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(英文原版)

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Fourth Edition

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Edited by
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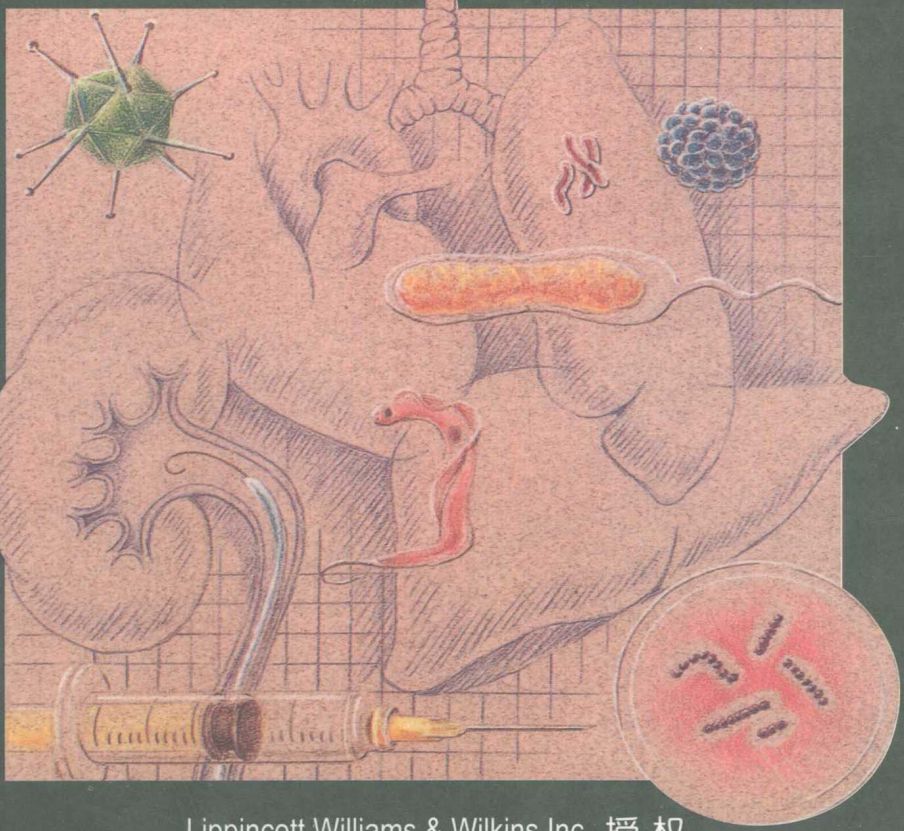

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Manual of Clinical Problems in Infectious Disease

FOURTH EDITION

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To my loving wife, Roberta, and our children Kimberly and David, as they pursue life's journey. To my parents, Joseph and Frances, for their invaluable support.—NMG

Many thanks to Bonnie, Scott, and Robin for providing a nurturing environment in which to work, and to Loxley for licking my feet during moments of stress.—RBB

To my parents, Sidney and Fritzie, for the value they placed on my education.—SLB

To my precious wife, Janet, and to my beloved children, Michael, Elizabeth, and Paul, for their abiding patience and support.—ALE

To my wife, Brenda, for her encouragement.—RAG

PREFACE

In 1979, at the request of our students and house officers, we prepared the first edition of *Manual of Clinical Problems in Infectious Disease.* At that time, our aim was to provide medical students, house officers, and practitioners with a contemporary approach to selected problems in infectious disease; key annotated references supported the text.

In 1986, with the help of two additional authors, Drs. Richard Brown and Anthony Esposito, the second edition of *Manual of Clinical Problems in Infectious Disease* was published and covered a list of new subjects.

Since that time, numerous new infectious agents have been recognized, new concepts have evolved, and new treatments have emerged. For the third edition, to satisfy the need for a contemporary text addressing this information, we prepared a new list of subjects and added Dr. Steven Berk to our team.

The fourth edition of *Manual of Clinical Problems in Infectious Disease* is not simply an updated version of the three earlier books: it reexamines some older material and explores new subjects such as Hepatitis C and VRE. Every effort has been made to add contemporary references to the text to enhance the accuracy of the manual and to provide a springboard for further reading; all references are annotated.

Like the three previous editions, this manual is not meant to be all-inclusive. Numerous major texts that fulfill this mission have already been published. The fourth edition of *Manual of Clinical Problems in Infectious Disease* represents an attempt to provide contemporary, scientifically accurate, and readable material on topics of concern to the practicing physician, house officer, and medical student. All of the editors are clinicians who see patients on a regular basis, and have written chapters based on a "real world" approach to patient care while keeping with a scientific basis of management. Chapters have been added, removed, or revised in keeping with changes in infectious diseases over the past five years. We are proud of our effort, and feel that this book will prove valuable to the clinician in the day-to-day management of patients with infections.

N.M.G.
R.B.B.
S.L.B.
A.L.E.
R.A.G.

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I. UPPER RESPIRATORY TRACT

1. TONSILLOPHARYNGITIS IN ADULTS

Tonsillopharyngitis (more simply, pharyngitis) is a common complaint characterized by inflammation of the mucous membranes of the throat. Erythema is generally present, but exudate is variably noted. Less commonly, ulceration or a membrane can be seen. Up to 40 million office visits are made annually by persons of all ages because of this illness, primarily during colder seasons, and it may account for up to 100 million days lost from work each year. Many patients and clinicians are aware of the importance of group A β-hemolytic streptococci (*Streptococcus pyogenes*) as a cause of pharyngitis, and concern for this pathogen must be a major focus in the management of sore throat. It is also felt to be the only commonly encountered pathogen for which treatment is clearly indicated. However, numerous other potentially treatable causes of this illness exist, and most cases of pharyngitis in adults are not caused by *S. pyogenes*. Table 1-1 lists some etiologies that need to be considered in the differential diagnosis of pharyngitis in adults. Patients who are immunosuppressed may be infected with additional pathogens—for example, enteric gram-negative bacilli or mixed anaerobes (granulocytopenia) and *Candida albicans* (T cell-mediated immunosuppression, HIV infection). Furthermore, HIV itself may be a cause of pharyngitis.

The clinical presentation of pharyngitis is usually a soreness in the throat. Dysphagia may also be noted, and if the uvula is involved, a rather discomforting feeling of a "lump" when swallowing may be felt. A major responsibility of all clinicians is to distinguish treatable from untreatable disease and to recognize potential complications. An important component of this process is the history. As an example, a sexual history may help define the likelihood of *Neisseria gonorrhoeae* pharyngitis, whereas an immunization history will help define the possibility of diphtheria. Risk factors for HIV infection should always be assessed. A patient's inability to manage secretions or severe dysphagia should alert the clinician to epiglottitis or abscess. Constitutional symptoms are variable. In many instances, initial assessment will not allow differentiation among etiologies. Streptococcal and adenoviral pharyngitis are commonly accompanied by significant fever; chills may also be present. The onset is generally abrupt, and patients are ill. Physical examination reveals pharyngeal erythema, and exudate is noted in at least 50% of cases. Exudate is uncommon in rhinovirus, coxsackievirus, and herpes simplex virus pharyngitis. Anterior cervical adenopathy often exists with streptococcal infection. Alternatively, the presence of posterior cervical adenopathy, laryngitis, diarrhea, or rhinorrhea generally indicates a viral etiology, and these symptoms have a negative predictive value of about 80% for disease caused by *S. pyogenes*. Infectious mononucleosis is often associated with severe pharyngitis, but other evidence of this disease is often present.

Gram's stain of pharyngeal exudate is an underemployed test that may be useful in determining the etiology of pharyngitis. In trained hands, groupable streptococci can be identified. The presence of polymorphonuclear leukocytes suggests bacterial or adenoviral infection. Additionally, although little literature exists, experience should allow differentiation of *Neisseria* species, *Haemophilus influenzae,* and *Corynebacterium* species (*C. diphtheriae* or *C. hemolyticum*). Infection with Epstein-Barr virus (EBV) is often associated with exudative pharyngitis; however, Gram's stain demonstrates only mixed organisms and no polymorphonuclear leukocytes. In the presence of EBV, Gram's stain demonstrating polymorphonuclear leukocytes suggests a confounding bacterial infection, usually with *S. pyogenes.*

A complete physical examination may help to identify the infection; splenomegaly or generalized lymphadenopathy with EBV, *S. pyogenes* with scarlet fever, *C. hemolyticum* with scarlatiniform or urticarial rash, adenovirus with conjunctivitis, *N. gonorrhoeae* with rectal or genital disease or disseminated infection, and *Mycoplasma pneumoniae* with pneumonia.

An immediate goal in the evaluation of pharyngitis is to detect cases caused by *S. pyogenes.* Although culture for *S. pyogenes* remains the gold standard for diagnosis, antigen testing of material from the tonsillopharyngeal area is the most expeditious means of identifying the organism. It is sensitive (80% to 90%) and specific (>95%) and

Table 1-1. Notable causes of pharyngitis in adults and percentages of cases

Bacterial/treatable	Viral/untreatable (42)
Streptococcus pyogenes (5–20)	Rhinovirus
Other "groupable" streptococci (6)	Adenovirus (19)
Haemophilus influenzae	Epstein-Barr virus (7–15)
Arcanobacterium hemolyticum (0.4–2)	Cytomegalovirus
Corynebacterium diphtheriae (rare)	Respiratory syncitial virus (2)
Neisseria gonorrhoeae (rare)	Myxovirus (10)
Mycoplasma pneumoniae (10–13)	
Chlamydia pneumoniae	

* Adapted from Carroll K, Reimer L. Microbiology and laboratory diagnosis of upper respiratory tract infections. *Clin Infect Dis* 1996; 23:442–448.

provides information while the patient is still in the office. The test results may be adversely affected if performed by unskilled personnel. A positive test result should prompt therapy. A negative test result should be followed by formal culture for this and possibly other bacterial pathogens, based on epidemiologic information. The easiest method is to swab the throat simultaneously with two swabs. If the first swab (for antigen detection) is negative, the second can be formally cultured. It is extremely important to sample the posterior pharynx and tonsils because yields from the tongue, gums, buccal mucosa, and other areas are far lower. *H. influenzae, C. hemolyticum,* and *N. gonorrhoeae* require special media and will not be identified by standard culture techniques or antigen-detection systems. Thus, when they are suspected, the clinician must communicate directly with the microbiology laboratory to access appropriate media and techniques.

A recent survey of board-certified pediatricians was conducted to determine actual practice patterns for the management of presumed streptococcal pharyngitis. Rapid tests were employed by about 64% of respondents, whereas 85% employed cultures. Only 42% of physicians in the survey employed the protocol of rapid test followed by culture if the result of the rapid test was negative. A third of physicians routinely discontinued antibiotics if studies for *S. pyogenes* were negative. Patients who are known to be immunosuppressed by virtue of underlying disease or therapy should be evaluated for other potential pathogens. Alternatively, persons who are demonstrated to have unusual etiologies or fail to respond to standard therapy may require evaluation for underlying diseases. For example, a patient with oral thrush should be evaluated for infection with HIV unless another risk factor is known. Similarly, when a patient has severe, unresolving pharyngitis, a CBC should be performed to assess for EBV or granulocytopenia.

Specific Etiologies of Pharyngitis

Groupable Streptococci

Streptococci remain the most commonly identified cause of sore throat. *S. pyogenes* is the most common and important of these organisms, but other groupable streptococci, including groups C and G, have been implicated. These may be associated with large food-borne or respiratory droplet outbreaks. However, only *S. pyogenes* is associated with rheumatic fever. Group C streptococcal pharyngitis has also been associated with glomerulonephritis. Reasons to treat *S. pyogenes* pharyngitis include (a) relief of symptoms, (b) prevention of spread, (c) prevention of immunologic sequelae, and (d) prevention of local suppurative complications. Rheumatic fever complicates *S. pyogenes* infections of the throat and can be prevented by administration of an appropriate antimicrobial agent within 8 to 9 days of disease onset. There is no evidence that poststreptococcal glomerulonephritis is preventable by use of antimicrobial agents. The most common local suppurative complication is peritonsillar abscess. Typical presentation is that of ongoing, generally unilateral pharyngitis and constitutional symptoms, often associated with dysphagia and the presence of a mass on digital palpation