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Viral respiratory diseases in children:
Classification, etiology, epidemiology,
and risk factors

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The epidemiology, molecular structure, cell tropism, and pathophysiology of many human disease-causing viruses have been painstakingly and elegantly characterized during the past 50 years. Vaccines and antiviral drugs of varying efficacy were developed and tested. Despite the relegation of smallpox to a freezer chest and the progress in the control of measles and hepatitis B, the viruses that cause respiratory tract infections remain significant causes of illness and death in pediatric populations worldwide. This discussion surveys the virus groups that contain nearly 200 distinct viruses that cause sporadic and epidemic respiratory infections in children. The epidemiology of infection with the influenza A and B, parainfluenza, and respiratory syncytial viruses and adenoviruses and their impact on infants and children and the groups at highest risk for morbid outcomes are discussed. (J Pediatr 1994;124:S13-S6)

Until the 1950s, little was known about the causes of acute upper respiratory tract infection or lower respiratory tract infection. It was evident that the bacterial causes of pneumonia, such as Streptococcus pneumoniae, Haemophilus influenzae, and the filterable agents responsible for swine and human influenza and measles, could not account for the majority of acute URTIs and LRTIs in children and adults. A real boom in respiratory virology came in the late 1950s and early 1960s, when markedly improved isolation and culture techniques and better serologic and biochemical methods were applied to the isolation and characterization of the viruses responsible for respiratory infections. Rhinoviruses, echoviruses, coxsackieviruses, adenoviruses, parainfluenza viruses, coronaviruses, and respiratory syncytial virus were added to influenza and measles viruses as causes of respiratory infections. Nearly 200 antigenically distinct viral agents were documented as causes of sporadic or epidemic URTI or LRTI in infants, children, and adults.

VIRUSES AND RESPIRATORY SYNDROMES

In 1963, Dr. Maxwell Finland chaired a symposium entitled "Problems in Definition of Respiratory Diseases and Respiratory Disease Agents." Papers presented by Dowling and Lefkowitz and by Parrott et al. defined the major clinical respiratory syndromes of adults and children and identified the major viruses responsible for these syndromes. Several respiratory syndromes were described in adults. The etiologic agents associated with these syndromes included coryza caused by rhinovirus, echovirus 28, and coxsackievirus A21; pharyngeal conjunctival syndrome caused by adenovirus; and pneumonia caused by influenza virus, parainfluenza virus, adenovirus, and coxsackievirus.

**Table:**

| LRTI | Lower respiratory tract infection |
| RSV | Respiratory syncytial virus |
| URTI | Upper respiratory tract infection |

The clinical syndromes in infants and children described by Parrott et al. were derived from a cross-sectional analysis and the results of respiratory cultures collected between 1957 and 1961 from approximately 8000 children with respiratory infections. Croup syndromes were associated with parainfluenza viruses, RSV, adenoviruses, and influenza vi-
ruses. Bronchopneumonia was most likely caused by RSV, but it may also have been caused by parainfluenza viruses (particularly parainfluenza type 3), adenoviruses, influenza viruses, or Mycoplasma pneumoniae. A syndrome that the investigators called "bronchiolitic bronchopneumonia" was predominantly associated with RSV or parainfluenza type 3 infection. Severe bronchitis and pharyngitis were associated with RSV, adenoviruses, the parainfluenza viruses, and influenza viruses. Outpatient rhinitis, pharyngitis, and bronchitis were associated with the same agents that caused bronchiolitic bronchopneumonia.

Table I summarizes current data on the common infectious pediatric respiratory syndromes and their usual causative agents. Little has changed in the three decades since the 1963 symposium. Indeed, although much more is known about etiology, pathogenesis, viral biochemistry, and genetics, the viruses described by the early 1960s continue to the 1963 symposium. Indeed, although much more is known about etiology, pathogenesis, viral biochemistry, and genetics, the viruses described by the early 1960s continue to be responsible for present-day sporadic or epidemic respiratory infections in adults and children. It is not surprising that there is substantial clinical overlap. Respiratory tract infections may be caused by a variety of different viruses, and individual viruses can cause variable clinical syndromes.

A prospective long-term study to examine patterns of respiratory illnesses in an American community was initiated in Tecumseh, Mich., in 1965 by Monto et al. This study surveyed representative segments of the Tecumseh population for respiratory infections from 1965 through 1971 and again from 1976 through 1981. The recovered viruses and the observed respiratory syndromes in nonhospitalized children and adults in Tecumseh mirrored the viruses and respiratory syndromes described by Parrott et al. Ultimately, more than 80 serotypes of rhinovirus were recovered from uncomplicated URTIs. In addition, RSV, parainfluenza viruses, influenza A and B, adenoviruses, and enteroviruses also were recovered from patients with URTI. The enteroviruses, however, were more likely to cause LRTI, to induce more severe illness, and to prompt reduc-
children of Central America, followed by those in Africa, South America, and Asia.

A number of observations can be added to the 1978 National Institutes of Health workshop data describing etiologic agents, clinical syndromes, infection rates, and outcome of viral respiratory diseases throughout the world. Acute respiratory infections are common causes of death in young children worldwide. Viruses cause more than half of these acute infections. The morbidity and mortality rates from viral respiratory infections are much higher in developing countries. The viruses documented as being responsible for respiratory infections in developed countries (RSV, parainfluenza and influenza viruses, adenoviruses, enteroviruses, and rhinoviruses) also are responsible for infections in developing countries.

**EPIDEMIOLOGY**

Epidemiologic studies have attempted to determine the modes of transmission for respiratory viruses. It has long been presumed that infectious viruses are carried on particles or droplets that are expelled from the respiratory tracts of infected persons. This mode of transmission was considered responsible for virus spread among human beings; however, experimental data show this mode to be only marginally important. Rather, the most successful route of viral spread is by the transmission of infectious mucosal secretions to the fingers and hands, and subsequently to the nose or eyes of a susceptible recipient. The simple act of timely hand washing may be the most effective method of breaking the chain of transmission and thereby interrupting virus spread.

Healthy infants, toddlers, and children are at high risk for encounter and infection with respiratory viruses. However, most will have a limited illness that will provoke the development of some immunity from subsequent infections with the same or similar agents. For most of the respiratory viruses, reexposure and reinfection are the rule. Usually, reinfections cause less severe disease and are less likely to induce LRTIs that result in bronchiolitis or pneumonia. Several risk factors (Table III) increase the rates of infection and the resulting severity of disease. These factors include young age, low birth weight, prematurity, chronic cardiopulmonary disease, some congenital or acquired immunodeficiency disorders, malnutrition (especially with vitamin A deficiency), crowding, the number of children residing in the household, the presence of large numbers of susceptible people in the community, lack of breast-feeding, and exposure of the susceptible child to other infected persons. There is substantial evidence of increased susceptibility to and complications of infection in children exposed to polluted air, which includes secondhand smoke in the infant's residence.

**Table III. Risk factors influencing the incidence and severity of viral respiratory tract infection in infants and children**

| Risk Factor                                |
|--------------------------------------------|
| Age, immunologic experience                |
| Prematurity, low birth weight              |
| Chronic cardiopulmonary diseases           |
| Immunodeficiency syndromes                 |
| Malnutrition                               |
| Exposure                                   |
| Other children in family                   |
| Crowding                                   |
| Care setting, family versus day care       |
| Environmental pollution, parental smoking  |
| Lack of breast-feeding                     |

Although vaccines for influenza A and B, RSV, parainfluenza virus type 3, and some adenoviral subtypes have been developed and tested only the vaccines for influenza A and B currently are available and recommended for use in children. The primary reasons for the desultory progress in vaccine development are the large number of agents responsible for disease, the poor or unpredictable immunologic response to vaccination of susceptible infants and children, and the high development costs of potential limited-use vaccines.

**SUMMARY**

In summary, 80 years ago the treatment of choice for bronchiolitis and bronchopneumonia was 15-minute hot baths, as hot as the child could tolerate twice a day, or mustard packs, or both. Since then, viral respiratory diseases and their etiology, epidemiology, pathophysiology, and natural histories are understood much more extensively. However, specific prevention and effective treatments remain elusive. Still, many treatments of viral respiratory diseases are homeopathic or supportive. The authors of the following articles expand on these observations. They offer new information on improved methods that provide for the prevention and treatment of these exceedingly prevalent pediatric respiratory disorders.

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