cases were characterized by coughing, polypnea, and gasping, with high fever most common in the pneumonia. Auscultatory signs, x-ray images characteristic for each ALRI syndrome, and hemograms raised suspicions of a bacterial etiology, with *S. aureus* and *S. pneumoniae* being the most frequent. Penicillin was effective in 70% of the bronchopneumonias and in 89% of the lobar or lobular pneumonias. For cases of suppurative pneumonia, rifampicin, isoxazolyl penicillin, and gentamicin were used with concomitant drainage in 84% of the cases. Mortality from ARI was 11.2 per 1,000 live births and lethality was 3.93%. Bronchopneumonia was four times more lethal than lobar pneumonia. In conclusion, in 2 of 7 hospitalized cases and in 3 of 5 consultations for ARI, coughing, polypnea, and heaving are useful in making primary care treatment decisions. The authors recommend giving penicillin parenterally in children with coughing and polypnea, and when these symptoms are associated with heaving, patients should be referred to a hospital without delay.

In the same Belén Hospital in Trujillo, a study was done of 1,193 children from 0 to 14 years of age, admitted as outpatients between January and December 1985 (26). To determine incidence, define high-risk groups, and identify determining factors of ALRI, random selection was made of 624 outpatients and 569 from the emergency unit without regard to the reason for seeking treatment. Children were excluded who had respiratory symptoms from measles, whooping cough, tuberculosis, chicken pox, German measles, diphtheria, foreign body, and asthma. The results demonstrated 583 cases of ARI per 1,000 outpatients. The vulnerable groups were children under 5 years of age (81.5%), males (55.3%), and those from urban

areas (45.3%) and suburban areas (43.5%). Moreover, the frequency of ARI was 68.1% in winter and took place in 57.9% of well-nourished children and in 60.3% of children with first-degree malnutrition, although malnutrition was associated in 30.9% of the children with ARI. Incidence was significant in cases of crowding with over two persons per bedroom (67.7%), in which parents were tobacco smokers (62.1%), and where firewood (68.7%) and kerosene (60.9%) were used. From these findings, it may be inferred that ARI are the main reason for outpatient pediatric consultations and that children under 5 years of age, males, and persons from urban and suburban areas are the most susceptible groups. Winter and bedroom crowding were found to be among the predisposing factors of ARI, whereas tobacco-smoking among parents and household fuels (firewood and kerosene) are determinant etiological factors.

In the Dominican Republic, a study was made of the clinical characteristics of 1,012 children with ARI in the upper respiratory passages in a semirural population, specifying the elements that should lead to more rational and economic management along with epidemiological characteristics, in particular the elevated proportion (46%) that these represent in the demand for medical care, which is 20% above the demand due to digestive disorders (26%). Attention was drawn to the statistically significant presence of ARI ($p < 0.001$) in nursing infants and children under 5 years, with no difference between the sexes. In addition, environmental contamination of the home was noted, with family tobacco-smoking aggravated by crowding and lack of rooms as contributing factors to these infections (27, 28).

V. LETHALITY AND MORTALITY

According to estimates from the late 1980s and early 1990s, in the Region of the Americas over 100,000 deaths from ARI a year are recorded in children under 1 year of age. Almost 90% of the deaths are due to pneumonia and 99% or more take place in developing countries in the Region. The situation reflects vast differences among countries, as seen in the notable rates of mortality from pneumonia in developing countries as compared to industrialized ones. In some case these differences have even grown. In looking at estimated mortality for infants under 1 year of age by country, one sees the differences indicative of the magnitude of the problem. According to the number of deaths recorded of infants under 1 year of age due to pneumonia and influenza between 1985 and 1990 as well as the estimated mortality per 100,000 live births, a classification could be made of the countries selected in the study (18) as shown in Table 1.

The developing countries of the Region show high infant mortality from pneumonia and influenza with a slightly declining trend. Comparing the figures from 1980 and 1990 (excepting Brazil, which showed an increase from 328 to 349 per 100,000 live births), all other countries showed declining trends, which were most pronounced in Canada (22 to 6) and the United States (28 to 15). Rates fell in Venezuela from 192 to 128; in Mexico from 771 to 324; and in Guatemala, where figures date from 1984, from 1,325 to 1,007. Rates fell in other countries as well; in Cuba from 161 to 88; in Uruguay from 158 to 97; in Argentina from 271 to 101; in Chile from 436 to 255; and in Peru from 628 to 279.

Table 1. Classification of countries selected according to estimated deaths per 100,000 live births in children under 1 year between 1985 and 1990.

Classification according to rate	Country	Number of deaths	Rate x 100,000 live births
> 2,000	Haiti	4,940	2,319.4
	Bolivia	6,793	2,220.0
	Peru	14,150	2,001.4
501 to 1,000	Guatemala	3,236	997.9
	Honduras	1,303	809.4
	Brazil	41,202	772.4
	Ecuador	1,608	760.9
	Mexico	19,415	756.0
	Paraguay	341	661.3
	El Salvador	940	647.1
	Nicaragua	642	645.1
201 to 500	Colombia	4,126	479.1
	Dominican Republic	684	465.0
	Chile	947	338.5
	Venezuela	1,239	239.6
100 to 200	Costa Rica	157	189.0
	Argentina	1,081	158.0
	Panama	77	133.0
	Uruguay	70	125.8
	Cuba	222	123.8
	Puerto Rico	73	113.7
<100	Canada	855	20.4
	United States	55	14.8

Source: PAHO/WHO. *Health Conditions in the Americas*. Scientific Publication No. 549, 1994 Edition. Pan American Health Organization/World Health Organization. Washington, DC.

In children between the ages of 1 and 4, the situation is similar. The lowest mortality rates of 1 per 100,000 were found in Canada and the United States in 1990. Guatemala presented a declining rate from 256 to 224 deaths from pneumonia and influenza with a greater difference observed in infants under 1 year of age. Between 1980 and 1990, mortality dropped from 2 to 1 in Canada and the United States; from 15 to 8 in Argentina; and 9 to 6 in Uruguay. The most pronounced annual decline was 9% in Cuba. In Chile the rates went from 17 to 13; in Venezuela from 25 to 13; in Mexico from 26 to 15. It should be emphasized that the examination of this situation is based on estimated rates in order to reflect the true situation. However, differences in the production of the data require that the figures be examined with care. In some cases, observations are influenced by marked under-reporting or they show important fluctuations in the figures from one year to the next.

A study was conducted in 1985 of annual demand due to ARI and overall and specific lethality from acute pneumonia in the Pediatrics Department of the School of the Santa Casa Medical Sciences in São Paulo, Brazil. The official statistics on mortality from respiratory diseases showed their importance as a public health issue in this city (29). The resulting data indicated a high incidence of ARI with a considerable level of serious cases. Demand, lethality, and mortality reached very high levels, mainly in the first year of life. There is a need for multicountry population studies and investigations on the characteristics of serious ARI-related diseases to learn about their epidemiology in several areas and prepare workable prevention and control programs.

In Porto Alegre, Brazil, a patterned questionnaire for relatives was used to study ARI-caused deaths among children up to 5 years of age, which were recorded between January and December 1986. Of 151 ARI-caused deaths, 139 (92.05%) were investigated. Of these cases, 61 (43.88%) occurred at home and 78 (56.12%) at hospitals. None of the family members in the cases of fatalities that occurred at home had sought prior medical treatment or had recognized the disease. In the deaths at the hospitals, there were references to difficulties in gaining access to more complex medical care (30). In 1987, Benguigui (31) described the State Program for Control of ARI in Children of the Secretariat of Health for Pará, Brazil. The Program was integrated into programs for primary health care and oral rehydration therapy, with the objective of standardizing diagnostic and therapeutic activities for these diseases. In 1982 the Program prepared a manual on rules and procedures for persons responsible for the basic health system in order to improve performance by standardizing treatment, rationalizing the use of antibiotics, and ensuring the effective use of medications. The author provides information on the structure of the program and the results of an analysis of data gathered from notification cards. These show that of 41,704 patients treated by the health system between 1981 and 1984 for what was categorized as ARI cases, classified as either moderate or serious, and treated according to the program criteria, 32,898 cases were re-evaluated, and of these 31,115 developed favorably, with 32 deaths recorded. The data were analyzed by age group, the drugs administered, evolution of the clinical picture, number of hospitalizations, recoveries, and deaths. The study also cited the partial results of investigations undertaken at the same time on

control activities performed in terms of evaluating through home visits moderate ARI cases that did not return to the unit for the corresponding re-evaluation and follow-up by the health team.

To learn the characteristics of patients who died as a result of ARI at the Roberto del Río Hospital in Santiago, Chile, D'Apromont Ormeño and César Callazo reviewed the clinical and laboratory background of selected patients between 1983 and 1984. In this period, 197 children died, 66 of them were over 28 days old and diagnosed as presenting respiratory infection. Data were studied according to age, sex, weight at birth, nutritional status, diagnosis of cause of death and associated pathologies, and therapeutic performance. Of the patients studied, 43% were under 6 months old; 66% under 1 year. The majority were male, 30% had a birth weight below 2.5 kg, and 37.5% were premature. At the time of death, 74% presented nutritional problems (from first to third degree) and 71% had previous hospital stays. The basic diagnosis was for ARI in only 26.8% of the cases; in the others the most frequent diagnosed problems were cardiopathic, multiple congenital defects, neurological diseases, and bronchopulmonary displacement. In treatment 96% received oxygen, 91% an antibiotic, and 58% a mechanical respirator (32).

In Costa Rica (33) ARI represented approximately 50% of the cases of diseases requiring health department notification and pediatric doctors' visits. ARI was also among the main diseases acquired in hospitals and main causes of death. In 1982, for example, they constituted 35% of the infections acquired in the National Children's Hospital of San José. Twenty-five percent of the patients had pneumonia and bronchopneumonia and, due in part to other serious complications, 16% of those affected died. Between 1970 and 1980, infant mortality from these diseases was reduced 70%. Among the specific measures that were believed effective were the extension of health coverage throughout the country, children's immunizations, and the immediate use of appropriate antibiotics. The Costa Rican experience shows that ARI control and prevention in developing countries is more likely to succeed when attention is paid to epidemiological and etiological research, appropriate standards for diagnosis and treatment are in place, health coverage is extended, and an effective holistic approach is used that takes account of many factors affecting ARI control.

González Ochoa, et al. (34) evaluated data for mortality and morbidity (doctor's visits) and the results of blood tests in Cuba in 1983. It was clear from mortality conditions that the elderly population was most at risk, whereas data for the population of children under five revealed a positive picture. The authors report that the last three months of the year saw an epidemic rise in the number of doctor's visits due to acute respiratory diseases (ARD), particularly RSV. Adults most commonly had the type A flu virus (H3N2), with an appreciable activity of A virus (H1M1) in some young population groups.

Attempts to define the scope of the problem in Central American countries (35, 36) suggest that mortality there is around 6.3%. ARI cause 56% of the deaths from respiratory infections in children under 1 year in developing countries. In El Salvador, ARI account for 13.2% of out-patient visits and the majority of visits due to infections. Along with diarrhea, ARI constitutes one of the two major causes of hospital admissions and of infant deaths due to infections. Of

the deaths, 70% occur in children under 1 year of age, and both causes represent 36% of all deaths in this age group. The possibility that these patients die as a result of immunological deficiency raises the need to find other options to treat immunodeficient children.

Of 150 children under 5 years of age who received medical care in the Professor Samuel B. Pessoa Health Center-Medical School in Brazil, about half presented with ARI at the time they were examined. An analysis of potential environmental risk factors revealed only one—the number of tobacco smokers in the family (37).

Among the diseases that affect children from birth up to 10 years of age, those of the respiratory tract figure prominently and passive tobacco smoking can exacerbate them. A representative sample of 482 children in this age group was selected for study; of these 190 (39.4%) were passive smokers, 292 (60.6%) were not. The presence of progressive pulmonary pathology was revealed through a questionnaire given to the mothers or responsible adults present. The results showed that 65.9% of this population presented symptoms of respiratory problems and that the most affected age group was between 0 and 2 years. The most frequent symptoms found were coughing (64.7%) and coryza (63.9%), probably as a result of infections of the upper respiratory tract. The presence of rales (26.1%) stands out in clinical importance due to the association with the risk factor of cigar smoke (passive smokers) in children until the age of 7 years (38).

In another group of 511 children between 0 and 10 years, in which 288 (56.4%) were passive smokers and 223 (43.6%) were not, selected by household from a representative sample, it was found that 30.7% presented respiratory symptoms, and that children under 2 years were the most affected. Symptoms of rales were found in 9.4% of the individuals interviewed. There is an association between the presence of the passive-smoking risk factor and the respiratory symptoms among all age groups studied. The need for treatment for “diseases of the lungs and bronchioles in the last 6 months” was found in 81 (15.8%) of the individuals studied, and 60 (74.1%) of these were in the passive-smoking group. It is concluded that passive smoking is associated with a higher prevalence of respiratory symptoms as well as an increase in the risk of seriousness of the ARI cases that require health service action (38).

In Colombia, a study of cases and controls at the Children's Hospital of Medellín was performed in 1985 (39) in order to establish the association between such factors as low birth weight, malnutrition, overcrowding, habitual smoking by the mother, and lack of breast-feeding in relation to serious ARI among children under 5 years. An association was found between each of these risk factors and ARI, and underscored the importance of ensuring breast-feeding for no less than 4 months and the negative impact of habitual smoking by the mother, particularly during the child's first year of life and particularly when more than five cigarettes a day are smoked.

VI. NUTRITION AND PNEUMONIA

Cruz and colleagues (40) used the indicators of weight in relation to age, height in relation to age, and weight in relation to height to determine the nutritional status of 678 children from 0 to 59 months of age who had been admitted with symptoms of ARI to the San Juan de Dios General Hospital in Guatemala City. Of these cases, 557 (82.2%) were classified as bronchopneumonia; 62 (9.1%) as pneumonia, and 43 (6.3%) as bronchiolitis. Five hundred and sixty were from metropolitan Guatemala City and 118 (17.5%) were from other municipalities in the Department of Guatemala. It was discovered that 188 (27.8%) had low weight for their age, 176 (25.9%) were small sized for their age, and 84 (12.4%) had low weight for their height. In general the children from the municipalities showed the highest proportions of malnutrition, even though in some parts of Guatemala City malnutrition has high prevalence. Furthermore, 78 (14.0%) of the bronchopneumonia cases showed low weight for height. Monitoring the nutritional status of patients admitted to pediatric wards due to infectious diseases may furnish valuable information not only for case management but also for education and health promotion among the patients' parents.

Between 1977 and 1978, Delgado et al. (41) carried out a study of 2-year-old children, living in several coffee plantations in southern Guatemala, who showed clinical manifestations of respiratory infections. The investigators examined the relationship between the disease, socio-economic characteristics, and the nutritional status of the population. They also evaluated the use of health posts, located on the plantations, that provided medical care for these infections. On the basis of consultations with health post staff and home visits conducted by a team of health promoters, information was collected in every area on the frequency and duration of nasal secretions, coughs, rales, the physical growth of each child, and his or her socio-economic characteristics. Observations were also made of clinical manifestations in relation to several risk factors that result from socioeconomic peculiarities such as the availability of drinking water at home, the literacy level of the head of the household, and the kind of dwelling occupied. Several obvious negative values were found on the Z scale for all of the anthropometric indicators with significant stunting in the physical growth of the children studied. Stunting was greater in those who had had one or more clinical episodes of ARI than in those who had not had any episodes.

VII. CONCLUSIONS

To make use of epidemiological information in developing ARI prevention and control strategies, the following elements must be taken into account:

- Timely treatment and diagnosis of coughs and respiratory difficulty (respiratory frequency according to age in months);
- Simplified care;

- Referrals of most serious cases for appropriate and timely treatment;
- Prophylaxis;
- Integrated training and prevention service;
- Increase in the use of and access to health services by the public;
- Timely and appropriate care for children under 5.

It is essential to have basic mortality and morbidity data available and to define, prioritize, and stratify the risks factors for getting sick or dying from ARI. Greater recognition must also be given to other determining factors such as:

- The genetic, molecular, and antigenic characteristics of ARI causative agents;
- Virulence, pathogenicity, and prevalence distribution of infectious agents and their different serotypes;
- Practical, sensitive, and specific diagnostic methods for timely identification of the genes and antigens of the etiological agents and for measuring or predicting the humoral and cellular immune response in infected children;
- Knowledge of the sources of infection and the transmission mechanisms;
- Validation of methods for the clinical and epidemiological study of responses to causative agents through environmental management, clinical treatment, and chemotherapy;
- Genetic risk factors and immunological safeguards in the infant and young child population;
- Development of effective immunizing agents to control high prevalence infectious agents, such as *S. pneumonia* and *H. influenzae*, in Latin American countries.

To reduce mortality from ARI and pneumonia, the member states of the World Health Organization have set the following priorities for case management:

- Define the etiologies of important strains of pneumonia, septicemia, and meningitis through studies simultaneously conducted in several countries;
- Define the clinical signs and etiology of ARI in malnourished children;
- Determine the best clinical signs for prognoses of severe strains of pneumonia and the need for referrals for young children;
- Use first line drugs such as co-trimoxazole (CTX, a mixture of trimethoprim [TMP] and sulfamethoxazole [SMX]) or penicillin in small children and amoxicillin in the event of resistance. In cases of malarial infections concomitant with ARI, it should be recalled that *Plasmodium falciparum* is often resistant to TMP mixed with the sulfamides and this medication is ineffective in controlling *Plasmodium vivax*;
- Develop a methodology to accommodate the results of ethnographic studies related to ARI;
- Perform tests of mothers on their interpretation of messages concerning care for children at home, in clinics, health centers, and hospitals;

- Compare the current resistance of common bacteria to antibiotics and perform a study of broader alternatives;
- Develop a methodology for a study of clinical episodes of ARI to be adapted for use by mothers at home; and
- Edit training manuals to strengthen the system of epidemiological surveillance for ARI.

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