MODULE 1
SUBSTANTIAL MODULE 2

THEME 5
PNEUMONIAS IN CHILDREN

Practical policies for students

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PNEUMONIA

Pneumonia and other lower respiratory tract infections are the leading causes of death worldwide. Because pneumonia is common and is associated with significant morbidity and mortality, properly diagnosing pneumonia, correctly recognizing any complications or underlying conditions, and appropriately treating patients are important. Although in developed countries the diagnosis is usually made on the basis of radiographic findings, the World Health Organization (WHO) has defined pneumonia solely on the basis of clinical findings obtained by visual inspection and on timing of the respiratory rate.

Pneumonia may originate in the lung or may be a focal complication of a contiguous or systemic inflammatory process. Abnormalities of airway patency as well as alveolar ventilation and perfusion occur frequently due to various mechanisms. These derangements often significantly alter gas exchange and dependent cellular metabolism in the many tissues and organs that determine survival and contribute to quality of life. Recognition, prevention, and treatment of these problems are major factors in the care of children with pneumonia.

One particular form of pneumonia present in the pediatric population, congenital pneumonia, presents within the first 24 hours after birth.

Practice Essentials

The United Nations Children's Fund (UNICEF) estimates that pediatric pneumonia kills 3 million children worldwide each year. These deaths occur almost exclusively in children with underlying conditions, such as chronic lung disease of prematurity, congenital heart disease, and immunosuppression. Although most fatalities occur in developing countries, pneumonia remains a significant cause of morbidity in industrialized nations.

International statistics

Pneumonia and other lower respiratory tract infections are the leading cause of death worldwide. The WHO Child Health Epidemiology Reference Group estimated the median global incidence of clinical pneumonia to be 0.28 episodes per child-year. This equates to an annual incidence of 150.7 million new cases, of which 11–20 million (7–13%) are severe enough to require hospital admission. Ninety-five percent of all episodes of clinical pneumonia in young children worldwide occur in developing countries.

Approximately 150 million new cases of pneumonia occur annually among children younger than 5 years worldwide, accounting for approximately 10–20 million hospitalizations. A WHO Child Health Epidemiology Reference Group publication cited the incidence of community-acquired pneumonia among children younger than 5 years in developed countries as approximately 0.026 episodes per child-year, and a study conducted in the United Kingdom showed that 59% of deaths from pertussis are associated with pneumonia.

Morbidity

Although viral pneumonias are common in school-aged children and adolescents and are usually mild and self-limited, these pneumonias are occasionally severe and can rapidly progress to respiratory failure, either as a primary manifestation of viral infection or as a consequence of subsequent bacterial infection.

Morbidity and mortality from RSV and other viral infections is higher among premature infants and infants with underlying lung disease. Significant sequelae occur with adenoviral disease, including bronchiolitis obliterans and necrotizing bronchiolitis. With neonatal pneumonia, even if the infection is eradicated, many hosts develop long-lasting or permanent pulmonary changes that affect lung function, the quality of life, and susceptibility to later infections.

Infants and postpubertal adolescents with TB pneumonia are at increased risk of disease progression. If TB is not treated during the early stages of infection, approximately 25% of children younger than 15 years develop extrapulmonary disease.

Bronchopneumonia occurs in 0.8–2% of all pertussis cases and 16–20% of hospitalized cases; the survival rate of these patients is much lower than in those with pneumonia that is attributed to other causes.

Immunocompromised children, those with underlying lung disease, and neonates are at high risk for severe sequelae, and they are also susceptible to various comorbidities. Cryptococcosis may occur in as many as 5–10% of patients with AIDS, and acute chest syndrome occurs in 15–43% of patients with sickle cell disease. Individuals with sickle cell disease not only have problems with their complement system, but they also have functional asplenia, which predisposes them to infection with encapsulated organisms such as S pneumoniae and H influenzae type B.

Mortality

The United Nations Children's Fund (UNICEF) estimates that 3 million children die worldwide from pneumonia each year; these deaths almost exclusively occur in children with underlying conditions, such as chronic lung disease of prematurity, congenital heart disease, and immunosuppression. Although most fatalities occur in developing countries, pneumonia remains a significant cause of morbidity in industrialized nations.

According to the WHO's Global Burden of Disease 2000 Project, lower respiratory infections were the second leading cause of death in children younger than 5 years (about 2.1 million [19.6%]). Most children are treated as outpatients and fully recover. However, in young infants and immunocompromised individuals, mortality is much higher. In studies of adults with pneumonia, a higher mortality rate is associated with abnormal vital signs, immunodeficiency, and certain pathogens.

Etiology

Pneumonia can be caused by a myriad of microorganisms. Clinical suspicion of a particular offending agent is derived from clues obtained during the history and physical examination. While virtually any microorganism can lead to pneumonia, specific bacterial, viral, fungal, and mycobacterial infections are most common in previously healthy children. The age of infection, exposure history, risk factors for unusual pathogens, and immunization history all provide clues to the infecting agent.

In a prospective multicenter study of 154 hospitalized children with acute community-acquired pneumonia (CAP) in whom a comprehensive search for an etiology was sought, a pathogen was identified in 79% of children. Pyogenic bacteria accounted for 60% of cases, of which 73% were due to Streptococcus pneumoniae, while the atypical bacteria Mycoplasma pneumoniae and Chlamydophila pneumoniae were detected in 14% and 9%, respectively. Viruses were documented in 45% of children. Notably, 23% of the children had concurrent acute viral and bacterial disease. In the study, preschool-aged children had as many episodes of atypical bacterial lower respiratory infections as older children. Multivariable analyses revealed that high temperature (38.4°C) within 72 hours after admission and the presence of pleural effusion were significantly associated with bacterial pneumonia.

Specific etiologic agents vary based on age groups (ie, newborns, young infants, infants and toddlers, 5-year-olds, school-aged children and young adolescents, older adolescents).

Newborns

In newborns (age 0–30 d), organisms responsible for infectious pneumonia typically mirror those responsible for early onset neonatal sepsis. This is not surprising in view of the role that maternal genitourinary and gastrointestinal tract flora play in both processes. Infections with group B Streptococcus, Listeria monocytogenes, or gram-negative rods (eg, Escherichia coli, Klebsiella pneumoniae) are common causes of bacterial pneumonia. These pathogens can be acquired in utero, via aspiration of organisms present in the birth canal, or by postnatal contact with other people or contaminated equipment.

Group B Streptococcus (GBS) was the most common bacterial isolate in most locales from the late 1960s to the late 1990s, when the impact of intrapartum chemoprophylaxis in reducing neonatal and maternal infection by this organism became evident. E coli has become the most common bacterial isolate among VLBW infants (1500 g or less) since that time. Other potential bacterial organisms include Nontypeable Haemophilus influenzae (NTHi).

Other gram-negative bacilli:
- Enterococci
- Staphylococcus aureus.

Some organisms acquired perinatally may not cause illness until later in infancy, including Chlamydia trachomatis, U urealyticum, Mycoplasma hominis, CMV, and Pneumocystis carinii. C trachomatis organisms are presumably transmitted at birth during passage through an infected birth canal, although most infants are asymptomatic during the first 24 hours and develop pneumonia only after the first 2 weeks of life.

Group B streptococci infections are most often transmitted to the fetus in utero, usually as a result of colonization of the mother's vagina and cervix by the organism. Agents of chronic congenital infection, such as CMV, Treponema pallidum (the cause of pneumonia alba), Toxoplasma gondii, and others, may cause pneumonia in the first 24 hours of life. The clinical presentation usually involves other organ systems as well.

Community-acquired viral infections occur in newborns, although less commonly than in older infants. The most commonly isolated virus is respiratory syncytial virus (RSV). The transfer of maternal antibodies is important in protecting newborns and young infants from such infections, making premature infants (who may not have benefited from sufficient transfer of transplacental immunoglobulin [Ig G]) especially vulnerable to lower-tract disease. In addition, premature infants may have chronic lung disease of prematurity, with associated hyperreactive airways, fewer functional alveoli, and baseline increased oxygen requirements.

Newborns may also be affected by the bacteria and viruses that commonly cause infections in older infants and children. Risk factors for infection include older siblings, group daycare, and lack of immunization.

Young infants

In the young infant (aged 1-3 mo), continued concern about the perinatally acquired pathogens mentioned above remains. However, most bacterial pneumonia in this age group is community acquired and involves S pneumoniae, S aureus, and nontypeable H influenzae. S pneumoniae is by far the most common bacterial pathogen in this age group. Infection with any of these pyogenic bacteria may be complicated by lung abscess, parapneumonic effusions, and empyema, although S aureus is notorious for such complications.

At this age, infants are incompletely immunized and remain at higher risk for H influenzae type B and pneumococcal disease, although herd immunity gained from widespread immunization of the population has been broadly protective. It is important to note that the current conjugate pneumococcal vaccine provides protection against 13 common pneumococcal types, but nonvaccine types remain problematic.

Most lower respiratory tract disease in young infants occurs during the respiratory virus season and is viral in origin, particularly in the patient with clinical bronchiolitis. The most common viral agents include RSV, parainfluenza viruses, influenza virus, adenovirus, and human metapneumovirus (hMPV).

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Atypical organisms may rarely cause infection in infants. Of these, C trachomatis, U urealyticum, CMV, and P carinii are described.

Bordetella pertussis infection leads to pneumonia in as many as 20% of infected infants (as a complication of the whooping cough infection).

Among other potential atypical bacterial pathogens, U urealyticum and U parvum have been recovered from endotracheal aspirates shortly after birth in very low birth weight (VLBW) infants and have been variably associated with various adverse pulmonary outcomes, including bronchopulmonary dysplasia (BPD). Whether these organisms are causal or simply a marker of increased risk is unclear.

Infants, toddlers, and preschool-aged children

Viruses remain the most common cause of pneumonia in this age group, accounting for approximately 90% of all lower respiratory tract infections. Tsolia et al identified a viral infection among 65% of hospitalized children with community-acquired pneumonia.

RSV is the most common viral pathogen, followed by parainfluenza types 1, 2, and 3 and influenza A or B. RSV infection occurs in the winter and early spring. Parainfluenza type 3 infection occurs in the spring, and types 1 and 2 occur in the fall. Influenza occurs in the winter.

Other viruses that cause pneumonia less frequently in infants and young children include adenovirus, enterovirus, rhinovirus, and coronavirus. A recent addition to this list is hMPV, which causes an illness similar to RSV and may be responsible for one third to one half of non-RSV bronchiolitis. The herpesviruses (HSV, VZV, and CMV) may rarely cause pneumonia, particularly in children with impaired immune systems.

Bacterial infections in this age group are seen on a regular basis. S pneumoniae is by far the most common bacterial cause of pneumonia. Among hospitalized children with bacterial pneumonia, S pneumoniae accounts for 21–44% of disease. Other agents to consider include H influenzae type B (HiB) (very uncommon in immunized children), S pyogenes, and S aureus.

Children younger than 5 years, children enrolled in daycare, or those with frequent ear infections are at increased risk for invasive pneumococcal disease and infection with resistant pneumococcal strains. Evidence suggests that breastfeeding has a protective effect against invasive pneumococcal infection.

School-aged children and young adolescents

M pneumoniae is the most frequent cause of pneumonia among older children and adolescents. Mycoplasma accounts for 14–35% of pneumonia hospitalizations in this age group. Children in homeless shelters and group homes and those with household contacts are at particular risk. Similarly, the diagnosis must be considered in immunocompromised children.

In this age group, pyogenic bacterial pneumonia remains a concern, usually caused by S. pneumoniae. Other pyogenic bacterial pathogens to consider include S. aureus and S. pyogenes.

Chlamydophila pneumoniae also causes pneumonia. The related organism, C. psittaci, is an unusual cause of pneumonia that occurs in people who work with and handle birds.

In immunosuppressed individuals, opportunistic infections with organisms such as Aspergillus species, Pneumocystis jirovecii, and CMV can occur.

Viral pneumonia remains common in this age group. Influenza pneumonia is a particular concern because ongoing infection with this virus predisposes to the development of bacterial superinfection, usually with S. pneumoniae or S. aureus.

Older adolescents

M. pneumoniae is the most common cause of community-acquired pneumonia during the teenage and young adult years. Atypical pneumonia caused by C pneumoniae can present with identical signs and symptoms. Bacterial pneumonia caused by S. pneumoniae is also seen.

Pulmonary infections caused by dimorphic fungi are also seen in this age group. Histoplasma capsulatum, which is found in nitrate-rich soil, is usually acquired as a result of inhalation of spores. Chicken coops and other bird roosts and decaying wood are often-cited sources. Cryptococcus neoformans is a common infection among pigeon breeders, but it is unusual in other immunocompetent individuals.

Blastomyces dermatitides, another dimorphic fungus, is found in certain geographic locations, most notably the Ohio and Mississippi River valleys. As with histoplasmosis, blastomycosis is acquired by inhalation of spores. Although 3 distinct forms of infection exist, the most common is acute pneumonia, which, in previously healthy individuals, most often resolves without treatment.

Viral pneumonias are common in this age group are usually mild and self-limited, but influenza pneumonia can be severe or protracted, particularly when a bacterial infection follows.

TB pneumonia in children warrants special mention. It can occur in any age group, and it is important to remember that children with TB usually do not present with symptoms until 1–6 months after primary infection. Any child with pneumonia who has a history of TB exposure, or who has traveled to a TB-endemic area of the world needs to be fully evaluated for the possibility of tuberculosis.

Legionella pneumophila, the agent of Legionnaires disease, can also cause pneumonia, although it is uncommon in the pediatric age group.

Not all pneumonia is caused by infectious agents. Children who have severe gastroesophageal reflux (GERD) may develop chemical pneumonitis secondary to recurrent aspiration. Inhalation of certain chemicals or smoke may cause pulmonary inflammation. Additionally, aspiration pneumonia is more common in children with neurologic impairment, swallowing abnormalities,

gastrointestinal motility, or a gastrostomy tube. Oral anaerobic flora, with or without aerobes, is the most common etiologic agent.

Immunocompromised children

Some children who are immunocompromised, whether secondary to HIV infection/AIDS, an immune disorder, or chemotherapy for a malignancy, are at risk for pneumonias with opportunistic agents. Virtually any bacteria, virus, fungus, or even parasite can invade and infect the lungs if the immune system is sufficiently impaired. Carefully obtained samples for appropriate microbiologic testing are paramount in such patients so that therapy can be optimized.

Children with cystic fibrosis are especially prone to develop infections with S. aureus, Pseudomonas aeruginosa, Burkholderia cepacia, and other multidrug-resistant organisms.

P. jirovecii pneumonia (PCP) is common in the most severely compromised children and can lead to respiratory failure and death in those who are profoundly immunocompromised. Adenovirus infections can be severe in these children as well, leading to bronchiolitis obliterans or hyperlucent lung syndrome. In addition, CMV poses a great risk to immunocompromised patients.

Fungal pneumonia, caused by Aspergillus, Zygomycetes, or other related fungi, occur in immunocompromised patients who undergo prolonged hospitalization, have prolonged neutropenia, and/or have received broad-spectrum antibiotics. Patients with underlying hematologic malignancies are at the highest risk.

Patients with sickle cell disease have problems with their complement system as well as functional asplenia, which predisposes them to infection with encapsulated organisms such as S. pneumoniae and H. influenzae type B. M. pneumoniae is also a common agent of pneumonia is this group of patients.

Pathophysiology

An inhaled infectious organism must bypass the host's normal nonimmune and immune defense mechanisms in order to cause pneumonia. The nonimmune mechanisms include aerodynamic filtering of inhaled particles based on size, shape, and electrostatic charges; the cough reflex; mucociliary clearance; and several secreted substances (eg, lysozymes, complement, defensins). Macrophages, neutrophils, lymphocytes, and eosinophils carry out the immune-mediated host defense.

Respiratory tract host defenses

To prevent and minimize injury and invasion by microorganisms and foreign substances, various defense mechanisms have evolved, both systemically and within the respiratory tract. Some mechanisms are nonspecific and are directed against any invasive agent, whereas others are targeted against only microbes or substances with specific antigenic determinants. Many of the defenses

are compromised in the fetus and newborn infant, resulting in more frequent breaches and consequent disruption of normal lung structure and function.

Nonspecific defenses include the glottis and vocal cords, ciliary escalator, airway secretions, migratory and fixed phagocytes, nonspecific antimicrobial proteins and opsonins, and the normal relatively nonpathogenic airway flora. Anatomic structures of the upper airway and associated reflexes discourage particulate material from entering, whereas coordinated movement of the microscopic cilia on the tracheal and bronchial epithelia tends to sweep particles and mucus up the airway and away from the alveoli and distal respiratory structures.

Mucoid airway secretions provide a physical barrier that minimizes epithelial adhesion and subsequent invasion by microorganisms. These secretions typically contain complement components, fibronectin, and other proteins that bind to microbes and render them more susceptible to ingestion by phagocytes. Alveolar and distal airway secretions also include whole surfactant, which facilitates opsonization and phagocytosis of pathogens, as well as surfactant-associated proteins A (Sp-A) and D (Sp-D), both of which modulate phagocytosis, phagocyte production of oxyradicals, and cytokine elaboration.

The secretions also contain directly inhibitory and microbicidal agents, such as iron-binding proteins, lysozymes, and defensins. Typical benign airway commensals, such as alpha-hemolytic streptococci and coagulase-negative staphylococci, occupy mucosal sites and elaborate bacteriocins and other substances that prevent more pathogenic organisms from adhesion, replication, and possible opportunistic invasion.

Newborns typically have sterile respiratory mucosa at birth, with subsequent uncontested colonization by microorganisms from the mother or environment. Accelerated access to distal respiratory structures and bypass of much of the ciliary escalator occur in infants who require endotracheal intubation. In these infants, increased physical disruption of epithelial and mucous barriers also occurs. In addition, interventional exposure to high oxygen concentrations, generous airway pressures, and large intrapulmonary gas volumes may interfere with ciliary function and mucosal integrity. The use of less invasive means of respiratory support, such as nasal ventilation, nasal continuous positive airway pressure (CPAP), and nasal cannula (conventional or humidified, high flow), may produce lesser degrees of pulmonary mucosal and parenchymal disruption, but some disruption is almost always present.

Systemic host defenses

Immunologic defense mechanisms targeted against particular pathogens typically emanate from specifically primed lymphocytes following presentation of processed antigens by macrophages. These mechanisms include cytotoxic, killer, suppressor, and memory functions; systemic and secretory antibodies;

and consequent cascades of cytokines, complement, vasomotor regulatory molecules, hemostatic factors, and other agents. Secretory antibodies are typically multimeric and contain secretory component and J chains that render them more opsonic and more resistant to microbial proteases.

Many of the biochemical cascades triggered by specific immune responses serve to localize microbial invasion, amplify and focus recruitment of phagocytes to the affected sites, and directly disrupt the structural and metabolic integrity of the microbes. The role that these cascades play in triggering apoptosis (programmed cell death) in host and invader cells is still undergoing exploration.

Secretory antibodies and mucosal lymphoid tissue are absent or minimally functional for the first month of life postnatally. Systemic antibodies may enter pulmonary tissues but usually consist primarily of passively transmitted maternal antibodies, with reduced transplacental transport of maternal antibodies before 32 weeks' gestation. Specific systemic antibodies can be generated, but many components of the necessary immunologic machinery are relatively sluggish. Circulating complement components are present at approximately 50% of the concentration found in older children, although components of the alternative pathway are present in sufficient quantities to serve as effective opsonins.

The neonatal granulocyte number frequently decreases in response to early infection (as well as noninflammatory processes such as maternal preeclampsia), whereas the phagocytes that are present often move much more sluggishly to the inflammatory focus, whether it is a microorganism or inanimate debris. Once at the targeted sites, phagocytes often ingest the invaders less efficiently, although intracellular microbicidal activities appear normal. Intercellular communication via cytokines and other mediators is blunted.

The net result of these and other developmental aberrations is that the fetal and neonatal inflammatory response is slower, less efficient, and much less focused than in older children. Infection is less likely to be localized and effectively inhibited by host defenses alone. Inflammation from particulate debris and other foreign substances is isolated less effectively, and the injurious effector portions of the inflammatory cascade are much less precisely targeted.

Pathogenesis

Pneumonia is characterized by inflammation of the alveoli and terminal airspaces in response to invasion by an infectious agent introduced into the lungs through hematogenous spread or inhalation. The inflammatory cascade triggers the leakage of plasma and the loss of surfactant, resulting in air loss and consolidation.

The activated inflammatory response often results in targeted migration of phagocytes, with the release of toxic substances from granules and other microbicidal packages and the initiation of poorly regulated cascades (eg, complement, coagulation, cytokines). These cascades may directly injure host tissues and adversely alter endothelial and epithelial integrity, vasomotor tone, intra-

vascular hemostasis, and the activation state of fixed and migratory phagocytes at the inflammatory focus. The role of apoptosis (noninflammatory programmed cell death) in pneumonia is poorly understood.

Pulmonary injuries are caused directly and/or indirectly by invading microorganisms or foreign material and by poorly targeted or inappropriate responses by the host defense system that may damage healthy host tissues as badly or worse than the invading agent. Direct injury by the invading agent usually results from synthesis and secretion of microbial enzymes, proteins, toxic lipids, and toxins that disrupt host cell membranes, metabolic machinery, and the extracellular matrix that usually inhibits microbial migration.

Indirect injury is mediated by structural or secreted molecules, such as endotoxin, leukocidin, and toxic shock syndrome toxin-1 (TSST-1), which may alter local vasomotor tone and integrity, change the characteristics of the tissue perfusate, and generally interfere with the delivery of oxygen and nutrients and removal of waste products from local tissues.

On a macroscopic level, the invading agents and the host defenses both tend to increase airway smooth muscle tone and resistance, mucus secretion, and the presence of inflammatory cells and debris in these secretions. These materials may further increase airway resistance and obstruct the airways, partially or totally, causing airtrapping, atelectasis, and ventilatory dead space. In addition, disruption of endothelial and alveolar epithelial integrity may allow surfactant to be inactivated by proteinaceous exudate, a process that may be exacerbated further by the direct effects of meconium or pathogenic microorganisms.

In the end, conducting airways offer much more resistance and may become obstructed, alveoli may be atelectatic or hyperexpanded, alveolar perfusion may be markedly altered, and multiple tissues and cell populations in the lung and elsewhere sustain injury that increases the basal requirements for oxygen uptake and excretory gas removal at a time when the lungs are less able to accomplish these tasks.

Alveolar diffusion barriers may increase, intrapulmonary shunts may worsen, and ventilation/perfusion (V/Q) mismatch may further impair gas exchange despite endogenous homeostatic attempts to improve matching by regional airway and vascular constriction or dilatation. Because the myocardium has to work harder to overcome the alterations in pulmonary vascular resistance that accompany the above changes of pneumonia, the lungs may be less able to add oxygen and remove carbon dioxide from mixed venous blood for delivery to end organs. The spread of infection or inflammatory response, either systemically or to other focal sites, further exacerbates the situation.

Viral infections are characterized by the accumulation of mononuclear cells in the submucosa and perivascular space, resulting in partial obstruction of the airway. Patients with these infections present with wheezing and crackles

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(see Clinical Presentation). Disease progresses when the alveolar type II cells lose their structural integrity and surfactant production is diminished, a hyaline membrane forms, and pulmonary edema develops.

In bacterial infections, the alveoli fill with proteinaceous fluid, which triggers a brisk influx of red blood cells (RBCs) and polymorphonuclear (PMN) cells (red hepatization) followed by the deposition of fibrin and the degradation of inflammatory cells (gray hepatization). During resolution, intra-alveolar debris is ingested and removed by the alveolar macrophages. This consolidation leads to decreased air entry and dullness to percussion; inflammation in the small airways leads to crackles.

Four stages of lobar pneumonia have been described. In the first stage, which occurs within 24 hours of infection, the lung is characterized microscopically by vascular congestion and alveolar edema. Many bacteria and few neutrophils are present. The stage of red hepatization (2–3 d), so called because of its similarity to the consistency of liver, is characterized by the presence of many erythrocytes, neutrophils, desquamated epithelial cells, and fibrin within the alveoli. In the stage of gray hepatization (2–3 d), the lung is gray-brown to yellow because of fibrinopurulent exudate, disintegration of RBCs, and hemosiderin. The final stage of resolution is characterized by resorption and restoration of the pulmonary architecture. Fibrinous inflammation may lead to resolution or to organization and pleural adhesions.

Bronchopneumonia, a patchy consolidation involving one or more lobes, usually involves the dependent lung zones, a pattern attributable to aspiration of oropharyngeal contents. The neutrophilic exudate is centered in bronchi and bronchioles, with centrifugal spread to the adjacent alveoli.

In interstitial pneumonia, patchy or diffuse inflammation involving the interstitium is characterized by infiltration of lymphocytes and macrophages. The alveoli do not contain a significant exudate, but protein-rich hyaline membranes similar to those found in adult respiratory distress syndrome (ARDS) may line the alveolar spaces. Bacterial superinfection of viral pneumonia can also produce a mixed pattern of interstitial and alveolar airspace inflammation.

Miliary pneumonia is a term applied to multiple, discrete lesions resulting from the spread of the pathogen to the lungs via the bloodstream. The varying degrees of immunocompromise in miliary tuberculosis (TB), histoplasmosis, and coccidioidomycosis may manifest as granulomas with caseous necrosis to foci of necrosis. Miliary herpesvirus, cytomegalovirus (CMV), or varicella-zoster virus infection in severely immunocompromised patients results in numerous acute necrotizing hemorrhagic lesions.

History

Newborns with pneumonia rarely cough; they more commonly present with poor feeding and irritability, as well as tachypnea, retractions, grunting, and hypoxemia. Grunting in a newborn suggests a lower respiratory tract disease and is due to vocal cord approximation as they try to provide increased positive end-expiratory pressure (PEEP) and keep their lower airways open.

After the first month of life, cough is the most common presenting symptom of pneumonia. Infants may have a history of antecedent upper respiratory symptoms. Grunting may be less common in older infants; however, tachypnea, retractions, and hypoxemia are common and may be accompanied by a persistent cough, congestion, fever, irritability, and decreased feeding. Any maternal history of Chlamydia trachomatis infection should be determined.

Infants with bacterial pneumonia are often febrile, but those with viral pneumonia or pneumonia caused by atypical organisms may have a low-grade fever or may be afebrile. The child's caretakers may complain that the child is wheezing or has noisy breathing. Toddlers and preschoolers most often present with fever, cough (productive or nonproductive), tachypnea, and congestion. They may have some vomiting, particularly posttussive emesis. A history of antecedent upper respiratory tract illness is common.

Older children and adolescents may also present with fever, cough (productive or nonproductive), congestion, chest pain, dehydration, and lethargy. In addition to the symptoms reported in younger children, adolescents may have other constitutional symptoms, such as headache, pleuritic chest pain, and vague abdominal pain. Vomiting, diarrhea, pharyngitis, and otalgia/otitis are other common symptoms.

Travel history is important because it may reveal an exposure risk to a pathogen more common to a specific geographic area (eg, dimorphic fungi). Any exposure to TB should always be determined. In addition, exposure to birds (psittacosis), bird droppings (histoplasmosis), bats (histoplasmosis), or other animals (zoonoses, including Q fever, tularemia, and plague) should be determined.

In children with evidence for recurrent sinopulmonary infections, a careful history to determine the underlying cause is needed. The recurrent nature of the infections may be unveiling an innate or acquired immune deficiency, an anatomic defect, or another genetic disease (cystic fibrosis, ciliary dyskinesia).

Physical Examination

The signs and symptoms of pneumonia are often nonspecific and widely vary based on the patient's age and the infectious organisms involved. Tachypnea is the most sensitive finding in patients with diagnosed pneumonia.

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Initial evaluation

Early in the physical examination, identifying and treating respiratory distress, hypoxemia, and hypercarbia is important. Visual inspection of the degree of respiratory effort and accessory muscle use should be performed to assess for the presence and severity of respiratory distress. The examiner should simply observe the patient's respiratory effort and count the respirations for a full minute. In infants, observation should include an attempt at feeding, unless the baby has extreme tachypnea.

Pulmonary findings in all age groups may include accessory respiratory muscle recruitment, such as nasal flaring and retractions at subcostal, intercostal, or suprasternal sites. Signs such as grunting, flaring, severe tachypnea, and retractions should prompt the clinician to provide immediate respiratory support. Retractions result from the effort to increase intrathoracic pressure to compensate for decreased compliance.

An emergency department (ED)-based study conducted in the United States found that respiratory rate alone and subjective clinical impression of tachypnea did not discriminate children with and without radiographic pneumonia. The WHO clinical criteria for pneumonia has also been reported to demonstrate poor sensitivity (34.3%) in diagnosing radiographic pneumonia in children presenting to a pediatric ED. However, children with tachypnea as defined by WHO respiratory rate thresholds were more likely to have pneumonia than children without tachypnea. The WHO thresholds are as follows:
- Children younger than 2 months – Greater than or equal to 60 breaths/min
- Children aged 2–11 months – Greater than or equal to 50 breaths/min
- Children aged 12–59 month – Greater than or equal to 40 breaths/min

Airway secretions may vary substantially in quality and quantity but are most often profuse and progress from serosanguineous to a more purulent appearance. White, yellow, green, or hemorrhagic colors and creamy or chunky textures are not infrequent. If aspiration of meconium, blood, or other proinflammatory fluid is suspected, other colors and textures reflective of the aspirated material may be seen.

Infants may have external staining or discoloration of skin, hair, and nails with meconium, blood, or other materials when they are present in the amniotic fluid. The oral, nasal, and, especially, tracheal presence of such substances is particularly suggestive of aspiration.

An assessment of oxygen saturation by pulse oximetry should be performed early in the evaluation of all children with respiratory symptoms. Cyanosis may be present in severe cases. When appropriate and available, capnography may be useful in the evaluation of children with potential respiratory compromise.

Cyanosis of central tissues, such as the trunk, implies a deoxyhemoglobin concentration of approximately 5 g/dL or more and is consistent with severe derangement of gas exchange from severe pulmonary dysfunction as in pneumonia, although congenital structural heart disease, hemoglobinopathy, polycythemia, and pulmonary hypertension (with or without other associated parenchymal lung disease) must be considered.

Chest pain may be observed with inflammation of or near the pleura. Abdominal pain or tenderness is often seen in children with lower lobe pneumonia. The presence and degree of fever depends on the organism involved, but high temperature (38.4°C) within 72 hours after admission and the presence of pleural effusion have been reported to be significantly associated with bacterial pneumonia.

Pneumonia may occur as a part of another generalized process. Therefore, signs and symptoms suggestive of other disease processes, such as rashes and pharyngitis, should be sought during the examination.

Auscultation

Auscultation is perhaps the most important portion of the examination of the child with respiratory symptoms. The examination is often very difficult in infants and young children for several reasons. Babies and young children often cry during the physical examination making auscultation difficult. The best chance of success lies in prewarming hands and instruments and in using a pacifier to quiet the infant. The opportunity to listen to a sleeping infant should never be lost.

Older infants and toddlers may cry because they are ill or uncomfortable, but, most often, they have stranger anxiety. For these children, it is best to spend a few minutes with the parents in the child's presence. If the child sees that the parent trusts the examining physician then he or she may be more willing to let the examiner approach. A small toy may help to gain the child's trust. Any part of the examination using instruments should be deferred as long as possible, because the child may find the medical equipment frightening. Occasionally, if the child is allowed to hold the stethoscope for a few minutes, it becomes less frightening. Even under the best of circumstances, examining a toddler is difficult. If the child is asleep when the physician begins the evaluation, auscultation should be performed early.

Children with respiratory symptoms may have a concomitant upper respiratory infection with copious upper airway secretions. This creates another potential problem, the transmission of upper airway sounds. In many cases, the sounds created by upper airway secretions can almost obscure true breath sounds and lead to erroneous diagnoses. If the etiology of sounds heard through the stethoscope is unclear, the examiner should listen to the lung fields and then hold the stethoscope near the child's nose. If the sounds from both locations are approximately the same, the likely source of the abnormal breath sounds is the upper airway.

Even when the infant or young child is quiet and has a clear upper airway, the child's normal physiology may make the examination difficult. The minute ventilation is the product of the respiratory rate and tidal volume. In young children, respiratory rate makes a very large contribution to the overall minute ventilation. In other words, babies take many shallow breaths as opposed to a few deep ones. Therefore, a subtle finding, particularly one at the pulmonary bases, can be missed.

The sine qua non for pneumonia has always been the presence of crackles or rales. Although often present, focal crackles as a stand-alone physical examination finding is neither sensitive nor specific for the diagnosis of pneumonia. Additionally, not all children with pneumonia have crackles.

Rales, rhonchi, and cough are all observed much less frequently in infants with pneumonia than in older individuals. If present, they may be caused by noninflammatory processes, such as congestive heart failure, condensation from humidified gas administered during mechanical ventilation, or endotracheal tube displacement. Although alternative explanations are possible, these findings should prompt careful consideration of pneumonia in the differential diagnosis.

Other examination findings suggestive of pneumonia include asymmetry of breath sounds in infants, such as focal wheezing or decreased breath sounds in one lung field, and asymmetry of chest excursions, which suggest air leak or emphysematous changes secondary to partial airway obstruction. Similarly, certain more diffuse lung infections (eg, viral infections) may result in generalized crackles or wheezing.

In lobar pneumonia, fibrinous inflammation may extend into the pleural space, causing a rub heard by auscultation. Pericardial effusion in patients with lower lobe pneumonia due to H influenzae may also cause a rub. Other signs and/or findings in lobar pneumonia include abdominal pain or an ileus accompanied by emesis in patients with lower lobe pneumonia and nuchal rigidity in patients with right upper lobe pneumonia.

Percussion may reveal important information. Occasionally, a child presents with a high fever and cough but without ausculatory findings suggestive of pneumonia. In such cases, percussion may help to identify an area of consolidation.

Systemic and localized findings

Systemic findings in newborns with pneumonia may provide clues to the etiology. Rash or jaundice at birth may indicate congenital infection. Nonspecific findings such as tachycardia, glucose intolerance, abdominal distention, hypoperfusion, and oliguria are very common is moderately to severely ill newborns, and are not specific for a lung focus of infection. Localized findings include conjunctivitis (consider C trachomatis), vesicles or other focal skin lesions (consider HSV), and unusual nasal secretions (consider congenital syphilis).

Adenopathy in older children suggests long-standing infection and should suggest a more chronic cause such as TB or a dimorphic fungal infection (eg, histoplasmosis, blastomycosis). Hepatomegaly from infection may result from the presence of some chronic causative agents, cardiac impairment, or increased intravascular volume. Apparent hepatomegaly may result if therapeutic airway pressures allow generous lung inflation and downward displacement of a healthy liver.

Other considerations

Infants infected with organisms in utero or via the maternal genital tract commonly present within the first few hours after birth, but if infection is acquired during the delivery, the presentation may be delayed. The usual presenting symptoms include tachypnea, hypoxemia, and signs of respiratory distress. Auscultation may reveal diffuse fine crackles.

Early onset group B streptococci infection usually presents via ascending perinatal infection as sepsis or pneumonia within the first 24 hours of life. C. trachomatis pneumonia should be considered in infants aged 2–4 weeks and is often associated with conjunctivitis. Infants infected with C. pneumoniae, U. urealyticum, Mycoplasma hominis, CMV, and P. carinii present between age 4 and 11 weeks with an afebrile pneumonia characterized by a staccato cough, tachypnea, and, occasionally, hypoxia.

Infants or toddlers with bacterial pneumonia may present with lethargy, irritability, acidosis, hypotonia, or hypoxia that is out of proportion to ausculatory findings; school-aged children and adolescents are often febrile and appear ill. Mycoplasma infections are indolent, with gradual onset of malaise, low-grade fever, headache, and cough. C pneumoniae is also fairly common in children aged 5 years and presents in a similar fashion.

Pneumonia caused by B. pertussis occurs predominantly in infants who have not completed their vaccinations or in children who did not receive vaccinations. Their clinical presentation includes coryza, malaise, fever, paroxysms of cough occasionally accompanied by emesis, apnea, poor feeding, and cyanosis. Older adolescents infected with pertussis present with a paroxysmal cough, which persists for more than 3 weeks and may last up to 3 months, unlike the whooping cough of younger children. Chest radiographs in this group of patients are almost always normal, despite the intensity of the cough illness.

Although infection with H. capsulatum is usually asymptomatic in older children and adolescents, infants and young children are at risk for symptomatic infection, which may cause respiratory distress and hypoxemia.

Pneumonia is the most common cause of acute chest syndrome, which occurs in 15–43% of patients with sickle cell disease. This syndrome is characterized by fever, chest pain, dyspnea, cough, tachypnea, crackles.

Patients With Recurrent Pneumonias

Occasionally, a patient has pneumonia that continues to manifest clinically (persistent or unresponsive pneumonia), radiographically (eg, 8 wk after antibiotic treatment), or both despite adequate medical management. Studies have documented that the usual pathogens (eg, pneumococcus, non-typeable H. influenza, Moraxella catarrhalis) are causative agents.

Other patients may present with a history of recurrent pneumonias, defined as more than 1 episode per year or more than 3 episodes in a lifetime and again the organisms responsible are the common pathogens.

These patients merit special mention because they require a more extensive workup by a specialist. One useful way to categorize these patients is based on radiographic findings with and without symptoms. This method places these children in 1 of 3 categories (see the Table 1 below) that help to narrow the differential diagnoses.

Table 1

Categorizing Patients Based on Symptoms, Which Assists in Differential Diagnosis of Those With Recurrent Pneumonias

Category	Laboratory and Imaging Findings	Clinical Findings	Differential Diagnosis
1	Persistent or recurrent radiologic findings	Persistent or recurrent fever and symptoms	Cystic fibrosis, immunodeficiencies, obstruction (intrinsic [eg, foreign body] or extrinsic [eg, compressing nodes or tumor]), pulmonary sequestration, bronchial stenosis, or bronchiectasis
2	Persistent radiologic findings	No clinical findings	Anatomic abnormality (eg, sequestration, fibrosis, pleural lesion)
3	Recurrent pulmonary infiltrates with interval radiologic clearing	No clinical findings	Asthma and atelectasis that has been misdiagnosed as a bacterial pneumonia; aspiration syndrome, hypersensitivity pneumonitis, idiopathic pulmonary hemosiderosis, or a mild immunodeficiency disorder

Approach Considerations
- Diagnostic tests for pneumonia may include the following:
- Pulse oximetry
- Complete blood cell (CBC) count
- Sputum and blood cultures
- Serology
- Chest radiography
- Ultrasonography

New data show that point-of-care ultrasonography accurately diagnoses most cases of pneumonia in children and young adults. In a study of 200 ba-

bies, children, and young adults (≤21 years), ultrasonography had an overall sensitivity of 86 % and a specificity of 89 % for diagnosing pneumonia. Ultrasonography may eventually come to replace x-rays for diagnosis.

Identifying the causative infectious agent is the most valuable step in managing a complicated case of pneumonia. Unfortunately, an etiologic agent can be difficult to identify as various organisms cause pneumonia. Bacterial (including mycoplasmal, chlamydial, and acid fast), viral, and fungal infections are relatively common and have similar presentations, complicating clinical diagnosis. Furthermore, basic laboratory testing and radiologic testing are often not helpful in determining the etiology of pneumonia, and the treatments widely vary.

In patients with complicated pneumonia who have not had a treatment response or who require hospital admission, several diagnostic studies aimed at identifying the infectious culprit are warranted, including cultures, serology, a CBC count with the differential, and acute-phase reactant levels (erythrocyte sedimentation rate, C-reactive protein).

Numerous factors may interfere with the ability to grow a likely pathogen in the microbiology laboratory, including (but not limited to) the following: pretreatment with antibiotics that limit in vitro but not in vivo growth, sputum contaminants that overgrow the pathogen, and pathogens that do not replicate in currently available culture systems. Techniques that may help overcome some of these limitations include antigen detection, nucleic acid probes, polymerase chain reaction (PCR)-based assays, or serologic tests.

Although once widely used, tests such as latex agglutination for detection of group B streptococcal antigen in urine, serum, or other fluids have fallen into disfavor because of poor predictive value; however, new generations of nonculture-based technologies continue to undergo development and may be more accurate and widely available in the future.

Complete Blood Cell Count.

Testing should include a CBC count with differential and evaluation of acute-phase reactants (ESR, CRP, or both) and sedimentation rate. The total white blood cell (WBC) count and differential may aid in determining if an infection is bacterial or viral, and, together with clinical symptoms, chest radiography, and ESR can be useful in monitoring the course of pneumonia. In cases of pneumococcal pneumonia, the WBC count is often elevated.

Before widespread pneumococcal immunization, Bachur et al observed that approximately 25% of febrile children with a WBC count of more than 20,000/µL, but without lower respiratory tract findings on examination, had radiographic pneumonia (termed occult pneumonia). Although blood testing was obtained less frequently in the post-Prevnar era, recent studies by the same group demonstrated that leukocytosis was still associated with occult pneumonia.

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Sputum Gram Stain and Culture

Sputum is rarely produced in children younger than 10 years, and samples are always contaminated by oral flora. In the cooperative older child with a productive cough, a sputum Gram stain may be obtained (see the image 1 below); however, very few children are able to cooperate with such a test. An adequate sputum culture should contain more than 25 PMN cells per field and fewer than 10 squamous cells per field.
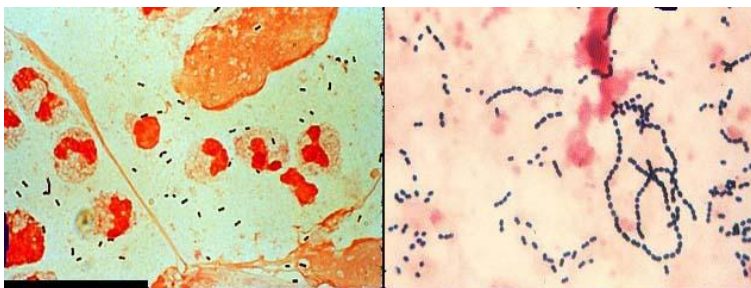

Image 1. (Left) Gram stain demonstrating gram-positive cocci in pairs and chains and (right) culture positive for Streptococcus pneumoniae.

In situations in which a microbiologic diagnosis is essential, endotracheal cultures and/or bronchoalveolar lavage culture can be sent for the isolation of offending pathogens. This is most important in patients with enigmatic and/or severe pneumonia, and it should be considered a priority in patients with compromised immune systems. Routine cultures for respiratory pathogens should be requested, along with special stains for PCP and special stains and cultures for Legionella, fungi, and acid-fast organisms. Viral cultures are also routinely requested.

Blood Culture

Although blood cultures are technically easy to obtain and relatively non-invasive and nontraumatic, the results are rarely positive in the presence of pneumonia and even less so in cases of pretreated pneumonia. In a study of 168 patients with known pneumonia, Wubbel et al found only sterile blood cultures.

In general, blood culture results are positive in less than 5% of patients with pneumococcal pneumonia. The percentage is even less in patients with Staphylococcus infection. However, a blood culture is still recommended in complicated cases of pneumonia. It may be the only way to identify the pathogen and its antimicrobial susceptibility patterns.

In neonates, blood culture with at least 1 mL of blood from an appropriately cleaned and prepared peripheral venous or arterial site is essential, because many neonatal pneumonias are hematogenous in origin and others serve as a focus for secondary seeding of the bloodstream. Older patients should have

larger-volume blood culture samples obtained based on their age and the ease with which blood can be obtained. Blood culture samples obtained through freshly placed indwelling vascular catheters may be helpful, but they generally are discouraged because of the possibility of contamination with skin flora. Multiple cultures of blood from different sites and/or those drawn at different times may increase the culture yield.

Serology

Because of the relatively low yield of cultures, more efforts are under way to develop quick and accurate serologic tests for common lung pathogens, such as M pneumoniae, Chlamydophila species, and Legionella.

In a Finnish study, of 278 patients diagnosed with community-acquired pneumonia, a total of 24 (9%) confirmed diagnoses of Mycoplasma infection were made, all of which had positive results with IgM-capture test with convalescent-phase serum. Acute and convalescent serum samples were collected and tested using enzyme immunoassay for M pneumoniae IgM and IgG antibodies. Nasopharyngeal aspirates were tested using PCR and cultured with a Pneumofast kit.

Positive results were confirmed with Southern hybridization of PCR products and an IgM test with solid-phase antigen. Using an IgM-capture test in acute-phase serum, 79% of results were positive, 79% were positive using IgG serology, 50% positive using PCR, and 47% positive using culture.

The authors of this study concluded that IgM serologic studies for Mycoplasma infection were not only quick but also sensitive and were the most valuable tools for diagnosis of M pneumoniae infection in any age group. IgM serology is much more sensitive than cold agglutinin assessments, which are more commonly used to aid in the diagnosis of Mycoplasma infection and which demonstrate positive results in only 50% of cases.

Chlamydophila and Legionella species can be grown by experienced microbiologists; however, serologic testing is also routinely performed to support or establish the diagnosis. Similarly, lung infections caused by dimorphic fungi (eg, histoplasmosis) are more commonly diagnosed serologically.

Inflammatory Markers

The use of markers of inflammation to support a diagnosis of suspected infection, including pneumonia, remains controversial because results are nonspecific. Various indices derived from differential leukocyte counts have been used most widely for this purpose, although noninfectious causes of such abnormal results are numerous. Many reports have been published regarding infants with proven infection who initially had neutrophil indices within reference ranges.

Quantitative measurements of CRP, procalcitonin, cytokines (eg, interleukin [IL]-6), inter-alpha inhibitor proteins (IaIp), and batteries of acute-phase reactants have been touted to be more specific but are limited by suboptimal positive predictive value.

Lag time from infection to abnormal values are noted for inflammatory markers; thus, serial measurements are often necessary and do offer a high negative predictive value. However, although these tests may be useful in assessing the resolution of an inflammatory process, including infection, they are not sufficiently precise to establish a diagnosis without additional supporting information. Decisions about antimicrobial therapy should not be based on inflammatory markers alone.

Polymerase Chain Reaction

Relatively rapid testing (1-2 d) of viral infections through multiplex PCR is available in many hospitals. PCR is more sensitive than antigen assays, and for some viruses (eg, hMPV), this study may be the only test available. PCR also shows promise of being useful in diagnosing streptococcal pneumonia. In one series of 63 children with empyema, a pathogen could be detected in 53 (84%) by PCR compared to only 24 (35%) by culture of blood and/or pleural fluid. The most frequently detected pathogen was pneumococcus, found in 45 patients.

PCR is noninvasive, an advantage over lung aspirate or bronchoalveolar lavage (BAL) cultures. Similarly, C pneumoniae infection is diagnosed more readily with PCR than with culture; however, positive test results must correlate with acute symptoms to have any validity, because 2–5% of the population may be asymptomatically infected with C pneumoniae.

PCR testing for TB is also widely available and is helpful in early identification of TB from other mycobacteria in acid-fast cultures.

Direct Antigen Detection

Although antiviral therapies are not often used, performing a nasal wash or nasopharyngeal swab for RSV and influenza enzyme-linked immunoassay (ELISA) and viral culture can help to establish a rapid diagnosis, which may be helpful in excluding other causes. Viral cultures can be obtained in 1–2 days using newer cell culture techniques and may permit discontinuation of unnecessary antibiotics. In addition, correct diagnosis allows for appropriate placement of patients in the hospital. For example, if necessary, 2 infants with RSV infection may share a room, whereas such patients would normally need isolation and may unnecessarily tie up a bed.

Chest Radiography

Chest radiography is the primary imaging study used to confirm the diagnosis of pneumonia. Well-centered, appropriately penetrated, anteroposterior chest radiography is essential (see the image 2 below), although other views may be warranted to clarify anatomic relationships and air-fluid levels.
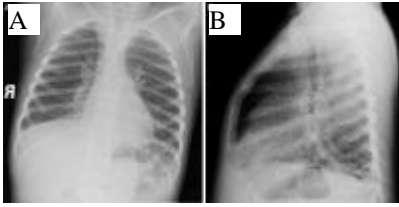
Image 2. (A) Anteroposterior radiograph from a child with presumptive viral pneumonia. (B) Lateral radiograph of the same child with presumptive viral pneumonia

When considering pneumonia, devote particular attention to the following:
- Costophrenic angles
- Pleural spaces and surfaces
- Diaphragmatic margins
- Cardiothymic silhouette
- Pulmonary vasculature
- Right major fissure
- Air bronchograms overlying the cardiac shadow
- Lung expansion
- Patterns of aeration

Be aware that any image reflects conditions only at the instant at which the study was performed. Because lung diseases, including pneumonia, are dynamic, initially suggestive images may require reassessment based on the subsequent clinical course and findings in later studies.

Radiographic patterns of pneumonia

Numerous radiographic patterns are consistent with pneumonia and a multitude of other pathologic processes. A synthesis of all available information and careful consideration of the differential diagnosis is essential to establishing the diagnosis, although empiric antimicrobial treatment usually cannot be deferred because of an inability to prospectively exclude the diagnosis.

Generalized hyperinflation with patchy infiltrates suggests partial airway obstruction from particulate or inflammatory debris, although the contribution of positive airway pressure from respiratory support must be considered. Pneumatoceles (especially with air-fluid interfaces) and prominent pleural fluid collections also support the presence of infectious processes.

Chest radiographs of infants infected with organisms in utero or via the maternal genital tract may demonstrate a ground-glass appearance and air bronchograms. Diffuse, relatively homogeneous infiltrates that resemble the ground-glass pattern of respiratory distress syndrome are suggestive of a hematogenous process, although aspiration of infected fluid with subsequent seeding of the bloodstream cannot be excluded.

Patchy, irregular densities that obscure normal margins are suggestive of antepartum or intrapartum aspiration, especially if such opacities are distant from the hilus. Patchy, irregular densities in dependent areas that are more prominent on the right side are more consistent with postnatal aspiration.

Except for patients with sickle cell disease, a significant pleural effusion usually indicates a bacterial etiology. Although these patterns are typical, the etiology cannot be reliably identified based solely on chest radiography findings. Other typical findings of bacterial pneumonia include a lobar consolidation with air bronchograms occasionally accompanied by a pleural effusion. Lobar consolidation and pleural effusion are seen in the images 3, 4 below.

Image 3. Right lower lobe consolidation in a patient with bacterial pneumonia

Image 4. Radiograph from a patient with bacterial pneumonia (same patient as in the preceding image) a few days later. This radiograph reveals progression of pneumonia into the right middle lobe and the development of a large parapneumonic pleural effusion

Single or multiple prominent air bronchograms 2 or more generations beyond the mainstem bronchi reflect dense pulmonary parenchyma (possibly an infiltrate) highlighting the air-filled conducting airways. A well-defined, dense lobar infiltrate with bulging margins is unusual. Lateral or oblique projections may help to better define structures whose location and significance are unclear.

Although unilateral and/or lobar infiltrates are often seen in bacterial pneumonia (see the image 5 below), several studies have found that the pattern of radiologic features cannot accurately distinguish a bacterial etiology from a viral etiology.
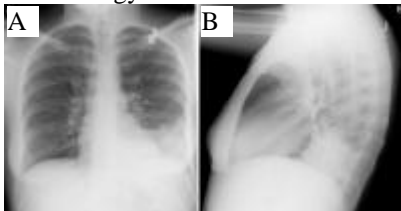

Image 5. (A) Anteroposterior radiograph from a child with a left lower lobe infiltrate. (B) Lateral radiograph of the same child with a left lower lobe infiltrate

In contrast, a large Finnish series concluded that an alveolar (equivalent to a lobar) infiltrate is an insensitive, but reasonably specific, indication of bacterial infection. Thus, a lobar infiltrate can be seen with viral infections, foreign body aspirations, and mucous plugging that results in atelectasis. Furthermore, pleural effusions, although usually parapneumonic (80%), may be observed in numerous disease processes.

At either extreme (from typical bronchiolitis with scattered infiltrates to dense lobar pneumonia with a large pleural effusion), the level of diagnostic certainty provided by radiologic findings increases.

Pneumatoceles and abscesses are less commonly found but may indicate a Staphylococcus aureus, gram-negative, or complicated pneumococcal pneumonia. Round pneumonia on chest radiographs should raise suspicion that the disease has a bacterial etiology, and particularly, that Streptococcus pneumoniae or S aureus is the causative agent. Round pneumonia is shown in the radiograph below (image 6).

Image 6. The radiographic appearance of Mycoplasma infection varies. Early in the infection, the pattern tends to be reticular and interstitial; as the infection progresses, patchy and segmental areas of consolidation are noted, along with hilar adenopathy and pleural effusions

For M pneumoniae, 3 radiographic patterns may be observed: peribronchial and perivascular interstitial infiltrates, patchy consolidations, and homogeneous acinar consolidations like ground glass. The lower fields of the lungs are most often affected, and enlargement of the hilar glands is common.

Although no radiographic findings are specific for Chlamydophilapneumoniae (formerly Chlamydia pneumoniae) , a combination of the clinical and radiographic findings strongly suggests the diagnosis before laboratory diagnosis is available.

In a study of 125 cases of Chlamydophila pneumonia, Radkowski et al demonstrated that most chest radiographs showed bilateral hyperexpansion and diffuse infiltrates with various radiographic patterns, including interstitial, reticular nodular, atelectasis, coalescence, and bronchopneumonia. Pleural effusion and lobar consolidation were not seen.

Chest radiography findings in children with tuberculous pneumonia may include hilar or mediastinal lymphadenopathy, atelectasis, or consolidation of a segment or lobe (usually right upper lobe), pleural effusion, cavitary lesions (in adolescents and adults only), or miliary disease.

In viral pneumonias, 4 common radiographic findings are generally detected: parahilar peribronchial infiltrates, hyperexpansion, segmental or lobar atelectasis, and hilar adenopathy.

Bronchoscopy

Flexible fiberoptic bronchoscopy is occasionally useful to obtain lower airway secretions for culture or cytology. This procedure is most useful in immunocompromised patients who are believed to be infected with unusual organisms (Pneumocystis, other fungi) or in patients who are severely ill.

The technique of direct rigid bronchoscopy may be used in larger infants; fiberoptic technique is occasionally possible in smaller infants or infants in whom the site is not easily reached using the rigid technique. Both this technique and protected brush tracheal aspirate sampling may not be well tolerated in infants with significant lung disease and poor gas exchange who are very dependent on continuous positive pressure ventilation.

Careful consideration of the diagnostic possibilities is necessary to send the samples for the appropriate tests. Contamination of the bronchoscopic aspirate with upper airway secretions is common; quantitative cultures can help distinguish contamination from infection. Culture and Gram stain of an endotracheal aspirate obtained by aseptic technique as soon as possible after intubation may be useful.

Under typical circumstances, airway commensals take as long as 8 hours to migrate down the trachea. At least one study demonstrated that culture of endotracheal aspirates obtained within 8 hours of birth correlates very well with blood culture results and probably reflects aspirated infected fluid. The longer the tube has been in place, the greater the likelihood that recovered organisms represent colonizing organisms rather than invasive pathogens; nonetheless, recovery of a single recognized pathogen in large quantities may be helpful in the selection of antibiotic therapy, especially if culture results from normally sterile sites are negative.

The absence of significant inflammatory cells in an endotracheal aspirate or other respiratory specimen suggests that organisms recovered from that site are unlikely to be truly invasive (unless the infant is markedly leukopenic). Thus, the organism represents colonization of the respiratory tract and not infection.

Bronchoscopic Alveolar Lavage

Quantitative culture techniques, such as bronchoscopic alveolar lavage have been assessed in non-neonatal populations and reportedly offer a specificity of more than 80%, depending on the threshold selected (values from >100–100,000 colony-forming units [CFU]/mL have been used).

Protected Brush Tracheal Aspirate Sampling

Sites distant from the larger bronchi often cannot be sampled. Specimens may have an increased risk of contamination with oral or airway commensals compared with bronchoscopic sampling but are thought to be more accurate than a conventional endotracheal aspirate.

Nondirected specimens have been obtained through endotracheal tubes 3 mm or greater in internal diameter and intuitively appear to offer decreased probability of contamination. Data from neonates are sparse. Unlike bronchoscopically obtained specimens, ensuring sampling from a particular involved site is more difficult.

Lung Aspiration

Lung aspiration is underused and is a significantly more efficient method of obtaining a culture. If a prominent infiltrate can be adequately localized in multiple planes, direct aspiration of the infected lung may be performed for culture or biopsy. Lung CT scanning may facilitate such localization.

Lung aspiration is associated with a greater risk of postprocedural air leak and usually requires a larger-bore needle than is used to obtain pleural fluid. Because the risk associated with this procedure is high, lung aspiration is usually reserved for patients who are ill enough to require hospitalization, have not improved with previous empiric treatment, or are immunocompromised and an exact etiology is needed. A lung aspirate should not be performed in patients who are on ventilators, who have a bleeding diathesis, or who are suspected of having an infection with Pneumocystis.

With advances in surgical techniques and increased experience, many clinicians prefer to seek open surgical biopsy or thoracoscopic sampling in such circumstances, especially because success and specimen size are greater and the ability to deal directly with any complication is enhanced.

A study demonstrated positive blood cultures implicated an organism in 18% of patients compared with 52% with positive lung aspirates. The investigators compared the incidence of positive culture results obtained with blood culture with positive culture results obtained with lung aspiration in 100 children aged 3–58 months with pneumonia. The organisms obtained in the blood and lung aspirate differed in 4 of 8 children in whom both culture results were positive, suggesting that a blood culture may not always accurately reveal the lung pathogen.

Other studies have demonstrated lung aspirate results to be positive in 50–60% of patients with known pneumonia. In these studies, 1.5-9 % of patients had a pneumothorax and 0.7–3% had transient small hemoptysis complicating their lung aspirations.

Lung Puncture

Although used much less frequently than in previous decades, diagnostic lung puncture may still be useful in circumstances in which pleural and sub-pleural lung surfaces are visibly involved and can be well localized. Risk-benefit ratio merits careful consideration given the risk of such complications as pneumothorax, bronchopleural fistula, and hemothorax, as well as sampling a nondiagnostic site. This is a high-risk procedure and should not be considered a routine procedure in the diagnosis or treatment of pneumonia in the neonate.

Thoracentesis

This procedure is performed for diagnostic and therapeutic purposes in children with pleural effusions (eg, when pleural fluid is impinging on lung or cardiac function) (see the image 7 below).
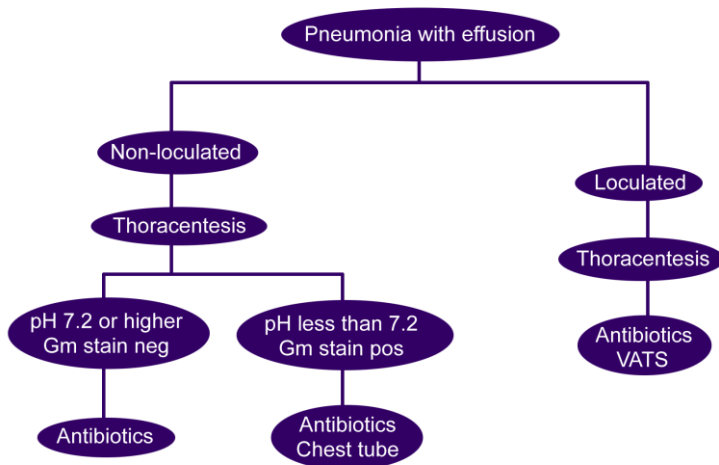

Image 7. A breakdown of test results and recommended treatment
for pneumonia with effusion.
Gm=Gram; neg=negative; pos=positive; VATS=video-assisted thoracic surgery.

In the presence of radiographically visible fluid, careful positioning of the infant and thoracentesis after sterile preparation of the sampling site may yield diagnostic findings on Gram stain, direct microscopy, and/or culture. If the Gram stain or the culture result from the pleural fluid is positive or the WBC count is higher than 1000 cells/mL, by definition, the patient has an empyema, which may require drainage for complete resolution. Ultrasonography may reveal smaller fluid pockets and facilitate safer sampling under direct visualization. Although data from neonates are insufficient to draw conclusions,

studies in older populations suggest a very high correlation with culture of lung tissue and/or blood. Other therapeutic decisions can be made based on the properties of the effusion.

The risk of pneumothorax or laceration of intercostal vessels is real but can be minimized by the use of proper technique, including use of the Z-technique (stretching the skin down over the entry site, so that release after the procedure will permit the return of tissues to their usual location with occlusion of the path of the needle), entry over the superior rib margin (to minimize inadvertent puncture of intercostal vessels) at a dependent site where fluid is most likely to collect, continuous aspiration once the skin is penetrated, and no further advancement once fluid is obtained.

Histology

No specific histologic findings are reported in most patients with pneumonias beyond evidence of inflammation and cellular infiltration and exudation into alveolar spaces and the interstitium. Sputum, lavage, or biopsy material may yield diagnostic findings.

Tissue samples of lung tissue in human infants have typically been obtained from an unrepresentative population. The sample population usually includes only infants with severe pulmonary disease that results in death or threatens to do so or infants who die of other causes and have coincidental sampling of the lung. Consequently, direct observations regarding histologic changes in mild or moderate pneumonia are sparse and are often supplemented by extrapolation from animal disease models, human adults with similar diseases, or more severe cases in human infants that resulted in death or biopsy. Despite these limitations, certain observations in congenital pneumonia recur, whether or not a specific pathogen is implicated.

Macroscopically, the lung may have diffuse, multifocal, or very localized involvement with visibly increased density and decreased aeration. Frankly hemorrhagic areas and petechiae on pleural and intraparenchymal surfaces are common. Airway and intraparenchymal secretions may range from thin and watery to serosanguineous to frankly purulent, and they are frequently accompanied by small to moderate pleural effusions that display variable concentrations of inflammatory cells, protein, and glucose.

Frank empyema and abscesses are unusual in newborn infants. Particulate meconium or vernix may be visible, especially in the more proximal airways, following aspiration episodes. Superimposed changes, such as air leak, emphysema, and sloughed airway mucosa, may be seen as a consequence of volutrauma, pressure-related injury, oxygen toxicity, and other processes that reflect the vigorous respiratory support often provided to these infants in an attempt to manage derangements of gas exchange caused by the underlying illness.

With conventional microscopy, inflammatory cells are particularly prominent in the alveoli and airways. Mononuclear cells (macrophages, natural killer cells,

small lymphocytes) are usually noted early, and granulocytes (eosinophils, neutrophils) typically become more prominent later. Microorganisms of variable viability or particulate debris may be observed within these cells. If systemic neutropenia is present, the number of inflammatory cells may be reduced. Alveoli may be atelectatic from surfactant destruction or dysfunction, partially expanded with proteinaceous debris (often resembling hyaline membranes), or hyperexpanded secondary to partial airway obstruction from inflammatory debris or meconium.

Hemorrhage in the alveoli and in distal airways is frequent. Vascular congestion is common; vasculitis and perivascular hemorrhage are seen less frequently. Inflammatory changes in interstitial tissues are less common in newborns than in older individuals.

Microscopic examination of tissue following immunohistochemical staining or other molecular biologic techniques can identify the herpes virus and an increasing number of other organisms. In patients with TB, acid-fast bacilli are present and can be detected using the Ziehl-Neelsen stain or can be grown on the Lowenstein-Jensen medium. Caseating granulomas are highly suspicious, even in the absence of detectable organisms. Findings of foamy alveolar casts are practically diagnostic for P jirovecii pneumonia, and the cup-shaped organisms are often found using Gomori methenamine silver staining or direct immunofluorescence.

Fungal elements may be seen using Gomori methenamine silver staining or periodic acid-Schiff (PAS) staining. Aspergillus and Zygomycetes species may be seen using simple hematoxylin and eosin (H&E) staining. The specific morphology of the organisms may be diagnostic, but, occasionally, culture or immunostaining is required.

Complications

Severe respiratory compromise may require intubation and transfer to a suitable intensive care unit (ICU) for more intensive monitoring and therapy. Indications for transfer include refractory hypoxia, decompensated respiratory distress (eg, lessening tachypnea due to fatigue, hypercapnia), and systemic complications such as sepsis.

Transfer may need to be initiated at a lower threshold for infants or young children, as decompensation may be rapid. Transfer of very sick infants or young children to a pediatric ICU is best done with a specialist pediatric transfer team, even if that entails a slightly longer wait, compared with conventional medical transport or even air transport.

Severe coughing, especially in the context of necrotizing pneumonias or bullae formation, may lead to spontaneous pneumothoraces. These may or may not require treatment depending on the size of the pneumothorax and whether it is under tension and compromising ventilation and cardiac output.

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Other complications include the following:
- Pleural effusion
- Empyema
- Pneumatocele
- Lung abscess
- Necrotizing pneumonia
- Systemic infection with metastatic foci
- Persistent newborn pulmonary hypertension
- Air leak syndrome, including pneumothorax, pneumomediastinum, pneumopericardium, and pulmonary interstitial emphysema
- Airway injury
- Obstructive airway secretions
- Hypoperfusion
- Chronic lung disease
- Hypoxic-ischemic and cytokine-mediated end-organ injury
- Sepsis

Approach Considerations

Treatment decisions in children with pneumonia are dictated based on the likely etiology of the infectious organism and the age and clinical status of the patient. Antibiotic administration must be targeted to the likely organism, bearing in mind the age of the patient, the history of exposure, the possibility of resistance (which may vary, depending on local resistance patterns), and other pertinent history.

After initiating therapy, the most important tasks are resolving the symptoms and clearing the infiltrate. With successful therapy, symptoms resolve much sooner that the infiltrate. In a study of adults with pneumococcal pneumonia, the infiltrate did not completely resolve in all patients until 8 weeks after therapy (although it was sooner in most patients). If therapy fails to elicit a response, the whole treatment approach must be reconsidered.

The Pediatric Infectious Diseases Society and the Infectious Diseases Society of America created evidence-based guidelines for the management of community-acquired pneumonia (CAP) in infants and children older than 3 months. These guidelines discuss site-of-care management, diagnosis, antimicrobial therapy, adjunctive surgical therapy, and prevention. While these guidelines do not represent the only approach to diagnosis and therapy, these recommendations may assist in decreasing morbidity and mortality rates in children with CAP.

Hospitalization

Pulse oximetry should be performed during the prehospital evaluation of children with suspected pneumonia, and supplemental oxygen should be administered, if necessary; however, many school-aged children do not require

hospitalization and respond well to oral antibiotics. Usually, these patients are not toxic or hypoxic enough to require supplemental oxygen. Unless they are vomiting, they do not require intravenous fluids or antibiotics. A parapneumonic effusion that requires drainage usually dictates a hospital admission.

Children younger than 5 years are hospitalized more often, but their clinical status, degree of hydration, degree of hypoxia, and need for intravenous therapy dictate this decision. Hospitalization should be considered for infants who are younger than 2 months or premature because of the risk of apnea in this age group.

Children who are toxic-appearing may require resuscitation and respiratory support. Treatment of critically ill children (those requiring ventilation) should include timely administration of appropriate antibiotics. Delays of only a few hours in one retrospective study were associated with significantly longer durations of ventilation, ICU stay, and total hospitalization. Chest radiography should be performed to identify the presence of an effusion/empyema. Drainage of a restrictive or infected effusion or empyema may enhance clearance of the infection and improves lung mechanics. Antibiotic therapy should include vancomycin (particularly in areas where penicillin-resistant streptococci have been identified) and a second- or third-generation cephalosporin.

Hemodynamic Support

RBCs should be administered to ensure a hemoglobin concentration of 13–16 g/dL in the acutely ill infant to ensure optimal oxygen delivery to the tissues. Delivery of adequate amounts of glucose and maintenance of thermoregulation, electrolyte balance, and other elements of neonatal supportive care are also essential aspects of clinical care.

Respiratory Management

Initial priorities in children with pneumonia include the identification and treatment of respiratory distress, hypoxemia, and hypercarbia. Grunting, flaring, severe tachypnea, and retractions should prompt immediate respiratory support. Children who are in severe respiratory distress should undergo tracheal intubation if they are unable to maintain oxygenation or have decreasing levels of consciousness.

Increased respiratory support requirements such as increased inhaled oxygen concentration, positive pressure ventilation, or CPAP are commonly required before recovery begins. Bi-level positive airway pressure (BiPAP) may also be used to help support respiratory effort as a stand-alone intervention or as a bridge to intubation. Criteria for institution and weaning of supplemental oxygen and mechanical support are similar to those for other neonatal respiratory diseases. Extra humidification of inspired air (eg, room humidifiers) is also not useful, although supplemental oxygen is frequently humidified for patient comfort.

Adequate gas exchange depends not only on alveolar ventilation, but also on the perfusion and gas transport capacity of the alveolar perfusate (ie, blood). Preservation of pulmonary and systemic perfusion is essential, using volume expanders, inotropes, afterload reduction, blood products, and other interventions (eg, inhaled nitric oxide) as needed. Excellent lung mechanics do little good if perfusion is not simultaneously adequate.

Be aware that lung disease is often structurally heterogeneous, with subpopulations of normally inflated, hyperinflated, atelectatic, obstructed, fluid-filled, and variably perfused alveoli that may require multiple adjustments of ventilatory pressures, flows, rates, times, and modalities.

Pharmacologic Therapy

The choice of an initial, empiric agent is selected according to the susceptibility and resistance patterns of the likely pathogens and experience at the institution, and the selection is tempered by knowledge of delivery of drugs to the suspected infected sites within the lung.

Antibiotic agents

Drug therapy for pneumonia is tailored to the situation. Because the etiologic agents vary, drug choice is affected by the patient's age, exposure history, likelihood of resistance (eg, pneumococcus), and clinical presentation. Beta-lactam antibiotics (eg, amoxicillin, cefuroxime, cefdinir) are preferred for outpatient management. Macrolide antibiotics (eg, azithromycin, clarithromycin) are useful in most school-aged children to cover the atypical organisms and pneumococcus. Local variations in resistance require different approaches to therapy, including cases caused by pneumococcus. Any child with a positive purified protein derivative (PPD) test result and infiltrate on chest radiographs requires additional testing for tuberculosis and polymicrobial treatment.

Agents typically used initially in the treatment of newborns and young infants with pneumonia include a combination of ampicillin and either gentamicin or cefotaxime. The selection of cefotaxime or gentamicin must be based on experience and considerations at each center and in each patient. Combination therapy provides reasonable antimicrobial efficacy against the pathogens that typically cause serious infection in the first days of life. Other agents or combinations may be appropriate for initial empiric therapy if justified by the range of pathogens and susceptibilities encountered in a particular clinical setting.

Isolation of a specific pathogen from a normally sterile site in the infant allows revision of therapy to the drug that is least toxic, has the narrowest antimicrobial spectrum, and is most effective. Dosing intervals for ampicillin, cefotaxime, gentamicin, and other antimicrobial agents typically require readjustment in the face of renal dysfunction or once the infant is older than 7 days (if the infant still requires antimicrobial therapy).

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The vast majority of children diagnosed with pneumonia in the outpatient setting are treated with oral antibiotics.

High-dose amoxicillin is used as a first-line agent for children with uncomplicated community-acquired pneumonia, which provides coverage for S pneumoniae. Second- or third-generation cephalosporins and macrolide antibiotics such as azithromycin are acceptable alternatives but should not be used as first-line agents because of lower systemic absorption of the cephalosporins and pneumococcal resistance to macrolides. Treatment guidelines are available from the Cincinnati Children's Hospital Medical Center and, more recently, from the Infectious Diseases Society of America (IDSA).

Macrolide antibiotics are useful in school-aged children, because they cover the most common bacteriologic and atypical agents (Mycoplasma, Chlamydophila, Legionella). However, increasing levels of resistance to macrolides among pneumococcal isolates should be considered (depending on local resistance rates). One study suggests that penicillin and macrolide resistance among S pneumoniae isolates has been increasing.

Hospitalized patients can be safely treated with narrow-spectrum agents such as ampicillin, and this is the mainstay of current guidelines for pediatric community-acquired pneumonia. Children who are toxic appearing should receive antibiotic therapy that includes vancomycin (particularly in areas where penicillin-resistant pneumococci and methicillin-resistant S aureus [MRSA] are prevalent) along with a second- or third-generation cephalosporin.

If gram-negative pneumonia is suspected and beta-lactam antibiotics are administered, some data suggest that continuous exposure to an antimicrobial concentration greater than the mean inhibitory concentration (MIC) for the organism may be more important than the amplitude of the peak concentration. Intramuscular treatment or intravenous therapy with the same total daily dose but a more frequent dosing interval may be advantageous if the infant's condition fails to respond to conventional dosing. Comparative data to confirm the superiority of this approach are lacking. Whether this approach offers any advantage with use of agents other than beta-lactams is unclear.

Studies in human adults have demonstrated that aminoglycosides reach the bronchial lumen marginally when administered parenterally, although alveolar delivery is satisfactory. Endotracheal treatment with aerosolized aminoglycosides has been reportedly effective for marginally susceptible organisms in bronchi, whereas cefotaxime appears to attain adequate bronchial concentrations via the parenteral route. Limited in vitro and animal data suggest that cefotaxime may retain more activity than aminoglycosides in sequestered foci, such as abscesses, although such foci are rare in congenital pneumonia, and adequate drainage may be more important than antimicrobial selection.

Recovery of a specific pathogen from a normally sterile site (eg, blood, urine, CSF) permits narrowing the spectrum of antimicrobial therapies and may thus reduce the selection of resistant organisms and costs of therapy. Repeated culture of the site after 24–48 hours is usually warranted to ensure sterilization and to assess the efficacy of therapy. Endotracheal aspirates are not considered to represent a normally sterile site, although they may yield a pathogen that is a true invasive culprit. Reculture of an endotracheal aspirate that identified the presumptive pathogen in a particular case may not be helpful because colonization may persist even if tissue invasion has been terminated.

Decreasing respiratory support requirements, clinical improvement, and resolution revealed on radiographs also support the efficacy of therapy. When appropriate, assess plasma antibiotic concentrations to ensure adequacy and reduce the potential for toxicity. Failure to recover an organism does not exclude an infectious etiology; continuation of empiric therapy may be advisable unless the clinical course or other data strongly suggests that a noninfectious cause is responsible for the presenting signs.

Continue to perform careful serial examinations for evidence of complications that may warrant a change in therapy or dosing regimen, surgical drainage, or other intervention.

Anti-inflammatory therapy

Evidence-supported options for targeted treatment of inflammation independent of antimicrobial therapy are severely limited. Considerable speculation suggests that current antimicrobial agents, directed at killing invasive organisms, may transiently worsen inflammatory cascades and associated host injury because dying organisms release proinflammatory structural and metabolic constituents into the surrounding microenvironment. This is not to imply that eradicating invasive microbes should not be a goal; however, other methods of eradication or methods of directly dealing with the pathologic inflammatory cascades await further definition. In pneumonia resulting from noninfectious causes, the quest for targeted, effective, and safe anti-inflammatory therapy may be of even greater importance.

A few small studies in adults suggest that glucocorticoid use might be beneficial in the treatment of serious (hospitalized) community-acquired pneumonia, although the study designs and sizes limit the ability to properly interpret this data. Until definitive studies are performed, steroids should not be routinely used for uncomplicated pneumonia.

Antiviral agents

Most infants with respiratory syncytial virus (RSV) pneumonia do not require antimicrobials. Serious infections with this organism usually occur in infants with underlying lung disease.

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Influenza A viruses, including 2 subtypes (H1N1) and (H3N2), and influenza B viruses currently circulate worldwide, but the prevalence of each can vary among communities and within a single community over the course of an influenza season. In the United States, 4 prescription antiviral medications (oseltamivir [Tamiflu], zanamivir, amantadine, rimantadine) are approved for treatment and chemoprophylaxis of influenza.

Influenza A pneumonia that is particularly severe or when it occurs in a high-risk patient may be treated with zanamivir or oseltamivir. The neuraminidase inhibitors have activity against influenza A and B viruses, whereas the adamantanes have activity against only influenza A viruses.

Check for resistance patterns for other antiviral agents indicated for treatment or chemoprophylaxis of influenza. Since January 2006, the neuraminidase inhibitors (oseltamivir, zanamivir) have been the only recommended influenza antiviral drugs because of widespread resistance to the adamantanes (amantadine, rimantadine) among influenza A (H3N2) virus strains.

In 2007–2008, a significant increase in the prevalence of oseltamivir resistance was reported among influenza A (H1N1) viruses worldwide. During the 2007–2008 influenza season, 10.9% of H1N1 viruses tested in the United States were resistant to oseltamivir.

These prompted the US Centers for Disease Control and Prevention (CDC) to issue revised interim recommendations for antiviral treatment and prophylaxis of influenza. Zanamivir (Relenza) is recommended as the initial choice for antiviral prophylaxis or treatment when influenza A infection or exposure is suspected.

A second-line alternative is a combination of oseltamivir plus rimantadine rather than oseltamivir alone. Local influenza surveillance data and laboratory testing can assist the physician regarding antiviral agent choice.

Complete recommendations are available from the CDC.

Herpes simplex virus pneumonia is treated with parenteral acyclovir.

CMV pneumonitis should be treated with intravenous ganciclovir or foscarnet.

Invasive fungal infections, such as those caused by Aspergillus or Zygomycetes species, are treated with amphotericin B or voriconazole.

Bronchodilators

Bronchodilators should not be routinely used. Bacterial lower respiratory tract infections rarely trigger asthma attacks, and the wheezing that is sometimes heard in patients with pneumonia is usually caused by airway inflammation, mucus plugging, or both and does not respond to bronchodilator. However, infants or children with reactive airway disease or asthma may react to a viral infection with bronchospasm, which responds to bronchodilators.

Nutritional Support

Attempts at enteral feeding often are withheld in favor of parenteral nutritional support until respiratory and hemodynamic status is sufficiently stable.

Prevention

Aside from avoiding infectious contacts (difficult for many families who use daycare facilities), vaccination is the primary mode of prevention. Since the introduction of the conjugated HIB vaccine, the rates of HIB pneumonia have significantly declined. However, the diagnosis should still be considered in unvaccinated persons, including those younger than 2 months, who have not received their first shot.

Conjugated and unconjugated polysaccharide vaccines for S pneumoniae have been developed for infants and children, respectively. The pneumococcal 7-valent conjugate vaccine (diphtheria CRM197 protein; Prevnar) that was introduced in 2000 contains epitopes to 7 different strains. Pneumococcal vaccine polyvalent (Pneumovax) covers 23 different strains. A new 13-valent conjugated vaccine (Prevnar 13) was approved in 2010 and replaces PCV7 for all doses. Children who have completed their vaccine schedule with PCV7 should get a booster dose with PCV13.

In a study to evaluate the effectiveness of heptavalent pneumococcal conjugate vaccine in prevention of pneumonia in children younger than 5 years, Black et al showed a 32.2% reduction in the first year of life and a 23.4% reduction between 1–2 years, but only a 9.1% reduction in children older than 2 years.

However, since the initiation of the heptavalent pneumococcal vaccine in 2000, researchers have found that nearly two thirds of invasive pneumococcal disease cases in young children have been caused by 6 serotypes not included in that vaccine. Those serotypes, along with the original 7, have been incorporated into pneumococcal vaccine valent-13 (Prevnar 13), which was approved in February 2010.

The 23-valent polysaccharide vaccine (PPVSV) is recommended for children 24 months or older who are at high risk of pneumococcal disease.

Influenza vaccine is recommended for children aged 6 months and older. The vaccine exists in 2 forms: inactivated vaccine (various products), administered as an intramuscular injection, and a cold-adapted attenuated vaccine (FluMist; MedImmune), administered as a nasal spray, which is currently licensed only for persons aged 2–49 years.

Although the influenza vaccine is especially recommended for children at high risk, such as those with BPD, cystic fibrosis, or asthma, the use of FluMist is cautioned in persons with known asthma because of reports of transient increases in wheezing episodes in the weeks after administration. However, in years when vaccine strains have been mismatched with the circulating influenza strains, FluMist has provided good protection (approximately 70%), even when the inactivated vaccine was entirely useless.

Clinical trials are ongoing to lower the age of administration of Fluzone (made by Aventis Pasteur), one of the inactivated intramuscular vaccines, to 2 months (currently approved for children 6 mo or older) to help protect this high-risk, but unvaccinated, population. The safety and efficacy of this approach remains unknown.

PCP prophylaxis with trimethoprim-sulfamethoxazole 3 times a week is widely used in immunocompromised children and has all but eradicated this organism in patients receiving prophylaxis.

The use of pneumococcal and H influenzae type B vaccines and penicillin prophylaxis in patients with sickle cell disease have helped reduce the incidence of bacterial infections in these children.

RSV prophylaxis consists of monthly intramuscular injections of palivizumab at a dose of 15 mg/kg (maximum volume 1 mL per injection; multiple injections may be required per dose). This strategy is currently recommended for high-risk infants only (ie, premature infants and newborns with congenital heart disease). Monthly injections during the RSV season approximately halve the rate of serious RSV disease that leads to hospitalization. This expensive therapy is generally restricted to infants at high risk, such as children younger than 2 years with chronic lung disease of prematurity, premature infants younger than 6 months (or with other risk factors), and children with significant congenital heart disease.

Malnutrition is a known risk factor for infections, but zinc deficiency in particular has been shown to increase the risk for childhood pneumonia. In areas of the world where zinc deficiency is common, supplementation may significantly reduce the incidence of childhood pneumonia.

Consultations

Consultation is not needed in the care of most children with pneumonia. However, children who have underlying diseases may benefit from consultation with the specialist involved in their long-term care. For example, most children with cystic fibrosis are monitored by a pulmonologist.

Consultation with a pediatric infectious disease specialist may be appropriate in the treatment of a child with persistent or recurrent pneumonia, and children with pleural effusions or empyema should be referred to a tertiary medical center, where thoracentesis can be performed. This procedure may be performed in an emergency department setting and may require subspecialty consultation.

Long-term Monitoring

Although some pneumonias are destructive (eg, adenovirus) and can cause permanent changes, most childhood pneumonias have complete radiologic clearing. If a significant abnormality persists, consideration of an anatomic abnormality is appropriate.

Careful longitudinal surveillance for long-term problems with growth, development, otitis, reactive airway disease, and other complications should be performed.

Prognosis

Overall, the prognosis is good. Most cases of viral pneumonia resolve without treatment; common bacterial pathogens and atypical organisms respond to antimicrobial therapy (see Treatment and Management). Long-term alteration of pulmonary function is rare, even in children with pneumonia that has been complicated by empyema or lung abscess.

Patients placed on a protocol-driven pneumonia clinical pathway are more likely to have favorable outcomes. The prognosis for varicella pneumonia is somewhat more guarded. Staphylococcal pneumonia, although rare, can be very serious despite treatment.

Control questions:

1. Right sided lower lobar pneumonia is suspected in a child of 6 years old. What examination will be less infofrmative?

A. Blood test.   D. X-ray of the chest.

B. Urine test.   E. Microbiological test of sputum.

C. Bilirubin level.

2. Numonia of pneumocystic etiology and moderate degree was diagnosed in a child of 3 months. What drug is it necessary to start the treatment with?

A. Penicillin.   C. Cefalexin.   E. Norphloxacin.

B. Biseptol.   D. Gentamicin.

3. Worsening of condition was diagnosed in a child of 5 years old with right-sided focal-confluent pneumonia provoked by Ps. Aeruginosa: appearance of lethargy, flabbiness, mottled skin, cold extremities, cyanosis of mucous membranes, increase of dyspnea and tachycardia, BP 60/40 mm Hg, weak pulse, oliguria. What complication is mostly probable?

A. Infectious-toxic shock, 2 stage.   D. Respiratory dystress-syndome

B. DIVC-syndrome.   of adult type.

C. Cardio-vascular insufficiency.   E. Synpneumonic pleuritis.

4. A child of 2,5 years has dry distressful cough, dyspnea of mixed character, RR 60/min, CR 110/min, t° 38,9°C, cyanosis of nasolabial triangle, at auscultation – isolated high-pitched dry and crepitation rales on both sides, at percussion – tympanic sound. At X-ray of the chest – reticular pattern with sponginess design. What is morphological form of pneumonia?

A. Focal-confluent.   C. Interstitial.   E. Croupous.

B. Segmental.   D. Focal.

5. A child of 10 years old had catarrhal symptoms during 14 days. Objectively: t° – 38,4°C, nonproductive cough, at auscultation – weak respiration in right

axillary region. Right-sided pneumonia was suspected. Which examination is necessary in the first place?

A. Blood test.

B. X-ray of the chest.

C. Spirography.

D. Proteinogram.

E. Clinical examination of sputum.

6. A child of 2 months old with pyodermia in inguinal folders, increase of t° up to 39,4°C, moist cough, refuse from food, dyspnea, acrocyanosis, dullness on percussion at the right side, at auscultation on the background of diminished breathing above dullness - small bubbling rales. Blood test: HB – 92 g/l, RBC – $3,0\times10^{12}$/l, WBC – 21×10^{9}/l, stab neutr. – 6%, segm. neutr. – 50%, eos – 5%, lymph. – 37%, mon – 6%, ESR – 28 mm/h. Right-sided focal pneumonia was diagnosed. What etiological factor is mostly probable?

A. Klebsiella.

B. Pneumococcus.

C. Staphylococcus.

D. E.coli.

E. Chlamidia.

7. A child of 9 years old is ill during 3 weeks. He complains of dry frequent cough, increase of temperature up to 37,2°C – 37,4°C. Objectively: condition is moderate, RR 18/min, at percussion – pulmonary sound, at auscultation – rough respiration, a few dry rales, predominantly at the right side lower scapular angle. Blood test: HB – 121 g/l, RBC – $3,75\times10^{12}$/l, WBC – 6.87×10^{9}/l, stab neutr. – 2%, segm. neutr. – 37%, eos – 5%, lymph. – 50%, mon – 6%, ESR – 8 mm/h. At X-ray – right-sided focal pneumonia. What etiological factor is mostly probable?

A. Mycoplasma pneumonia.

B. Ps. aeruginosa.

C. St. Aureus.

D. Str. pneumonia.

E. Legionella pneumophilia.

8. A child of 7 years old is ill during 3 days. He fell ill abruptly with elevation of t° up to 39,2°C, chills, headache, dry cough appeared, pain in right hypochondrium at cough and deep inspiration. Skin is pale, RR 26/min, right half of the chest is backward the left, at persussion - dullness above posterior lower parts at the right side, at auscultation diminished breathing above dullness, pleural friction rub. At X-ray – intensification of pulmonary pattern design of focal character in lower lobe of right lung, in right sinus – horizontal level of fluid. What is your diagnosis?

A. Right-sided fibrinous pleuritis.

B. Right-sided focal pneumonia conplicated with synpneumonic exudative pleuritis.

C. Right-sided lobar pneumonia complicated with pyopneumothorax.

D. Right-sided exudative pleuritis.

E. Right-sided pneumonia, uncomplicated, severe course.

9. Right-sided nosocomial pneumonia of low lobe complicated with exudative pleuritis was diagnosed in a child of 4 years old. Klebsiella was isolated from

pleural contents. What antibacterial drugs are necessary for treatment of pneumonia in this child?

    A. Tetracycline.   *D. Cefalosporines of III generation.*

    B. Macrolides of II generation.   *E. Aminoglycosides a of I generation.*

    C. Aminopenicillines.

10. Atypical chlamidial pneumonia was diagnosed in a child of 8 months. What is optimal antibacterial therapy?

    A. Tetracycline.   *D. Aminoglycosides.*

    B. Cefalosporines of II generation.   *E. Macrolides of II generation.*

    C. Aminopenicillines.

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MODULE 1
SUBSTANTIAL MODULE 2

THEME 5
PNEUMONIAS IN CHILDREN

Practical policies for students