pleuropulmonary infections are the *Fusobacterium* species *F. necrophorum*, *F. nucleatum*, and *F. varium*; *P. melaninogenica*; the *Prevotella oralis* group; *Porphyromonas gingivalis*; *Porphyromonas asaccharolytica*; *Peptostreptococcus* species; and the *Bacteroides ureolyticus* group.

The *B. fragilis* group contains the anaerobic pathogens most frequently isolated from clinical infections. Members of this group are part of the normal bowel microbiota; they include several distinct species, such as *B. fragilis*, *B. thetaiotaomicron*, *B. vulgatus*, *B. uniformis*, *B. ovatus*, and *P. distasonis*. *B. fragilis* is the most important clinical isolate, although it is isolated in lower numbers than some other *Bacteroides* species from cultures of the commensal fecal microbiota.

In female genital tract infections, organisms normally colonizing the vagina (e.g., *Prevotella bivia* and *Prevotella disiens*) are the most common isolates. However, *B. fragilis* is not uncommon.

PATHOGENESIS

Anaerobic bacterial infections usually occur when an anatomic barrier is disrupted and constituents of the local microbiota enter a site that was previously sterile. Because of the specific growth requirements of anaerobic organisms and their presence as commensals on mucosal surfaces, conditions must arise that allow these organisms to penetrate mucosal barriers and enter tissue with a lowered oxidation-reduction potential. Therefore, tissue ischemia, trauma, surgery, perforated viscus, shock, and aspiration provide environments conducive to the proliferation of anaerobes. The introduction of many bacterial species into otherwise sterile sites leads to a polymicrobial infection in which certain organisms predominate. Three major factors are involved in the pathogenesis of anaerobic infections: bacterial synergy, bacterial virulence factors, and mechanisms of abscess formation. The ability of different anaerobic bacteria to act synergistically during polymicrobial infection contributes to the pathogenesis of anaerobic infections. It has been postulated that facultative organisms function in part to lower the oxidation-reduction potential in the microenvironment, allowing the propagation of obligate anaerobes. Anaerobes can produce compounds such as succinic acid and short-chain fatty acids that inhibit the ability of phagocytes to clear facultative organisms. In experimental models, facultative and obligate anaerobes synergistically potentiate abscess formation.

Virulence factors associated with anaerobes typically confer the ability to evade host defenses, adhere to cell surfaces, produce toxins and/or enzymes, or display surface structures such as capsular polysaccharides and lipopolysaccharide (LPS) that contribute to pathogenic potential. The ability of an organism to adhere to host tissues is important to the establishment of infection. Some oral species adhere to the epithelium in the oral cavity. *P. melaninogenica* actually attaches to other microorganisms. *P. gingivalis*, a common isolate in periodontal disease, has fimbriae that facilitate attachment. Some *Bacteroides* strains appear to be piliated, a characteristic that may account for their ability to adhere.

The most extensively studied virulence factor of the nonsporulating anaerobes is the capsular polysaccharide complex of *B. fragilis*. This organism is unique among anaerobes in its potential for virulence during growth at normally sterile sites. Although it constitutes only 0.5–1% of the normal colonic microbiota, *B. fragilis* is the anaerobe most commonly isolated from intraabdominal infections and bacteremia. In an animal model of intraabdominal sepsis, the capsular polysaccharide was identified as the major virulence factor of *B. fragilis;* this polymer plays a specific, central role in the induction of abscesses. A series of detailed biologic and molecular studies of this virulence factor showed that *B. fragilis* produces at least eight distinct capsular polysaccharides, far more than the number reported for any other encapsulated bacterium. *B. fragilis* can exhibit distinct surface polysaccharides either alone or in combination by regulating the expression of these different capsules in an on–off manner through a reversible inversion of DNA segments within the promoters for operons containing the genes required for polysaccharide synthesis. Structural analysis of two of these polysaccharides, PSA and PSB, revealed that each polymer consists of repeating units with positively charged free amino groups and negatively charged groups. This structural feature is rare among bacterial polysaccharides, and the ability of PSA—and, to a lesser extent, PSB—to induce abscesses in animals depends on this zwitterionic charge motif. Intraabdominal abscess induction is related to the capacity of this polysaccharide to stimulate macrophages to release cytokines and chemokines—in particular, interleukin (IL) 8, IL-17, and tumor necrosis factor α (TNF-α)—from resident peritoneal cells through a Toll-like receptor 2–dependent mechanism. The release of cytokines and chemokines results in the chemotaxis of polymorphonuclear neutrophils (PMNs) into the peritoneum, where they adhere to mesothelial cells induced by TNF-α to upregulate their expression of intercellular adhesion molecule 1 (ICAM-1). PMNs adherent to ICAM-1-expressing cells probably represent the nidus for an abscess. PSA also activates T cells to produce certain cytokines, including IL-17 and interferon γ, that are necessary for abscess formation.

B. fragilis produces other virulence factors that allow it to predominate in disease. This organism synthesizes pili, fimbriae, and hemagglutinins that aid in attachment to host cell surfaces. In addition, *Bacteroides* species produce many enzymes and toxins that contribute to pathogenicity. Enzymes such as neuraminidase, protease, glycoside hydrolases, and superoxide dismutases are all produced by *B. fragilis.* Anaerobic bacteria produce a number of exoproteins that can enhance the organisms' virulence. The collagenase produced by *P. gingivalis* may enhance tissue destruction. An association of *B. fragilis* strains positive for the enterotoxin BFT with clinical episodes of diarrhea in children and adults has been suggested. BFT is a metalloprotease that is cytopathic for intestinal epithelial cells and induces fluid secretion and tissue damage in ligated intestinal loops of experimental animals. Recent evidence from mouse models indicates that enterotoxin-producing strains of *B. fragilis* may play a role in colon carcinoma.

Exotoxins produced by clostridial species, including botulinum toxins, tetanus toxin, *C. difficile* toxins A and B, and five toxins produced by *Clostridium perfringens*, are among the most virulent bacterial toxins in mouse lethality assays. Anaerobic gram-negative bacteria such as *B. fragilis* possess LPSs (endotoxins) that are 100–1000 times less biologically potent than endotoxins associated with aerobic gram-negative bacteria. This relative biologic inactivity may account for the lower frequency of disseminated intravascular coagulation and purpura in *Bacteroides* bacteremia than in facultative and aerobic gram-negative bacillary bacteremia. An exception is the LPS from *Fusobacterium*, which may account for the severity of Lemierre's syndrome (see "Complications of Anaerobic Head and Neck Infections," below).

APPROACH TO THE PATIENT: Infection Due to Anaerobic Bacteria

The physician must consider several points when approaching the patient with possible infection due to anaerobic bacteria.

1. Most of the organisms colonizing mucosal sites are commensals; very few cause disease. When these organisms do cause disease, it often occurs in proximity to the mucosal site they colonize.
2. For anaerobes to cause tissue infection, they must spread beyond the normal mucosal barriers.
3. Conditions favoring the propagation of anaerobic bacteria, particularly a lowered oxidation-reduction potential, are necessary. These conditions exist at sites of trauma, tissue destruction, compromised vascular supply, and complications of preexisting infection, which produce necrosis.
4. Frequently, a complex array of infecting microbes can be found. For example, as many as 12 species of organisms can be isolated from a suppurative site.
5. Anaerobic organisms tend to be found in abscess cavities or in necrotic tissue. The failure of an abscess to yield organisms