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Infections Associated with Indwelling Devices: Infections Related to Extravascular Devices

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The use of indwelling prosthetic devices, on either a temporary or a permanent basis, has become routine in modern medical practice. The number and types of such devices have increased greatly over the past few decades. Despite surgical advances and improvements in the materials and design of devices, infection continues to be a major complication of their use. Such infections quite frequently cause serious dysfunction of the prosthesis, requiring its removal, or may even be associated with life-threatening local or systemic consequences. In the preceding article, we outlined current concepts of the pathogenesis of foreign body infections and described the nature and consequences of infections associated with intravascular foreign bodies (16). We now deal with the clinical and microbiologic aspects of extravascular infections associated with implanted medical devices.

ENDOTRACHEAL AND TRACHEOSTOMY TUBES

Prosthetic airways are used principally in hospitalized patients, usually for brief periods. Occasional patients are equipped with tracheostomy tubes on a prolonged basis in the outpatient setting. The most serious infection in patients with artificial airways is pneumonia, although tracheitis, otitis, and sinusitis occur as well. Because these devices are typically used in patients at high risk for pneumonia, it is difficult to define the role of the airway in the pathogenesis of infection.

Artificial airways interfere with a number of respiratory tract defense mechanisms. The current of inhaled air passing through the smooth lumen of the endotracheal tube bypasses the angulations and mucosa of the upper respiratory tract, structural features which normally ensnare particles of 10-μm diameter or larger (41). The endotracheal airway prevents closure of the glottis; this allows aspiration. Of perhaps greater importance, the vital role of the closed glottis in the initiation of an effective cough is vitiated. The cuffs on airways, whether of the rigid, high-pressure type or of the soft, low-pressure variety, do not prevent aspiration (8, 53). The airway also may traumatize the tracheal mucosa and interrupt normal ciliary cell clearance functions (28, 30).

Colonization of the oropharynx by potential pathogens is a frequent occurrence among seriously ill patients (25). Such patients have increased salivary protease activity and loss of cellular fibronectin, which may predispose them to enhanced adherence of gram-negative bacilli (63). The role of artificial airways in this colonization is undefined. Distal airways also become colonized with these organisms following intubation (26). The bacteria that cause pneumonia in patients with artificial airways are predominantly gram-negative aerobic bacilli, but *Staphylococcus aureus*, streptococci, and anaerobes may also be involved (13, 25, 63). *Staphylococcus epidermidis*, the organism most commonly recognized in association with foreign body infection, is not a respiratory pathogen in patients with artificial airways. Inhibition of gastric acidity with antacids or blockers of the histamine H2 receptor may allow growth of gram-negative bacteria and subsequent colonization of the airways of critically ill patients (17).

The prevention of infection associated with artificial airways is best achieved by limiting the duration of intubation whenever possible, meticulous attention to frequent suctioning, and strict adherence to infection control guidelines (particularly hand washing) to avoid transmission of nosocomial pathogens from one patient to another. Contaminated reservoir solutions, formerly a source of infection for intubated patients, are no longer a major problem since the introduction of appropriate methods of decontamination.

INDWELLING UROLOGICAL DEVICES

A significant proportion of hospitalized patients, especially those undergoing major surgery, have a urethral catheter placed for a short time; and many patients who are unable to control bladder function because of spinal cord injury, stroke, or generalized debility must permanently use an indwelling catheter.

The incidence of bacteriuria rises from 0.5 to 1% for a single "in-and-out" catheterization to 10 to 30% for catheters in place for up to 4 days (20, 31) and up to 95% for catheters in place for 30 days or more (20, 31).

There are several mechanisms through which catheters contribute to the pathogenesis of urinary tract infections. The most obvious is the disruption of the normal valvular function of the urethra. Catheters serve as a direct conduit for pathogens. Microorganisms may be carried from the external meatus to the bladder when the catheter is introduced, they may spread along the external surface of the catheter from the meatal area, or they may pass in a retrograde fashion through the lumen. Catheters also may traumatize urethral and bladder mucosa, disrupting the normal mucopolysaccharide coating of the epithelium, damaging its cellular structure and rendering it more susceptible to the attachment of bacteria (44), and allowing ingress of bacteria through surface erosions.

The bacteria that cause urinary tract infections in patients with catheters in place for short durations are similar to those seen in hospitalized patients without catheters. They are primarily gram-negative bacilli of enteric origin that have the ability to adhere to and multiply in the lower urinary tract. The list of pathogens is headed by *Escherichia coli* and includes *Klebsiella* and *Proteus* species, a number of miscellaneous enteric gram-negative bacilli, and enterococci. Patients who require long-term catheterization tend to acquire bacteriuria caused by a different spectrum of microorganisms, including multiple-antibiotic-resistant strains of *Pseudomonas aeruginosa* and *Enterobacter*, indole-positive *Proteus*, and *Providencia* species. Such organisms are not

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usually found in the gastrointestinal tracts of normal nonhospitalized individuals. They are, however, well-recognized denizens of the hospital environment, where they persist in part because of selective pressure exerted by antimicrobial use. These multiply resistant gram-negative bacilli may enter the urinary tract after colonization of the bowel, but frequently they are directly inoculated by health care workers manipulating the catheter or collecting system. Recurrent invasion of the urinary tract is inevitable with long-term catheterization (61), but certain bacteria have the ability to persist for long periods. Some of these persistent strains have been shown to form a glycocalyceal film on the catheter surface (42).

Attempts to prevent catheter-associated infection have included the introduction of closed drainage systems (now universally used in the United States), application of antimicrobial ointments, instillation of antimicrobial agents into the bladder or collection bag, administration of systemic antimicrobial agents, and a change from permanent catheters to intermittent clean catheterization (32). The use of closed collection systems decreases the rate of acquisition of bacteriuria (31, 56), although with prolonged catheterization the incidence of infection eventually is quite high. Application of periurethral ointment has never been documented to decrease the incidence of infection (59). Antimicrobial bladder rinses are of no benefit with closed drainage systems (4, 21, 60), and instillation of an antimicrobial agent into the collection bag has generally not been of benefit (59). Systemic antimicrobial prophylaxis is effective, but only for short-term catheterization (7), and tends to select for resistant organisms (35).

Intermittent clean catheterization, used by paraplegics and other patients able to perform self-catheterization, is clearly an alternative to permanent catheterization (32). Although significant bacteriuria is reported to range from 27 to 100% (59), the incidence of febrile infections is decreased.

Penile prostheses, an accepted form of treatment for certain forms of impotence, and prostheses implanted to restore sphincter function are now widely used, although the actual number of devices implanted is probably low. Infection is the major complication and is frequently caused by *S. epidermidis* (55). In addition to the administration of systemic antibiotics, removal of the device is usually necessary to eradicate the infection (55).

CENTRAL NERVOUS SYSTEM SHUNTS

Prosthetic devices are inserted into the cerebrospinal fluid (CSF) circulatory pathways either for monitoring and control of increased CFS pressure or for administration of therapeutic agents. Monitoring devices include subarachnoid screws or cup catheters and intraventricular catheters. In patients with hydrocephalus, CSF is frequently diverted from the central nervous system to the periphery, usually by means of ventriculoperitoneal or ventriculoatrial shunts. External ventriculostomies are occasionally used for this purpose as well, particularly in situations associated with an acute increase in CSF pressure. Internal ventriculostomies, on the other hand, are used to bypass the blood-brain barrier and allow direct intraventricular administration of antimicrobial and antineoplastic drugs.

The reported incidence of infection varies widely, depending upon factors such as patient selection, type of device, and definition of infection. Schoenbaum et al. (52) studied 442 shunts inserted for hydrocephalus in 289 patients at Children's Hospital Medical Center in Boston, Mass., from 1959 through 1968. Twenty-two percent of the shunts became infected. Including shunt revisions, the patients underwent a total of 743 operations. The proportion of operations resulting in infections was 17.7% for the period 1959 to 1965 but declined to 6.2% for the final 3 years of the study. Sixty-two percent of the infections occurred within 1 month of the most recent surgical procedure.

Two recent studies (3, 36), conducted primarily with adult patients, found infection rates of 11% for intracranial pressure monitors. Risk factors identified by these studies included the presence of intracranial hemorrhage, maintenance of the device in place for 5 days or more, and irrigation of the pressure-monitoring system. The latter finding reinforces the impression that most infections of CSF prostheses occur as the result of implantation of the organism at the time of surgery or of contamination of the device by ward personnel during manipulation. This impression is buttressed by the fact that most infections of CSF prosthetic devices are caused by skin floras. *S. epidermidis* is by far the most frequent pathogen, with *S. aureus* in second place. A variety of other organisms may be involved, including corynebacteria, propionibacteria, enterococci, and gram-negative bacilli.

The clinical syndromes associated with CSF prostheses range from wound infections to nondescript febrile states to ventriculitis or meningitis. Patients with ventriculoatrial shunts may present a septicemic picture, while those with ventriculoperitoneal shunts may develop intra-abdominal cysts or frank peritonitis. Shunt dysfunction may produce signs and symptoms of increased intracranial pressure. Some patients with ventriculoatrial infections develop a form of glomerulonephritis (shunt nephritis) characterized by mesangial hypercellularity and granular deposits of immunoglobulins and complement along the glomerular membrane. These findings are characteristic of immune complex glomerulonephritis.

The details of management of CSF prosthetic infections are complex, depending as they do on the type of infection, age of the patient (open or closed fontanels), nature of the pathologic process, urgency of maintaining continuous access to the ventricular system, and antimicrobial susceptibility of the infecting pathogen. Moreover, there are few controlled studies, and opinions as to optimal modes of therapy vary widely. In general, once signficant infection of the CSF has occurred, most studies (24, 52, 64) indicate the need for removal of the infected apparatus and the administration of appropriate systemic antibiotics. In many instances, it may be advisable to administer intraventricular antibiotics as well, by either a newly inserted external drainage device or reinsertion of a new prosthetic device or, in infants, by ventricular taps. A recent study (37) suggested that many patients with ventriculoperitoneal shunt infections may be treated effectively by externalization of the peritoneal catheter, intravenous and intraventricular antibiotic therapy, and later replacement of the peritoneal catheter.

For infections of CSF shunts caused by *S. epidermidis*, surface characteristics of the infecting microorganism may influence prognosis. Bayston and Penny's original description of a slime layer associated with coagulase-negative staphylococci (5) dealt with strains isolated from CSF shunt infections. Diaz-Mitoma et al. (15) reported that, in ventriculoperitoneal infections caused by coagulase-negative staphylococci, failure to eradicate the organism by antimicrobial therapy was significantly more frequent with slime-producing than with non-slime-producing organisms. Younger et al. (64) found great difficulty in curing certain

CSF shunt infections caused by adherent *S. epidermidis* strains (as defined in their assay) by antimicrobial therapy alone; removal of the shunt was usually necessary.

OCULAR PROSTHESES

Ocular prostheses, once limited to artificial globes used for cosmetic purposes, now include intraocular lenses, ocular explants, and contact lenses. There are three basic types of contact lenses. Hard lenses are made of polymethylmethacrylate, a substance that is impermeable to water and gas. Hydrophilic, or soft, lenses are made of cross-linked hydrogel polymer or copolymer and contain 38 to 85% water by weight; they are permeable to both water and gas. Gas-permeable hard lenses, composed of silicone, cellulose acetate butyrate, or polymethylmethacrylate-silicone copolymers, allow the passage of gas but not fluids. The hard lenses are designed to be worn only during waking hours because they limit the oxygen available to the avascular cornea to the amount present in tears. Hydrophilic lenses, on the other hand, permit the free passage of oxygen and can be worn continuously. Infection may result from damage to the corneal epithelium by the artificial lens. Recent epidemiologic studies have implicated predisposing factors which include damage to the corneal epithelium by the artificial lens and improper cleaning and handling of the lens.

Conjunctivitis and keratitis are the two principal infections that occur in association with lenses (9). The causative bacteria are primarily *S. aureus*, streptococci, and *Pseudomonas* species. Improperly maintained cleansing solutions are an important source of pseudomonads. Fungi may also cause lens-related infection. It should be noted that the soft or hydrophilic lens can serve as a reservoir of infection when bacteria penetrate the lens matrix and are not removed by proper cleaning. Treatment is usually readily accomplished by removal of the lens and topical application of antibiotics for several days.

A rare but devastating infection with the free-living fresh water protozoan *Acanthamoeba* sp. has been reported in association with lens use (11, 39). This protozoan contaminates the lens when proper sterility of the cleansing solution is not maintained. Cleansing solutions prepared by the user have been implicated as the usual source. *Acanthamoeba* sp. is not susceptible to available antiparasitic agents, and the chronic keratitis produced has been complicated by perforation and loss of the eye (22, 39, 54).

The most effective preventive measure against contact lens-associated infection is strict adherence to the manufacturer's guidelines for wearing and cleaning the lens.

The rate of infection of intraocular lenses is low, and such infections virtually always occur in the postoperative period. *S. aureus* and *S. epidermidis* are the major pathogens, although occasionally a gram-negative bacillus is encountered. Permanent loss of vision is the usual outcome.

ORTHOPEDIC PROSTHESES

Orthopedic devices include not only prostheses to replace hip, knee, and other joints but also a wide assortment of screws, pins, plates, and rods for stabilization of bone defects. Infections involving orthopedic prosthetic devices are often catastrophic events leading to removal of the device and weeks of hospitalization. The clinical manifestations of infection may be insidious and related primarily to device dysfunction. Infection may arise from bacteremic seeding of the device, but most of these infections are introduced at the time of surgery. The rate of infection related to surgery is affected by many variables: the presence of underlying disease, the type of surgery, the duration of the operation, previous surgery or infection at the site, surgical technique, and the composition of the material implanted. The rate of infection for first-time implantation of an artificial hip is generally less than 2% (18, 19, 33, 40), while knee replacement is reported to carry a <0.6 to 11% risk of infection, depending upon the type of implant (48, 49).

The major pathogen causing orthopedic-prosthetic-device-associated infection is *S. aureus*, followed by coagulase-negative staphylococci. The list of other microorganisms associated with such infections is lengthy but includes members of the family *Enterobacteriaceae*, *P. aeruginosa*, streptococci, and anaerobes (1, 23, 48, 49).

The consequences of infection are so serious that antibiotic prophylaxis, usually reserved for contaminated or "dirty" surgery, is recommended for surgery involving implantation of orthopedic prostheses. Some surgeons use antibiotic-loaded acrylic cement to prevent infections, but the efficacy of this approach is unproven (49). Because the risk of infection associated with the use of pins or screws for stabilization of a bony defect is considerably lower, prophylaxis is dependent upon considerations unique to the patient undergoing the surgery.

Some controversy has arisen over the question of whether antibiotic prophylaxis should be given to patients with prosthetic joints who undergo dental procedures. Because the typical causative pathogens are not oral floras and because a clear temporal association between dental procedures and prosthetic infections has not been demonstrated (23), we do not recommend routine prophylaxis.

PERITONEAL DIALYSIS CATHETERS

Peritoneal dialysis for treatment of renal failure has been widely used for more than 20 years. It is now a standard method for treatment of both acute, short-term renal failure and chronic renal failure in patients in whom return of renal function is not anticipated. The basic technique has evolved from the short-term dialysis performed through a simple straight rigid catheter into a long-term method performed through a silicone catheter that is permanently implanted and used for either intermittent peritoneal dialysis or continuous ambulatory peritoneal dialysis. Advances in dialysis technology have permitted the use of intermittent and continuous ambulatory peritoneal dialysis by patients outside the medical facility. Infection was a limiting factor during the developmental stages of these techniques, and it remains the major complication (45).

The rapid exchange of dialysate fluid results in an intraperitoneal medium that is deficient in complement and immunoglobulins (29). The phagocytic capability of peritoneal macrophages is normal (58), but the deficiency of opsonins may well be a significant factor in the pathogenesis of intermittent and continuous ambulatory peritoneal dialysis infections.

Estimates of rates of peritonitis have ranged from 1.2 to 6.3 episodes per patient year (14, 50). Most infections in patients on chronic dialysis are probably related to breaks in sterile technique during the manipulation of the external tubing and bags. Infection may also occur if contaminated dialysate fluid is used and, infrequently, during the course of a bacteremia. Most episodes of peritonitis can be managed with antibiotic instillation into the dialysate without removal of the catheter (6).

Major improvements in the packaging and techniques of administration of dialysate have reduced the risk of infection. Recognition of the dangers related to manipulation of the external catheter has decreased the introduction of pathogens into the system, although this is still an important route of infection. The permanent catheters now in use are surgically placed under sterile conditions. They have Dacron cuffs that are placed just under the skin and just above the peritoneal surface; fibrous tissue grows into the cuffs and forms impermeable obstacles to bacterial growth spreading along the catheter from the skin surface.

IUDs

A large variety of intrauterine devices (IUDs) have been available in the past, but in the United States there are currently only two such devices on the market (2). IUDs produce an inflammatory reaction which is thought to interfere with fertilization. Bacteria are frequently undetectable by usual culture techniques once the IUD is in place (38); however, IUDs are uniformly coated with a biofilm that contains bacteria (34).

Recognizable patterns of IUD-associated infections include (i) an acute endometritis which may follow insertion, (ii) typical pelvis inflammatory disease, and (iii) unilateral ovarian abscess. The common anerobic and aerobic floras of the female genital tract account for most IUD infections. In addition, there have been a number of reports of pelvic actinomycosis in wearers of IUDs (51, 57).

AUGMENTATION MAMMAPLASTY

The use of silicone prostheses for cosmetic augmentation of breasts is associated with a low rate of infection; the usual pathogen has been *S. aureus* (12). Since 1978, a number of reports have documented infections caused by *Mycobacterium fortuitum* and *Mycobacterium chelonei* (10). These infections are characterized by an absence of systemic signs, spontaneous drainage of odorless serosanguinous or purulent fluid, and a poor response to treatment (10). The source of these pathogens has not been identified.

MANAGEMENT OF PROSTHETIC INFECTIONS: GENERAL COMMENTS

The experience gained with prosthetic-device-associated infections permits some generalizations about management. For each device, a small number of pathogens accounts for the majority of infections. Infections of central nervous system shunts, intravascular catheters, heart valves, and prosthetic joints are frequently associated with staphylococci, especially coagulase-negative staphylococci. This association is revealing of the nature of foreign body-pathogen interaction because of the normally innocuous relationship between coagulase-negative staphylococci and the host. The pathogens usually encountered in catheter-associated urinary tract infections are gram-negative bacilli, either those commonly found among bowel floras or more highly antibiotic-resistant, nosocomially acquired organisms.

Despite an ever-enlarging antimicrobial armamentarium that now includes potent agents against virtually all bacterial pathogens, most foreign body infections require removal of the device before cure is achieved. Notable exceptions to this rule are peritoneal catheters in patients receiving continuous ambulatory peritoneal dialysis and intraocular lenses in patients with pseudophakic endophthalmitis (62). Likewise, some patients with prosthetic valve endocarditis—particularly those with late-onset infections caused by penicillin-susceptible streptococci—may be cured by antimicrobial therapy alone.

The most effective approach to foreign body infections is prevention. Most microorganisms associated with permanently implanted devices are introduced with the device at the time of surgery. Preventive measures that have been advocated to decrease the incidence of infection have included the use of laminar air flow and high-volume air filtration in the operating theater, preoperative skin preparation with aseptic soap, and administration of prophylactic antibiotics. Minimizing operative time and tissue trauma are of obvious importance. Certain materials used to make medical devices may predispose to infection because they provide more favorable substrates for pathogens (27). Cement used to hold artificial joints in place, methylmethacrylate, has inhibitory action against polymorphonuclear cell chemotaxis and phagocytosis (43, 46, 47).

Prophylactic antibiotics appear to be appropriate when used at the time of surgical implantation of permanent prosthetic devices, such as heart valves, vascular grafts, and artificial joints, although their effectiveness has only rarely been demonstrated in controlled trials (A. B. Kaiser, *in* A. L. Bisno and F. A. Waldvogel, ed., *Infections Associated with Indwelling Medical Devices*, in press). The low frequency of infection associated with many prosthetic implant procedures has posed the need for a prohibitively high number of study subjects to document the efficacy of prophylaxis.

Research into newer prosthetic materials may provide devices with lower affinities for pathogens—or possibly with antimicrobial properties—and enhanced biocompatibility with the tissue environment into which the device is placed. Such materials could conceivably have a major impact on the incidence and natural history of infections associated with indwelling medical devices.

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