Paparella: Volume I: Basic Sciences and Related Disciplines

Section 5: Microbiology

Chapter 24: Bacteriology

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It is the purpose of the authors to bring to the attention of the practicing clinician more recent information on some of the bacteria that have been causing disease in humans. A complete review of all the bacteria would result in writing another textbook on bacteriology. This obviously is not our purpose. The authors with to focus the reader's attention on changes in the course of certain disease processes that have resulted from physicians' intervention with antibiotics, bactericidals, and other forms of therapy. To reach the authors' objective would result in a freshness of approach to the understanding of the current presentation of bacterial disease processes.

Haemophilus Influenzae

Haemophilus influenzae is a gram-negative, aerobic coccobacillus. There are six capsular serotypes (a through f). Although *Haemophilus influenzae* b was sensitive to ampicillin in the past, up to 25 per cent of infections are caused by Haemophilus strains producing beta-lactamase (Yamamoto and Iwanaga, 1986). Cultures of secretions from tissue thought to contain *Haemophilus influenzae* are very important, because such cultures can identify those strains of *Haemophilus influenzae* that may be resistant to the usual antibiotic regimens. In the seriously ill person, chloramphenicol therapy with intravenous ampicillin may be necessary while awaiting the results of cultures.

Probably the most common type of infection due to *Haemophilus influenzae* is otitis media. However, a study to determine the incidence of Haemophilus infections in serial patients has not been done. Attention has been focused on meningitis, followed by pneumonia and supraglottitis, each of which can be a life-threatening infection. It has been reported that there is a 8.5 per cent incidence of multiple site involvement with *Haemophilus influenzae* b (Dajani et al, 1979).

In the recent past, *Haemophilus influenzae* was recognized by physicians as primarily a disease process of the very young in so far as otolaryngologic infections were concerned. Certainly, Haemophilus infections in the aged were known, since Sir William Osler died from infection with a "Pfeiffer bacillus", or *Haemophilus influenzae*, empyema, and pneumonia. The disease has not been associated with older people. However, the incidence of isolation of *Haemophilus influenzae* in infections of the aged appears to be increasing.

Certainly, in the pre-antibiotic era, acute suppurative otitis media, suppurative sinusitis, acute epiglottitis, and facial cellulitis were more commonly seen and reported in children 2 to 5 years of age and less. Today, such infections are seen in much older age groups, and indeed epiglottitis has been reported in patients in their 70s. Although the cause of a change in the presentation of infections due to *Haemophilus influenzae* has not been carefully documented, it is likely that the herd-resistance to Haemophilus influenza has been reduced

by the prompt administration of antibiotics, such as the cephalosporins, to children with otitis media and other similar types of infections.

Similarly, as the herd-resistance of the human host has been reduced, the incidence of isolation of *Haemophilus influenzae* from cultures from the human host has not only increased, but the incidence of strains of *Haemophilus influenzae* resistant to the cephalosporins has increased. An example of this was seen in central West Virginia in the spring of 1987 (United Hospital Center, Clarksburg, WV, 1987), where a three-fold increase in the isolation of *Haemophilus influenzae* occurred. Many such increases might be documented from other hospitals throughout the nation in other seasonal changes.

The combination of an increased resistance of this bacteria to antibiotics, coupled with the decrease in the resistance of the host, has produced what appears to be an increase in virulence of *Haemophilus influenzae.* Such infections have resulted in more gram-negative septicemias and life-threatening infections than in the past. Such infections should be kept in mind, since they can severely tax the armamentarium of the individual physician. Under such life-threatening circumstances of gram-negative septicemia, the appropriate antibiotic may be chloramphenicol (Chloromycetin), rifampin, or the newest generations of cephalosporins.

Use of support measures such as intravenous steroids, fluids, and maintenance of the airway, could be appropriate therapy. The maintenance of the airway may include the implementation of a tracheotomy. Certainly, airway preservation in the individual case may also require consultation with specialists in other disciplines including, but not limited to, pediatrics, anesthesia, and infectious diseases.

Facial cellulitis secondary to *Haemophilus influenzae* has been described by a number of authors and must be differentiated from erysipelas secondary to *Streptococcus pyogenes* and, on occasions, periorbital facial cellulitis differentiated from an acute ethmoid sinusitis that has ruptured through the lamina papyracea of the ethmoid into the periorbital area. This distinction can be readily accomplished by a simple Gram stain of secretions or exudate. Similarly, an x-ray study of the facial cellulitis secondary to *Streptococcus pyogenes* would show no evidence of an ethmoid infection. Certainly, a facial cellulitis secondary to *Haemophilus influenzae* and a facial cellulitis secondary to rupture of acute ethmoiditis into the periorbitum may, on occasion, extend beneath the periorbitum, causing ophthalmoplegia, blindness, and cavernous sinus thrombosis.

Finding gram-negative or gram-positive cocci in overwhelming numbers may aid in determining the need for early implementation of the appropriate antibiotic or antibiotic combination. Early diagnosis may be made by a simple Gram stain of a secretion or exudate.

Haemophilus influenzae infections of the upper respiratory tract in children produce a high incidence of bacteremia. As in adults, there appears to be fewer positive blood cultures (Shalin et al, 1987). Although serious life-threatening situations or *Haemophilus influenzae* orbital complications require the immediate implementation of the appropriate antibiotic, the presence of infection with *Haemophilus influenzae* may require rifampin prophylaxis. A single dose of rifampin, 20 mg/kg for 4 days, with 600 mg/dose maximum, is recommended by the American Academy of Pediatrics on Infectious Diseases for the following contacts: (1) all household members less than 4 years of age, (2) day care center and nursery school classroom

contacts (all ages, including adult staff), and (3) the index case before discharge from the hospital (Centers for Disease Control, 1985).

The Food and Drug Administration has approved a marginally effective *Haemophilus influenzae* type b vaccine. The vaccine contains a capsular polysaccharide that the Disease Control Center recommends for all children between the ages of 2 and 5 years. Only those children at high risk and who are under 24 months of age should be offered the vaccine. Although more vaccines are being developed at present, it should be emphasized that the current vaccines are recommended, even though continued studies on their full effectiveness are still being done. Other efforts are also under way to improve the antibody response to the vaccine itself (JAMA, 1987).

Mycobacterium Tuberculosis

Mycobacterium tuberculosis is another organism whose clinical presentation has been altered by the antitubercular medications used during recent years. Certainly, tuberculosis must be considered and reconsidered even in this modern era. In 1986, there was an increase in the number of cases of tuberculosis in the USA over 1985, as reported by the Journal of the American Medical Association (JAMA, May 1987). Clearly, the downward trend in the incidence of tuberculosis has reversed itself. The reasons for this increase, although not fully known, would have to include an increase in tuberculosis among minorities, in the influx of persons born and raised in foreign countries, and certainly in those persons with human immunodeficiency virus (HIV).

Since the human host may be compromised by HIV, the incidence of primary as well as secondary tuberculosis has been noted in patients with AIDS as well as in persons with other diseases that produce an immunocompromised state.

It is the authors' recommendation that all persons who have had a recent diagnosis of tuberculosis be examined for HIV because the data obtained from 24 states and four localities indicates that 625 or 4.2 per cent of the 15,181 patients with AIDS also had tuberculosis (JAMA, 1987).

Today a quick universal method of testing the immune competence of the human host is being developed. The testing of T-cell subsets and diagnosis of increased T-cell suppression of immunity is available to almost every laboratory. However, a broad understanding of immune competence of the human host, is only beginning to develop. Certainly, the opportunistic infections as seen in patients with AIDS and other similar disease processes will need considerable clarification in the future for the practicing physician to be as competent in the treatment of bacterial disease as he or she should be.

Another excellent example of how antibacterial drugs have modified the course of the usual clinical presentation of tuberculosis is seen in the recent reports of laryngeal tuberculosis. Today, laryngeal tuberculosis has been reported in the absence of pulmonary involvement and has been associated with a syndrome relatively new to laryngeal tuberculosis.

Levenson and associates reported on hoarseness and progressive dysphagia in some 20 cases in which cavitary tuberculosis was usually found on chest x-ray studies, leading to

the suggestion that a chest x-ray study should be performed early when evaluating hoarseness as well as dysphagia of obscure origin (Levenson et al, 1984).

Ramages and co-workers discussed 25 cases of tuberculous otitis media in children. These children had presented courses of otorrhea, and there was a relatively high incidence of facial paralysis (Ramages and Gertler, 1985). In summary, tuberculosis is constantly changing its clinical presentation and is increasing in incidence in the USA.

Streptococcus Pneumoniae

Streptococcus pneumoniae can be isolated from approximately 50 per cent of patients with acute suppurative otitis media. This organism has been suspected of being the cause of otitis in the otitis-prone child. Although the definition of the otitis-prone child has not been clearly made, the term generally refers to those children who have had recurrent episodes of acute suppurative otitis media beginning in the early childhood and associated often with persistent or recurrent episodes of acute serous otitis media. The child who is otitis prone may have recurrent episodes of otitis media because of the immediate or recurrent use of antibiotics. Clearly, this condition was not described in the older literature. It is doubtful that physicians practicing in the pre-antibiotic era would have missed such a persistent abnormality in children. This suggests that other factors, such as antibiotics, may be involved in the etiology of this condition.

As antibiotics may have modified the clinical presentation of *Streptococcus pneumoniae* infections in the middle ears of children, an attempt to make an effective pneumococcic vaccine has been tried. The vaccine contains the six types of pneumococcus that are more frequently involved in acute suppurative otitis media. Such a vaccine has been tried and was found to be only marginally successful, similar to the vaccine associated with *Haemophilus influenzae.* The difficulty seems to be in the addition of an adjuvant of sufficient potency to provoke an adequate antigenic response on the part of the host. The host must produce an antigenic response sufficient to enable him or her to reduce the frequency and severity of such attacks of otitis media. Although the vaccine was marginally successful, it has not been generally applied clinically to all otolaryngologic patients, but continued study of such pneumococcic vaccines is being done.

Streptococcus pneumoniae type 3 produces a mucous-type colony covered by a sclera that reduces the effectiveness of the antibiotic, making this particular capsular type of *Streptococcus pneumoniae* more virulent that a more usual strain (Sugita et al, 1985). *Streptococcus pneumoniae* type 3 is a major cause of otitis media in adults, but it is a rare cause of otitis media in children. These latter two facts are nearly identical to the clinical findings 40 to 60 years ago in the pre-antibiotic era. *Streptococcus pneumoniae* is a common clinical pathogen in otitis media and suppurative maxillary sinusitis, though it is usually responsive to antibiotic therapy.

One must resist the notion that infections secondary to *Streptococcus pneumoniae* can be readily controlled by antibiotic therapy. Twenty-five per cent of cases of infection with pneumococcic pneumonia still result in death. Meningitis secondary to pneumococcic otitis still results in deafness, dementia, and death. Such infections may still result in irreversible host changes despite our modern armamentarium of antibiotics.

Virtually every structure associated with the upper and lower respiratory tract may carry pneumococcic proliferation and tissue invasion.

Streptococcus Pyogenes

Streptococcus pyogenes is still a common cause of infection in the region of the head and neck. However, its clinical presentation has also been modified, most likely due to the general use of antibiotics throughout the world. Before the use of antibiotics, group A beta hemolytic streptococcus was the causative organism in 50 per cent of all cases of acute otitis media. However, it accounted for only 10 per cent of such cases in Sweden from 1970 to 1983 (Prellner and Ryder, 1986). It is also interesting to note that *Streptococcus pyogenes* is a facultative anaerobe, and as such, can modify its growth to anaerobic conditions. It has been reported that *Streptococcus pyogenes* has been found in large numbers of colony-forming units in the pus of peritonsillar abscesses (Sprinkle et al, 1984). Also, as noted by Maharaj, it has been seen in conjunction with other anaerobes in the mastoid (Maharaj et al, 1987). *Streptococcus pyogenes* is seen with other organisms in abscess formation and may be encountered anywhere in the head and neck as well as producing systemic complications that result in infection in regions distant from the original site of the infection.

The organism may produce disease processes in the ear, the sinuses, the epiglottis, the throat, and the tonsils. Also it may be associated with other organisms, most notably the anaerobes.

A clinical variant of otitis media, acute necrotizing otitis media, still occurs but was much more common before the antibiotic era. If not quickly recognized and treated, the severe sequela of destructive exotoxin from the streptococcus may necrose all layers of the tympanic membrane, interrupt the ossicular chain, and cause facial nerve paralysis (Stiernburg et al, 1986). Acute necrotizing otitis media may occur in combination with measles or may be found in the transiently immunocompromised patient whose ability to respond to *Streptococcus pyogenes* is limited. Such a streptococcal infection in the immunocompromised patient would appear clinically more virulent than in the normal person. Although otolaryngologists should always be aware of this particular organism, it is also seen in the metabolically compromised diabetic who cannot maintain the host defenses against such an organism.

Anaerobes

The anaerobes of the Bacteroidaceae family are among the most numerous of the microorganisms found in the normal intestinal flora. However, it is unusual to find a throat culture that is positive for one of the anaerobic bacteria. Although they are not commonly identified organisms in the usual throat culture, the clinician should not be lulled into not considering the anaerobes when a patient presents with the clinical diagnosis of an abscess of the head and neck.

The host response to the presence of the microorganism may result in a pyogenic abscess in some circumstances and a nonpyrogenic one in others. Nevertheless, abscess formation is still a common finding and is associated with severe and fatal complications.

The difficulty in the laboratory isolation of anaerobes from clinical materials has prevented the true assessment of their significance and frequency in human infections, particularly when considering infections of the head and neck. The clinician may have been lulled into believing that anaerobes are not usual inhabitants of the head and neck and are not usually found in throat cultures.

Anaerobic bacteria were found in the majority of abscesses reported by the author (Sprinkle et al, 1984), and have been reported in otitis media.

Because the culture and identification of the anaerobes may take from 5 to 7 days, treatment must not depend upon identification of a pathogen but should be started at once. Remember that approximately 50 per cent of anaerobic infections results in bacterioses, and prompt surgical incision and drainage should accompany appropriate antibiotic therapy. It is clinically important that whenever foul-smelling or putrid pus is encountered, anaerobes should be suspected since pure *Escherichia coli* infections do not cause foul-smelling pus. Similarly, a negative culture from exudate or tissue that is strongly suspected of having bacterial infection should suggest to the physician the presence of anaerobes since they are often difficult to grow in the usual clinical laboratory setting.

An immediate study of Gram-stained smear of the pus from an abscess may be helpful because the bacteroidaceae appear as pleomorphic gram-negative bacilli.

Pathogenic Streptococci that are anaerobic are also commonly associated with abscess formation and require appropriate penicillin therapy for the best clinical response. However, the Bacteroidaceae are not sensitive to the usual doses of penicillin and a newer generation cephalosporin, Chloromycetin, or clindamycin should be considered.

Staphylococcus Aureus

Staphylococcus aureus is still commonly associated with abscess formations in the head and neck region whereas Staphylococcus aureus was seen in approximately 50 per cent of abscesses of the head and neck in the study presented (Sprinkle et al, 1984), *Staphylococcus aureus* is more commonly seen in abscesses as an infection containing a single organism. Its ability to form a pyogenic membrane makes this understandable. However, it also has been reported in conjunction with other organisms.

In an unpublished study conducted by the authors, recurrent Staphylococcal abscesses have been found to be associated with a T-cell suppression. The authors have found that those patients who have repeated abscess formation secondary to *Staphylococcus aureus* had an excellent response to anti-inflammatory agents. Certainly, each of these individuals should be thoroughly screened for diabetes and other metabolic defects as well.