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Anaerobic bacteria: Infection and Management

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Abstract: *Anaerobic bacteria are important pathogens in many different infections. Empiric antimicrobial therapy is frequently used in the treatment of anaerobic infections as it might take several days for bacterial cultures to grow and, in many cases, the patient needs care without delay. The patient's condition and the nature of the infecting microorganisms are of extreme importance.Since anaerobic infections are generally polymicrobial, where anaerobes are mixed with aerobic organisms, therapy should provide coverage of both types of pathogens. The isolation of anaerobes requires appropriate methods of collection, transportation and cultivation of specimens. The lack of use of any of these methods can lead to inadequate recovery of anaerobes and inappropriate therapy. Treatment of anaerobic infection is complicated by the slow growth of these organisms and the growing resistance of anaerobic bacteria to antimicrobials. The primary role of antimicrobials is to limit the local and systemic spread of infection. Surgical drainage is of primary importance. The antibiotic resistance patterns are no longer predictable in anaerobic bacteria and the first choice of antibiotic might not be sufficient. Antimicrobial susceptibility testing of the infecting microorganisms will give essential information of the alternatives for treatment.*

Keywords**:** *Anaerobic bacteria, anaerobic infections,polymicrobial,Antimicrobial susceptibility.*

I. Introduction

Anaerobic infections are caused by anaerobic bacteria.Anaerobic means "life without air." Anaerobic bacteria grow in places which completely, or almost completely, lack oxygen. Anaerobic bacteria do not grow on solid media in room air (0.04% carbon dioxide and 21% oxygen). Anaerobes have been encountered.in infections at virtually all anatomic sites, although the frequency of recovery is highly variable. These bacteria are naturally occurring and plentiful in and on the body. They are the most common flora in the body. They don't cause infection in their natural state, but can cause infection after injury or trauma to the body. Anaerobic infections commonly affect the abdomen, genitals, heart, bone, joints, central nervous system (CNS), respiratory tract, skin, and mouth.[1]

Now-a-days, anaerobic infections are showing evidence of increasing virulence, rising incidence, unresponsiveness to metronidazole therapy and worse outcomes. Some of these infections are serious and have high mortality rate and can no longer be overlooked as in the past and need to be properly identified.[2] Anaerobic microbiology has fallen out of the spotlight of infectious disease, due to extraordinary efforts required to recognize these infections as also the availability of generally effective antimicrobials against these organisms.[3]

II. Historical background

Anaerobes were first discovered by Louis Pasteur in 1862. The year 1965 marked the start of the renascence of anaerobic microbiology, largely spearheaded by Sidney Finegold, who is often referred to as the father of anaerobic microbiology. In India, interest in anaerobic microbiology started a little later but soon caught up, and by the 1980s, anaerobes had been cultured from all types of infections, starting with brain abscesses, otitis media, oro-dental infections, cutaneous abscesses, lung abscesses, intra-abdominal sepsis, pelvic infections, etc.[4]Subsequently, over the next three decades, anaerobes were documented to be the major causative agents of puerperal sepsis, lung abscesses and intra-abdominal sepsis.[5]Since the early 1990s there have been many evaluations of the utility of the anaerobic bottle in the blood culture set and results have varied widely. In 1992, Dr. Patrick R. Murray, a well-known blood culture expert, published a study which concluded that "…bacteraemia caused by obligate anaerobic bacteria is decreasing relative to sepsis caused by other bacteria and fungi and that the routine use of unvented anaerobic blood culture bottles reduces the recovery of common aerobic bloodstream pathogens."[6]

However, not much research was done on the non-sporing anaerobes in the next few decades and the scientific community concentrated on the spore-bearing organisms causing invariably fatal diseases like tetanus and gas gangrene. One of the reasons for this could have been the increasing number of these cases observed in soldiers during the world war. Difficulty in culturing the anaerobes and lack of standardization in nomenclature prevented progress in the field of anaerobic microbiology.

III. Clinical infection

The frequency of isolation of anaerobic bacteria varies in different infectious sites.[7]Mixed infections caused by numerous aerobic and anaerobic bacteria are often observed.The genera or groups of anaerobes most frequently isolated from pyogenic infections are *Bacteroides*, *Clostridium*, gram-positive cocci and *Fusobacterium*. Anaerobes are able to cause all types of intracranial infections. These often cause subdural empyema, and brain abscess, and rarely cause epidural abscess and meningitis. The origin of brain abscess is generally an adjacent chronic ear, mastoid, or sinus infection oropharynx, teeth or lungs.[8]

The anaerobes often isolated from brain abscesses caused by anaerobic Gram-negative bacilli (including Prevotella,*Porphyromonas*, Bacteroides), *Fusobacterium*,Peptostreptococcus spp. Anaerobes can be isolated from most types of upper respiratory tract and head and neck and infection that include tonsillar, peritonsillar and retropharyngeal abscesses, chronic otitis media, sinusitis and mastoiditis, all deep neck space infections, parotitis, odontogenic infections, and postsurgical and nonsurgical head and neck wounds and abscesses.[9, 10]Anaerobes can also be isolated in about 35% of individuals who suffer from nosocomial-acquired aspiration pneumonia.[11]

Abdominal infections are characteristically biphasic: an initial stage of generalized peritonitis associated with *Escherichia coli* sepsis, and a later stage, in which intra-abdominal abscesses harbouring anaerobic bacteria (including *B. fragilis* group) emerge. Female genital tract infections caused by anaerobic bacteria are polymicrobial and include: soft-tissue perineal, vulvar and Bartholin gland abscesses; bacterial vaginosis; endometritis; salpingitis; adnexal abscess; tubo-ovarian abscesses; intrauterine contraceptive device-associated infection; pelvic inflammatory disease.[12]The anaerobes often recovered from female genital tract include *Prevotellabivia*, *Prevotelladisiens*, and *Peptostreptococcus*, *Porphyromonas* and *Clostridium* spp. *Bacteroidesfragilis* group is rarely recovered in these infections compared to intra-abdominal infection. *Actinomycesspp*.And *Eubacteriumnodatum* are often recovered in infections associated with intrauterine devices. *Mobiluncusspp*. can be associated with bacterial *vaginosis.*[13]

The incidence of anaerobic bacteria in bacteremia varies between 5% to15%,this is explained by a greater number of anaerobic bacteraemia in patients with complex underlying disease or those that are immunosuppressed. The commonest isolates are B. fragilis group (over 75% of anaerobic isolates), *Clostridium* spp. (10–20%), *Peptostreptococcus* spp. (10–15%), *Fusobacterium* spp. (10–15%) and *P. acnes* (2–5%).[14]

The newborn`s exposure to the maternal vaginal bacterial flora which contains aerobic and anaerobic bacterial flora can lead to the development of anaerobic bacterial infection. These infections include cellulitis of the site of fetal monitoring (caused by *Bacterodes* spp.), bacteremia, aspiration pneumonia (caused by *Bacterodes* spp.), conjunctivitis (caused by clostridia,) and infant botulism.[15]

IV. Laboratory diagnosis

Anaerobes require properly collected and transported samples before they could be isolated.The approaches for isolation and identification of anaerobic bacteria are gas pack, Coy anaerobic chambers, pre reduced anaerobically sterilized media (PRAS), brain heart infusion agar supplemented with haemin and vitamin K, L-cysteine, yeast extract with preliminary disks like metronidazole (5 µg), vancomycin (5 µg) and colistin (10 µg) sodiumpolyanetholsulphonate (SPS) discs for anaerobic incubation, Robertson cooked meat media and sodium azide selective media. Identification is based upon morphological characteristics like pigment production, susceptibility to penicillin, rifampicin, kanamycin, vancomycin, and colistin.[16]

Due to more turnaround time for their culture, identification and sensitivity and the cost, routine anaerobic bacteriology of various clinical isolates was not considered in many clinical laboratories. Anaerobic bacteria considered to act synergistically with coexisting aerobic pathogens. Bacteremia by anaerobic pathogen though not so infrequent, blood culture for anaerobe is still not regularly practiced in many clinical laboratories.[17]

V. Resistance pattern of anaerobic bacteria

Resistance among anaerobic pathogens was thought to be low. However, the susceptibility patterns of anaerobic bacteria are undergoing changes and decreased *in vitro* susceptibility to various antimicrobials has been reported in recent years.[18]The most frequently isolated antibiotic-resistant anaerobe is *B. fragilis*. However, resistance is also seen among anaerobes that were previously considered to be highly susceptible to antibiotics, raising concerns about appropriate empirical therapy.

Resistance to metronidazole is also on the rise. An increasing number of clinical failures with metronidazole treatment of *C. difficile* infection have been reported during the past few years.[19] Resistant rates up to 63% have been reported with metronidazole in clinical anaerobic isolates This poses a problem since metronidazole is a frequent choice for empirical anaerobic coverage over the other antibiotics.

Low-level metronidazole-resistant strains may be overlooked because the breakpoint of 32 mg/L that was set by the Clinical and Laboratory Standards Institute (CLSI) is much higher than the 4 mg/L cutoff level

for strains isolated in the community. Specific resistance genes (nim) conferring resistance to nitroimidazoles have been isolated in different genera of gram-positive and gram-negative anaerobic bacteria, including Bacteroides species. The nim genes encode an alternative reductase that can convert nitroimidazole to a nontoxic derivative, thereby circumventing the toxic effect that causes breakage of the DNA.[20]This should make us realize that it is high time susceptibility testing of anaerobes be undertaken by clinical microbiology laboratories. This has always been an arduous task. However, with a special set of guidelines for anaerobic sensitivity introduced by CLSI standardization, it no longer remains an issue.

VI. Therapeutic approach for anaerobic infection

Recovery from an anaerobic infection depends on adequate and rapid management. The main principles of managing anaerobic infections are neutralizing the toxins produced by anaerobic bacteria, preventing the local proliferation of these organisms by altering the environment and preventing their dissemination and spread to healthy tissues.

Antibiotic prophylaxis is often practiced to combat anaerobic infection. The available parenteral antimicrobials for most infections are metronidazole, clindamycin, chloramphenicol, cefoxitin, a penicillin (i.e. ticarcillin, ampicillin, piperacillin) and a beta-lactamase inhibitor (i.e. clavulanic acid, sulbactam, tazobactam), and a carbapenem (imipenem, meropenem, doripenem, ertapenem).[21]An antimicrobial effective against Gram-negative enteric bacilli (i.e. aminoglycoside) or an anti-pseudomonal cephalosporin (i.e. cefepime) are generally added to metronidazole, and occasionally cefoxitin when treating intra-abdominal infections to provide coverage for these organisms. Clindamycin should not be used as a single agent as empiric therapy for abdominal infections. Penicillin can be added to metronidazole in treating of intracranial, pulmonary and dental infections to provide coverage against microaerophilic streptococci, and Actinomyces.[22]Therapy with hyperbaric oxygen (HBO) may also be useful. The main goal of antimicrobials is in restricting the local and systemic spread of the microorganisms.

VII. Recent perspective of anaerobic infection

Anaerobic microbial bacteriology went from a period of intense neglect to a period of intense activity. Once the etiology and clinical manifestations of anaerobic infections were documented, anaerobic microbiology again took a backseat in most clinical microbiology laboratories. Several factors were responsible for this. Hospital administrators also felt that anaerobic microbiology was not cost effective. The cost of an anaerobic culture and sensitivity was five times that of an aerobic culture and sensitivity.[2]Empirical treatment for anaerobes became a routine practice.

Interest on anaerobic microbiology has taken a new upsurge due to increasing reports of infections with anaerobic bacteria including *Bacteroides* group, *Clostridium difficle*and animal infection outbreaks caused by *Clostridium botulinum*.[23]Bacterial therapeutics, use of bacteria for drug delivery, a new area of research concentrating on treatment of cancers with use of anaerobic bacteria to carry the antibiotics or anti-cancer reagents to the hypoxic, low pH and microenvironments inside the cancerous tissue has been instrumental in generating some interest in anaerobic bacteria.[24]

In most developing countries, less financial establishment for separated anaerobic section in diagnostic laboratory. Though many aerobic blood cultures are negative, no efforts are made to process blood for anaerobic culture. Previous reports have suggested significance of anaerobic blood cultures in ICU's and a 3% positivity of obligate anaerobes among the study group.[25, 26]No adequate data is available either on the frequency of anaerobic bacterial infections, predisposing factors or on the in vitro antimicrobial susceptibility patterns of anaerobic bacteria isolated from clinical specimens.

VIII. Conclusion

Interest in anaerobic microbiology has waxed and waned. Anaerobic bacterial identification and their susceptibility towards various antimicrobial agents can only be attained if clinicians suspect anaerobic bacterial infections and availability of trained laboratory staff on the necessary precautions to be taken for proper collection and transport of specimens where ever anaerobic bacteria are to be suspected. Routine sensitivity testing of clinical isolates of anaerobes seems to be the need of the hour. Unless judicious use of antimicrobials is planned for the anaerobic bacteria based on their sensitivity patterns, they will soon follow their counterparts, the aerobes, in developing into "super bugs" which do not respond to commonly used drugs. It is a critical time for clinical microbiologists. We must reinvigorate our interest in these pathogens to prevent future clinical disasters from resistant microorganisms.

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