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Historical, Physical, and Laboratory Clues to the Diagnosis of Pneumonia

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Pneumonia may be defined as an infectious process involving the lungs. It may be acute, subacute, or chronic, and it may be due to a wide variety of infectious agents including bacteria, viruses, and fungi, with bacterial pneumonias the lungs are the primary site of organ involvement, but with viral and atypical bacterial pathogens extrapulmonary manifestations are common. Tuberculosis and fungal disease may be limited to the lung or, if the infection is disseminated, result in extrapulmonary manifestations involving multiple organs. The clinical problem is to differentiate the treatable pneumonias from untreatable infectious processes and non-infectious conditions mimicking pneumonia. Because the bacterial and atypical pneumonias are the most common and readily treatable with antimicrobial therapy, the diagnostic approach is directed at ruling out or identifying specific bacterial pathogens.

Patients present with a variety of signs and symptoms, so the syndromic approach to diagnosis is the most sensible, the best, and sometimes the only way to arrive at a reasonable working differential diagnosis. Careful analysis of the history combined with pertinent physical findings help to narrow diagnostic possibilities and suggest specific etiologies for the patient's pulmonary complaints.[1–4] It is the chest roentgenogram, however, that defines the process as pulmonary and suggests broad diagnostic categories in which to classify the pulmonary process. Therefore the chest roentgenogram is helpful for differentiating a typical pneumonia from an atypical pneumonia but is not usually helpful for arriving at a specific etiologic diagnosis. It is even more helpful for eliminating whole categories from diagnostic consideration. This purpose is the real strength of the plain film, which reveals what the process is not rather than what it is in most cases. For example, a diffuse honeycomb pattern on a chest film suggests that the process is not infectious but does not reveal what the initial pulmonary process was that resulted in end-stage pulmonary disease manifested by "honeycombing" on the plain chest film.[5–8]

The critical factor in syndromic diagnosis is combining nonspecific findings, whether they are laboratory findings or chest film abnormalities,

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so as to increase diagnostic specificity. Always look for uncommon but specific findings that immediately point to a specific diagnosis. For example, the finding of hypophosphatemia in a patient with an atypical pneumonia presentation immediately suggests the possibility of legionnaires' disease.

This approach works even by combining nonspecific findings with long differential diagnoses if one can "bunch" and "clump" diagnostic data with mental dexterity and adroitness. For example, the differential diagnosis for pleural effusion is considerable, as is the differential diagnosis for hilar nodal involvement. When a pulmonary infiltrate is found in conjunction with a pleural effusion and hilar adenopathy, the differential diagnosis is quickly limited to a relatively few disease entities by combining these three findings, which when taken by themselves would have not provided the answer. The search for diagnostic clues, preferably specifically but also nonspecifically in groups, directs the astute clinician to arrive quickly, with minimal information, at a fairly precise diagnosis that permits early empiric antimicrobial therapy.[9,10] For this reason, the chapter contains many tables of differential diagnostic features to assist the clinician in finding diagnostic information that can be combined to assist in the diagnosis of the patient with pneumonia.

The use of diagnostic "pearls" represents another important aspect of medical education and diagnostic decision making. Aphorisms help decide between two conditions that are similar or provide information to allow a specific diagnosis. This information is helpful adjunctively when combined with conflicting or difficult diagnostic dilemmas suggested by the history, physical examination, and chest film. For example, if the differential diagnosis is between Wegener's granulomatosis and Churg-Strauss allergic granulomatosis, the presence of eosinophilia, if due to the pulmonary process, immediately eliminates Wegener's granulomatosis as a diagnostic possibility. Similarly, eosinophilia is not part of pulmonary or disseminated tuberculosis; and in the absence of other causes of eosinophilia, this finding alone goes strongly against the diagnosis of *Mycobacterium tuberculosis* in any of its myriad manifestations.[1,11]

It is also not often appreciated that a patient presents with a nonspecific syndrome complex that nevertheless has the "diagnostic flavor" of certain diseases. For example, an elderly emaciated man with a pulmonary infiltrate and pulmonary symptoms that have persisted for weeks immediately suggests a chronic pulmonary process, which may be tuberculous, neoplastic, or fungal. Just as importantly, it immediately eliminates nearly all common bacterial and viral pathogens. This "feeling" that patients give you immediately suggests the appropriate diagnostic approach that may be refined with additional laboratory tests.[9,10]

Although the focus of this chapter is on arriving at a syndromic diagnosis on which to base early empiric therapy, which is important because it is of the greatest benefit to the patient, it should not be forgotten that the aim of the diagnostic workup is to arrive at a specific etiologic diagnosis.[2,3] A

definitive diagnosis should be sought in all cases but is not always available in a timely fashion and in some cases, is not possible at all. The clinician, however, should endeavor to make every effort to arrive at a specific etiologic diagnosis. It may be done by blood cultures or by recovery of a specific pathogen from pleural fluid or tissue samples. Techniques vary from a variety of staining techniques to culture of the organism or serologic methods. Because definitive diagnosis, except for the common bacterial pneumonias, is often delayed or not possible, every effort must be directed to use the syndromic diagnostic approach to efficiently and effectively devise a diagnostic and therapeutic approach to the patient's pulmonary problems.[12–14]

Clues from the History

It has long been said that "the history is the diagnosis." This Oslerian aphorism remains true today and is helpful in many patients with noninfectious and infectious pulmonary disorders.[1] The historical clues to pneumonia begin with questioning the patient about exposure to sick people or special environmental conditions. More important diagnostic information is available by analyzing underlying diseases, the age of the individual, and any associated condition that may suggest the predisposition to specific pulmonary pathogens.[2,5] For example, pneumonia in children and young adults is likely to be due to *Mycoplasma*, one of the respiratory viruses, or *Chlamydia pneumoniae*, but it must be appreciated that bacterial pneumonias also are not uncommon in this age group. Similarly, elderly patients may have viral pneumonias but, excluding viral influenza, are more likely to have bacterial or atypical pneumonias. Alcoholics are predisposed to infection by the pneumococcus, *Klebsiella*, and *M. tuberculosis*, and to aspiration pneumonia. Individuals coming from chronic care facilities with pneumonias are likely to have *Streptococcus pneumoniae*, *Hemophilus influenzae*, or *Klebsiella* as a cause for their infectious pneumonia, other factors aside.[15] Patients with human immunodeficiency virus (HIV) presenting initially almost invariably have *Pneumocystis carinii* pneumonia (PCP), but on subsequent admissions may have a relapse of PCP or a variety of other pathogens including *Mycobacterium avium-intracellulare*, *Salmonella*, or *Legionella*.[2,12] Infections in leukopenic compromised hosts are determined by the profoundness and duration of the leukopenia. Early after chemotherapy, most infections tend to be nonpulmonary and due to aerobic gram-negative bacilli (e.g., *Pseudomonas aeruginosa*). After more than 2 weeks of profound leukopenia, the possibility of disseminated fungal diseases (e.g., *Aspergillus*) increases with time. These patients do not have gram-positive infections except as related to intravenous access devices, and gram-positive pneumonias in these patients are distinctly uncommon.[1,2]

These patients also may have a variety of noninfectious pulmonary problems, including leukoagglutination reactions involving the lungs, radiation pneumonitis, or a variety of drug-induced pulmonary diseases secondary to chemotherapeutic agents.[16] By examining the data in this way, one uses historical information to suggest specific diagnostic possibilities or, at the very least, broad diagnostic categories.

Symptoms are less specific in general and therefore provide less useful information. Combining nonspecific symptom clues with other information, however, enhances their value. For example, dyspnea is a common symptom of a wide variety of pulmonary diseases, but severely progressive dyspnea that develops over a week or more suggests PCP.[2] Once again the rapidity of the time course combined with the relatively nonspecific symptoms of dyspnea helps eliminate a variety of pulmonary disorders that may produce dyspnea more slowly (e.g., a variety of interstitial lung diseases).[11,12] Viral pneumonias may also some produce some dyspnea over a week, but again there should be other associated symptoms (e.g., fevers or myalgias) that would point toward a viral etiology. Similarly, severe bacterial pneumonias would not present solely with dyspnea after a week or more of acute shortness of breath in the absence of any other symptoms.[17] In contrast, if one is fortunate enough to have a patient with symptoms that do not ordinarily accompany most pneumonias, the uncommon but specific finding is of great diagnostic significance. For example, if an adult patient presents with an ill-defined pulmonary infiltrate and abdominal pain, *Legionella* is the most likely diagnostic possibility. Once again we have combined a typical pneumonia presentation on the chest film with an extrapulmonary finding to rapidly limit diagnostic possibilities.[9] Analogously, ear pain in a patient with pneumonia suggests pneumococcus, group A streptococci, *H. influenzae*, *Branhamella catarrhalis*, or *Mycoplasma* pneumonia, and the finding of the less common but more specific bullous myringitis immediately points to *Mycoplasma* as the cause of the patient's problems.[10] Similarly, a sore throat due to pharyngitis in a patient with pneumonia eliminates immediately pneumococcus and *H. influenzae* from diagnostic consideration, as these organisms are not associated with pharyngitis but commonly colonize the oropharynx.[18]

Underlying medical diseases also suggest specific putative pathogens. The diagnostic approach here is to recognize that the underlying condition is associated with a specific host defense defect, which in turn predisposes to a limited number of possible pathogens.[1,2] A patient with pneumonia and asplenia should have *S. pneumoniae*, *H. influenzae*, or *Neisseria meningitidis* pneumonia.[19] Patients with silicosis or pneumoconiosis are predisposed to *M. tuberculosis*; similarly, patients with *M. tuberculosis* or silicosis, which results in scarred and fibrosed lungs, may in turn predispose to adenocarcinoma; rarely, the two may even coexist. The most important part of the diagnostic approach is to appreciate the value

of the method of looking for findings with high diagnostic specificity and in combining nonspecific findings to increase diagnostic accuracy.[9,10] Clues from the history are presented in Table 5.1.

Clues from the Physical Diagnosis

Physical diagnosis is most helpful for determining if the patient has consolidation or pleural effusion. Other physical diagnostic findings are helpful in specific situations (e.g., apical dullness suggesting tuberculosis, chest wall sinuses suggesting actinomycosis or bronchogenic carcinoma, or the relatively "quiet lungs" on auscultation typical of the viral pneumonias). Except for pleural effusion and consolidation, the most important physical findings are generally not helpful for diagnosing specific causes of pulmonary disease.[20] The physical examination is somewhat more helpful by providing extrapulmonary findings that may provide clues to the cause of the pulmonary process. In a patient with an atypical pneumonia and

TABLE 5.1. Pneumonia: historical clues.

Clues	With lung infiltrates suggest
Environmental clues	
Soil/plant contact	Legionnaires' disease
	Histoplasmosis
	Blastomycosis
	Sporotrichosis
Zoonotic clues	
Bird contact	Psittacosis
	Blastomycosis
	Histoplasmosis
	Cryptococcosis
	Q fever
Cat contact	Tularemia
	Q fever
Rabbit contact	Tularemia
Dog contact	*Dirofilaria immitis*
Host clues	
Age	
Children/young adults	*Mycoplasma*
	C. pneumoniae
	Viral pneumonias
Elderly	*Streptococcus pneumoniae*
	Hemophilus influenzae
	Klebsiella
	Legionnaires' disease
	Viral influenza
	Aspiration pneumonia/anaerobic abscess
	M. tuberculosis

TABLE 5.1. *Continued*

Clues	With lung infiltrates suggest
Special populations	
Alcoholics	*S. pneumoniae*
	Klebsiella
	M. tuberculosis
	Aspiration pneumonias/anaerobic abscess
Chronic care facilities	*S. pneumoniae*
	H. influenzae
	Klebsiella
	M. tuberculosis
	C. pneumoniae
IV drug abusers	*Staphylococcus aureus*
	Septic pulmonary embolism
	Pseudomonas aeruginosa
	Pneumocystis carinii[a]
	M. tuberculosis/*M. avium-intracellulare*
HIV	PCP
	M. tuberculosis
	M. avium-intracellulare
	Salmonella
	Legionella
	CMV
	Histoplasmosis
	S. pneumoniae
	Klebsiella
	H. influenzae
Leukopenia (prolonged and profound)	*Aspergillus*
	Mucormycosis
	Cryptococcosis
	Pseudomonas
Organ transplant	Cytomegalovirus
	Herpes simplex virus
	Aspergillus
	Cryptococcosis
	PCP
Foreign travel	*M. tuberculosis*
	Q fever
	Melioidosis
	Paragonamiasis
Symptom clues	
Cough (nonproductive)	*Mycoplasma*
	Legionella
	Q fever
	C. pneumoniae
	Tularemia
	Viral pneumonia
Chest pain (pleuritic)	Bacteremic pneumonia
	Viral influenza
Dyspnea (severe)	Viral pneumonia
	PCP
	Severe bacteremic pneumonia

(*continued*)

TABLE 5.1. *Continued*

Clues	With lung infiltrates suggest
Night sweats	*M. tuberculosis*
	Histoplasmosis
Abdominal pain	*Legionella*
Ear pain	*Mycoplasma*
	S. pneumoniae
	H. influenzae
	B. catarrhalis
Sore throat	*Mycoplasma*
	C. pneumoniae
	Viral influenza
	Group A streptococci
	Adenovirus
Hoarseness	
Acute	Viral influenza
	C. pneumoniae
Chronic	*M. tuberculosis*
Diarrhea	*Mycoplasma*
	Legionella
Headache (severe)	Psittacosis
	Q fever
Mental confusion	*Legionella*
	Mycoplasma
Abdominal pain	Legionnaires' disease
Muscle aches (severe)	Cocci
	Viral influenza
	Mycoplasma
	Psittacosis
Nosebleed	Psittacosis
Underlying condition/disease	
Asplenia	*S. pneumoniae*
	H. influenzae
	N. meningitidis
Uremia	*M. tuberculosis*
COPD	*S. pneumoniae*
	H. influenzae
	Klebsiella
	B. catarrhalis
Pulmonary alveolar proteinosis	*Nocardia*
	Cryptococcosis
Silicosis/coal mining	*M. tuberculosis*
Sarcoidosis	*M. tuberculosis*
Lymphoma/malignancy	*M. tuberculosis*
Blood transfusion	PCP
Chickenpox exposure	Varicella
Corticosteroid therapy	*M. tuberculosis*
	Aspergillosis
Urinary tract infection	*E. coli*
Periodontal disease	Actinomycosis
	Aspiration pneumonia/anaerobic abscess

TABLE 5.2. Pneumonia: physical diagnosis clues.

System clues	With pneumonia suggests
HEENT	
Horder's spots	Psittacosis
Seborrheic dermatitis (severe)	PCP
Conjunctivitis	Adenovirus
Otitis/bullous myringitis	*Mycoplasma*
Pharyngitis	*Mycoplasma*
	Chlamydia pneumoniae
	Viral infection
	Adenovirus
Nose ulcer	Histoplasmosis
Tongue ulcer	Histoplasmosis
Oral ulcers (severe)	PCP
	Histoplasmosis
Hairy leukoplakia	PCP
Perioral ulcerations/ conjunctivitis (Steven-Johnson syndrome)	*Mycoplasma*
Chest	
Erythema multiforme	*Mycoplasma*
Chest wall sinuses	Actinomycosis
	M. tuberculosis
	Sporotrichosis
Seborrheic dermatitis (severe)	PCP
Abdomen	
Hepatosplenomegaly	*M. tuberculosis*
	Histoplasmosis
	Q fever
	Psittacosis
Extremities	
Erythema multiforme	*Mycoplasma*
Folliculitis (severe)	PCP
Erythema nodosum	Coccidioidomycosis
	Histoplasmosis
	Blastomycosis
	M. tuberculosis
	Group A streptococci
Ecthyma gangrenosum	*Pseudomonas*
	Serratia
Skin ulcers	Blastomycosis
	Sporotrichosis
	Tularemia
	Histoplasmosis
Vesicular lesions	Varicella
Obscure phlebitis	Psittacosis

HEENT = head, eyes, ears, nose, and throat.

macular facial spots, the diagnosis of psittacosis is highly likely. Conjunctivitis in the neonate with pneumonia immediately suggests *Chlamydia*, where as conjunctivitis in an adult points to adenoviral pneumonia.[2,4] Certain associations are nearly pathognomonic and, although unusual, are virtually diagnostic when found (e.g., tongue ulcers for disseminated histoplasmosis and hairy leukoplakia in HIV patients with PCP pneumonia).

Unfortunately, all findings are not present in every case, and one must be constantly alert to seize on the diagnostic significance of uncommon but specific findings.[9] For example, an atypical pneumonia plus erythema multiforme on the skin is virtually diagnostic of *Mycoplasma* pneumonia, as no other pneumonia is associated with this skin manifestation.[21] The clinician must be cautious when associating erythema multiforme with a pneumonia, as the patient could be receiving an antibiotic (e.g., trimethoprim-sulfamethoxazole) for the pneumonia or an unrelated urinary tract infection that could result in a drug reaction manifested by erythema multiforme.[1] Once again, never analyze findings in a vacuum, but always apply them in the proper clinical context and preferably in concert with other findings to avoid diagnostic errors.[9,10] Clues from the physical diagnosis are presented in Table 5.2.

Clues from the Chest Film

It is not commonly appreciated that the behavior of the infiltrate on the chest film is as important to the diagnosis as its general appearance. Rapidly developing pulmonary infiltrates suggest limited processes that are capable of producing such roentgenographic abnormalities.[6,8] Gram-negative bacillary pneumonias, *Staphylococcus aureus* infection, aspiration pneumonia, and legionnaires' disease characterize infectious possibilities, whereas congestive heart failure and adult respiratory distress syndrome (ARDS) are the most common noninfectious entities that appear rapidly. Similarly, infiltrates that rapidly resolve are almost never infectious and suggest left ventricular failure, localized pulmonary edema, and acute eosinophilic pneumonias or pulmonary drug reactions.[1,4]

The predominant location of the infiltrate on the chest film or lobar predisposition has important diagnostic significance.[7,8] Symmetric peripheral infiltrates suggest a noninfectious etiology (e.g., pulmonary drug reactions). Unilateral pulmonary infiltrates suggest bacterial pneumonias, actinomycosis, nocardiosis, Q fever, or *Crytococcus neoformans*. Noninfectious asymmetric pulmonary infiltrates suggest such entities as adenocarcinoma, large-cell anaplastic carcinoma, vasculitis, systemic lupus erythematous (SLE), or Loeffler syndrome.[16] In contrast, perihilar infiltrates suggest viral pneumonias, fungal disease, pertussis, or PCP, as well as a wide variety of noninfectious processes.[22–25]

Focal infiltrates are a difficult diagnostic problem but usually represent a bacterial process rather than a noninfectious one. Most of the noninfectious causes of pulmonary infiltration are generalized processes and tend not to be focal (e.g., chemical pneumonitis, pulmonary drug reactions). Radiation pneumonitis, however, tends to be focal and confined to the radiation fields; similarly, pulmonary embolus and infarction as well as localized pulmonary edema or bronchogenic carcinomas may present with localized or focal infiltrates.[25,26] In general, diffuse infiltrates are noninfectious but may be a manifestation of any of the viral pneumonias or PCP.

Lastly, the speed of resolution of an infiltrate provides important diagnostic information regarding the cause of the pulmonary infiltrate. Among the infections, tuberculosis and lung abscesses are the commonest examples in this category.[27] Noninfectious conditions are more commonly responsible for slowly resolving infiltrates (e.g., chronic pulmonary drug reactions, Wegener's granulomatosis, repeated aspiration).[26] An infiltrate that resolves slowly or not at all suggests a postobstructive pneumonia or underlying carcinoma. However, do not forget the entity known as "delayed resolution of pneumococcal pneumonia," in which pulmonary abnormalities may persist on the chest roentgenogram for up to 14 weeks after initial diagnosis (Table 5.3).

Certain diseases, infectious or noninfectious, have a predilection for certain areas of the lung. This information may be used diagnostically in a general sense but is useful only when combined with other historical, physical, or laboratory features. In general, the upper lung zone involvement is characteristic of tuberculosis, histoplasmosis, and coccidioidomycosis.[27–30] Anaerobic aspiration pneumonia due to mechanical causes is commonest in the upper lung fields, as is *Proteus* and *Klebsiella* among the bacterial pneumonias. It should be appreciated that any bacterial pneumonia may

TABLE 5.3. Pneumonia: clues from the chest film—infiltrates.

Infectious agents	Noninfectious agents
Rapidly progressive infiltrates	
Legionnaires' disease	Congestive heart failure
Aspiration pneumonia	Noncardiac pulmonary edema
S. aureus	ARDS
Gram-negative pneumonia	Systemic lupus erythematosus (SLE)
Peripheral infiltrates	
Actinomycosis	Loeffler syndrome
Nocardiosis	Pulmonary drug reactions
	Adenocarcinoma
	Large-cell anaplastic carcinoma
	Vasculitis
	SLE
	Fat emboli

(*continued*)

TABLE 5.3. *Continued*

Infectious agents	Noninfectious agents
Perihilar infiltrates	
Viral pneumonias	Squamous cell carcinoma
Pertussis	Small-cell anaplastic (oat cell) carcinoma
PCP	
Histoplasmosis	Silicosis
Cryptococcosis	Congestive heart failure
Coccidioidomycosis	Pulmonary alveolar proteinosis
Chlamydia trachomatis	Sarcoidosis
Focal infiltrates	
Bacterial pneumonia	Bronchogenic carcinoma
	Chemical pneumonitis
	Pseudolymphomas
	Localized pulmonary edema
	Pulmonary infarct
	Pulmonary drug reactions
	Radiation pneumonitis
Diffuse infiltrates	
PCP	Pulmonary edema
Viral pneumonias	Noncardiac pulmonary edema
	Chemical pneumonitis
	Radiation pneumonitis
	Cancer with lymphangitic spread
	Pulmonary fibrosis
	Pulmonary alveolar proteinosis
	Wegener's granulomatosis
	Bilateral massive aspiration
	SLE
	Uremia
	Drug reactions
	ARDS
	Sarcoidosis
Rapidly resolving infiltrates	
None	Pulmonary edema
	"Vanishing tumor" (localized pulmonary edema)
	Acute pulmonary drug reactions
	Acute eosinophilic pneumonias
Slowly resolving infiltrates	
Abscesses	Repeated aspiration
Inadequate/inappropriate therapy	Pulmonary emboli
Legionnaires' disease	Postobstructive pneumonias/carcinoma
Tuberculosis	Bronchoalveolar carcinoma
S. pneumoniae	Lymphomas
PCP	Chronic pulmonary drug reactions
	Bronchopulmonary aspergillosis
	Wegener's granulomatosis

involve the upper lungs, but *Klebsiella* is found in the upper lobes more commonly than group A streptococcal pneumonia or *B. catarrhalis* pneumonia, for example.[2,4] Noninfectious disorders with an upper lung zone preference include eosinophilic granulomas, psittacosis, and Loeffler syndrome. Midlung zones are affected by infectious bacterial pneumonias (e.g., *S. pneumoniae*, *H. influenzae*) or a wide variety of noninfectious conditions (e.g., sarcoidosis, hypersensitivity pneumonitis, lymphomas). Infectious diseases have a predilection for the lower zones of the lung; pneumococcus and *H. influenzae* have a predilection for the right lower

TABLE 5.4. Pneumonia: chest film clues—lung zone predilection.

Infectious agents	Noninfectious agents
Upper lung zone	
Tuberculosis	Eosinophilic granulomas
Histoplasmosis	Silicosis
Coccidioidomycosis	Bronchial adenoma
Atypical tuberculosis	Loeffler syndrome
Klebsiella	Extrinsic allergic alveolitis
Proteus	Sarcoidosis
Aerobic aspiration pneumonia/abscess	Radiation pneumonitis
	Ankylosing spondylitis
Mid-lung zone	
S. pneumoniae	Metastatic carcinoma
H. influenzae	Bronchial adenomas
	Eosinophilic granulomas
	Lymphomas
	Idiopathic pulmonary hemosiderosis
	Goodpasture syndrome
	Sarcoidosis
	Extrinsic allergic alveolitis
	Silicosis
	Hypersensitivity pneumonitis
Lower lung zone	
Cryptococcosis	Idiopathic hemosiderosis
Sporotrichosis	Metastases
Mycoplasma	Goodpasture syndrome
Melioidosis	Drug-induced pulmonary disease
H. influenzae	Extrinsic allergic alveolitis
S. pneumoniae	Arteriovenous malformation
Group A streptococci	Pulmonary infarct
Tularemia	Rheumatoid nodules
Q fever	Wegener's granulomatosis
Psittacosis	Fibrosing alveolitis
Legionella	
C. pneumoniae	
Amebiasis	
E. coli	
Hydatid cysts	

lobe, for example.[31] Noninfectious lower lung processes include Goodpasture syndrome, drug-induced pulmonary disease, hypersensitivity pneumonitis, pulmonary infarcts, and metastatic disease.[25,26] Again, care must be taken to avoid trying to diagnose the problem based on these isolated, nonspecific findings alone. Always try to combine such nonspecific findings with other nonroentgenographic clues (Table 5.4).

Cavitary lesions, when present, are important diagnostic clues. Relatively few pulmonary diseases, infectious or noninfectious, result in cavities. When cavities are present they are usually thick-walled. The finding of a thin-walled cavity quickly limits differential diagnostic possibilities to sporotrichosis, coccidioidomycosis, paragonamiasis, or atypical tuberculosis, among the infectious etiologies.[4] It should be remembered that most of the thick-walled cavitary lesions, over time, develop into thin-walled lesions. If the process is subacute versus chronic, argue against the noninfectious etiology.[6,7] Thick-walled cavitary lesions that are noninfectious are usually due to squamous cell carcinoma, Wegener's granulomatosis, rheumatoid nodules, lymphoma, metastatic carcinoma, or bronchoalveolar carcinoma.[25,26] The clinician should combine the cavitary lesion with the presence of other features of the chest film; for example, rapidly progressive infiltrates with cavitary lesions favor the diagnosis of a bacterial pneumonia or anaerobic pneumonitis versus a granulomatous or noninfectious pneumonia (Table 5.5).

TABLE 5.5. Pneumonia: clues from chest film—cavitary lesions.

Infectious agents	Noninfectious agents
Thick-walled lesions	
Staphylococcus aureus	Squamous cell carcinoma
Klebsiella	Pulmonary infarction
Escherichia coli	Silicosis
Pseudomonas	Wegener's granulomatosis
Tuberculosis	Rheumatoid nodules
Histoplasmosis	Lymphoma
Blastomycosis	Sarcoidosis
Aspergillus	Metastatic carcinoma
Melioidosis	Metastatic sarcoma
Anaerobic lung abscess	Bronchioalveolar carcinoma
Septic pulmonary emboli	Melanoma
Nocardia	
Thin-walled lesions[a]	
Sporotrichosis	Wegener's granulomatosis
Coccidioidomycosis	
Paragonamiasis	
Atypical tuberculosis	

[a] Many thick-walled cavitary lesions become thin-walled over time.

Hilar adenopathy alone is not confused with pneumonia; but when it is found in concert with a pulmonary infiltrate it is helpful for limiting diagnostic possibilities. Hilar adenopathy may be viewed as unilateral or bilateral in terms of differential diagnosis. *Mycoplasma* and viruses are unusual causes of hilar adenopathy, and when hilar adenopathy occurs it is only in children.[32–34] In adults, hilar adenopathy suggests tuberculosis, fungus infection, or, if the patient has an atypical pneumonia, tularemia. Noninfectious etiologies are more common causes of both unilateral or bilateral hilar adenopathy (e.g., bronchogenic carcinoma, lymphomas, SLE).[12] Bilateral hilar adenopathy is most strongly associated with sarcoidosis but is also a feature of lymphomas. Once again, associated clues may provide the key to the differential diagosis. For example, if a patient presents with bilateral hilar adenopathy, a pulmonary infiltrate, and pleural effusion, the diagnosis of lymphoma is favored over sarcoidosis, as pleural effusions are uncommon with sarcoidosis.[5,6] Similarly, if there is a clear channel between the hilar nodes and the cardiac shadow, the diagnosis of sarcoidosis is enhanced. The same thing is true of right paratracheal adenopathy in concert with symmetric bilateral hilar adenopathy, suggesting the diagnosis of sarcoidosis.[8] Calcification of the hilar nodes, except for silicosis, is usually due to tuberculosis or histoplasmosis. Be careful not to confuse calcifications in adjacent structures as being in the hilar nodes (e.g., a calcified aortic aneurysm[7,8] (Table 5.6).

Pleural effusions occurring alone do not indicate pneumonia; but when present in conjunction with an ipsilateral pulmonary infiltrate, they provide an important diagnostic clue to the etiology of the pulmonary process. Pleural effusions may be classified according to their size,

TABLE 5.6. Pneumonia: clues from the chest film—hilar adenopathy.

Infectious agents	Noninfectious agents
Bilateral hilar adenopathy	
Fungi	Sarcoidosis
Tularemia	Bronchogenic carcinoma
Tuberculosis	Lymphomas
Mycoplasma	Leukemias
Viral pneumonias	Silicosis
	Systemic lupus erythematosus
Unilateral hilar adenopathy	
Tuberculosis	Bronchogenic carcinoma
Fungi	Metastases
Tularemia	Lymphomas
Mycoplasma	Atypical measles
Calcified hilar nodes	
Tuberculosis	Silicosis
Histoplasmosis	

rapidity of accumulation or reaccumulation, and their bilaterality.[35,36] Unilateral pleural effusion on an infectious basis suggests *H. influenzae* or *S. pneumoniae* as the most likely bacterial pathogen. Among the granulomatous diseases, primary tuberculosis is the most common cause of unilateral pleural effusion.[1,4] Noninfectious causes of pleural effusion include a wide variety of disorders; but most commonly unilateral pleural effusions are due to congestive heart failure, pancreatitis, malignancy, or pulmonary infarction. Bilateral pleural effusions are never infectious, even if associated with pulmonary infiltrates.[36] The most common cause of bilateral pleural effusion by far is congestive heart failure. Unilateral or bilateral pleural effusions without pulmonary infiltrates suggest a subdiaphragmatic collection, or abscess. A good example of an abdominal cause for pleural effusion in concert with a pulmonary infiltrate is pancreatitis-induced ARDS. The size of a pleural effusion is also somewhat helpful in the differential diagnosis. Moderate pleural effusions are characteristic of *H. influenzae*, tularemia and primary tuberculosis, whereas a large pleural effusion that is infectious immediately points to group A streptococci.[8,10] Among the noninfectious causes, a large pleural effusion or a rapidly recurring pleural effusion immediately points to a neoplastic etiology. Small to moderate effusions are due to a wide variety of noninfectious conditions (e.g., pulmonary infarction, pancreatitis, SLE, congestive heart failure nephrosis, cirrhosis, or ascites).[35] Combining the pleural effusion with other findings to increase diagnostic accuracy again emphasizes the principle of "bunching" information to increase diagnostic accuracy. Pleural effusion occurs with cardiomegaly virtually only with primary tuberculosis or with associated tuberculous pericarditis. Almost all other etiologies are noninfectious. Pleural effusion with hilar enlargement, argues against the fungal etiology, and favors tuberculosis.[27,30] Among the noninfectious etiologies, bronchogenic carcinomas and lymphomas head the list. Focal infiltrates suggest a bacterial process, although, again, neoplastic disorders and pulmonary embolism may present in this fashion. The diagnostic clues from pleural effusions are presented in Table 5.7.

Chest nodules by themselves usually represent granulomatous disease or malignancy. When found in association with a pulmonary infiltrate, however, they suggest a wider range of diagnostic possibilities.[12] Pulmonary nodules may be classified as solitary or multiple, diffuse, localized, or cavitating. Multiple nodules in a patient with atypical pneumonia suggest *Legionella micdadei* or Q fever. The only viral pneumonia with nodular densities is adenoviral pneumonia.[1,36] The ovoid densities are not truly nodules and are therefore not considered in this differential diagnostic list. Septic pulmonary emboli are characterized by temperatures of more than 102°F and an identifiable distant source in the pelvis or arm in a patient with a history of intravenous drug abuse. Most other infectious multiple pulmonary nodules are caused by subacute or chronic diseases due to the higher bacteria, *M. tuberculosis*, or fungi. Noninfectious causes

TABLE 5.7. Pneumonia: chest film clues—pleural effusion.

Infectious agents	Noninfectious agents
Unilateral pleural effusion	
S. pneumoniae	Chronic heart failure
Klebsiella	Neoplasms
H. influenzae	Metastases
Tularemia	Meig syndrome
Mycoplasma	Postthoracotomy
Primary tuberculosis	Postmyocardial infarction syndrome (Dressler syndrome)
	SLE
	Pancreatitis/ARDS
	Pulmonary infarction
	Subphrenic collection/abscess
Bilateral pleural effusion	
None	Congenital heart failure
	Cirrhosis/ascites
	Pancreatitis
	Subdiaphramatic abscess
	Pulmonary infarction
	Metastases
	SLE
	Postmyocardial infarct syndrome
	Nephrosis
	Hypothyroidism
	Drug-induced pulmonary disease
	Meig syndrome
Size of pleural effusion	
None or small effusion	Small to moderate effusion
Streptococcus pneumoniae	Pancreatitis
Mycoplasma	Pulmonary infarct
Legionella	Meig syndrome
	Drugs
Moderate	Nitrofurantoin
H. influenzae	Methysergide
Tularemia	Drug-induced SLE
Primary tuberculosis	SLE
	Rheumatoid nodules
	Cirrhosis or ascites
	Congestive heart failure
	Nephrosis
Large	Large
Group A streptococci	Malignancy
Pleural effusion with cardiomegaly	
Viral infection (only with CHF)	Congestive heart failure
Primary tuberculosis	Pulmonary embolism
	Neoplasms
	Rheumatoid nodule
	Postpericardiotomy syndrome
	SLE

(*continued*)

TABLE 5.7. *Continued*

Infectious agents	Noninfectious agents
Pleural effusion with hilar enlargement	
Primary tuberculosis	Pulmonary embolism
Pertussis	Bronchogenic carcinoma
	Lymphomas
	Metastases
Pleural effusion with focal infiltrates	
Pneumonia/empyema	Pulmonary embolism
Primary tuberculosis	Neoplasms
H. influenzae	Bronchogenic cardinoma
S. pneumoniae	Lymphomas
Group A streptococci	
Mycoplasma	
Tularemia	

SLE = systemic lupus erythematosus; ARDS = adult respiratory distress syndrome; CHF = congestive heart failure.

include such diverse entities are metastatic carcinoma, Wegener's granulomatosis, rheumatoid nodules, ateriovenous malformations, and nonsepticpulmonary emboli.[23,25] Diffuse fine nodules are suggested by eosinophilic granulomas, sarcoidosis, or hypersensitivity pneumonitis. Among the noninfectious causes of cavitary nodules are squamous cell carcinoma and bronchoalveolar carcinoma, which are often confused with anaerobic lung abscesses. Similarly, cavitation is a feature of Wegener's granulomatosis, and sometimes this entity can be confused with infectious causes. Wegener's granulomatosis is frequently associated with hemoptysis, which is less common in the infectious conditions it mimics.[12] The patient with septic pulmonary emboli is seriously ill and has an underlying recognizable source of the emboli. Patients with *Nocardia* do not commonly present with hemoptysis, nor do those with cryptococcosis.[16] Tuberculosis with fibrocaseous disease do not present predominantly with nodules as do those with Wegener's granulomatosis. In this way, by combining other features with a chest roentgenogram, one can quickly eliminate possibilities. The differential diagnosis of nodules in the chest film is presented in Table 5.8.

There are a variety of other findings on the chest film that limit the diagnostic possibilities if not suggest a specific etiology. For example, the "bulging fissures sign" indicates volume expansion and is most commonly associated with *Klebsiella* pneumonia. However, any infectious or noninfectious process that can result in lobar expansion may produce the same sign.[8,12] Therefore do not forget other infectious etiologies or bronchoalveolar carcinoma as a cause for this roentgenographic finding. Moreover, spontaneous pneumothorax is usually associated with bullous lung diseases; and do not fail to consider eosinophilic granuloma,

TABLE 5.8. Pneumonia: chest film clues—nodules.

Infectious agents	Noninfectious agents
Solitary pulmonary nodule	
Tuberculosis	Bronchogenic cancer
Histoplasmosis	Metastasis (kidney, colon, ovary, testis, Wilms' tumor, sarcoma
Coccidioidomycosis	Lymphoma
Cryptococcosis	Plasmacytoma
Nocardia	Rheumatoid nodules
Dirofilaria	Wegener's granulomatosis
Abscess	Arteriovenous malformation
	Pulmonary infarct
	Hamartoma
	Hematoma
	Bronchial adenomas
	Sarcoidosis
Multiple pulmonary nodules	
Legionella micdadei	Wegener's granulomatosis
Septic pulmonary emboli	Caplan syndrome
Abscesses	Metastasis (kidney, colon, ovary, testes, melanoma)
Histoplasmosis	Lymphoma
Coccidioidomycosis	Arteriovenous malformation
Cryptococcosis	Pseudolymphoma
Nocardia	Pulmonary infarction
Tuberculosis	Rheumatoid nodules
Q fever	Silicosis
Hydatid cyst	Atypical measles
Paragonamiasis	
Adenovirus	
Diffuse fine nodules	
Viral pneumonia	Hypersensitivity pneumonitis
Miliary tuberculosis	Eosinophilic granuloma
	Sarcoidosis
Cavitating nodules	
Septic pulmonary emboli	Squamous cell carcinoma
Nocardia	Bronchoalveolar cell carcinoma
Cryptococcosis	Melanoma
Coccidioidomycosis	Osteosarcoma
Aspergillosis	Lymphoma
Abscesses	Wegener's granulomatosis
	Rheumatoid nodules

metastatic osteogenic sarcoma, or beryliosis as a cause of spontaneous pneumothorax in the appropriate clinical setting.[7,8] Similarly, legionnaires' disease and PCP have been associated with spontaneous pneumothorax, albeit uncommonly, although one would never diagnose legionnaires' disease or PCP on this basis alone. It is always inadvisable to diagnose "in a vacuum" basing one's impressions solely on the chest film. Rather, one

should always endeavor to synthesize the diagnostic clues as an aid in diagnosis.[10]

Laboratory Clues

Basic laboratory tests provide useful adjunctive indirect clues to the pulmonary process. A complete blood count (CBC) is commonly obtained on all patients with pneumonia, and one should specifically look for leukopenia, eosinophilia, basophilia, or thrombocytopenia. Any of these findings provides useful diagnostic information when no extrapulmonary process is responsible for the abnormality. For example, eosinophilia in concert with a pulmonary infiltrate always suggests a noninfectious etiology with the exception of helminthic migration through the pulmonary vasculature or a fungal pneumonia, most commonly coccidiodomycosis.[2,37] Basophilia is associated only with varicella pneumonia among all of the infectious diseases but suggests the possibility of carcinoma or lymphoma when the etiology of the pulmonary infiltrate is obscure. Monocytosis suggests tuberculosis, lymphoma, SLE, or carcinoma.[4] Leukopenia in an acutely ill patient suggests a viral process, usually viral influenza, overwhelming pneumococcal or streptococcal sepsis, disseminated histoplasmosis, or tuberculosis; it is also an indirect indicator of PCP in a patient with HIV.[27] Liver function tests should be obtained on all patients with pneumonias because abnormalities of liver function immediately suggest an atypical pathogen in a patient with acute pneumonia or miliary tuberculosis or lymphoma in a patient with a subacute or chronic illness.[1,21] Laboratory tests from routine blood work are presented in Table 5.9.

Blood cultures should be performed on all patients with pneumonias, as they may provide a retrospective specific bacterial diagnosis. Blood cultures should always be preposed when the patient is first seen—before antimicrobial therapy is started. Positive blood culture results must be interpreted in the appropriate clinical context, as is true with all laboratory tests, but it may be the only way to make the diagnosis in a patient incapable of producing sputum. Blood culture positivity relates to the timing of the blood culture sample (i.e., in relation to the onset of the infectious pneumonia). Blood culture positivity is directly related to the *volume* of blood obtained rather than the number of specimens. Blood culture positivity also is related to the pathogen causing the pneumonia; that is, certain pathogens have a high bacteremic potential (e.g., *S. pneumoniae*, *H. influenzae*), whereas others are rarely recovered from blood cultures (e.g., *Serratia* or *Acinetobacter*).[2,4] If a sputum specimen is unobtainable, the diagnosis may be mode retrospectively by testing the patient for urinary antigens to *Hemophilus*, pneumococcus, or *Legionella*. It should be remembered that antigen urea is slow to develop and may be

TABLE 5.9. Pneumonia: laboratory clues from serum tests.

Abnormality	Infectious associations
Leukopenia	Viral influenza PCP Miliary tuberculosis *Streptococcus pneumoniae* *Staphylococcus* Histoplasmosis (disseminated)
Eosinophilia	Coccidioidomycosis Helminths
Basophilia	Varicella
Monocytosis	Tuberculosis Lymphoma SLE Carcinoma
Thrombocytopenia	Sarcoidosis SLE Lymphoma Miliary tuberculosis Histoplasmosis (disseminated) Influenza ARDS PCP (HIV) Drug-induced
Hypergammaglobulinemia	Sarcoidosis PCP (HIV)
Abormal liver function tests	Psittacosis Miliary tuberculosis Legionnaires' disease Q fever

negative initially, but once the process is initiated it persists over long periods. Therefore be careful not to misinterpret an initial negative urinary antigen test as evidence against a particular pathogen. The test should be considered negative only if it remains negative weeks into the infectious process. Similarly, serum serologic tests, which are useful for epidemiologic purposes or a retrospective serologic diagnosis, should be negative initially during the acute pneumonia but become positive weeks or months later. Once again, be careful not to ascribe acute pulmonary infiltrates to a positive *Legionella* or *Mycoplasma* serology, especially in low titer, as the positive test usually indicates previous exposure rather than acute disease.[1,2,4]

Sputum, when available, provides the most immediate and useful clue to the diagnosis of community-acquired bacterial pneumonia. For a sputum sample to be correctly interpreted, it must be properly collected, represent

TABLE 5.10. Pneumonia: diagnostic clues from sputum.

Sputum findings	Infectious agents
Foul smell	Oral anaerobes (aspiration)
Creamy yellow or salmon color	*Staphylococcus aureus*
Currant-jelly color	Pneumococcus
	Klebsiella
Raspberry-syrup color	Pneumonic plague
Red color (pseudohemoptysis)	*Serratia*
Blood-streaked (hemoptysis)	*Klebsiella*
	Viral influenza
	Meningococcus
	Pneumonic plague
No PMNs	Q fever
PMNs	Bacterial pneumonia
Eosinophils	Helminths (pulmonary migration phase)
Mononuclear cells	*Legionella*
	Mycoplasma
Mixed flora	Aspiration pneumonia

the lower respiratory tract flora, and be void of oropharyngeal contamination. Such contamination is evidenced on microscopic examination of the sputum by finding epithelial squamous cells in the specimen. This specimen should be disregarded and the culture results ignored. The gross examination of the sputum in terms of its color, consistency, and odor provide an initial impression. Purulent, fixed sputum favors a bacterial etiology, whereas thin or mucoid sputum suggests an atypical pneumonia or a malignant process. Blood-flecked sputum suggests most commonly pneumococcus or *Klebsiella*. The finding of purulence correlates well with the presence of polymorphonuclear neutrophils (PMNs) in the microscopic examination of the sputum. In general, the more purulent the sputum, the higher the PMN count, a condition that favors a bacterial etiology.[12] Atypical pneumonias, in general, with the occasional exception of *Legionella*, present with a mononuclear cell predominance, although usually in low numbers[31,38] (Table 5.10).

Gram stain of the sputum provides specific information as to the cause of the bacterial pneumonia. Gram-stained sputum may be misleading in a patient with chronic obstructive pulmonary disease (COPD) or anaerobic pneumonitis, where the results of the sputum Gram stain and culture show mixed or normal flora and provide no useful diagnostic information. A properly collected sputum sample that shows a predominant organism is the most useful. The type of organism (i.e., bacilli versus cocci) and the configuration of the organism provide specific diagnostic information. Gram-positive cocci in the smear may represent streptococci, pneumococci, or staphylococci. Overly decolorized streptococci may even resemble

TABLE 5.11. Pneumonia: diagnostic clues from sputum (Gram stain).

Finding	Organism	Comments
Gram positive		
Diplococci	*Streptococcus pneumoniae*	Coffee bean configuration (lancet-shaped)
Cocci (grape-like clusters)	*Staphylococcus aureus*	May be seen together with short chains or pairs
Cocci (short chains or pairs)	Group A streptococci	Length ≈ virulence Smaller than streptococci
Comma-shaped	*Nocardia*	Sometimes appear like "Chinese letters" on Gram stain
Gram negative		
Coccobacillary (pleomorphic)	*Hemophilus influenzae*	Encapsulated
Bacilli	*Klebsiella*	Plump and encapsulated
Diplococci	*Neisseria meningitidis* *Branhamella catarrhalis*	Kidney-bean-shaped

H. influenzae, *Branhamella*, or *Acinetobacter*.[22] The configuration of organisms among gram-positive organisms is most useful. Gram-positive cocci in pairs may represent pneumococci, streptococci, or an early staphylococcal infection. However, if grape-like clusters are present, even if in small number, *S. aureus* can be reliably diagnosed. If the Gram stain shows predominantly diplococci with occasional short chains, the diagnosis of *S. pneumoniae* can be made with confidence. A Gram stain showing many short chains of small cocci, even if some are present in pairs, points immediately to a group A streptococcal etiology. Gram-negative bacillary enteric organisms cannot be differentiated by Gram stain,[2,4] although the trained observer can differentiate *Pseudomonas* from *Klebsiella* from *H. influenzae*. An experienced microscopist can also easily distinguish the oral pigmented *Bacteroides* found in aspiration pneumonia/anaerobic lung abscesses from other aerobic gram-negative bacilli by Gram stain alone. The presence of gram-negative diplobacilli immediately suggests the diagnosis of *Neisseria meningitidis* or *B. catarrhalis*. Sputum Gram stain findings are presented in Table 5.11.

Although the presence of a pleural effusion adds another dimension to the chest film differential diagnosis, analysis of the fluid provides more definitive information and further limits diagnostic possibilities. The gross appearance of the pleural effusion fluid is usually helpful and in some cases can be diagnostic (e.g., hydatid cyst fluid, mesothelioma, chylous effusion). Much emphasis is usually given to differentiating transudates from exudates, but this information generally adds little diagnostic help to the case. There are only three causes of transudates: heart failure, nephrosis, and cirrhosis.[1,36] These conditions should be clinically obvious and not require lactate dehydrogenase (LDH) ratio analysis to make

TABLE 5.12. Pneumonia: diagnostic clues from pleural fluid.

Findings	Infectious agents	Noninfectious agents
Bloody	Tuberculosis Tularemia	Mesotheliomas Pulmonary infarct Carcinoma Metastases
Whitish	Empyema Hydatid cysts	Chylous effusion
Brownish	Empyema Amebic cysts	Parapneumonic effusion
Yellow-green	—	Rheumatoid arthritis
pH $\leq$ 7.3	Tuberculosis Rheumatoid arthritis	Bronchogenic carcinoma (rarely)
$\downarrow$ Glucose	Tuberculosis Bacteria Fungi *Mycoplasma*	Carcinoma Rheumatoid nodules SLE Lymphomas Esophageal rupture
$\uparrow$ Protein	Tuberculosis	Carcinoma Rheumatoid arthritis
$\uparrow$ Amylase	None	Pancreatitis/pseudocyst Adenocarcinoma Esophageal rupture
Extracellular debris	Abscesses Anaerobic empyema	Rheumatoid arthritis
PMNs	Bacteria Early tuberculosis	Idiopathic pleural effusion Pancreatitis Abdominal abscess CHF
Lymphocytes	Tuberculosis	Carcinoma
Eosinophils	Fungi Helminths	Lymphomas Mesotheliomas Pleural effusion Pneumothorax Pulmonary drug regimens Idiopathic effusions

the diagnosis from pleural effusion fluid. Virtually all other causes are exudative in nature and do not require further tests to document what should be obvious. There are some exceptions, but in general differentiation of a exudate from a transudate is not helpful.

Microscopic examination of the pleural fluid is somewhat helpful. PMN predominance usually suggests early tuberculosis or a bacterial pneumonia but is also found with idiopathic pleural effusions, pancreatitis, and

abdominal abscesses. PMNs are found in low numbers in effusions due to congestive heart failure. Lymphocytic predominance suggests tuberculosis or carcinoma, whereas eosinophils point to fungi or a variety of noninfectious causes.

Usually neglected but of great diagnostic importance is the pH of the fluid. A pH of less than 7.3 usually points to tuberculosis or rheumatoid arthritis but rarely is associated with bronchogenic carcinomas.[36] A low glucose level points to a bacterial, tuberculous, or fungal etiology among the infectious causes but is also associated with carcinoma, rheumatoid nodules, SLE, or lymphomas. An elevated pleural fluid protein level suggests rheumatoid arthritis, carcinoma, or tuberculosis.

Once again, the findings should be combined to increase diagnostic specificity, and therefore finding decreased glucose and increased protein in a patient with a pleural fluid pH of less than 7.3 strongly favors the diagnosis of tuberculosis. Extracellular debris is characteristic of rheumatoid arthritis, as is a yellow-greenish fluid. A grossly bloody fluid suggests malignancy or pulmonary infarction and argues against the diagnosis of tuberculosis.[1,25] Among the atypical pneumonias, bloody pleural effusion is associated only with tularemia. A serosanguineous pleural effusion suggests tuberculosis, group A streptococci, or malignancy.[2,3] Clues that can be obtained pleural fluid are outlined in Table 5.12.

Synthesis of Diagnostic Clues

The clinician uses whatever historical physical chest film or laboratory clues that are available in combination to rule in or exclude a bacterial or atypical pneumonia. The diagnostic approach is directed at identifying a treatable disease so empiric therapy may be begun as soon as possible. A definitive diagnosis of collagen vascular diseases and malignant disorders is secondary because they usually do not present an immediate threat to the patient's health on presentation. Using the syndromic approach and differential diagnosis, each disease usually presents with a particular profile.

It is not coincidental that diseases occur in some individuals with certain underlying diseases or host defense defects; it is the age, underlying disease, and host defect that predisposes the patient to specific pathogen groups. Furthermore, pathogens pathophysiologically cause disease in a stereotyped fashion, and therefore they "behave" in a predictable fashion most of the time. For example, the pneumococcus prefers the lower lobe and does not cavitate. Therefore if there is a lower lobe segmental or lobar defect that is cavitating, one can confidently state that the process is not due to pneumococcus, remembering that the chest film is more useful in a negative sense, to exclude diagnostic possibilities, than it is to make a specific etiologic diagnosis. If a patient with a lower lobe process also has an increased bilirubin level, the only bacterial pneumonia that routinely

TABLE 5.13. Pneumonia: common bacteria—differential diagnosis.

Organism	Historical host factors	Sputum	Chest film	Pleural effusion	Cavitation	Comments
S. pneumoniae	Elderly; COPD/ CHF; alcoholism; asplenia	Encapsulated; may be blood-tinged; gram-pos. diplococci	RLL preference; multilobe involvement common; occasional bronchopneumonia pattern	Usually none but may be small unilateral effusion; empyema uncommon	None	In ETOH may have associated ABE or meningitis; ↑ bilirubin; bacteremia common
H. influenzae	Elderly; chronic care facilities/ nursing home patients; children ≤6 years old; COPD	Encapsulated pleomorphic gram-neg. bacilli	RLL common, but any lobe possible; occasional bronchopneumonia pattern	Common (⅓) small to moderate sized; empyema uncommon	None	Both encapsulated and unencapsulated strains pathogenic; bacteremia common
Group A streptococci	Postviral influenza uncommon, history of pharyngitis in 2/3	Gram-pos. cocci in chains	Lower lobe preference	Large (hydrothorax) effusion often obscuring infiltrate; empyema not uncommon	None	Pleuritic chest pain common early feature; pleural effusion fluid is serosanguineous; bacteremia occasionally
S. aureus	Usually in the postinfluenza setting; children; IV drug	Gram-pos. cocci in clusters; may be blood-tinged	No lobar predilection; multilobar involvement common	Effusion uncommon; empyema common	Early common feature; thick-walled cavitation; pneumatoceles in children	Severe hypoxemia/ cyanosis; patient clinically very "sick"; bacteremia common

Klebsiella	ETOH; chronic care facility/ nursing home patients; postviral influenza	Encapsulated plump pleomorphic gram-neg. bacilli; may be blood-tinged	Upper lobe preference; "bulging fissure sign"	Effusion uncommon; empyema common	Common thick-walled cavities	Chronic *Klebsiella* may mimic reactivation tuberculosis; bacteremia occasionally
B. catarrhalis	COPD; elderly	Gram-neg. diplococci	Lower lobe preference	None	None	Uncommon in normal hosts; resembles *H. influenzae*, *Acinetobacter*, or *N. meningitidis* on sputum Gram stain; bacteremia uncommon
E. coli	Elderly; recent urinary tract manipulation, prostatitis	Unencapsulated gram-neg. bacilli	Lower lobe preference; bronchopneumonia pattern common	Effusion uncommon; empyema not uncommon	Uncommon	Usually from antecedent or concomitant *E. coli* urinary tract infection; bacteremia common

COPD = chronic obstructive pulmonary disease; CHF = congestive heart failure; ETOH = alcohol abuse; RLL = right lower lobe; ABE = acute bacterial endocarditis.

does that is pneumococcus, not *H. influenzae* or *B. catarrhalis*. Similarly, if a patient presents with an ill-defined lower lobe infiltrate and has diarrhea, the likelihood of *Mycoplasma* or *Legionella* is enhanced. Approaching diseases in this way gives pathogens certain "profiles" that are a compilation of diagnostic clues ascribable to an organism or process.[9,10] This information for the common community-acquired bacterial pneumonias is presented in Table 5.13.

The atypical pneumonias are usually differentiated from the typical bacterial pneumonias by their less acute onset, except for *Mycoplasma* and legionnaires' disease, and by their extrapulmonary findings. All of the pathogens responsible for the atypical pneumonias cause systemic diseases that have predominant pulmonary manifestations; however, the clue to diagnosing an atypical pneumonia resides in combining the extrapulmonary features.

The chest film is most helpful for differentiating an atypical from a typical bacterial process. In general, bacterial pneumonias usually produce segmental or lobar infiltrates unless the process is a bronchopneumonia.[1,2] If the process is diffuse and ill-defined, an atypical etiology is favored. It must be kept in mind that atypical pneumonias may present with segmental or lobar infiltrations that closely resemble a bacterial pneumonia, (most characteristic of psittacosis and legionnaires' disease). Being careful never to diagnose in a vacuum solely on the basis of the chest film, the clinician should endeavor to use the extrapulmonary findings that are present with the atypical pneumonias to readily differentiate them from the bacterial pneumonias as well as from each other. A pulse temperature deficit in a patient with an ill-defined lower lobe infiltrate immediately suggests legionnaires' disease, psittacosis, or Q fever, and definitely excludes *Mycoplasma* pneumonia, tularemia, or *C. pneumoniae*.[26] Liver function abnormalities are not characteristic of typical bacterial pneumonias and immediately suggest an atypical pathogen. Elevated liver function test results argue against the diagnosis of *Mycoplasma* pneumonia, tularemia, and *C. pneumoniae*. Elevated cold agglutinins ($\geq$1:64) strongly suggest at *Mycoplasma* etiology for the patient's symptoms. Acute hoarseness usually suggests a viral pneumonia; but among the atypical pneumonias, it is a common feature of *Chlamydia pneumoniae* infection in young adults.[26] The diagnostic features of the atypical pneumonias are presented in Table 5.14.

The subacute or chronic pneumonias are a problem unto themselves. Most of these disorders are not infectious, but the common infectious etiologies include tuberculosis and the fungal pneumonias. Tuberculosis and histoplasmosis have nearly the same clinical spectrum of disease. Crytococcosis, sporotrichosis, and blastomycosis can usually be readily differentiated from tuberculosis or histoplasmosis. Reactivation tuberculosis is manifested by apical disease with or without fibrocavitary involvement of the upper lobes. Histoplasmosis may present in a similar

TABLE 5.14. Diagnostic features of atypical pneumonias.

Manifestations	Mycoplasma pneumonia	Legionnaires' disease	Psittacosis	Q fever	Tularemia	Chlamydia pneumoniae
Symptoms						
Mental confusion	−	+	±	−	−	−
Headache	±	+	+	+	−	−
Meningismus	−	−	+	−	−	−
Myalgias	+	+	+	+	−	−
Ear pain	±	−	−	−	−	±
Pleuritic pain	±	+	±	±	−	−
Abdominal pain	−	+	−	−	−	−
Diarrhea	±	+	±	±	−	−
Hoarseness	−	−	−	−	−	+
Signs						
Rash	± (erythema multiforme)	−	± (Horder's spots)	−	−	−
Raynaud's phenomenon	±	−	−	−	−	−
Nonexudative pharyngitis	+	+	−	−	−	+
Hemoptysis	−	±	±	±	−	−
Lobar consolidation	−	±	±	±	±	−
Cardiac involvement	±	±	±	±	−	−
Splenomegaly	−	−	+	−	−	−
Relative bradycardia	−	+	+	+	−	−
Chest film findings						
Infiltrate	Patchy	Patchy/ consolidation	Patchy/ consolidation	Multiple rounded pleura-based opacities	Ovoid, bodies	Single circumscribed infilitrate
Bilateral hilar adenopathy	−	−	−	−	+	−
Pleural effusion	± (small)	±	±	−	+ (bloody)	±
Laboratory findings						
WBC count	Elevated	Elevated	Normal	Normal	Normal	Normal
Hypophosphatemia	−	+	−	−	−	−
Increase in SGOT/SGPT	−	+	+	+	−	−
Cold agglutinins	+	−	−	−	−	−
Microscopic hematuria	−	+	−	−	−	−

Source: Adapted from Cunha.[21]

TABLE 5.15. Pneumonias: clinical spectrum of histoplasmosis.

Hematologic signs
Thrombocytopenia
Anemia
Leukopenia
Pancytopenia
Splenomegaly
Generalized adenopathy
Eosinophilia
Dermatologic signs
Erythema nodosum
Skin ulcers
Gastrointestinal signs
Granulomatous hepatitis
Intestinal ulceration
Pulmonary signs
"Thick-walled" cavities
Apical infiltrates
Coin lesions
Hilar adenopathy
"Buckshot" calcifications
Miliary calcifications
"Marching cavities"
Mediastinal fibrosis
Obstruction of pulmonary/artery vein[a]
Obstruction of superior vena cava[a]
Cardiac
Endocarditis
Pericarditis
Ear, nose, and throat signs
Nose ulcers
Lip ulcers
Gum ulcers
Mouth ulcers
Tongue ulcers
Laryngeal ulcers
Neurologic signs
Chronic meningitis
Other signs
Addison's disease

Source: Adapted from Cunha BA: Histoplasmosis. Infect Dis Pract 1986;9:1–8.

[a] Secondary to lymph node compression/mediastinal fibrosis.

fashion. Acute primary tuberculous pneumonia is associated with a pleural effusion, but it is not a feature of reactivation tuberculosis. Histoplasmosis in the commonest fungal disease likely to be encountered and may present in disseminated form in HIV patients and compromised hosts. Once again, the diagnostic approach involves looking for specific features (e.g., tongue ulcers, which suggest the diagnosis of histoplasmosis, or a constellation of nonspecific findings that when combined may provide as nearly specific information).[28–30] For example, a patient with pulmonary infiltrates and erythema nodosum may have tuberculosis or histoplasmosis. However, if eosinophils are present in the periphery, the diagnosis of histoplasmosis is favored because eosinophilia is not a feature of tuberculosis.[1] In this way, the diagnostic workup can be directed until a specific diagnosis is made. The many manifestations of histoplasmosis are presented in Tables 5.15 and 5.16.

TABLE 5.16. Infectious granulomatous pneumonias.

Findings	Histoplasmosis	Tuberculosis	Blastomycosis
Fever			
Double quotidian fever	−	±	−
Laboratory tests			
Pancytopenia	+[a]	+	−
Hypergammaglobulinemia	−	−	−
Leukemoid reaction	−	+	−
Chest roentgenogram			
Miliary calcification	+	±	−
Hilar adenopathy	+	−	−
Pleural effusion	−	+	−
Abdominal roentgenogram			
Liver/spleen calcification	+	−	−
Organ involvement			
Meningitis	+[a]	+	−
Oropharyngeal ulcers	+[a]	±	−
Pulmonary infiltrates	+	+	±
Endocarditis	+	−	−
Addison's disease	+[a]	+	−
Granulomatous hepatitis	+	+	±
Splenomegaly	+[a]	±	±
Generalized adenopathy	+	±	−
Intestinal ulcers	+[a]	±	−
Bone/joint lesions		+	+
Glomerulonephritis	−	−	−
Epididymoorchitis	−	+	+
Granulomatous prostatitis	+	−	+
Skin ulcers	+[a]	±	+
Erythema nodosum	+	+	±

Source: Adapted from Cunha BA: Histoplasmosis. Infect Dis Pract 1986;9:1–8.
[a] Only in disseminated histoplasmosis.

The diagnosis of nosocomial pneumonia in the febrile leukopenic compromised host, organ transplant patient, and HIV-positive patient depend on demonstrating the putative pathogen in tissue. General principles apply to these as well as other patients, but a specific diagnosis depends on a definitive test or demonstration of the organism in tissue.[39,40] One can predict, in general, the group of pathogens likely to infect an organ transplant patient early versus later but cannot differentiate among pathogens in each category. For example, cytomegalovirus (CMV) and HIV commonly coexist with PCP pneumonia in organ transplant patients. Only lung biopsy can differentiate these two disease entities, which present in a similar fashion and frequently coexist.[2,4] In the leukopenic compromised host, only generalities can be made, but these principles are nontheless useful for the initial approach to the patient. Early, after induction chemotherapy, aerobic gram-negative pathogens predominate. The longer that intravenous access devices remain, the more likely is intravenous line sepsis to occur due to gram-positive organisms or fungi. The longer the neutropenia persists, the more likely it is that a disseminated fungal mycoses will supervene. Definitive diagnosis of disseminated fungal disease depends on demonstrating tissue invasion, not superficial recovery of, the organism from mucosal surfaces.[1,3] Similarly, the HIV patient initially may present with PCP if diffuse infiltrates are present. However, focal infiltrates suggest a bacterial etiology that may be due to common pathogens or intracellular organisms (e.g., *Salmonella*, *Legionella*). HIV patients presenting with recurrent pulmonary infiltrates require a definitive diagnostic procedure, as it may be due to a variety of opportunistic pathogens as well as noninfectious diseases (e.g., Kaposi sarcoma of the lung).

In addition to clues from the history, physical examination, chest film, and laboratory tests, the clinician needs other diagnostic caveats to help with the differential diagnosis of community-acquired pneumonias. This aphorismic approach utilizing diagnostic "pearls" frequently is the way to solve complex clinical problems. Aphorisms provide bits of clinical wisdom that are helpful in telling what the diagnosis is not or in differentiating between two similar disease entities. Pneumonia aphorisms and diagnostic pulmonary pearls should be applied to the case in addition to, not instead of, the aforementioned diagnostic process.

Pneumonia Aphorisms

1. Recurrent pneumonias may be due to immunodeficiencies (antibody deficiency, complement deficiency, cell-mediated deficiency, or phagocyte disorders).

2. Hypereosinophilic immunoglobulin E (IgE) syndrome or Job syndrome is associated with recurrent pneumonitis.

3. Patients prone to recurrent pneumonia may have an underlying disorder. Do not forget to consider seizure disorder, alcoholism, intravenous drug abuse, diabetes, sickle cell anemia, renal failure, esophageal diverticulum, or tracheoesophageal fistula.

4. Kartagener syndrome is suggested by the combination of pneumonia, recurrent sinusitis, and otitis plus situs inversus.

5. Pulmonary sequestration is a development abnormality involving lung sequestered from bronchi, predisposing to recurrent pneumonia.

6. Myeloma or chronic lymphatic leukemia with pneumonia is usually due to *Hemophilus influenzae*, *Streptococcus pneumoniae*, or *Staphylococcus aureus* because of defects in patient's the B lymphocytes.

7. Selective IgA deficiency is a rare cause of recurrent pneumonias. Recurrent sinopulmonary infections are uncommon; and although IgA deficiency is the most common immunodeficiency, it is usually asymptomatic.

8. The usual pathogens in chronic granulomatous disease are *S. aureus* and occasionally gram-negative aerobic bacilli. Remember that infections with coagulase-negative organisms, streptococci, *H. influenzae*, or pneumococci are rare. Look for associated hepatosplenomegaly and lymphadenopathy.

9. The conditions associated with recurrent pneumonias include chest abnormalities: bronchogenic carcinomas, silicosis, kyphoscoliosis, previous pulmonary surgery, previous pulmonary tuberculosis, asthma, chronic bronchitis, or congestive heart failure.

10. Systemic diseases associated with recurrent pneumonias include alcoholism, diabetest, chronic lymphocytic leukemia, lymphoma, myeloma, sickle cell disease, cerebrovascular accident, neutropenia, systemic steroid treatment, hypogammaglobulinemia, and systemic lupus erythematosus (SLE).

11. Aspiration pneumonia rarely requires more than penicillin therapy, as most aspirated oral anaerobes are sensistive to most antibiotics. However, if "pigmented" oral *Bacteroides* is present in large numbers, or if *S. aureus* is present, the β-lactamases produced by these organisms inactivate penicillin, and treatment with a β-lactamase-resistant drug (e.g., clindamycin) is required.

12. Invasive *Aspergillus* infections (e.g., *Aspergillus* pneumonia) are associated with negative or low-titer *Aspergillus* precipitins in the peripheral blood. High levels of *Aspergillus* precipitins are associated with bronchopulmonary aspergillosis, which is a noninfectious immunologic reaction to the fungus.

13. Nasal cultures are worthless for the diagnosis of pneumonia, except in the case of febrile, leukopenic compromised hosts where surveillance nasal cultures positive for *Aspergillus* predict subsequent invasive or disseminated *Aspergillus* infection.

14. *Candida* pneumonia probably does not exist. Similarly *Torulopsis glabrata* pneumonias are also exceedingly rare or do not exist at all.

15. Be careful not miss the diagnosis of PCP pneumonia with a near-normal chest roentgyenogram. The patient's severe and progressive dyspnea suggesting PCP can be verified by finding a greatly reduced carbon monoxide diffusing capacity and a positive gallium scan of the lungs.

16. Cytomegalovirus (CMV) pneumonia is virtually never found in normal hosts. In immunocompromised hosts it is most commonly associated with PCP.

17. In renal transplant patients, common community-acquired organism (e.g., *S. pneumoniae*, *H. influenzae*, *S. aureus*) are important pathogens up to day 30 after transplantation and after day 120, but not during the intervening 30–120 days.

18. Viral and fungal pathogens are most common 30–120 days after renal transplant, when cell-mediated immunity is maximally depressed. Pathogens include CMV, *Nocardia*, and *Aspergillus*.

19. *Legionella* pneumonia may be community-acquired and has the same presentation when nosocomially acquired. Look for the organism in the hospital's water supply.

20. Pneumonia in a patient with herpes labialis is pneumococcal until proved otherwise. Herpes labialis occurs in up to 30% of patients with pneumococcal pneumonia.

21. Pneumococcal pneumonia may be associated with leukopenia or leukocytosis. Be wary of a patient presenting with right upper quadrant pain and isolated elevation of the bilirubin level. Indirect hyperbilirubinemia may be a clue to pneumococcal pneumonia or represent Dubin-Johnson syndrome in a patient with a pneumonia due to another etiology.

22. Asplenic individuals may present with fulminant shock and sepsis disseminated intravascular coagulation (DIC) due to overwhelming pneumococcal infection, which rarely can produce the same picture in apparently "normal" individuals.

23. Pneumococcal empyema is unusual today, and pleural effusion is uncommon.

24. Complete histologic resolution is the rule with pneumococcal pneumonia; however, delayed resolution of pneumococcal pneumonia may take up to 14 weeks.

25. Pneumococcal bacteremia is particularly associated with cirrhosis, hypergammaglobulinemia, and asplenism.

26. The pneumococcal vaccine does not protect everyone who is immunized. Serotypes in the pneumococcal vaccine do not represent all organisms responsible for pneumococcal pneumonria. Furthermore, compromised hosts have impaired antibody responses that frequently result in inadequate or no protection.

27. More than 60% of patients with group A streptococcal pneumonia have an antecedent history of pharyngitis, but only 20% of these patients have positive throat cultures for the organism.

28. With group A streptococcal pneumonia, the higher the pleural fluid white blood cell count is over 20,000 cells/mm^3, the more likely is empyema.

29. The longer the chains of streptococci in Gram-stained sputum, the more pathogenic and virulent is the organism.

30. Group A streptococcal pneumonia is characterized in virtually all cases by large pleural effusions. Persistent pleuritic chest pain heralds empyema.

31. Group B streptococcal pneumonia occurs only in neonates and is the most common manifestation of early-onset group B streptococcal infection. The chest film appearance mimics that of pneumococcal pneumonia, but cyanosis is a clue to the group B streptococcal etiology.

32. Staphylococcal pneumonia follows not only viral influenza infection but may follow measles or other minor upper or lower respiratory infections.

33. Pneumothorax commonly is associated with staphylococcal pneumonia, but pneumatoceles are found primarily in children and not adults.

34. After viral influenza, *S. aureus* is the most common pathogen, but pneumococcus, *H. influenzae*, and *Klebsiella* should also be considered.

35. Staphylococcal pneumonia is characterized by widely scattered pulmonary infiltrates, but pneumatoceles and consolidation are unusual. Multiple abscesses that cavitate occur in approximately 25% of cases.

36. *Nocardia* species are obligate aerobes, are weakly acid-fast, and produce branching filaments. In contrast, *Actinomyces* are anaerobic, are non-acid-fast, and have sulfa granules.

37. Aspiration pneumonia that occurs after a week or more of hospitalization should be treated as a nosocomial pneumonia because "hospital" flora are aspirated. For this reason, specific antianaerobic coverage should not be added to the regimen.

38. *Acinetobacter* pneumonia is nearly always nosocomial, and its treatment includes respiratory support equipment. Be wary because *Acinetobacter* is a common nosocomial colonizer of the wounds, skin, and sputum.

39. *Serratia* pneumonia is uncommon; and when it does occur, it does not cavitate.

40. Community-acquired *Acinetobacter* pneumonia is rare but is as sociated with positive blood cultures, whereas nosocomial *Acinetobacter* infection is never associated with bacteremia.

41. Chronic *Klebsiella* pneumonia resembles tuberculosis. However, chronic *Klebsiella* pneumonia is associated with thin-walled cavities, unlike *Mycobacterium* tuberculosis, which is associated with thick-walled cavities.

In addition, the sputum shows gram-negative encapsulated bacilli with *Klebsiella* pneumonia and not with pulmonary tuberculosis.

42. *Proteus* pneumonia is the only nosocomial pneumonia with a predisposition for the upper lobes.

43. *Pseudomonas* pneumonia is always nosocomial except in patients with cystic fibrosis.

44. Virtually all *Proteus* pneumonias originate from the urinary tract. On roentgenogram, *Proteus* pneumonia resembles *Klebsiella* pneumonia, except that cavitation is unusual. In a patient with an antecedent history of urinary tract infection, *Escherichia coli* and *Proteus* pneumonias are the most likely diagnostic possibilities.

45. Hemoptysis associated with a nosocomial pneumonia suggests *Serratia marcescens* pneumonia. It may be differentiated from true hemoptysis of testing the sputum for hemoglobin. Pseudohemoptysis is related to prodigiosin, which gives the red color to sputum.

46. A "pertussoid cough" in a young infant with peripheral eosinophilia suggests *Chlamydia* rather than *Bordetella* pertussis.

47. In a child with pneumonia, more than 60% lymphocytes on the peripheral smear suggests pertussis. The "shaggy heart sign" may be seen on chest roentgenogram.

48. The only pneumonias associated with epistaxis are psittacosis and pertussis. Subconjunctival hemorrhage in the pneumonia patient immediately suggests pertussis.

49. Meningococcal pneumonia occurs primarily in closed military recruit populations and is usually due to group Y serotypes. The usual presentation is that of a diffuse bronchopneumonia, and bacteremia occurs in fewer than 10% of patients.

50. The only pneumonia presenting with a low serum phosphorus level in the absence of other causes of hypophosphatemia is that due to *Legionella*.

51. Ovoid densities on the chest film suggest *Legionella micdadei*, tularemia, or adenoviral pneumonia.

52. With primary tuberculous pneumonia with a large effusion, the PPD test is often negative. Primary tuberculosis, which occurs most of ten in the very young and the very old, is characterized by a lower lobe infiltrate and a pleural effusion.

53. False-positive tuberculin skin tests may be attributed to technical difficulties, nonspecific pertubations and immunity such as from recent acute viral infections (e.g., measles, Ebstein-Barr virus, CMV), steroid therapy, dehydration, malnutrition, hypothyroidism, and old age. Viral immunization, sarcoidosis, immunosuppressive therapy, radiotherapy, and lymphoreticular malignancies may also be responsible for a negative skin test.

54. Be careful not to miss tuberculosis (TB) with a negative PPD if the patient has primary TB with a large tuberculous effusion, miliary TB, far-

advanced TB, or very early TB. The patient can also have TB and be rendered anergic by a superimposed disease (e.g., HIV infection).

55. Cold agglutinin titers seen in *Mycoplasma* infection peak during the second and third weeks of illness. Cold agglutinins are IgM antibodies that bind to the big I antigen on the erythrocyte.

56. A lobar infiltrate with consolidation in the absence of pleuritic chest pain suggests psittacosis. Splenomegaly occurs in 10–70% of patients with psittacosis. Splenomegaly in a patient with pneumonia suggests psittacosis or Q fever.

57. Respiratory syncytial virus (RSV) causes tracheobronchitis in adults but pneumonia in children.

58. Measles pneumonia predominantly involves the lower lobes, and the disease parallels the cutaneous manifestations. Measles pneumonia may be fatal in severely immunocompromised hosts and in the very young and the malnourished patient.

59. *Staphylococcus aureus*, pneumococcus, and *H. influenzae* are the most common pathogens in postmeasles pneumonia.

60. Ebstein-Barr virus (EBV) mononucleosis rarely presents with interstitial infiltrates. Hilar adenopathy, paratracheal node enlargement, and pleural effusions have been reported. Patients with EBV mononucleosis do not get secondary bacterial pneumonias.

61. The patient with pneumonia and skin petechial hemorrhages or purpura, not in shock or in DIC, suggests adenvirus as a cause.

62. The physical examination in viral influenza pneumonia patients is unremarkable, as is the chest film. Rales and rhonchi in these patients suggest superimposed bacterial pneumonia.

63. Secondary bacterial pneumonia in a patient with viral influenza usually occurs about a week after the beginning of the influenza illness when the patient is clinicallyimproving. There is a recrudescence of fever, and the chest film shows a segmental or lobar defect.

64. Uncomplicated asthma is not associated with pulmonary infiltrates or fever.

65. Aspergillomas have been associated with chronic cavitary pulmonary diseases including tuberculosis, histoplasmosis, sarcoidosis, and ankylosing spondylitis. *Aspergillus* precipitins are positive in 80% or more of patients. The chest film usually reveals a soft-tissue density surrounding by a crescent of air that delineates the fungus ball in the cavity.

66. Invasive pulmonary aspergillosis occurs only in severely immunocompromised hosts (e.g., patients with leukemia or lymphoma, those on chemotherapy, renal transplant patiens). Do not forget that invasive aspergillosis is also associated with prolonged treatment with antibiotics and therapy with corticosteroids.

67. The diagnosis of all invasive fungal infections of the lung requires biopsy proof of tissue invasion. Mere recovery of an organism from a

protected brush or bronchoalveolar lavage (BAL) specimen does not prove its pathogenicity in the lung.

68. Blastomycosis does not involve the gastrointestinal tract or the central nervous system. Calcification is not a feature of blastomycosis.

69. Crytococcal pneumonia sometimes is characterized by blood-streaked sputum and pleuritic chest pain. Cryptococcal pneumonia occurs almost always in immunosuppressed individuals. Sputum cultures are usually negative with cryptococcal pneumonia. If skin lesions are present, they should be biopsied, as the organism is present in large numbers in these lesions.

70. In a patient with pneumonia and meningitis, do not fail to consider cryptococci, tuberculosis, *Toxoplasma*, CMV, *Nocardia*, legionnaires' disease, or *Mycoplasma* meningoencephalitis.

71. Herpes simplex meningitis is rarely if ever associated with herpes pneumonitis.

72. The patient with malaria may have noncardiac pulmonary edema or adult respiratory distress syndrome (ARDS), but pulmonary infiltrates are not due to secondary pneumonia.

73. An elevated right hemidiaphragm in association with pulmonary infiltrates suggests amebiasis or echinococcosis. Neither of these diseases is associated with peripheral eosinophilia.

74. Except with congenitally acquired disease, toxoplasmosis never causes pneumonia by itself in adults. Toxoplasmosis is a common co-pathogen in patients with HIV. Lung infiltrates due to *Toxoplasma* are difficult to differentiate from those due to other pathogens. LUNG Biopsy is needed for a definitive diagnosis.

75. Eosinophilia is uncommon with dog heartworm (Dirofilaria immitis). The chest film shows one or more coin lesions, but most patients are asymptomatic. Some have chest pain, cough, fever, or hemoptysis.

76. In a patient with hemoptysis from Southeast Asia, tuberculosis, melioidosis, or paragonamiasis should be considered. Be careful not to forget that paragonamiasis frequently coexists with pulmonary tuberculosis.

77. Bacterial pneumonia can activate quiescent tuberculosis, a common phenomenon in elderly patients. Therefore if an elderly patient is recovering from a bacterial pneumonia and subsequently becomes worse and develops a new pulmonary infiltrate, consider reactivated tuberculosis in the differential diagnosis.

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