45 - 162 Haemophilus and Moraxella Infections

162 Haemophilus and Moraxella Infections

Gonococcal meningitis and endocarditis should be treated in the hospital with high-dose IV ceftriaxone (1–2 g IV every 12–24 h); therapy should continue for 10–14 days for meningitis and for at least 4 weeks for endocarditis. All persons who experience more than one episode of DGI should be evaluated for complement deficiency.

■ ■PREVENTION AND CONTROL Condoms, if properly used, provide effective protection against the transmission and acquisition of gonorrhea as well as other infections that are transmitted to and from genital mucosal surfaces. Spermici dal preparations used with a diaphragm or cervical sponges impreg nated with nonoxynol-9 offer some protection against gonorrhea and chlamydial infection. However, the frequent use of preparations that contain nonoxynol-9 is associated with mucosal disruption that paradoxically may enhance the risk of HIV infection in the event of exposure. All patients should be instructed to refer sex partners for evaluation and treatment. All sex partners of persons with gonorrhea should be evaluated and treated for N. gonorrhoeae and C. trachomatis infections if their last contact with the patient took place within

60 days before the onset of symptoms or the diagnosis of infection in the patient. If the patient's last potential sexual exposure to infection was >60 days before onset of symptoms or diagnosis, the patient's most recent sex partner should be treated. Partner-delivered medications or prescriptions for medications to treat gonorrhea and chlamydial infec tion diminish the likelihood of reinfection (or relapse) in the infected patient. This approach is permissible (or potentially allowable) in all 50 states and is an option for partner management. Patients should be instructed to abstain from sexual intercourse until therapy is com pleted and until they and their sex partners no longer have symptoms. Greater emphasis must be placed on prevention by public health education, individual patient counseling, and behavior modification, particularly the use of condoms. Sexually active persons, especially adolescents, should be offered screening for STIs. For most male patients, NAAT of urine or a urethral swab may be used for screening. Preventing the spread of gonorrhea may help reduce the transmis sion of HIV. No effective vaccine for gonorrhea is yet available, but efforts to test several candidates are underway including a field trial of a licensed group B meningococcal vaccine (4CMenB or Bexsero®), which in retrospective epidemiologic analyses has been associated with reduced rates of gonorrhea. PART 5 Infectious Diseases ■ ■FURTHER READING Bolan GA et al: The emerging threat of untreatable gonococcal infec tion. N Engl J Med 366:485, 2012. Bolan GA et al: Morb Mortal Wkly Rep 70 (No. 4), 2021. Gonococcal Infections, in Sexually Transmitted Infections Treatment Guidelines, 2021. U.S. Centers

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Haemophilus and

Moraxella Infections HAEMOPHILUS INFLUENZAE ■ ■MICROBIOLOGY Haemophilus influenzae was first recognized in 1892 by Pfeiffer, who erroneously concluded that the bacterium was the cause of influenza. H. influenzae is a small (1- × 0.3-µm) gram-negative organism of vari able shape; thus, it is often described as a pleomorphic coccobacillus. In clinical specimens such as cerebrospinal fluid (CSF) and sputum,

H. influenzae frequently stains only faintly with safranin and therefore can easily be overlooked. H. influenzae grows both aerobically and anaerobically. As the Latin name implies, Haemophilus is the “blood-loving bacterium.” A prereq uisite for growth is a requirement for the media to contain blood, but the blood substrate needs to be preheated; hence, H. influenzae grows on chocolate agar plates (slowly heated to 80°C [176°F]), whereas ordinary blood plates (without preheating) will not sustain growth. Its aerobic growth requires two factors: hemin (designated X factor) and nicotinamide adenine dinucleotide (V factor). While MALDI-ToF (Matrix-Assisted Laser Desorption/Ionization - Time of Flight) is now widely used for bacterial identification, these requirements are still sometimes applied in clinical laboratories. However, using phenotypic methods for differentiating among Haemophilus species has limitations, as the growing number of whole-genome sequences of Haemophilus isolates from the human respiratory tract is revealing complex genetic relationships among Haemophilus species (see “Diagnosis,” below). Six major serotypes of H. influenzae have been identified; designated a through f, they are based on antigenically distinct polysaccharide capsules. In addition, some strains lack a polysaccharide capsule and are referred to as nontypeable strains. Type b and nontypeable strains are the most relevant strains clinically (Table 162-1), although encapsulated strains other than type b can cause disease. An H. influ enzae type b isolate was the first free-living organism to have its entire genome sequenced in the early 1990s. The antigenically distinct type b capsule is a linear polymer composed of ribosyl-ribitol phosphate. Strains of H. influenzae type b (Hib) cause disease primarily in infants and children <6 years of age, although it is nowadays rare due to effective vaccine campaigns. Nontypeable strains are primarily mucosal pathogens but occasionally cause invasive disease, particularly in immunocompromised hosts and the elderly. ■ ■EPIDEMIOLOGY AND TRANSMISSION H. influenzae, an exclusively human pathogen, is spread by airborne droplets or by

direct contact with secretions or fomites. Between TABLE 162-1 Characteristics of Type b and Nontypeable Strains of Haemophilus influenzae FEATURE TYPE b STRAINS NONTYPEABLE STRAINS Capsule Ribosyl-ribitol phosphate Unencapsulated Pathogenesis Invasive infections due to hematogenous spread Mucosal infections due to contiguous spread Clinical manifestations Meningitis and invasive infections in incompletely immunized infants and children Otitis media in infants and children; lower respiratory tract infections in adults with chronic bronchitis Evolutionary history Basically clonal Genetically diverse Vaccine Highly effective conjugate vaccines Protein D used as carrier protein in pneumococcal vaccine approved in Europe: GSK Synflorix. Others under development

30 and 60% of healthy preschool children are intermittent carriers. Colonization with nontypeable H. influenzae is a dynamic process; new strains are acquired and other strains are replaced periodically. This is particularly evident in patients with chronic obstructive pulmonary disease (COPD). The widespread use of Hib conjugate vaccines in many indus trialized countries has resulted in striking decreases in the rate of nasopharyngeal colonization by Hib and in the incidence of Hib infection (Fig. 162-1). On a global basis, invasive Hib disease occurs predominantly in unimmunized children and in those who have not completed the primary immunization series. Most World Health Organization member countries have introduced Hib conjugate vac cination, but a large number of the world’s children remain unimmu nized, principally in countries without national vaccine programs. In addition to immunocompromised hosts, certain groups have a higher incidence of invasive disease with encapsulated H. influenzae (along with capsular serotypes other than Hib) than the general population, including African Americans, Australian Aboriginal children, and Native American groups. Although this increased incidence has not yet been accounted for, several factors may be relevant, including age at exposure to the bacterial species, socioeconomic conditions, and genetic differences. ■ ■PATHOGENESIS Hib strains cause systemic disease by invasion and hematogenous spread from the respiratory tract to distant sites such as the meninges, Incidence of Invasive H. influenzae Disease, United States Hib Non-b serotypes Nontypeable

Incidence per 100,000

A Estimated U.S. Incidence of Invasive H. influenzae Disease by Age Group and Serotype

Incidence per 100,000

<1 ≥65 50–64 35–49 18–34 Age (years) 1–4 5–17 ABCs cases from 2018–2022 and estimated to the U.S. population *2022 data are preliminary B FIGURE 162-1 Estimated incidence rates (per 100,000) of invasive disease due to Haemophilus influenzae caused by Hib, non-b serotypes, and nontypeable bacteria in the United States, 1994–2022. A. Disease caused by Hib remains low. In 2020–2021, disease caused by non-b serotypes and nontypeable bacteria increased. B. Estimated incidence rates (per 100,000) of invasive H. influenzae disease by serotype and age in the United States, 2018–2022. (Source: Active Bacterial Core surveillance, Centers for Disease Control and Prevention, https://www.cdc.gov/hi-disease/surveillance.html.)

bones, and joints. The type b polysaccharide capsule is an important virulence factor affecting the bacterium’s ability to avoid opsonization and cause systemic disease.

Nontypeable strains cause disease by local invasion of mucosal sur faces. Otitis media results when bacteria reach the middle ear by way of the eustachian tube. Adults with COPD experience recurrent lower respiratory tract infection due to nontypeable strains. In addition, nontypeable H. influenzae persist in the lower airways of adults with COPD in both extracellular and intracellular locations, contributing to the airway inflammation that is a hallmark of the disease. Nontypeable strains that cause infection in adults with COPD differ in pathogenic potential and genome content from strains that cause otitis media. In the middle ear, nontypeable strains form biofilms. More resistant to host clearance mechanisms and to antibiotics than are planktonic bac teria, biofilms are associated with chronic and recurrent otitis media. Nontypeable H. influenzae persist in the human respiratory tract and cause infection by altering expression of genes through slipped-strand mispairing and through phase-variable expression of DNA methylase genes that control the expression of multiple genes that play a role in virulence. The incidence of invasive disease caused by nontypeable strains is low but appears to have increased over the past decade; one possible explanation for this increase might be that unencapsulated and hence nontypeable H. influenzae were overlooked in the past during the pre vaccine era due to the high incidence of Hib. Most strains that cause invasive disease are genetically and phenotypically diverse. ■ ■IMMUNE RESPONSE Antibody to the capsule is important in protection from infection by Hib strains. The level of (maternally acquired) serum antibody to the capsular polysaccha ride, which is a polymer of polyribitol ribose phosphate (PRP), declines from birth to 6 months of age and, in the absence of vaccination, remains low until ~2 or 3 years of age. The age at the antibody nadir correlates with that of the peak incidence of type b disease. Antibody to PRP then appears partly due to exposure to Hib or cross-reacting antigens. Systemic Hib disease is unusual after the age of 6 years because of the presence of protective antibody. Vaccines in which PRP is conju gated to protein carrier molecules have been developed and are now used widely. These vaccines generate an antibody response to PRP in infants and effectively prevent invasive infections in infants and children. CHAPTER 162 Haemophilus and Moraxella Infections Since nontypeable strains lack a capsule, the immune response to infection is directed at noncapsu lar antigens. These antigens have generated consider able interest as immune targets and potential vaccine components. The human immune response to non typeable strains appears to be strain-specific, a charac teristic that accounts in part for the propensity of these strains to cause recurrent otitis media and recurrent exacerbations of chronic bronchitis in immunocom petent hosts. Hia Hib Hic Hid Hie Hif Non-typeable ■ ■CLINICAL MANIFESTATIONS Hib The most serious manifestation of infection with Hib is meningitis (Chap. 143), which primarily affects children <2 years of age. The clinical manifesta tions of Hib meningitis are similar to those of menin gitis caused by other bacterial pathogens. Fever and altered central nervous system function are the most common features at presentation. Nuchal rigidity may or may not be evident. Subdural effusion, the most common complication, is suspected when, despite 2 or 3 days of appropriate antibiotic therapy, the infant has seizures, hemiparesis, or continued obtundation. The overall mortality rate from Hib meningitis is ~5%, and the morbidity rate is high. Of survivors, 6% have

permanent sensorineural hearing loss, and about one-fourth have a significant disability of some type. If more subtle disabilities are sought, up to half of survivors are found to have some neurologic sequelae, such as partial hearing loss and delayed language development.

Epiglottitis (Chap. 37) is a life-threatening Hib infection involving cellulitis of the epiglottis and supraglottic tissues. It can lead to acute upper-airway obstruction. Its unique epidemiologic

features are its occurrence in an older age group (2–7 years old) than other Hib infec tions and its absence among Navajo Native Americans and Alaskan Eskimos. Sore throat and fever rapidly progress to dysphagia, drooling, and airway obstruction. In countries with Hib vaccine child immuniza tion programs, epiglottitis now occurs primarily in adults. Cellulitis (Chap. 134) due to Hib occurs in young children. The most common location is on the head or neck; the involved area some times takes on a characteristic bluish-red color. Most patients have bacteremia, and 10% have an additional focus of infection. Hib causes pneumonia in infants. The infection is clinically indistin guishable from other types of bacterial pneumonia (e.g., pneumococcal pneumonia) except that Hib is more likely to involve the pleura. Several less common invasive conditions can be important clinical manifesta tions of Hib infection in children. These include osteomyelitis, septic arthritis, pericarditis, orbital cellulitis, endophthalmitis, urinary tract infection, abscesses, and bacteremia without an identifiable focus. Non–type b encapsulated strains of H. influenzae (types a, c, d, e, and f) are unusual causes of invasive infection manifested predomi nantly by bacteremia and pneumonia. H. influenzae type a infections are seen with increased frequency in indigenous populations of North America, and these strains are predominantly clonal. Most infections due to non–type b encapsulated strains occur in the setting of underly ing conditions including immunosuppression. PART 5 Infectious Diseases Nontypeable H. influenzae Nontypeable H. influenzae is the most common bacterial cause of exacerbations of COPD; these exacerba tions are characterized by increased cough, sputum production, and shortness of breath. Fever is low-grade, and no infiltrates are evident on chest x-ray. Nontypeable strains also cause community-acquired bacterial pneumonia in adults, especially among patients with COPD or HIV or other immunocompromised hosts. The clinical features of H. influenzae pneumonia are similar to those of other types of bacte rial pneumonia, including pneumococcal pneumonia. In recent years, pneumonia due to nontypeable H. influenzae has been more common than pneumonia caused by Streptococcus pneumoniae (Fig. 162-2). Nontypeable H. influenzae is one of the three most common causes of childhood otitis media (the other two being S. pneumoniae and Moraxella catarrhalis) (Chap. 37). Infants are febrile and irritable, while older children report ear pain. Symptoms of viral upper-respi ratory infection often precede otitis media. The diagnosis is made by M. catarrhalis (12%) H. influenzae (33%) S. aureus (12%) Other microbes (15%) S. pneumoniae (5%) S. pneumoniae (28%) A FIGURE 162-2. Importance of nontypeable Haemophilus influenzae and Moraxella catarrhalis in community-acquired pneumonia (CAP) and in exacerbations of COPD patients. A. Meta-analysis of bacterial detection in lower respiratory tract specimens using molecular panels or quantitative assays from patients with CAP. B. Cumulative results of a prospective study (1994–2004) of bacterial infection in chronic obstructive pulmonary disease (COPD) showing etiology of exacerbations. Numbers of exacerbations shown indicate acquisition of a new strain simultaneous with clinical symptoms of an exacerbation. (Data source for A: NJ Gadsby et al: Clin Infect Dis 62:817, 2016; DN Gilbert et al: Diagn Microbiol Infect Dis 99:115246, 2021; S Serigstad et al: Sci Rep 12:326, 2022; M Fally et al: Infect Dis (Lond) 53:122, 2021.)

pneumatic otoscopy. An etiologic diagnosis, although not routinely sought, can be established by tympanocentesis and culture of middleear fluid. Clinical features associated with H. influenzae otitis media include a history of recurrent episodes, treatment failure, concomitant conjunctivitis, bilateral otitis media, and recent antimicrobial therapy. The increasing use of pneumococcal polysaccharide conjugate vaccines in most countries has resulted in an overall decrease in otitis media and its complications. However, a relative increase in the proportion of otitis media caused by H. influenzae in children failing initial anti microbial therapy or with recurrent episodes has

occurred. Contin ued monitoring of the incidence and etiology of otitis media will be important. Nontypeable H. influenzae also causes puerperal sepsis and is an important cause of neonatal bacteremia. These nontypeable strains, provisionally named Haemophilus quentini, are closely related to but distinct from H. haemolyticus, tend to be of biotype IV, and cause inva sive disease after colonizing the female genital tract. Nontypeable H. influenzae causes sinusitis (Chap. 37) in adults and children. In addition, the bacterium is a less common cause of various invasive infections. These infections include bacteremia, empyema, adult epiglottitis, pericarditis, cellulitis, septic arthritis, osteomyelitis, endocarditis, cholecystitis, intraabdominal infections, urinary tract infections, mastoiditis, and aortic graft infection. Most H. influenzae invasive infections in countries where Hib vaccines are used widely are caused by nontypeable strains, and a recent increased incidence of such infections has been observed. Although most strains of nontypeable

H. influenzae that cause invasive infections are genetically diverse, recent localized clusters of infections have been caused by clonally related strains. Continued monitoring will be important. Many patients with H. influenzae bacteremia have an underlying condition, such as HIV infection, cardiopulmonary disease, alcoholism, or cancer. ■ ■DIAGNOSIS The most reliable method for establishing a diagnosis of invasive

H. influenzae infection is recovery of the organism in culture in a normally sterile body site, such as blood, CSF, or joint fluid. Isolation of bacteria is important for antimicrobial susceptibility testing. Rapid polymerase chain reactions (PCR) and other DNA-based methods are commonly used in modern clinical laboratories. H. influenzae isolated from the respiratory tract must be distin guished from a complex flora and from other Haemophilus species. Particular caution must be used to distinguish H. influenzae from Haemophilus haemolyticus, a respiratory tract commensal with identi cal growth requirements. H. haemolyticus has classically been distin guished from H. influenzae by the hemolysis of the former species on horse blood agar. However, a significant proportion of isolates of H. haemolyticus have now been recognized as nonhemolytic. Analysis of M. catarrhalis (39%) H. influenzae (48%) P. aeruginosa (8%) B

various genotypic markers, including 16S ribosomal sequences, super oxide dismutase, outer-membrane protein P6, protein D, and fuculose kinase, can be used to distinguish these two species. The availability of whole genome sequences of an increasing number of Haemophilus isolates from the human upper respiratory tract has revealed com plex genomic relationships among Haemophilus species, suggesting a genetic continuum between some Haemophilus species. The presence of gram-negative coccobacilli in Gram-stained CSF is strong evidence for Hib meningitis. Recovery of the organism or detec tion of H. influenzae DNA from CSF confirms the diagnosis. The same applies for other normally sterile body fluids, such as blood, joint fluid, pleural fluid, pericardial fluid, and subdural effusion, and are thus also confirmatory in other infections. Because nontypeable H. influenzae is primarily a mucosal pathogen, it is a component of a mixed flora; thus, etiologic diagnosis is chal lenging. Nontypeable H. influenzae infection is strongly suggested by the predominance of gram-negative coccobacilli among abundant polymorphonuclear leukocytes in a Gram-stained sputum specimen from a patient in whom pneumonia is suspected. Although bacteremia is detectable in a small proportion of patients with pneumonia due to nontypeable H. influenzae, most such patients have negative blood cultures. A diagnosis of otitis media is based on the detection by pneumatic otoscopy of fluid in the middle ear. An etiologic diagnosis requires tympanocentesis but is not routinely sought. An invasive

procedure is also required to determine the etiology of sinusitis; thus, treatment is often empirical once the diagnosis is suspected in light of clinical symptoms and sinus radiographs. TREATMENT Haemophilus influenzae Initial therapy for meningitis due to Hib should consist of a cepha losporin such as ceftriaxone or cefotaxime. For children, the dosage of ceftriaxone is 75–100 mg/kg daily given in two doses 12 h apart. The pediatric dosage of cefotaxime is 200 mg/kg daily given in four doses 6 h apart. Adult dosages are 2 g every 12 h for ceftriaxone and 2 g every 4–6 h for cefotaxime. An alternative regimen for initial therapy is ampicillin (200–300 mg/kg daily in four divided doses) plus chloramphenicol (75–100 mg/kg daily in four divided doses). Therapy should continue for a total of 1–2 weeks. Administration of glucocorticoids to patients with Hib menin gitis reduces the incidence of neurologic sequelae. The presumed mechanism is reduction of the inflammation induced by bacterial cell-wall mediators of inflammation when cells are killed by antimi crobial agents. Dexamethasone (0.6 mg/kg per day intravenously in four divided doses for 2 days) is recommended for the treatment of Hib meningitis in children >2 months of age. Invasive infections other than meningitis are treated with the same antimicrobial agents. For epiglottitis, the dosage of ceftriax one is 50 mg/kg daily, and the dosage of cefotaxime is 150 mg/kg daily, given in three divided doses 8 h apart. Epiglottitis constitutes a medical emergency, and maintenance of an airway is critical. The duration of therapy is determined by the clinical response. A course of 1–2 weeks is usually appropriate. Many infections caused by nontypeable strains of H. influenzae, such as otitis media, sinusitis, and exacerbations of COPD, can be treated with oral antimicrobial agents. Approximately 30–40% of nontypeable strains produce β-lactamase (with the exact proportion depending on geographic location), and these strains are resistant to ampicillin as well as amoxicillin. Several agents have excellent activity against nontypeable H. influenzae, including amoxicillin/ clavulanic acid, various extended-spectrum cephalosporins, and the macrolides azithromycin and clarithromycin. Fluoroquinolones are highly active against H. influenzae and are useful in adults with exacerbations of COPD. However, fluoroquinolones are not currently recommended for the treatment of children or pregnant women because of possible effects on articular cartilage.

In addition to β-lactamase production, alteration of penicillinbinding proteins—a second mechanism of ampicillin resistance— has been detected in isolates of H. influenzae. Although still rare in the United States, these β-lactamase-negative ampicillin-resistant strains are common in Japan and are increasing in prevalence in Europe. Resistance to macrolides is also being observed with increasing frequency globally. Continued monitoring of the evolving antimicro bial susceptibility patterns of H. influenzae will be important.

■ ■PREVENTION Vaccination (See also Chap. 129) Three monovalent conjugate vaccines that prevent invasive infections with Hib in infants and chil dren are licensed in the United States. In addition to eliciting protective antibodies, these vaccines prevent disease by reducing rates of pharyn geal colonization with Hib. The widespread use of conjugate vaccines has dramatically reduced the incidence of Hib disease in developed countries. Even though the manufacture of Hib vaccines is costly, vaccination is cost-effective. The Global Alliance for Vaccines and Immunizations has recognized the underuse of Hib conjugate vaccines. The disease burden has been reduced in developing countries that have implemented routine vaccination (e.g., The Gambia, Chile). An important obstacle to more widespread vaccination is the lack of data on the epidemiology and burden of Hib disease in many developing countries. All children should be immunized with a Hib conjugate vaccine, receiving the first dose at ~2 months of age, the rest of the primary series at

2–6 months of age, and a booster dose at 12–15 months of age. Specific recommendations vary for the different conjugate vaccines. The reader is referred to the recommendations of the American Acad emy of Pediatrics (Chap. 129 and https://www.aap.org/en/patient-care/immunizations/vaccination-recommendations-by-the-aap/). CHAPTER 162 Currently, no vaccines are available specifically for the prevention of disease caused by nontypeable H. influenzae. However, a vaccine that contains protein D—a surface protein of H. influenzae—conjugated to pneumococcal polysaccharides is licensed in other countries and is used widely throughout the world. The vaccine has shown partial efficacy in preventing H. influenzae otitis media in clinical trials. Vac cine formulations that include surface protein antigens are currently in clinical trials, and additional progress in the development of vaccines against nontypeable H. influenzae is anticipated. Haemophilus and Moraxella Infections Chemoprophylaxis The risk of secondary disease is greater than normal among household contacts of patients with Hib disease. There fore, all children and adults (except pregnant women) in households with an index case and at least one incompletely immunized contact <4 years of age should receive prophylaxis with oral rifampin. When two or more cases of invasive Hib disease have occurred within 60 days at a child-care facility attended by incompletely vaccinated children, administration of rifampin to all attendees and personnel is indicated, as it is for household contacts. Chemoprophylaxis is not indicated in nursery and child-care contacts of a single index case. The reader is referred to the recommen dations of the American Academy of Pediatrics. HAEMOPHILUS DUCREYI Haemophilus ducreyi is the etiologic agent of chancroid (Chap. 141), a sexually transmitted disease characterized by genital ulceration and inguinal adenitis. In addition to being a cause of morbidity in itself, chancroid is associated with HIV infection because of the role played by genital ulceration in HIV transmission. Chancroid increases the efficiency of transmission of and the degree of susceptibility to HIV infection. H. ducreyi has also been recognized as an important cause of non–sexually transmitted cutaneous ulcers. ■ ■MICROBIOLOGY H. ducreyi is a highly fastidious coccobacillary gram-negative bacte rium whose growth requires X factor (hemin). Although in light of this requirement, the bacterium has been classified in the genus Haemophi lus, DNA homology and chemotaxonomic studies have established substantial differences between H. ducreyi and other Haemophilus

species. Taxonomic reclassification of the organism is likely in the future but awaits further study. Ulcers contain predominantly T cells. The fact that patients who have had chancroid may have repeated infections indicates that infection does not confer protection.

■ ■EPIDEMIOLOGY AND PREVALENCE The prevalence of chancroid has steadily declined in the United States and worldwide over the past decade and a half. The infection appears to be more common in developing countries. Transmission is predomi nantly heterosexual, and cases in males have outnumbered those in females by ratios of 3:1 to 25:1 during outbreaks. Contact with com mercial sex workers and illicit drug use are strongly associated with chancroid. Most cases in developed countries are sporadic. H. ducreyi has emerged as a major cause of cutaneous ulcers in children in developing countries, particularly in the South Pacific and Africa. Strains that cause cutaneous ulcers have genome sequences that are nearly identical to class I strains (of two related classes) of

H. ducreyi that cause genital ulcers. ■ ■CLINICAL MANIFESTATIONS AND DIFFERENTIAL DIAGNOSIS Infection is acquired as the result of a break in the epithelium during sexual contact with an infected individual. After an incubation period of 4–7 days, the initial lesion—a papule with

surrounding erythema— appears. In 2 or 3 days, the papule evolves into a pustule, which sponta neously ruptures and forms a sharply circumscribed ulcer that generally is not indurated (Fig. 162-3). The ulcers are painful and bleed easily; little or no inflammation of the surrounding skin is evident. Approxi mately half of patients develop enlarged, tender inguinal lymph nodes, which frequently become fluctuant and spontaneously rupture. Patients usually seek medical care after 1–3 weeks of painful symptoms. PART 5 Infectious Diseases The presentation of chancroid does not usually include all of the typical clinical features and is sometimes atypical. Multiple ulcers can coalesce to form giant ulcers. Ulcers can appear and then resolve, with inguinal adenitis (Fig. 162-3) and suppuration following 1–3 weeks later; this clinical picture can be confused with that of lympho granuloma venereum (Chap. 194). Multiple small ulcers can resemble folliculitis. Other differential diagnostic considerations include the various infections causing genital ulceration, such as primary syphilis, secondary syphilis (condyloma latum), genital herpes, and donovano sis. In rare cases, chancroid lesions become secondarily infected with bacteria; the result is extensive inflammation. Non–sexually transmitted cutaneous ulcers caused by H. ducreyi resemble those of yaws caused by Treponema pallidum subspecies FIGURE 162-3 Chancroid with characteristic penile ulcers and associated left inguinal adenitis (bubo).

pertenue, which is endemic in regions where H. ducreyi cutaneous ulcers are seen. Ulcers caused by H. ducreyi are less likely than those of yaws to show central granulating tissue and less likely to have indurated edges, but substantial overlap in clinical characteristics exists. ■ ■DIAGNOSIS Clinical diagnosis of chancroid is often inaccurate, and laboratory confirmation should be attempted in suspected cases. An accurate diagnosis of chancroid relies on culture of H. ducreyi from the lesion or from an aspirate of suppurative lymph nodes. Since the organism can be difficult to grow, the use of selective and supplemented media is nec essary. DNA detection by PCR is in use in larger clinical laboratories. A probable diagnosis of sexually transmitted chancroid can be made when the following criteria are met: (1) one or more painful genital ulcers; (2) no evidence of T. pallidum infection by dark-field examination of ulcer exudate or by a negative serologic test for syphilis performed at least 7 days after ulcer onset; (3) a typical clinical presen tation for chancroid; and (4) a negative test for herpes simplex virus in the ulcer exudate. A serologic test for syphilis does not distinguish cutaneous ulcers due to H. ducreyi from those due to yaws, but PCR should be performed. TREATMENT Haemophilus ducreyi Treatment regimens for both genital and cutaneous infections include either (1) a single 1-g oral dose of azithromycin; (2) ceftri axone (250 mg intramuscularly in a single dose); (3) ciprofloxacin (500 mg by mouth twice a day for 3 days); or (4) erythromycin base (500 mg by mouth three times a day for 7 days). Isolates from patients who do not respond promptly to treatment should be tested for antimicrobial resistance. In patients with HIV infection, healing may be slow and longer courses of treatment may be neces sary. Clinical treatment failure in HIV-seropositive patients may reflect co-infection, especially with herpes simplex virus. Contacts of patients with chancroid should be identified and treated, whether or not symptoms are present, if they have had sexual contact with the patient during the 10 days preceding the patient’s onset of symptoms. MORAXELLA CATARRHALIS ■ ■MICROBIOLOGY M. catarrhalis is an unencapsulated gram-negative diplococcus whose ecologic niche is the human respiratory tract. The organism was initially designated Micrococcus catarrhalis. Its name was changed to Neisseria catarrhalis in 1970 because of phenotypic similarities to commensal Neisseria species. On the basis of more rigorous analysis of genetic relatedness, Moraxella catarrhalis is now the widely accepted name for this species. ■ ■EPIDEMIOLOGY Nasopharyngeal colonization by M. catarrhalis is common in infancy, with colonization rates ranging between 33 and 100% and depend ing on geographic location. Several factors probably account for this geographic variation,

including living conditions, day-care attendance, hygiene, household smoking, and population genetics. The prevalence of colonization decreases steadily with age. The widespread use of pneumococcal conjugate vaccines in some countries has resulted in alterations in patterns of nasopharyngeal colonization in resident populations. A relative increase in colonization by nonvaccine pneumococcal serotypes, nontypeable H. influenzae, and M. catarrhalis has occurred. These changes in colonization pat terns may be altering the distribution of pathogens of both otitis media and sinusitis in children. ■ ■PATHOGENESIS M. catarrhalis causes mucosal infections of the respiratory tract by con tiguous spread from its colonizing site in the upper airway. A preceding

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