

8.6.11 Anaerobic bacteria

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8.6.11 Anaerobic bacteria 1055 8.6.11 Anaerobic bacteria Anilrudh A. Venugopal and David W. Hecht ESSENTIALS Anaerobic bacteria will not grow when incubated with 10% CO₂ in room air, but they vary in their tolerance of different levels of oxygen. Anaerobic bacteria are important commensal flora of the skin and oral, intestinal, and pelvic mucosae, and are classified according to their Gram-staining characteristics and ability to produce spores: (1) Gram-positive—cocci, non-spore-forming bacilli, and spore-forming bacilli (notably the *Clostridium* spp.); (2) Gram-negative—cocci and bacilli. Many anaerobic bacteria possess virulence factors that facilitate their pathogenicity (e.g. histolytic enzymes and various toxins). Clinical features—anaerobes typically cause clinically significant infections when there is tissue compromise, ischaemia, or mucosal injury. These infections are often polymicrobial in nature and can include (1) bacteraemia; (2) central nervous system infection— intracranial abscesses by contiguous spread, for example, from chronic otitis media, or haematogenous spread (e.g. from tooth abscess); (3) head and neck infections—periodontal and pharyngeal infections from spread of gingival disease; (4) pleuropulmonary infections (e.g. lung abscess from aspirated oropharyngeal flora); (5) intra-abdominal infections—often caused by mixed colonic flora that have been displaced by bowel injury; (6) gastrointestinal infections; (7) genitourinary infections; (8) skin and soft tissue infections— ranging from cellulitis to necrotizing fasciitis; should be considered in cases of infected animal and human bites, and in intravenous drug users; diabetic foot ulcers often have polymicrobial infections that include anaerobes. Diagnosis—a putrid odour of the affected tissue or drainage is highly suggestive of an anaerobic infection, as is the presence of gas in tissues. Care must be taken when collecting specimens for anaerobic culture because many of the organisms are very sensitive to oxygen, and some cannot tolerate more than a few minutes at ambient oxygen levels. However, anaerobic spores are aerotolerant, can survive in harsh oxygen-laden environments, and will germinate under appropriate conditions. Treatment and prevention—aside from supportive care, treatment requires (1) drainage of abscesses and resection of devitalized tissue; and (2) antibiotics—agents that are active against anaerobes include clindamycin, metronidazole, vancomycin, β -lactam/ β -lactamase inhibitor combinations, carbapenems, moxifloxacin, tigecycline, chloramphenicol, and even macrolides but resistance patterns have been

changing and the choice of empirical therapy is best guided by knowledge of local susceptibility testing results. Prophylaxis against anaerobic bacteria significantly reduces postoperative infection rates following intra-abdominal surgery. History In 1690 Antonie van Leeuwenhoek first described anaerobic bacteria as 'animalcules' that could survive in the absence of air. This observation was overlooked until nearly 200 years later. In 1861 Louis Pasteur had observed that the bacteria near the surface of a droplet of water had stopped moving while the organisms at the centre of the droplet continued to move about. He hypothesized that oxygen in the air had caused the death of the surface bacteria. Pasteur's early experiments with bacterial fermentation led to the development of anaerobic bacteriology. Years later in 1916 it was the invention of the anaerobic jar by James McIntosh and Paul Fildes that allowed for the repeated culture and study of anaerobes. This led to the discovery of many anaerobic bacteria responsible for various human diseases.

Definition Anaerobic bacteria are organisms that cannot grow in the presence of various levels of oxygen. Room air is approximately 20% oxygen and when cultured in this environment, anaerobes will not grow on solid media. Reduced oxygen tensions are required for their growth. Anaerobes are described as strict, moderate, or facultative anaerobes, according to their tolerance of oxygen. Strict anaerobes may grow only at oxygen levels of less than 0.5%. They are usually catalase negative and lack superoxide dismutase rendering them susceptible to toxic oxygen radicals, although this is not always the case. Moderate anaerobes also grow poorly in air and prefer media that have oxygen levels of 2-8%. Facultative anaerobic bacteria are organisms that can grow in various levels of oxygen including normal oxygen tensions.

Taxonomy of important anaerobic organisms Table 8.6.11.1 lists the species of anaerobes that colonize human mucosal surfaces and skin or produce clinically significant disease. They are classified according to their Gram-staining characteristics and ability to produce spores.

Epidemiology Limited data about the incidences of anaerobic infections are available. Most anaerobic infections occur as contamination of endogenous flora into neighbouring sites. There are some notable exceptions that can occur after exposure to environmental sources of anaerobes can include but are not limited to infections with *Clostridium tetani*, *Clostridium perfringens*, *Clostridium botulinum*, *Clostridium difficile* (see Chapter 8.6.25), *Enterotoxigenic Bacteroides fragilis*.

Human commensal flora Commensal bacteria are organisms that live on both mucosal surfaces and skin of humans but under normal circumstances do not cause disease. They play an important role in normal host physiology by colonizing and helping to prevent infections by pathogenic organisms. By producing toxic metabolites, lowering the local pH, and depleting the area of nutrients they make the surrounding area

section 8 Infectious diseases 1056 uninhabitable for other pathogenic organisms. Anaerobes make up a large part of this commensal flora in humans, as outlined next.

Skin The commensal flora of the skin consists predominantly of aerobes, anaerobes, and yeasts. The principal anaerobes present are Gram-positive bacilli of the genus *Cutibacterium* (formerly *Propionibacterium*) and the Gram-positive cocci from the genus *Peptostreptococcus*. The three main species of *Cutibacterium* include *C. acnes*, *C. granulosum*, and *C. avidum*. They occur mainly in hair follicles and sebaceous glands. *C. acnes* produce free fatty acids from triglycerides, but, while this may control the growth of pathogenic bacteria on the surface of skin, it has also been associated with the development of acne.

Upper respiratory tract and oral cavity The nasal cavity mucosa tends to be colonized with organisms that are similar to the organisms found on skin surfaces and the sebaceous glands.

Oropharyngeal flora typically includes *Peptostreptococci*, *Tannerella forsythia*, and *Fusobacterium*. In the oral cavity, areas such as the tonsillar crypts, gingival crevices, and the clefts on the tongue

have a more favourable atmosphere for anaerobes. Their lower oxygen levels promote colonization with *Prevotella*, *Peptostreptococci*, *Fusobacterium*, and other anaerobic Gram-positive bacilli.

Gastrointestinal tract The upper gastrointestinal tract from oesophagus to jejunum is relatively free of microorganisms but can become transiently colonized with bacteria following meals or from the swallowed secretions of the upper airway. The terminal ileum tends to have a flora more closely resembling that of the large intestines where anaerobes can outnumber the aerobes from 100 to 1000:1. Among a diverse group of anaerobes, the *Bacteroides fragilis* group predominates. *B. vulgatus* and *B. thetaiotaomicron* are more common than *B. fragilis*. Another group of colonizing anaerobes found in the stool are *Clostridium* spp., including *C. perfringens* and *C. novyi*. There have been reports in both adults and children of colonization with *C. difficile* where they have displayed positive stool test results but without symptoms.

Genitourinary tract The kidneys, ureters, urinary bladder, and proximal part of the urethra are normally free of organisms as they are constantly flushed with urine if the anatomy of the urinary tract is normal. The distal portion of both male and female urethras have a scanty flora including aerobic skin colonizers and some anaerobic organisms including *Bacteroides*, *Fusobacterium*, *Peptostreptococcus*, and *Clostridium* spp. The vaginal flora can include both aerobes and anaerobes but, by adulthood, anaerobes such as *Lactobacillus*, *Prevotella*, *Fusobacterium*, and *Peptostreptococci* predominate (Fig. 8.6.11.1).

Pathogenesis Several factors predispose to the pathogenesis of anaerobic infections, including tissue injury and destruction, impaired blood supply, or any breakdown in the integrity of mucosa or skin. Many anaerobic bacteria possess one or more characteristics that enhance their pathogenic virulence. These can include enzyme production, toxins, polysaccharide capsules, lipopolysaccharides, and spore formation. Histolytic enzymes such as collagenases, fibrinolysins, lipases, and other enzymes are produced by *Bacteroides* and *Prevotella*. These enzymes cause tissue destruction, whereas the α -toxin found in *C. perfringens* can also cause haemolysis. *Porphyromonas gingivalis*, *Bacteroides* spp., and *Fusobacterium* produce heparinases that can promote coagulation leading to tissue ischaemia. *Porphyromonas gingivalis*, *B. fragilis*, and *Fusobacterium nucleatum* produce catalase and superoxide dismutase which are believed to help the organisms tolerate higher levels of oxygen. Various organisms, including *C. perfringens* and *C. difficile*, have also been found to have enterotoxins that alter intestinal cell function and cause cell death, leading to diarrhoea. Certain species of clostridium, including *C. botulinum* and *C. tetani*, produce neurotoxins that block neuromuscular transmissions leading to paralysis or spasms plus rigidity, respectively. Endotoxins can cause macrophage and complement activation leading to fever, hypotension, and oedema from the release of cytokines. Enterotoxigenic *B. fragilis* is known to produce a metalloproteinase toxin that causes cell proliferation and protein shedding resulting in a diarrhoeal illness. Gram-negative anaerobes, like their aerobic counterparts, have a lipopolysaccharide layer in their outer membrane that can act as an endotoxin. The lipopolysaccharide of the anaerobic Gram-negative cell walls are typically less potent than the lipopolysaccharide of Table 8.6.11.1

Taxonomy of important anaerobic bacteria

Gram-positive anaerobes	Gram-negative anaerobes
Cocci	Bacilli
Bacilli	Cocci
Non-spore forming	Spore forming
<i>Actinomyces</i> spp.	<i>Clostridium</i> spp.
<i>Veillonella</i> spp.	<i>Bacteroides fragilis</i> group
<i>Peptostreptococcus</i> spp.	<i>Bifidobacterium</i> spp.
Other <i>Bacteroides</i> spp.	<i>Streptococcus</i> spp.
<i>Eubacterium</i> spp.	<i>Bilophila wadsworthia</i>
<i>Fingoldia magna</i>	<i>Eggerthella</i> spp.
<i>Fusobacterium</i> spp.	<i>Lactobacillus</i> spp.
<i>Porphyromonas</i> spp.	<i>Mobiluncus</i> spp.
<i>Prevotella</i> spp.	<i>Cutibacterium</i> spp.

8.6.11 Anaerobic bacteria 1057 aerobic Enterobacteriaceae. One exception to this rule is the lipopolysaccharide of *F. nucleatum* which is believed to be involved in its pathogenic role in periodontal

disease and Lemierre's disease. The capsular polysaccharides associated with the *B. fragilis* group, *Prevotella melaninogenica*, and *Peptostreptococcus*, are associated with impaired phagocytosis by host cells and can lead to abscess formation. Finally, spore-producing organisms like the *Clostridium* species can survive in harsh oxygen-laden environments by developing spores that will later germinate when environmental conditions become favourable again.

Clinical spectrum

Anaerobic bacteraemia Anaerobes account for about 5% of all positive blood cultures. The predisposing factors for anaerobic bacteraemia in newborns include prematurity, prolonged labour, chorioamnionitis, and necrotizing enterocolitis. Underlying risk factors for anaerobic bacteraemia in children and adults include malignancies, immunosuppression, hepatic failure, and diabetes mellitus. The organism isolated depends on the underlying infectious condition. In cases of gastrointestinal or necrotic skin infections it is usually a member of the *B. fragilis* group. *Peptostreptococcus* and *Clostridium* spp. are other commonly found blood isolates. The isolation of *Clostridium septicum* or the facultative anaerobe *Streptococcus bovis* in bacteraemic patients should raise the suspicion of underlying cancer, especially of colonic origin.

Central nervous system infections Intracranial infections with anaerobes can arise by contiguous spread from surrounding structures (e.g. with chronic otitis media, mastoiditis, or sphenoidal sinusitis). This can lead to abscess formation, septic thrombophlebitis, or venous sinus infections. When frontal sinusitis spreads to involve the frontal bone, it can lead to osteomyelitis and subperiosteal abscess known as Pott's puffy tumour. Intracranial abscesses can also arise as a result of haematogenous seeding of the brain parenchyma from suppurative distant foci such as dental abscesses and alveolar infections. Abscesses that arise may be single or multiple in number and involve any portion of the brain, although the site involved depends on the mode of infection. Anaerobic organisms commonly associated with infections of the central nervous system include *Prevotella*, *Peptostreptococci*, and *Fusobacterium* spp., although these are often polymicrobial infections involving aerobes.

Head and neck infections The origin of oral, head, and neck infections is often the anaerobic flora of the oral cavity. Lower oxygen tension in the gingival crevices promotes colonization with anaerobes. When dental hygiene is poor, dental plaque develops leading to gingivitis, periodontal infections, and abscesses. Periodontal infections result from spread of gingival disease to the surrounding tissue. As infection spreads from more superficial gingival disease to deeper infections there is a shift in the pathogenic organisms from Gram-positive cocci and bacilli to Gram-negative bacilli. Anaerobic pharyngeal infections may arise in relation to gingivitis. Complications might arise by contiguous spread of these infections along medial, lateral, or submaxillary spaces. Ludwig's angina is described as a brawny induration of the submaxillary and sublingual spaces with

Anaerobic Infections Brain Abscess Animal and Human Bites Cellulitis Foot ulcers Bacteraemia Pelvic Abscess Endometritis Salpingitis Tubo-ovarian Abscess Septic Abortion Gingivitis Periodontal Infections Periodontal Abscess Vincent's Angina Ludwig's Angina Lemierre's Syndrome Lung Abscess Empyema Aspiration Pneumonitis Necrotizing Pneumonia *C. difficile* associated Disease Appendicitis Peritonitis Pericolonic Abscess Intra-abdominal Abscess Chronic Otitis Media Sinusitis and Mastoiditis Commensal Flora spp. Oral Cavity and Upper Respiratory Tract Gastrointestinal Tract Genitourinary Tract Skin *Bacteroides fragilis* group Other *Bacteroides* spp. *Clostridium* spp. *Peptostreptococci* spp. *Fusobacterium* spp. *Fusobacterium* spp. *Peptostreptococci* spp. *Clostridium* spp. Other *Bacteroides* spp. *Prevotella* spp. *Lactobacilli* spp. *Cutibacterium* spp. *Peptostreptococci* spp. *Fusobacterium* spp. *Tannerella forsythia* *Prevotella* spp. *Veillonella* spp.

Fig. 8.6.11.1 Human anaerobic commensal flora (left) and clinical spectrum of anaerobic infections (right).

section 8 Infectious diseases 1058 poor, dental plaque develops leading to gingivitis, periodontal infections, and abscesses. Periodontal infections result from spread of gingival disease to the surrounding tissue. As infection spreads from more superficial gingival disease to deeper infections there is a shift in the pathogenic organisms from Gram-positive cocci and bacilli to Gram-negative bacilli. Anaerobic pharyngeal infections may arise in relation to gingivitis. Complications might arise by contiguous spread of these infections along medial, lateral, or submaxillary spaces. Ludwig's angina is described as a brawny induration of the submaxillary and sublingual spaces with

cellulitis usually arising from spread of lower molar dental infections. Severe infections threaten the airway and can extend to the mediastinum. Vincent's angina is an acute necrotizing ulcerative gingivitis manifested by inflamed gingivae, interdental ulcerations, and halitosis. Otitis media and sinusitis occasionally involve anaerobes, although they are more common in chronic infections of these spaces. *Fusobacterium necrophorum* may be a cause of pharyngitis in up to 10% of cases. Lemierre's syndrome frequently occurs in young, previously healthy patients as the result of spread of an oropharyngeal infection leading to septic thrombophlebitis of the internal jugular vein. Clinical features helpful in diagnosing this condition are recent oropharyngeal infection, clinical evidence of thrombophlebitis including ipsilateral neck tenderness with fevers and chills, as well as isolation of the anaerobic pathogen. Most commonly, the organism isolated is *Fusobacterium necrophorum*, although other organisms have been identified. Early diagnosis is required to reduce morbidity associated with distant septic emboli and mortality.

Pleuropulmonary infections The spectrum of anaerobic lung infections includes lung abscesses, empyema, aspiration pneumonia, and necrotizing pneumonias. The origins of these anaerobes are usually from the oropharyngeal flora. *Peptostreptococcus*, *Fusobacterium*, pigmented *Prevotella*, *Porphyromonas*, and *Bacteroides* spp. are most commonly isolated, often in combination with aerobes and other microaerophilic anaerobes such as *Streptococcus* spp. Patients with an anaerobic lung abscess will often complain of fevers, weight loss, and foul-smelling or foul-tasting sputum. This odour may be detectable on entering the patient's room.

Intra-abdominal infections The presence of an intra-abdominal infection can usually be diagnosed clinically from a thorough history and physical examination. If the patient is not being taken for an immediate laparotomy, then patients with suspected intra-abdominal infection should undergo computed tomography (CT) scanning to evaluate the abdomen. Intra-abdominal infections are often caused by mixed colonic flora that have been displaced by surgery, penetrating trauma, intestinal malignancy, inflammatory bowel disease, or perforation of colonic diverticula. Intra-abdominal abscesses, pericolic abscesses, and peritonitis may develop. Isolates are most commonly mixed facultative and strict anaerobes, notably the facultative anaerobe *Escherichia coli* and the anaerobe *B. fragilis* group. Other commonly occurring anaerobes include *Peptostreptococcus* spp., *Fusobacterium* spp., and *Clostridium* spp.

Gastrointestinal infections *C. difficile* infection is discussed in Chapter 8.6.24. Clinical symptoms often include abdominal pain and distension, fevers, and profuse foul-smelling watery diarrhoea. Laboratory findings include leucocytosis (leukaemoid reactions) and hypoalbuminaemia. Polymerase chain reaction assays of stool samples that target the presence of the toxin B gene have sensitivities ranging from 85 to 95% and specificities of 95–99%, which are improved compared to the toxin immunoassays. Recommendations about the use of oral metronidazole and vancomycin are discussed in detail in the adult clinical practice guidelines (see Further reading). Fidaxomicin is another treatment option that offers the advantage of lower recurrence rates compared to oral vancomycin. It is important to perform strict contact isolation measures for patients suspected of *C. difficile* disease to prevent nosocomial transmission and encourage proper hand hygiene with soap and water.

Enterotoxigenic *Bacteroides fragilis* has been associated with a diarrhoeal illness in humans. The Enterotoxigenic *Bacteroides fragilis* organism produces a metalloprotease *B. fragilis* toxin that is proinflammatory and causes disruption of the colonic epithelial cells. Patients often present with tenesmus, abdominal pain, and an inflammatory diarrhoea.

Genitourinary infections Like the oral cavity and colon, the female genital tract has an increased colonization ratio of anaerobes to aerobes of nearly 10:1. Disruption of the integrity of the tissues of the female genital tract increases the risk of anaerobic infections such as periurethral and labial pyogenic infections, pelvic abscesses, postpartum endometritis, salpingitis, tubo-

ovarian abscess, and septic abortions. *B. fragilis* group, *Prevotella* spp. including *P. bivia*, *P. disiens*, and *P. melaninogenica*, *Peptostreptococci*, and *Clostridium* spp. are commonly isolated. *Actinomyces* have been associated with intrauterine device-related infections. Bacterial vaginosis (see Chapter 9.4) is an infection characterized by malodorous vaginal discharge caused by a polymicrobial infection often including *Prevotella*, *Peptostreptococci*, *Mobiluncus*, and the facultative anaerobe *Gardnerella vaginalis*. *Clostridium sordellii* is a toxin-producing Gram-positive anaerobe that has been known to cause pelvic infections. This usually presents with vague symptoms caused by deep infections following childbirth, medically induced abortions, or trauma. There is rapid clinical deterioration with profound hypotension, an intense leukaemoid reaction, and it is associated with a high mortality rate. Skin and soft tissue infections These usually arise after the integrity of the skin has been lost from injury, ischaemia, or surgery, and there is contamination by either faecal or oral secretions. These are usually polymicrobial infections with aerobic and anaerobic bacteria. The spectrum of disease ranges from cellulitis to necrotizing fasciitis. Anaerobic skin infections should also be considered in cases of infected animal and human bites and decubitus ulcers, and with intravenous drug users. Diabetic foot ulcers are often polymicrobial infections that include anaerobes. Common isolates from soft tissue infections include *B. fragilis* group, *Peptostreptococci*, and *Clostridium* spp. Bone and joint infections Osteomyelitis and septic arthritis from anaerobes are rare but can result when infection spreads from surrounding soft tissue, as in the case of diabetic foot ulcers. Diagnosis is made by the careful collection of fluids in anaerobic containers or by bone biopsy cultures.

8.6.11 Anaerobic bacteria 1059 *Fusobacterium* spp. and other *Bacteroides* spp. have been isolated from joint infections on a few occasions. Diagnosis Clinical clues A putrid odour of the affected tissue or discharge is very suggestive of anaerobic infections. Underlying illnesses such as diabetes mellitus, abscess formation, tissue ischaemia, and necrotic tissue are predisposing factors. Another important clue is the location of the infection in relation to mucosal surfaces that are normally colonized by anaerobes such as intra-abdominal and oral infections. Gas in tissues suggests anaerobic infection. It can often be detected on radiographs in cases of skin and soft tissue infections or with CT or MRI in deeper infections. However, gas formation in tissues is not specific to anaerobes and can be found in many aerobic infections as well. Some anaerobic infections, such as actinomycosis, might be identified on smears or tissue biopsy by the presence of filamentous Gram-positive bacilli and 'sulphur granules', although these may be easily missed. Collection of specimens The greatest barrier to the diagnosis of anaerobic infections (aside from not considering anaerobes) is faulty collection and transport of specimens. Aspirated pus or excised infected tissue should be sent to the microbiology laboratory under anaerobic conditions as soon as possible. The use of swabs is discouraged because of the low yield of organisms. Gram's stains and plating of the specimens should be done promptly with minimal exposure to air to minimize the loss of obligate anaerobes. Immediately after inoculation, the media should be kept under anaerobic conditions in either anaerobic jars or chambers at 35–37°C. Most microbiology laboratories will not set up anaerobic cultures if the specimens have been collected or transported improperly. Another method to isolate anaerobes is to inoculate from 1–10 ml of the suspected infected fluid into an anaerobic blood culture bottle with proper labelling of the specimen source. Anaerobic blood cultures Recent studies have confirmed their importance in detecting both anaerobic and early facultative anaerobic bacteraemias. Paired cultures should be drawn, including both aerobic and anaerobic bottles, and these should be collected from peripheral sites. This is important as positive cultures for anaerobes often occur when not suspected. Treatment Susceptibility and resistance The Clinical Laboratories and Standards Institute (CLSI) and the

European Committee on Antimicrobial Susceptibility Testing (EUCAST) each respectively will publish their own breakpoints to determine the cut offs for the susceptibility of various anaerobic bacteria. The breakpoints recommended by each committee do not always correlate, and this can lead to variations in reported rates of resistance. The recommendations for testing and breakpoints is regularly reviewed by these committees. Resistance to various classes of antibiotics will vary according to the species of the anaerobic bacteria and these are discussed in more detail next. β -Lactam antibiotics β -lactams like penicillin have traditionally been used to treat anaerobic infections. Penicillin G continues to have activity against many anaerobes, but resistance has been growing particularly in the anaerobic Gram-negative bacilli. There are three main ways that anaerobes can develop resistance to β -lactam antibiotics: (1) β -lactamase enzymes including penicillinases and cephalosporinases; (2) reduced affinity of the penicillin binding proteins present in the cell wall; and (3) alterations in the porin channels leading to decreased permeability of the cell walls to β -lactams. The most common mechanism of resistance is the development of the inactivating enzymes like β -lactamases. β -lactam/ β -lactamase inhibitor combinations such as ampicillin/sulbactam, piperacillin/tazobactam, and ticarcillin/clavulanate demonstrate a high degree of in vitro activity against many anaerobes including members of the *B. fragilis* group. Many anaerobes can produce cephalosporinases, which limits the use of cephalosporins as single agents in the treatment of anaerobic infections. Since cephalosporinases have little activity against second generation cephalosporins we still see moderate antianaerobic in vitro activity with cephamycins such as cefoxitin particularly in the *Bacteroides fragilis* group. Newer cephalosporins like ceftolozane/tazobactam and ceftazidime/avibactam have limited anaerobic activity, including variable activity against the *Bacteroides fragilis* group. They should be combined with metronidazole when treating serious anaerobic infections. Carbapenems such as imipenem/cilastatin, meropenem, ertapenem, and doripenem typically demonstrate excellent in vitro activity against nearly all anaerobes. The presence of carbapenemases are less common among anaerobes. Chloramphenicol Chloramphenicol is a bacteriostatic drug that has been used to treat severe anaerobic infections. Although resistance is rare, use of the drug does carry risks of significant side effects that can include aplastic anaemia and haemolytic anaemia. The drug requires vigilant monitoring when used. It is rarely used in the United States. Clindamycin Clindamycin is a bacteriostatic lincosamide that has demonstrated good activity against anaerobes in the past. Resistance rates have been increasing globally in *Bacteroides fragilis* group anaerobes and non-*Bacteroides* anaerobes. It is often used for dental infections and aspiration pneumonias but is no longer recommended as empiric therapy for anaerobic coverage in intra-abdominal infections due to increased resistance among Enterobacteriaceae. Nitroimidazoles Metronidazole has demonstrated excellent activity against most anaerobic bacteria. The rates of resistance in the anaerobic Gram-negative bacilli, including the *Bacteroides fragilis* group, has been low. Aerobic and facultative anaerobic organisms often show high rates of resistance and, as such, microaerophilic Streptococci often demonstrate resistance. Other nitroimidazoles like tinidazole and secnidazole also have anaerobic activity but are mainly used for the treatment of bacterial vaginosis. Others Tigecycline has activity against many Gram-positive and Gram-negative anaerobic bacteria including the *Bacteroides fragilis* group, *C. perfringens* and *Peptostreptococcus* spp. Among fluoroquinolones,

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