



## VIRAL AND BACTERIAL PNEUMONIAS

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### I. GENERAL CONSIDERATIONS

**P**neumonia, the infection of the pulmonary parenchyma, is brought on by an attack of viruses, bacteria, or even other microorganisms. In children under the age of 5, pneumonia is a serious health problem, especially in developing countries, where its incidence and role in early childhood mortality make effective control actions imperative (1, 2).

In developing countries, the majority of pneumonia cases have a bacterial etiology, according to data from studies conducted in several regions, which identified bacteria in pulmonary aspirate or blood cultures (3, 4). In the developed countries, most pneumonia cases are believed to have a viral origin (5). Nevertheless, recent publications suggest that the incidence of bacterial infections may be higher than earlier studies had indicated (6).

Epidemiological data on acute respiratory infections (ARI) of the lower respiratory tract in the countries of Latin America are scarce, which makes it difficult to assess the magnitude of the problem. Knowledge of the predominant microorganisms in each area and of the serotypes and antibiotic resistance of the most common bacteria is essential for the development of local strategies (7). This information is also critical to the identification of the antibiotics of choice and the administration of specific vaccines (8,9).

The isolation of the etiologic agents of bacterial pneumonia through cultures or rapid antigen identification presents considerable technical challenges, but these difficulties become extreme in vicinities where adequately equipped laboratories do not exist (10). Another complicating factor is the high frequency of mixed etiology, which occurs in 25-75% of cases, according to several studies (11, 12).

A physician who treats a child with pneumonia will therefore generally base his diagnosis of bacterial or viral origin on clinical findings, blood tests, and x-rays, relating them to factors such as age, characteristics of the host, and the prevailing epidemiological situation. Hence, in treating a child with a presumptive diagnosis of pneumonia, the physician must:

- 1) Determine whether the etiology of the illness is viral or bacterial to decide whether or not to administer antibiotics (13); and
- 2) Assess the degree of severity of the illness and watch for the appearance of complications, which will determine whether the child can be treated on an outpatient basis or requires hospital care, and if so, at what level of complexity.

It should be emphasized that to carry out these activities the members of the health team must be adequately trained in clinical diagnosis. They must also be capable of recognizing the factors that may lead to severe pneumonia, which is most likely to have a fatal outcome. These factors were analyzed in 987 hospitalized children in a study conducted in Papua New Guinea (14). The following section will explore the clinical-therapeutic aspects of pneumonia, first establishing some of the physiopathological correlations that are essential for a better understanding of these problems.

## II. ETIOLOGY AND PATHOGENESIS

Pneumonia is generally caused by viruses and bacteria present in the environment. Most enter the respiratory tract via the airborne route. Less frequently, the infection may spread hematogenously or via the lymphatic system. The microorganisms are transmitted from person to person through contact with contaminated respiratory secretions or through microaspiration of germs that colonize the nasopharynx (15).

Normal flora contains numerous aerobic and anaerobic Gram-positive and -negative bacteria. *Streptococcus pneumoniae*, unencapsulated *Haemophilus influenzae*, *Staphylococcus aureus*, *Branhamella catarrhalis*, *Streptococcus* sp., and anaerobic penicillin-susceptible bacteria, such as *Peptostreptococcus* and others, commonly occur in low concentrations of 10<sup>3</sup>-10<sup>4</sup>/ml. Epidemiological studies (16) have shown a direct correlation between nasopharyngeal colonization by *S. pneumoniae* and pneumonia and/or bacteremia caused by the same serotypes. The bacteria most frequently associated with pneumonia in children under 5 are *S. pneumoniae* and *H. influenzae*, both of which are commonly found in the throats of healthy children (17).

### a) Pulmonary defense mechanisms

The respiratory system boasts mechanical actions and immune responses among its defense mechanisms (18), to safeguard the sterility of the lower respiratory tract and protect against bacterial invasion. The first line of defense is the cough reflex; the bifurcations of the bronchial

atrium favor the impaction of germs and particles on the mucosal walls when a turbulent air-flow is established. The mucociliary apparatus is responsible for mucous clearance, which is accomplished by means of the sweeping movement of the cilia. If these defenses are overcome, the alveolar macrophages phagocytose pathogenic bacteria and viruses, thereby constituting a formidable barrier to microbial infection (19). This action is complemented by the activity of the granulocytes and polymorphonuclear leukocytes, the complement system, and specific humoral (immunoglobulins) and cell-mediated immunity.

Various factors may interfere with these mechanisms. Respiratory viruses destroy cilia and alter their genetic code, diminishing their motility and effectiveness for clearance. This leads to a significant increase in bacteria, with concentrations rising to more than 10<sup>5</sup>/ml, which overwhelms the phagocytic capacity of the alveolar macrophages and creates favorable conditions for invasion. Similar damage is caused by drugs such as cough suppressants and expectorants, hypnotics, cigarette smoke, and other factors in the environment, including by-products from the combustion of organic waste.

It has been demonstrated that certain conditions may predispose poor immune response in the host. Malnutrition reduces levels of 11S immunoglobulin A in the secretions (20) responsible for impeding adherence, which also have specific antibody functions. Various immune disorders predispose the host to severe or recurrent pneumonia, including a deficit of IgG, especially some subtypes: Ig2 and Ig4 (21, 22).

Among the conditions that are conducive to lower respiratory tract infections and increase the risk of severe ARI are low levels of antibody against pneumococcal polysaccharides in infants under the age of 6 months (23).

### **b) Bacterial mechanisms of action**

Germs possess mechanisms that enable their pathogenic action. For example, the capsule of *S. pneumoniae* enables it to resist phagocytosis, while *Mycoplasma pneumoniae* has a specialized organelle, the P protein, that allows it to adhere to the respiratory epithelium (24). Unencapsulated *H. influenzae* has fimbriae that facilitate adherence to the respiratory epithelium, but not invasiveness (25). This last property is inherent in capsulated *H. influenzae*, generally of type b, which produces systemic infections and may cause secondary pneumonia.

Viruses multiply within ciliated cells, causing damage through cytopathic action and inflammatory response, sometimes resulting in cilioepithelial lesions and necrosis in the bronchi and bronchioles, hypersecretion of mucus, formation of plugs that block light, mononuclear infiltrates, and large quantities of fluid and leukocytes in the alveoli (26).

Three stages are recognized in the development of bacterial pneumonia (27):

- 1) Colonization of pathogens, which invade the bronchial mucosa and release toxins such as the pneumolysins of *S. pneumoniae*, the phenazine of *Pseudomonas*, or the hyaluronidase

of *S. aureus*. The phenomenon of inflammation begins with recruitment of neutrophils and secondary impairment of the action of released superoxidant anions and proteins, in addition to other mediators such as interleukin-1 (IL-1) and tumor necrosis factor (TNF). Significantly elevated levels of IL-1 have been found in bronchoalveolar washings from patients with pneumonia (28).

- 2) As a result of the damage to the mucosa, specific receptors are exposed, which facilitates the adherence of pathogens and subsequent invasion.
- 3) Invasion and spread are generally almost simultaneous. When the viruses penetrate the macrophages, they depress their bactericidal activity, reducing their interaction with cytotoxic T-lymphocytes (T-L) and increasing the risk of pneumonia.

The association between severe pneumonia and several factors has been studied extensively. For example, hypercoagulation with fibrinolytic activity and consumption coagulopathy, and hypocoagulation with fibrinolysis, are factors associated with a poor prognosis (29). Infants with severe pneumonia and a small or absent thymus may have alterations of T-lymphocyte subpopulations and a reduced level of serum thymic factor, expressing a deficit of specific cell-mediated immunity (30). Some particularly virulent bacteria and viruses, such as those listed in Table 1, may produce fulminant pneumonia.

In conclusion, severe pneumonia is generally associated with three factors:

- 1) Absence of effective defense mechanisms;
- 2) Degree of selectivity of the inflammatory response for destroying pathogens with little damage to the pulmonary parenchyma;
- 3) Incapacity for repair of pulmonary tissue.

There are also numerous situations in which a severe impairment of immune function may increase the risk of death. This was observed in an epidemic outbreak of measles that occurred in Argentina between 1974 and 1976 (31).

### **III. CLINICAL EVALUATION**

The physician who finds a pulmonary infection in the patient must consider several diagnostic and therapeutic strategies. Different etiological agents can give rise to quite similar manifestations, while a single microorganism can cause very different clinical pictures.

Identifying the etiological agent of pneumonia is a difficult task, especially in pediatric cases (32). A clinical evaluation, thorough interview, and an exhaustive physical examination can, in a great number of cases, afford sufficient information for making therapeutic decisions, particularly when access to radiological or laboratory diagnosis is limited or nonexistent. Identification of the risk factors and associated pathologies and quantification of their severity provide the basis for therapeutic decisions (Tables 2 and 3).

In the majority of cases it is possible to establish a presumptive diagnosis of pneumonia in any child who initially presents with tachypnea or subcostal retraction (33-35). Retractions express greater respiratory distress, at times in conjunction with nasal flaring, grunting, or cyanosis (36). The physical examination may reveal minor respiratory compromise secondary to pain on the affected side, lessening of vocal vibrations in the event of effusion and dullness to percussion, which is a telling sign of extensive pneumonia.

**Table 1.** Progressive or fulminant pneumonia: Most frequent etiologies

<b>Bacterial</b>	<b>Viral</b>
Gram-negative enterobacteria	Influenza
<i>Klebsiella pneumoniae</i>	Adenovirus
<i>Enterobacter</i>	Herpes zoster
<i>Escherichia coli</i>	Measles
<i>Pseudomonas aeruginosa</i>	Cytomegalovirus
	Epstein-Barr
	herpes simplex
<b>Others</b>	
<i>S. aureus</i> (methicillin-resistant)	
<i>Chlamydia psittaci</i>	
<i>Mycobacterium tuberculosis</i>	

Auscultation reveals a diminished vesicular murmur on the affected side. This asymmetry is often the most frequent and sometimes the only finding, particularly in small children. Crepitant stertor unaffected by coughing or kinesic maneuvering, a tubular murmur at the end of an inspiration, bronchophony, and aphonic pectoriloquy fill out the classic picture of pulmonary condensation. The antalgic position, secondary to thoracic pain, may indicate pleural distress. The cough is initially dry and scratchy, sometimes barking is present and may become productive with dense, even rust-colored, sputum. The pediatric patient will commonly present an axillary fever between 38.5° and 40° C and signs of general involvement such as discomfort, loss of appetite, difficulty in drinking liquids, paleness, anxiety-ridden appearance, vomiting, epigastria, and abdominal swelling. In some instances a reddening has become evident in the homolateral cheek on the affected side. Sleepiness and irritability may also be observed. When a severe case presents, care must be given to detecting any signs of heart failure such as tachycardia, gallop rhythm, crepitant stertors in the base of both lungs, and cardiomegaly. There have also been reports of meningeal signs (37), splenomegaly, pain in the right iliac fossa appearing like an appendicular picture, cutaneous exanthem, and diffuse hemorrhagic rash.

This broad description of signs and symptoms—some of which are systemic, others closely related to the respiratory apparatus—may have special characteristics in nursing infants and newborns.

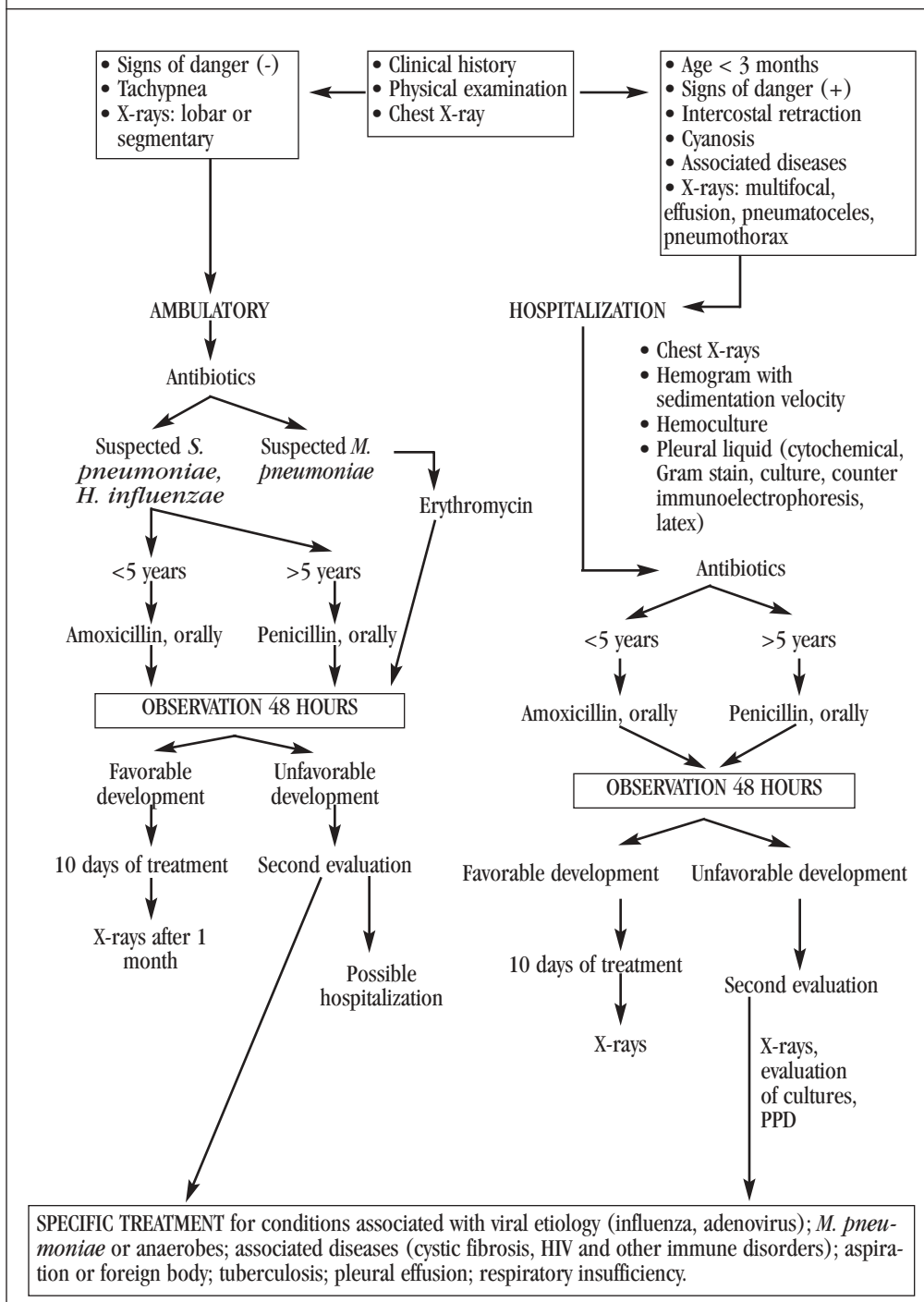
<b>Table 2.</b> Basic methodology for diagnosis of pneumonia		
<b>Evaluation</b>	<b>Methodology</b>	<b>Objectives</b>
Clinical	<ul style="list-style-type: none"> <li>• Clinical history</li> <li>• Physical examination</li> </ul>	If pneumonia is suspected, determine: <ul style="list-style-type: none"> <li>• Degree of severity</li> <li>• Etiology</li> <li>• Possible associated pathologies</li> </ul>
Radiological	<ul style="list-style-type: none"> <li>• Chest X-ray</li> </ul>	Confirm diagnosis of pneumonia: probable etiology
Laboratory	<ul style="list-style-type: none"> <li>• Hemogram</li> <li>• Gram stain</li> <li>• Cultures</li> <li>• Rapid methods</li> </ul>	Confirm etiology of pneumonia
Treatment	<ul style="list-style-type: none"> <li>• Ambulatory</li>   <li>• Referral</li> </ul>	<ul style="list-style-type: none"> <li>• Antibiotics</li> <li>• Clinical observation (48 hours)</li> </ul> Hospitalization: <ul style="list-style-type: none"> <li>• Pediatrics ward</li> <li>• Intensive care unit</li> </ul>

In nursing infants and newborns, pneumonia often begins with the abrupt onset of fever, and sometimes convulsions that precipitate the visit. As the symptoms develop, manifestations of greater severity appear: restlessness or lethargy, loss of appetite, subcostal indrawing, rapid and shallow breathing (over 50 per minute in nursing infants from 2 to 12 months), expiratory grunting, peripheral cyanosis, abdominal swelling, and tachycardia. The physical examination does not always reveal the presence of pneumonia. Sometimes the only indication is auscultatory asymmetry with diminished respiratory noise on the affected side. The general condition of nursing infants with fever may be lightly or moderately affected, without respiratory manifestations, which is known as “fever without origin” and indicates a likely viral etiology. The absence of signs in this age group does not rule out the presence of pneumonia; thus, a chest x-ray is indicated within 3 days of the onset of symptoms.

In newborns respiratory manifestations are even less obvious. General signs of sepsis prevail, such as refusal to eat, lethargy, hypotonia, convulsions, vomiting, abdominal swelling, paleness, cyanosis, hypothermia, and with a varying degree of respiratory effect: tachypnea (over 60 per minute), apneic episodes, retractions, nasal flaring, and grunting.

The constant concern of the physician is to determine specific and sensitive clinical signs that are easily applicable and will predict with the least possible error the presence of pneumonia.

**Table 3.** Algorithm for diagnosis and therapeutic decisions concerning locally acquired pneumonias



Many publications have offered retrospective and prospective analysis of the aforementioned clinical signs and symptoms. The majority concur in finding tachypnea to be the most useful predictive sign (33, 34, 36, 38). For some sources, high fever, refusal to eat, and vomiting are also sensitive indicators (34). For others the clinical impression (“doesn’t look well”) is the most telling parameter (39, 40). Attempts have also been made to study the rates for respiratory frequency in relation to patient age and various other physiological aspects. The consensus is to accept the figure of 60 per minute as the threshold for defining respiratory distress in the newborn. As for accurate predictors of severity, subcostal retractions are widely accepted as a valid indicator (33, 34). (For a more extensive and detailed discussion on ARI in newborns and nursing infants under 2 months of age, see Chapter 17 in this volume by Gerardo Cabrera Meza.)

Shann determined that several signs foretold death (41), particularly prolonged sickness and pneumonia in undernourished children without fever, and Spooner et al. (14) concur with this author in pointing to refusal to eat, cyanosis, and nasal flaring as signs of death. Table 4 details these data and summarizes criteria for hospital admission.

Many authors have attempted to correlate clinical, hematological, and radiological findings to a likely viral or bacterial etiology of pneumonia cases, or to specify the underlying bacterial type. However, most have concluded that no categorical evidence allows such differentiation (42, 43).

The above clinical description corresponds to pneumonia as produced most generally by *S. pneumoniae*. We examine below the characteristics of pneumonia produced by other agents.

*Haemophilus influenzae* causes approximately 30% of the pneumonia, with positive cultures, found in children under 2 years of age; 35% of these positive findings are type B (44). Their pathognomonic findings are no different from those produced by *S. pneumoniae*. However, *H. influenzae* type B (45) can have an abrupt onset, sometimes with toxemia (46), pleural effusion is common and pericarditis exceptional (47, 48). An association is observed with meningitis in some patients and acute otitis media in 50% of the cases.

Although pneumonia from *S. aureus*, which predominates in infants under 1 year of age, is less frequently reported than in the past, increases in older children and adolescents have been reported by some authors (49). Prior viral history with influenza, measles, or chicken pox is a predisposing factor. The initial presentation is similar to that described for *S. pneumoniae*, however with a slower evolution, significant general malaise, and prostration. Fever and respiratory difficulty were the principal signs presented in 61 cases reported by Chartrons and McCracken (50). The most severe forms presented shock, cyanosis, abdominal swelling, and hepatomegaly in association with marked anemia and/or dehydration. Bacteremia is common, 29% in primary pneumonia (50) and even greater in secondary cases with presentation of other origins such as pyodermitis, osteoarthritis, or abscesses. Mechanical and functional decompensation may progress to respiratory insufficiency, aggravated by the appearance of pressure from pyopneumothorax that should be drained quickly (51). Given the abrupt changes that may occur, hospital admission and strict control are indicated when this etiology

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2 Para uma documentação mais extensa e detalhada sobre as IRA nos recém-nascidos e nos lactentes menores de dois meses de idade, consultar o capítulo correspondente neste mesma publicação, a cargo do Dr. Gerardo Cabrera Meza.

<b>Table 4.</b>	
<p><b>Clinical signs that predict death in children from pneumonia</b></p> <p><i>According to Shann (41):</i></p> <ul style="list-style-type: none"> <li>• Prolonged sickness</li> <li>• Inability to eat</li> <li>• Wheezing</li> <li>• Chest retractions</li> <li>• Cyanosis</li> <li>• Hepatomegaly</li> <li>• Leukocytosis</li> <li>• Severe changes in radiology</li> <li>• Malnourished and febrile</li> </ul> <p><i>According to Spooner (14):</i></p> <ul style="list-style-type: none"> <li>• Cyanosis</li> <li>• Inability to eat</li> </ul> <p>Others:</p> <ul style="list-style-type: none"> <li>• Nasal flaring</li> <li>• Under 1 year of age</li> <li>• Malnourished</li> <li>• Fever for more than 7 days</li> <li>• First child</li> </ul>	<p><b>Clinical signs that indicate need for hospital admission</b></p> <ul style="list-style-type: none"> <li>• Signs of severe respiratory difficulty: <ul style="list-style-type: none"> <li>- intercostal retraction</li> <li>- nasal flaring</li> <li>- cyanosis</li> </ul> </li> <li>• Toxic appearance</li> <li>• Under 3 months of age</li> <li>• Neurological signs <ul style="list-style-type: none"> <li>- convulsions</li> <li>- drowsiness</li> <li>- irritability</li> </ul> </li> <li>• Malnourished</li> <li>• Small febrile nursing infant</li> <li>• Inability to eat or drink</li> <li>• Underlying diseases, immunocompromised</li> <li>• Recurrence of pneumonia</li> <li>• Lack of response to oral therapy</li> <li>• Nuclear family at high social risk</li> </ul>

is suspected. Nosocomial staphylococcus is more serious and brings greater complications as a result of the aggressiveness of the agent and the patient's more vulnerable condition (52).

Pneumonia from group A  $\beta$ -hemolytic Streptococcus (53) is occasionally found as a complication of viral infections, particularly from influenza (54), measles, chicken pox, German measles, or bacterial infections such as whooping cough. The clinical picture varies widely, from a sudden onset with chills to an insidious evolution. Empyema and bacteremia have been reported, as have scarlatiniform eruption and purpuric exanthem. And there have been recent reports of fulminant forms (54) with apnea, shock, hypoxia, and hypercapnia.

An increase has been observed, for example in the United States, in the incidence of pneumonia in neonates from group B Streptococcus. It may present as a precocious infection, within 4 days of birth, or as a later infection, not until week 6, with greater incidence of serotype III. Predisposing factors include premature rupture of membranes, maternal colonization, and low birth weight. A possible relationship has also been suggested with a low antibody concentration for type III native capsular polysaccharides (55). This is difficult to differentiate from other clinical neonate pictures of respiratory distress, particularly from hyaline membrane syndrome (56).

Gram-negative enterobacteria and *Pseudomonas aeruginosa* are opportunistic pathogens that occasionally cause pneumonia when risk factors such as prolonged hospitalization are present and invasive practices, such as mechanical ventilation and intravascular catheters, are employed. An increase in occurrence has been attributed to longer survival of patients carrying primary or secondary immunodeficiencies, the proliferation of intensive care units, and the generalized and sometimes irrational use of antimicrobial drugs.

Pneumonia brought on by *Klebsiella pneumoniae* is rare in nursing infants and small children. It may present in normal hosts, but is more frequently found in immunocompromised patients, and epidemic outbreaks in hospital neonate nurseries are known to occur (57). The clinical picture at the onset is very similar to pneumococcal pneumonia, but it can have a more gradual evolution or a fulminant course. It is characteristic to find thick and abundant mucus secretion with a marked tendency toward destruction of the parenchyma with the formation of abscesses and empyema (58). Frequently, there are also found signs of bacteremia with a generally distressed condition (59).

Pneumonia from *P. aeruginosa* presents in hospitalized patients with underlying diseases, such as fibrocystic diseases or leukemia (60). Young nursing infants are at high risk of contamination from equipment used for aerosol therapy and assisted breathing (61). Both pulmonary fields become affected with abscess formation and the patient's skin presents petechial and purpuric lesions from thromboembolism and vasculitis. Ecthyma gangrenosum is a highly suggestive lesion of this etiology.

*Escherichia coli*, *Proteus mirabilis*, *Enterobacter*, and *Acinetobacter* are other enterobacteria that have been isolated in cases of pneumonia and always constitute a severe clinical picture and guarded prognosis.

There is consensus that lobar or massive condensation, purulent pleurisy, and the presence of pneumatoceles are highly suggestive of bacterial etiology. An obstructive clinical picture, however, with hyperresonance upon percussion, prolonged inspiration, and rales is characteristic of bronchiolitic syndrome, with respiratory syncytial virus (RSV) being the most common cause.

Many patients with ARI of the lower tract are not included in the two groups mentioned, which raises serious etiological doubts and may correspond to so-called atypical pneumonia. The causative agents most commonly associated with clinical manifestations of atypical pneumonia are *M. pneumoniae*, *Chlamydia (trachomatis, psittaci, pneumonia)*, and some respiratory viruses (62) with quite similar systemic and respiratory manifestations.

In school-aged children *M. pneumoniae* is the most frequent cause of atypical pneumonia and presents clinical pictures running from mild or moderate in the most common cases to severe manifestations (63). Most commonly there is a gradual onset with malaise, fever, headache, and scratchy cough manifested by the third or fifth day. Auscultation is of little significance: high pitched stertors and rales, rather subdued for the intensity of the accompanying cough (64, 65). Occasionally, when there appear what are generally small effusions, the course is prolonged and beset by more complications (Table 5) (66, 67). *M. pneumoniae* is ubiquitous and can bring on many kinds of distress; bullous myringitis or severe otitis media, macu-

lar-papular exanthem, Steven-Johnson syndrome, and meningitis (67). Differential diagnosis for respiratory viral infections, particularly when rales predominate, is difficult to establish. Lack of response to b-lactam antibiotics with a presumptive pneumococcal pneumonia points to other etiologies, possibly *M. pneumoniae*, especially in school-aged children.

In recent decades afebrile pneumonia syndrome has come to be recognized, most often in nursing infants up to 4 months of age (68). The onset is gradual and the course subacute. Produced by *Chlamydia trachomatis*, it is transmitted at the time of birth through the cervix. Characteristically, this pneumonia presents prolonged fits of intense coughing, tachypnea, and fine bilateral stertors. A study conducted in Argentina found positive serology for *C. trachomatis* in 19.2% (49) of 255 children between 1 and 18 months of age, presenting as bronchiolitis in 17% (43) and pneumonia in 20% (51) of the pediatric patients (69). This syndrome is rarely found in children 1 year of age (70).

The TWAR strain of *Chlamydia pneumoniae* is a rare cause of pneumonia in small children. The majority of these cases are mild or asymptomatic, and rarely severe (71). There is often pharyngeal distress, prolonged hoarseness, and subsequent cough. The other signs and symptoms are similar to those from *M. pneumoniae* (72) with a possible causal relation to posterior hyperreactivity of the air passage just as described for RSV (73).

*Chlamydia psittaci* is the causative agent of psittacosis. Although parrots are its major reservoir, it can be harbored by any bird species, and is observed, albeit infrequently, in association with epidemic outbreaks (74). The manifestations usually begin abruptly with high fever, intense cephalalgia, myalgia, pharyngitis, epistaxis, and with predominant respiratory symptoms—persistent cough, tachypnea, and signs of severe pneumonia with hypoxia. Further complications may present such as encephalitis, convulsions, and hemolytic or other types of anemia. Splenomegaly is frequent.

**Table 5.** Pneumonia from *Mycoplasma pneumoniae*: Frequency of signs, symptoms, and radiological findings

Signs and symptoms		Radiological findings	
Cough	97%	Lobar condensation	8%
Discomfort	82%	Partial condensation	13%
Vomiting	40%	Interstitial pattern	20%
Abdominal pain	35%	Lobar and interstitial	10%
Headache	32%	Pleural effusion	14%
Fever	60%		
Stertors	70%		
Pharyngitis	50%		
Adenopathy	50%		
Otitis media	2%		

Viral pneumonia presents many different clinical pictures as demonstrated conclusively in virological research conducted among hospitalized patients (75). After a few days of nasal discharge and listlessness, there appear painful coughing, vomiting and fever between 38° and 40° C. In nursing infants, however, fever may be very mild or altogether absent, and in severe cases, bouts of apnea are common (76). The course evolves with faster breathing, retraction, nasal flaring, minimal findings from percussion, subcrepitant rales, sometimes crackling rales (both focalized and bilateral), hoarseness, protracted expiration, and/or sibilant rales. In some children it is difficult to diagnose whether the pneumonia is caused by *S. pneumoniae* or by *H. influenzae*. If it evolves into necrotizing bronchopneumonia, which is infrequent, manifestations may arise of respiratory insufficiency as a result of alveolar-capillary blockage. One sees aggravation of cough, apnea, cyanosis at rest, and marked alterations in arterial gases.

Adenovirus is an infrequent cause of pneumonia in children (77, 78). It commonly manifests in varying intensities of obstructive syndrome, atypical pneumonia, or parenchymatous condensations. Severe cases usually are caused by serotypes 2, 5, and 21 (79). There is a risk of sequelae, such as bronchiectasis or obliterating bronchiolitis (80). The type A strain of influenza virus is a cause of lower ARI in the course of epidemic outbreaks and poses greater risk to nursing infants, the elderly, and immunocompromised persons. It presents varying clinical manifestations. Severe forms requiring hospitalization represent only 1% of the cases (81), with percussion revealing fine bilateral rales in the lung base. As the process is aggravated, signs are presented of respiratory insufficiency, protracted apnea, bradycardia, and digestive and neurological complications with encephalitic manifestations or convulsions, similar to those in other severe viral infections (82).

The type B strain of influenza virus causes pneumonia only when there are predisposing conditions, such as chronic pulmonary disease, cardiopathy, or immunosuppression, in which cases the respiratory distress may be very severe (83).

Parainfluenza virus was identified in children with bronchiolitic syndrome, with the type 3 strain most often found in patients requiring hospitalization. The virus has also been isolated in pneumonia cases with limited condensation, as has been described for other virus types. It generally has a moderate course, although fatalities have also been reported (84).

*Bordetella pertussis*, the measles virus, and *Mycobacterium tuberculosis* are three agents of secondary (as a complication) pneumonia in children under 5, which give rise to high risk. These three microorganisms are of special interest for several reasons:

- a) The infections they produce are susceptible to specific vaccinations, which can prevent them altogether or at least reduce the risk of complications.
- b) These are prevalent diseases in developing countries where vaccination programs may achieve adequate coverage, but where living conditions and access to health services are usually troublesome.
- c) The rates of morbidity and mortality are significant during epidemic outbreaks, with greater risk posed to nursing infants and malnourished and immunocompromised patients (31).

Whooping cough or pertussis characteristically manifests in small children with paroxysms of cough, preceded by dry cough common in other processes in the upper respiratory tract. The picture in the nursing infant is less defined, but includes prolonged bouts of apnea and cyanosis. The most frequent complications are bronchopneumonia from opportunistic germs and hypoxic encephalopathy, which may cause death. Presentation of pertussis syndrome in the nursing infant poses problems in diagnosing etiology; whether the agent is *B. pertussis*, viral agents such as type 3 or 5 adenovirus, or others. In a study of 51 children with clinical manifestations of pertussis syndrome caused by *B. pertussis*, RSV, or mixed infection, apnea was the most common sign (18 to 21%) with paroxysms of emetic cough, sibilant rales, and cyanosis appearing in equal frequency in the three groups that were evaluated (85).

The measles virus is the cause of infrequent giant-cell pneumonia that usually presents severe respiratory difficulty in the intra-eruptive stage. This process is the result of viral proliferation in the pulmonary atrium, which form large syncytia that invade the pulmonary structures. The clinical manifestations include nonproductive cough and the respiratory distress described above, with elevated case mortality (86). Bacterial pneumonia secondary to measles is a frequent complication in nursing infants and small children; it has a varied etiology, including opportunistic pathogens.

Tuberculosis as a cause of pediatric pneumonia merits special comment. In developing countries it must always be assessed in the diagnosis of children with lower ARI, presumably bacterial, who fail to respond to antimicrobial therapy within the time anticipated. In most instances these are non-characteristic primary infections and identification of Koch's bacillus is very involved. Thus, specific treatment is generally initiated on the basis of clinical-radiological findings, known contact with a bacilliferous source or tuberculous conversion.

#### IV. RADIOLOGICAL EVALUATION

The radiograph (x-ray) is an extremely useful instrument in the diagnosis of pneumonia, even though at times it fails to provide definitive confirmation (87).

If a child has a cough and difficulty in breathing, then pneumonia must be suspected. A finding of so-called condensation syndrome should be considered as presumptive evidence. Radiological images will confirm the presence and location of the pathology.

Radiological examination may also assist in distinguishing between a viral or bacterial etiology (88, 89), bearing in mind variables such as the child's age, clinical manifestations, and other laboratory data (49, 90-93). In an appreciable portion of the cases, however, it is not possible to achieve such specificity, and consequent doubts require patient evaluation and consistent follow-up (94).

Certain aspects of the radiological examination warrant close consideration; pneumonia mainly involves the pulmonary parenchyma, although it may also affect other airways and the pleura.

Topographic location in the radiograph of condensation either centered in the lobar region or with segmentary distribution requires thorough knowledge of pulmonary segmentation and



**Photograph No. 1.** Three-year-old patient with pneumococcal pneumonia in the right pulmonary base and parapneumonial effusion

application of the concepts of the sign of the silhouette (95), which makes it possible to determine the placement of intrathoracic opacity that will erase the contour of a mediastinal or diaphragm structure only if it is in contact with them. The pneumonia may affect one or various segments or lobules or take on a diffuse distribution. The density of the images of condensation may be uniform or heterogeneous with borders that can be defined by the incisions or be blurry-edged.



**Photograph No. 2.** Two-year-old patient diagnosed with sepsis, meningitis, and pneumonia mainly affecting the apical segment of the left inferior lobe. Type B *H. influenzae* was isolated from the cephalorhachidian fluid and in the hemoculture.

The images in pneumonia usually reveal an alveolar, cottony pattern with blurry, ill-defined edges, and a tendency to coalesce. The air bronchogram is an essential sign of alveolar involvement in the diagnosis. It consists of the visualization of clear tubular images corresponding to air-filled intrapulmonary bronchi, offset by the surrounding opaque parenchyma. This sign clearly suggests the presence of pneumonia, although absence of the signs does not rule it out. These images are typically found in pneumonia caused by *S. pneumoniae*, *H. influenzae*, *Klebsiella*, or *Pseudomonas*.

If the lesion progresses, the parenchyma usually exhibits necrosis, which is confirmed by signs of cavity-like images showing a destructive pattern. These rounded hyperclear images reveal fine walls in the case of pneumatoceles and thick walls in the presence of abscesses that may contain liquid. When they are in contact with the air passage, a water-air line can be visualized. They are frequently found in secondary pneumonia from *S. aureus*, *Klebsiella*, anaerobes, and Koch's bacillus, and rarely in the pneumococci. Interstitial involvement, radiologically characterized by linear and diffuse micronodular images, is usually secondary to viral infections from *M. pneumoniae* or a characteristic miliary appearance may indicate the presence of hematogenous tuberculosis.



**Photograph No. 3.** Five-year-old patient with feverish manifestations 5 days after onset, regular general condition, and pneumonia in the right pulmonary base that evolved toward pyopneumothorax. *S. aureus* was isolated in the pleural liquid.



**Photograph No. 4.**  
Six-year-old patient  
infected with *M.*  
*pneumoniae*, as  
diagnosed by com-  
plement fixation.



**Photograph No. 5.**  
Eight-year-old patient  
with bilateral basal  
involvement;  
immunofluorescence  
of nasopharyngeal  
aspirate rendered a  
positive diagnosis for  
adenovirus.



**Photograph No. 6.** Twenty-day-old newborn hospitalized with presumptive diagnosis of sepsis. The chest x-ray revealed right-lung hypoventilation evolving into pneumonia, which responded well to antibiotic treatment.

The radiological pattern of viral pneumonia, classically interpreted as the interstitial type, probably corresponds only to the initial stage of this process; after progressing to the alveoli, it displays a pattern similar to that of bacterial pneumonia.

Extrinsic or intraluminal canicular involvement in most cases results in atelectasis. This can be demonstrated in the radiography by a decrease in the volume of the distal parenchyma and the displacement of the fissures, mediastinum, and diaphragm to the affected side. When the obstructive mechanism is valvular in nature, hyperclarities or distal air entrapment is observable. Pneumococcal or *H. influenzae* pneumonia is normally associated with partial atelectasis; the presence of atelectasis secondary to adenopathies is suggestive of a tuberculoid etiology.

Pleural involvement may be manifested by effusions, most frequently in clinical pictures produced by *S. aureus*, *H. influenzae*, and *Klebsiella*. The magnitude may vary; a small pleural discharge, opacification of the costodiaphragmatic or costophrenic angles, or hemothoracic opacification and mediastinal displacement to the contralateral side are all signs that may present. In the event of minimal or hypertensive pneumothorax, the hyperclarity is accompanied

by pulmonary collapse. When the pneumothorax encloses on itself, many airy images appear that are difficult to distinguish from pneumatoceles, bullae, or abscesses.

The following descriptions concern the radiological characteristics of the most common etiological agents.

Pneumococcal pneumonia habitually presents with homogenous consolidation in the peripheral air spaces with a non-segmentary distribution (Photograph No. 1). As seen in the air bronchogram, the radiological pattern is of the alveolar type, with defined borders that affect the superior and inferior lobules. Cavitation is not frequent and the radiographic resolution is quick when the appropriate antimicrobial treatment is employed. In exceptional instances, the entire lobule is affected (96), the image is rounded (97), or it appears like diffuse bronchopneumonia. The association with secondary atelectasis and intraluminal exudate is common. The small parapneumonic effusion can be difficult to identify through radiology, except in the lateral cubit position or if ultrasound, a useful method in this situation, is employed. Reports have also described massive effusion, necrotic cavitations, and pneumothorax as secondary manifestations of more virulent strains or in more susceptible patients. The radiological signs present after the onset of clinical symptoms, and often persist up to three months after the symptoms have remitted.

The radiological signs in *H. influenzae* pneumonia are often similar to those of the *S. pneumonia* type. Sometimes they present an interstitial pattern or present nonhomogenous opacities with segmentary distribution as in bronchopneumonia. These opacities proceed to consolidation of the airspace, especially the inferior lobules, and affect more than one lobule in 25% of the cases (Photograph No. 2). Pleural effusion is frequent, estimated to occur in between 50% and 75% of all cases (98) and associated in 5% with pericardiac effusion.

Staphylococcal pneumonia differs from the above types in the frequency of pneumatoceles, effusion, and pneumothorax (Photograph No. 3) (49). The pneumatoceles are secondary to the mechanism of valvular obstruction in the peribronchial abscesses and the bronchial lumen, and may reach considerable size. They are seen in 50% of the cases (99, 100). Condensation in the parenchyma commonly presents as a confluent bronchopneumonia and it is exceptional to have a finding of an air bronchogram. Pleural effusion is found in 50% to 60% of the cases and as many as 90% in older series; it may evolve into empyema, pyopneumothorax, or hypertensive pneumothorax. The wide variability of radiological images, sometimes taken within hours of each other, requires close attention, frequent controls, and in some cases, urgent surgical drainage. Sudden death has occurred in small children due to tension pneumothorax.

Pneumonia from *Streptococcus pyogenes* is manifested in segmentary-type bronchopneumonic images. It affects the inferior lobules, but may be bilateral. Pleural effusion is common and abscesses occasionally appear.

Radiology for *B. pertussis* whooping cough is not at all specific. Traditionally, rather diffuse pericardiac images exhibiting a velvety or spiny aspect have been described. They correspond to small atelectasis. Interstitial-type images are also observed running from the hilus to the

periphery, hyperinsufflation, atelectasis, confluent segmentary bronchopneumonia, and hilar lymphadenopathies.

*Klebsiella pneumoniae* is similar to the first presentation of *S. pneumoniae*; there presents nonsegmentary, homogenous, parenchymatous condensation, predominantly in the upper lobules and also an air bronchogram. There is a characteristic tendency to produce abundant, thick mucous exudate that amasses in the sulci. Frequent observations are made of multiple abscesses and cavities, pleural involvement with empyema, that simulate the course of a staphylococcal infection or post-primary tuberculosis.

*P. aeruginosa* pneumonia affects both pulmonary bases and presents extensive bilateral parenchymatous consolidations and diffuse patch- or nodule-like shadows. These may appear like small abscesses or effusions.

Pneumonia caused by anaerobes secondary to bronchoaspiration develops in the posterior segments of the superior lobules and in the apical segment of the inferior lobules. It may present segmentary condensations that easily turn into abscesses.

Atypical pneumonia such as that produced by *M. pneumoniae*, shows highly nonspecific radiological signs and images that appear more like viral than bacterial pneumonia. The fine rectilinear pattern predominates, suggesting interstitial inflammation, segmentary distribution that evolves toward consolidation of the pneumococcal type. Likely location is the right inferior lobule or possibly bilateral (Photograph No. 4) (101, 102). The pleural effusions are small, observed in 20% of the cases; 25% present hilar adenopathies.

Radiographic findings of *C. trachomatis* suggest that the pulmonary damage is greater than the clinical findings. Bilateral involvement with hyperinsufflation, alveolar or diffuse perihilar infiltrates, patchy consolidations and lineal densities associated with subsegmentary atelectasis. Lobar consolidation is exceptional, found in only 5 of the 125 cases reported by Radkowski (103).

Radiographic confirmation of viral pneumonia often reveals incipient interstitial infiltrates that quickly develop toward an alveolar pattern, with the two patterns often coexisting (104). Parenchymatous condensation is seen in the inferior lobules and associated with subsegmentary atelectasis. In infants and young children, trapped air, hilar infiltrates, and areas of consolidation secondary to atelectasis are found, whereas in older children the lobar involvement is more defined, although the affected areas do not consolidate altogether. Adenovirus pneumonia is commonly described as exhibiting thickening in the bronchial walls, peribronchial densities, air blockage, and patchy or confluent infiltrates (Photograph No. 5).

Radiological diagnosis of pneumonia in a newborn poses serious difficulties. Images tend to be less defined and diffuse, and differential diagnosis should be performed to check for other frequent problems in the neonatal period, such as hyaline membrane disease, congenital cardiopathies, and meconium inhalation (Photograph No. 6) (105).

## V. LABORATORY DATA

The most important benefits to be expected from laboratory studies are to distinguish between bacterial and viral pneumonia, and if possible, to identify the causative agents (32).

Conventional studies permit with difficulty the differentiation: leukocytosis above 15,000 and neutrophil bands above 500/mm<sup>3</sup>, suggest bacterial pneumonia, but are also seen with other diseases. Leukopenia in patients who are undergoing severe processes or are immunosuppressed poses high risk, but is not specific. Quantitative C-reactive protein (CRP) is considered useful in distinguishing bacterial from viral pneumonia. According to a study conducted with 30 children with bacterial pneumonia (106), values of 35 mg/l or higher are considered significant.

The search for the etiological agent is indicated for children who present a clinical picture of pneumonia that is sufficiently severe to warrant hospitalization. At least two blood samples for taking cultures should be obtained at 20- to 30-minute intervals, and if possible, before antibiotic therapy is initiated. Immediate placement of the sample in appropriate culture media is essential because of the lability of the bacteria under study.

If effusion is present, an etiologic diagnosis should be afforded in 80% of cases through tests using a Gram-stained smear and a pleural fluid culture in combination with rapid diagnostic tests for type B *H. influenzae*, *S. pneumoniae*, and group B *Streptococcus*. Agglutination tests with latex particles are more sensitive than counterimmunoelectrophoresis (CIE), but may give false positives, particularly when there are other foci of infections caused by *H. influenzae* or when the child has recently received a specific conjugated vaccination for this germ. The tests, however, allow bacterial antigens to be detected in patients whose pleural fluid has been sterilized after administration of antibiotics (107, 108). It should be noted that hemoculture yield is low, less than 20%, even when adequate equipment and instruments are used (109-111).

Other more active procedures have been employed, although they are largely not indicated in children unless for very specific situations:

- 1) Conventional sputum culture is a technique that yields low sensitivity and specificity, with little predictive value. Only samples that contain fewer than 10 salival cells and over 25 polymorphonuclears per field should be processed.
- 2) Transtracheal puncture is not recommended due to the high risk it poses.
- 3) Bronchial aspirate is useful for identifying certain pathogenic agents, such as *Mycobacterium*, *Pneumocystis carinii*, and fungi. However, it is of little value for common bacteria, due to contamination of the material extracted from the upper respiratory tract.
- 4) Bronchoalveolar washings, bronchial brushing either with or without protected catheter, is used more in adults, because for technical reasons it is a difficult procedure in children.
- 5) Pulmonary puncture aspiration is indicated only in patients whose pneumonia evolves rapidly, with extensive and peripheral infiltrates, and in immunocompromised patients, and the procedure should be controlled by using ultrasound or tomography, and requires adequate training.

- 6) Invasive pulmonary biopsy is a surgical technique that should be limited for pneumonia cases that evolve sluggishly, particularly in immunocompromised patients. Despite high diagnostic efficacy, it has sporadic indications.

Cytochemical study of pleural fluid may be useful when germs are not detected, particularly to consider which procedures will best treat persistent pleural effusion. The flowchart shown in Table 6 is suggested for handling pleural effusions; it was proposed by the consensus at a meeting of the Committees on Pneumology and Infectology of the Argentine Society of Pediatrics.

When *M. pneumoniae* is suspected, the simple method for determining cryoagglutinins has severe limitations because of the high number of false positives and false negatives (112). Titers above 1/32 are significant. Searching for antibodies by using complement fixation, with a 4-fold titer elevation, is the most commonly used method. Other methods such as culture isolation, ELISA to determine antigens, and ribosomal RNA detection have not been widely used.

With *C. trachomatis* culture isolation or detection by fluorescent antibodies has had considerable success (49). Microimmunofluorescence is a very specific technique to determine IgM antibodies, demonstrable three weeks after the onset of the disease (113).

Finally, the growing availability of rapid methods for viral diagnosis has increased the efficacy of laboratory microbiology. Immunofluorescence can be used to detect respiratory syncytial virus (RSV), adenovirus, influenza, and parainfluenza in nasopharyngeal aspirate. The enzyme-linked immunosorbent assay (ELISA) has proven to be a reliable and fast technique for antigen determination (114).

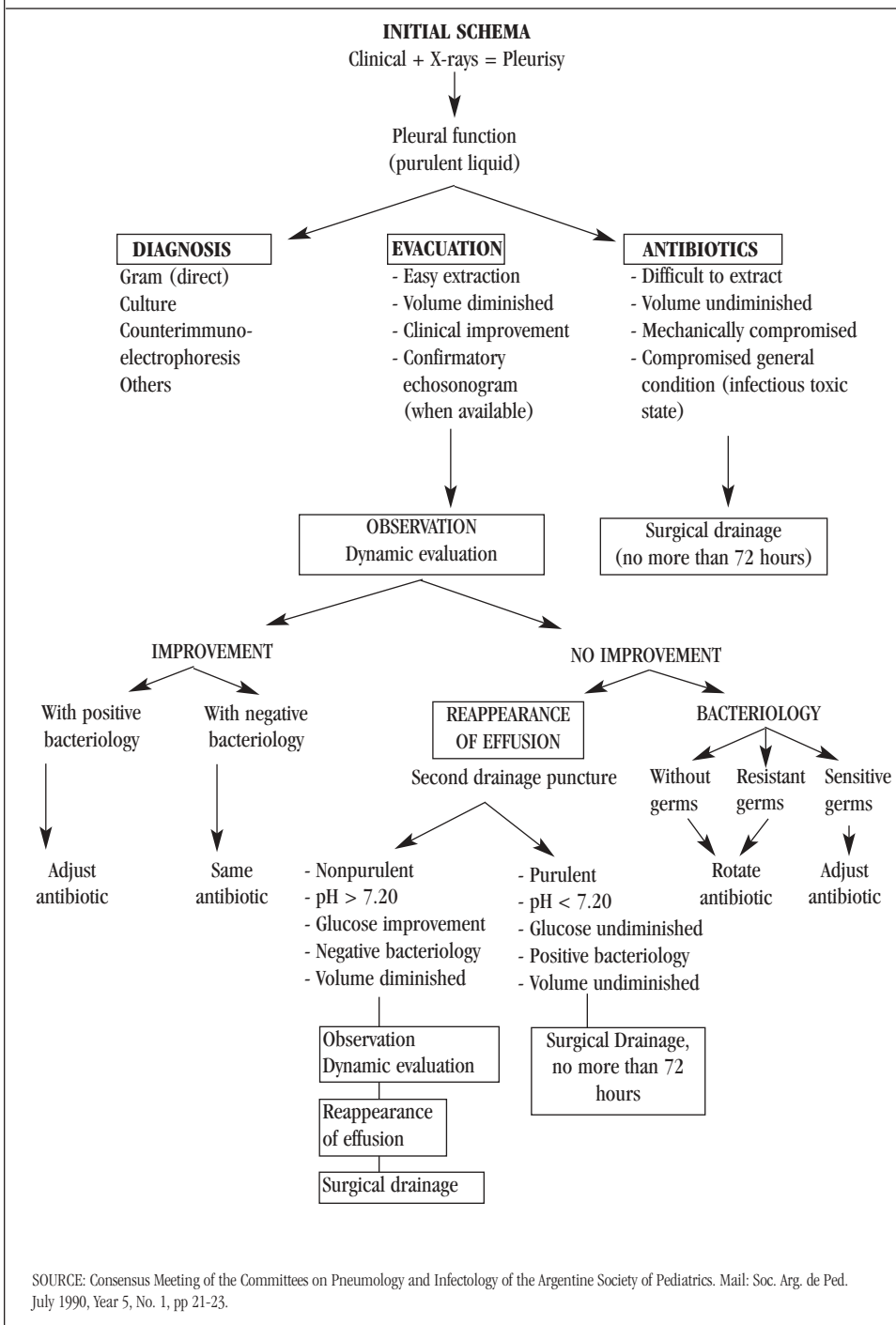
## VI. TREATMENT

The technical limitations inherent in etiological diagnosis sometimes hinder a decision on antibiotic treatment (115). The physician diagnosing pneumonia in a child should begin antibiotic treatment and assess whether follow-up can be conducted on an outpatient basis or if hospitalization is required (Tables 3 and 6). The criteria mentioned above allow different therapeutic options to be chosen on the basis of the most likely etiological agent (116).

Listed below are some problems that should be assessed when initiating empirical antibiotic treatment:

1. Impossibility of confirming the etiological diagnosis in most cases;
2. Ongoing alterations in bacterial sensitivity;
3. Experimental studies that have demonstrated that antibiotic concentrations in serum, bronchial secretions, and pulmonary parenchyma do not always coincide (117-119). The capillary alveolar membrane, which is semipermeable and regulates the passage of antibiotics from the capillary endothelium toward the alveolar lumen, may be affected in the event of infection (27);
4. Continuous supply of new antibiotic drugs that can induce confusion among physicians.

**Table 6.** Algorithm for follow-up of pleural effusions (in non-immunocompromised hosts)



Each region may present different levels of bacterial sensitivity, making it useful to propose criteria based on consensus over choice initial empirical treatment and optional guidelines, rather than inflexible rules.

The basic selection criteria for antibiotics to treat pneumonia are similar to those proposed for other kinds of infections:

- a) Use those that cover the germs most likely to be causing the infection (Table 7);
- b) Indicate the most limited spectrum to diminish the likelihood of resistant strains;
- c) Preferably use single medications rather than combinations of antibiotics;
- d) Choose those that maintain adequate bioavailability in the site of infection;
- e) Attain a sufficiently low minimum inhibitory concentration, yet avoid failures such as the need to raise dosage to a level that risks toxicity;
- f) Consider those that have few side effects;
- g) Consider an adequate cost-benefit ratio in making the selection.

Most community-acquired bacterial pneumonia in children under 5 years of age is caused by *S. pneumoniae* and noncapsulated or type B *H. influenzae*. These germs generally respond to b-lactamase antibiotics or amoxicillin administered orally in mild or moderate cases or intravenous ampicillin in more severe cases requiring hospitalization. A favorable response with clinical improvement within 3 days is considered positive therapeutic evidence, with a likely etiology of pneumococcus or ampicillin-sensitive *H. influenzae*.

Intestinal absorption of amoxicillin is quicker and less affected by the presence of ingested food, compared to ampicillin. It has a longer average life that allows it to be administered every 8 hours. When ampicillin is given intravenously, oral administration is indicated between 48 and 72 hours, if feasible, to avoid prolonged hospitalization and diminish the risk of nosocomial infections from multiresistant bacteria (120).

Trimethoprim-sulfamethoxazole (TMP-SMX or cotrimoxazole) has been proposed as the drug of choice in countries with scarce resources. In a random study with 614 children in Zimbabwe, it was shown to have an effect similar to procaine penicillin (121). However, *S. pneumoniae* was found to resist cotrimoxazole in 20% of the children attending day-care centers (122).

In areas with low incidence of b-lactamase producing *H. influenzae*, the response to amoxicillin is generally favorable.

In severe cases or in the event of poor antibiotic response, intravenous administration of a combination of ampicillin and chloramphenicol is indicated (123), because only rarely has a strain been detected that is resistant to both of these drugs (124, 125). In recent years, however, there have been findings of type B *H. influenzae* strains that are resistant to both these drugs, with high rates reported in Spain and Thailand (126, 127).

If *S. pneumoniae* is identified in a microbiological study, penicillin is the drug of choice. Amoxicillin and ampicillin are effective and conserve their activity in sputum and bronchial

<b>Table 7. Initial empirical antibiotic treatment of bacterial pneumonia</b>			
AGE	OUTPATIENT	HOSPITALIZED * ** *** **** *****	PREDOMINANT PATHOGENS
0 to 2 weeks		(E) ampicillin (iv) + gentamicin (im-iv) (A) ampicillin (iv) + cefotaxime (iv)	<ul style="list-style-type: none"> <li>• <i>E. coli</i></li> <li>• b-Streptococcus</li> <li>• Nosocomial enterobacteria</li> </ul>
> 2 to 4 weeks		(E) ampicillin + cefotaxime or ceftriaxone (iv)  (A) erythromycin (po)	<ul style="list-style-type: none"> <li>• <i>E. coli</i></li> <li>• <i>Klebsiella</i></li> <li>• <i>Enterobacter</i></li> <li>• Nosocomial enterobacteria</li> <li>• b-Streptococcus</li> <li>• <i>C. trachomatis</i></li> </ul>
> 1 a 2 months		(E) ampicillin (iv) + gentamicin (im-iv) (A) ceftriaxone or cefotaxime (iv) (A) erythromycin (po)	<ul style="list-style-type: none"> <li>• <i>E. coli</i> and other enterobacteria</li> <li>• <i>H. influenzae</i></li> <li>• <i>S. pneumoniae</i></li> <li>• <i>C. trachomatis</i></li> </ul>
> 2 mo to 5 years	(E) amoxicillin (po) (A) axetil cefuroxime (po) (A) cefixime (po)	(E) ampicillin (iv or po) (A) ampicillin (iv) + chloramphenicol (iv) (A) cefuroxime (iv) or ceftriaxone (iv-im)	<ul style="list-style-type: none"> <li>• <i>S. pneumoniae</i></li> <li>• <i>H. influenzae</i></li> </ul>
> 5 years	(E) penicillin V (po) (A) amoxicillin erythromycin (po)	(E) penicillin G (iv) (A) cefuroxime (iv) ceftriaxone (iv-im) vancomycin (iv) erythromycin (po)	<ul style="list-style-type: none"> <li>• <i>S. pneumoniae</i></li> <li>• <i>Mycoplasma p.</i></li> </ul>
<p>* If there is suspicion of: <i>S. aureus</i> methicillin-sensitive = cephalothin (iv) or nafcillin (iv); <i>S. aureus</i> or <i>S. epidermidis</i> methicillin-resistant = vancomycin (iv);</p> <p>** Suspicion of <i>C. trachomatis</i>: erythromycin or other macrolide;</p> <p>*** If suspicion of <i>P. aeruginosa</i>: ceftazidime = gentamicin or vancomycin;</p> <p>**** If suspicion of resistant enterobacteria, replace gentamicin with amikacin.</p> <p>(po) = orally; (im) = intramuscularly; (iv) = intravenously; (E) = Elective; (A) = Alternative.</p>			

**Table 8.** Antibiotics, dose per kilogram of weight and suggested intervals for treatment of lower respiratory infections

ANTIBIOTIC	DOSE	INTERVAL
• Penicillin	150,000 u.	Every 6 hours
• Ampicillin	150 mg	Every 6 hours
• Amoxicillin	40 to 50 mg	Every 8 hours
• Erythromycin	40 mg	Every 6 hours
• Chloramphenicol	75 mg	Every 6 hours
• Nafcillin	150 mg	Every 6 hours
• Cephalexin	100 to 150 mg	Every 6 hours
• Cephalothin	150 mg	Every 6 hours
• Cefotaxime	150 mg	Every 6 hours
• Ceftriaxone	50 to 75 mg	Every 24 hours
• Ceftazidime	150 mg	Every 6 hours
• Cefuroxime	125 to 150 mg	Every 8 hours
• Vancomycin	40 mg	Every 6 hours

secretions for several hours before becoming degraded by b-lactamases, which are able to penetrate the pulmonary parenchyma and maintain adequate levels therein. Macrolides and fluoroquinolones possess similar properties (27). Recent modifications have been seen in the behavior of *S. pneumoniae*, and inadequate responses have been observed in children with pneumonia (128). The minimum inhibitory concentration (MIC) for penicillin, which used to be a low level (0.02 mg/l) has risen to a range of 0.05-0.10 mg/l. It is generally accepted that 5-10% of the strains possess intermediate resistance; that is, they present an MIC between 0.1 and 1.0 mg/l. These strains are inhibited by increasing the penicillin dose without the need to change the antibiotic. When resistance is high (MIC  $\geq$  1.0 mg/l), it is imperative to use other drugs, such as cefuroxime or third-generation cephalosporins.

Should a patient fail to respond positively to initial treatment the following options should be evaluated:

- a) The causal germs could be bacteria that do not respond to b-lactamase-resistant drugs such as *M. pneumoniae*, *C. trachomatis*, and *B. pertussis*, all of which are sensitive to erythromycin and the new macrolides. The effectiveness of erythromycin against *Chlamydia pneumoniae* is controversial; tetracycline or doxycycline in children over 9 years of age is indicated.
- b) There may be present *S. pneumoniae* with intermediate or high resistance to penicillin. If it has intermediate resistance a higher dose of penicillin or ampicillin is recommended. If it is a highly resistant strain, a different type of drug will have to be administered as indicated above;

- c) b-Lactamase-producing *H. influenzae* may be present, in which case adding chloramphenicol or changing to second- or third-generation cephalosporins is suggested;
- d) If the cause is *S. aureus*, it is usually sensitive to first-generation cephalosporins and anti-staphylococcal penicillin;
- e) If *M. tuberculosis* is suspected a specific treatment is indicated;
- f) The pneumonia may be of a viral etiology.

Of the 50 pneumonia patients in the Rouskanen series who failed to respond to b-lactam drugs, 3 suffered from a viral infection, 3 had a mixed etiology, and another 3 were infected with *M. pneumoniae* (129).

The tables in this chapter propose criteria for administering antibiotics, considering age group, whether outpatient or inpatient care is indicated, and on the basis of predominant bacteria.

On rare occasions other pathogens are observed such as *Chlamydia pneumoniae* or *Acinetobacter baumannii*, the latter of which is sensitive to very few antibiotics, sometimes only to imipenem-cilastatin and to fluoroquinolones.

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