Joint infection

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Background—where we stand today

Short historical background

Based on a knowledge of Louis Pasteur's discovery that microorganisms caused problems in the beer and silk industry, by 1864 Joseph Lister had begun using the antiseptic carbolic acid for surgery. In 1867 he published his manuscript *"The Antiseptic System"* (Lister, 1867). Lister's familiarity with the microscope allowed him to confirm that bacteria were the cause of suppurative wounds. He quickly designed techniques to prevent tissue contamination making elective surgery feasible. Until Lister, surgical intervention commonly lead to infection half the time. His antiseptic treatment for established infection also met with success. Lister's methods were quickly adopted world wide and used to prevent and treat infection. Koch's postulates developed the principles of specific diagnosis of the organism. By the 1930's, sulfa drugs were introduced to be followed by penicillin a decade later. Success in control and treatment led to the explosive rise of surgical interventions. The eruption of implant surgery during this century led in great part by orthopaedic surgeons provoked the need to optimize better techniques of preventing and treating infection. Earlier and improved methods of diagnosis and treatment have reduced postoperative infection rate and the morbidity of hematogenous or trauma induced bone and joint infection. Even so, joint infection is still among the most common serious problems faced by the orthopaedic surgeon.

Incidence, frequency, morbidity, mortality, cost to society

The annual incidence of septic arthritis in recent years varies in reports between 9.2 per 110,000 (Morgan et al. 1966) and 37.1 (Yagupsky et al. 1995). The problem is more common in children and the aged (Ryan et al. 1997). Staphylococcal and streptococcal species comprise more than half the cases. *Streptococcus pneumonia* and Lancefield group A *beta-hemolytic Streptococcus* accounted for almost two thirds of the streptococcal infections. Knee and hip together account for two thirds of the sites of joint infection. About half the infections have a predisposing factor, usually a connective tissue disease, often on immunosuppresive medication or else parenteral drug abuse (Amo et al. 1997).

Pathophysiology including morphology, biochemistry, genetic

For many decades the role of the host immune system reacting to the bacteria and causing articular cartilage destruction has been well documented. Within 48 hours of infection 40% of the glycosaminoglycans can be lost from the articular cartilage and by three weeks 50% of the collagen. The bacteria itself can secrete a factor that accelerates the loss of proteoglycan from cartilage (Smith and Schurman 1986). The loss of proteoglycan is associated with increase in chondrocyte-derived neutral metalloproteinases (Williams et al. 1991). Bacteria that have a collagen receptor can mediate adhesion and add to the virulence of the organism (Witalski et al. 1993). Chemokines working with cytokines can recruit leukocytes into tissues and up-regulate adhesion molecules (Luster 1998). Some staphylococcal enterotoxins display superantigen properties stimulating large numbers of T-cell lymphocytes. Animal models indicate that these bacteria are especially arthritogenic (Bremell and Tarkowski 1995). Using a similar model, MHC class II molecular expression were shown to increase the prevalence and severity of arthritis (Abdelnour et al. 1997). Nitric oxide is an important mechanism used by the macrophage for killing ingested bacteria. When nitric oxide synthase was inhibited in an animal model mortality and arthritogenicity greatly increased (Sakiniene et al. 1997).

Diagnostic procedures

DNA hybridization combined with polymerase chain reaction is a hopeful new field for sensitive and early

microbial identification (Canvin et al. 1997). Sensitivity is exceptional but probes for portions of a bacterial gnome may have success long after live bacteria no longer exist making interpretation clinically less helpful under some situations. Magnetic resonance imaging is frequently the best of the imaging modalities to diagnose and anatomically pinpoint most soft tissue infections including septic arthritis and promises to improve with new advances (Beltran 1995). Radionuclide imaging improves with continuing certainty. The most useful scans are radiolabeled granulocyte tests though newer multiphased scintillation scans with computed tomography are fascinating if not increasingly expensive. Isotope bone scans of painful joint replacements are deservedly playing less of a role in diagnosis of infection (Owenn et al. 1995) (Palestro and Torres 1997). Histologic help in diagnosis can be critical and better guidelines have been established using frozen sections for decision making at surgery of potentially infected total joint arthroplasty (Feldman et al. 1995).

Treatment modalities

Appropriate antibiotic treatment with surgical debridement, drainage and nutritional supplements if necessary continues as the primary basis of therapy. Passive range of motion, physical therapy, irrigations and local antibiotics have an advocacy and importance.

Outcome

Early diagnosis and treatment are the best guarantors of a good outcome. For example, acute septic arthritis of the hip joint in infancy and childhood when treated within 4 days of the onset of symptoms almost always had a satisfactory outcome. Associated osteomyelitis or infection with *Staphylococcus aureus* had a worse outcome (Bennett and Namnyak 1992).

Future perspectives

Epidemiologic changes in the future

The impaired host with predispostion to septic arthritis is an increasing phenomenon. In economically advanced countries, longer life spans lead to larger numbers of aged people with compromised immune systems and a predisposition to infection. Septic arthritis in the impaired host commonly includes relatively otherwise uncommon infections and other opportunistic microbes including fungus, tuberculosis and viruses.

Therapeutic developments

Technology advancements that are predictable include improvement in virtually all current modes of treatment including better antibiotics and better antibiotic delivery systems. Local antibiotics are of special interest to orthopaedic surgeons from which there are many strong advocates. It is in this arena where orthopaedic surgeons may contribute most easily to important advances leading to more effective and safer antibiotic delivery systems. Dissolvable time released antibiotic local delivery systems will make further inroads in clinical settings. The computer age guarantees antibiotic therapy with feedback loops and 'designer' individualized or boutique regimens will come to fruition in the foreseeable future. Better outcome studies will continue to improve almost every aspect of our knowledge adding steady increments of success to clinical treatment.

Prevention

In children the use of vaccination can effectively prevent infection of *Haemophilus influenzae* and could have major importance world wide (Bowerman et al. 1997). Prophylactic antibiotics will in the future move away from systemic delivery and become local controlled release medications from biodegradable vehicles left behind at surgery or injected into the joint.

Stopping and reverting damage

Joint sepsis is stopped most easily the sooner it is treated with antibiotics. The earlier the treatment the less important and the less necessity for the use of drains or operative intervention. Even infected total joint arthroplasties have a chance at cure with retention of the implant if infection occurs in the early post operative period and is quickly diagnosed and aggressively treated. Reverting damage to articular cartilage is not well documented after intervention. Post infectious inflammation is minimized by early intervention and thus minimizes progressive cartilage destruction once the bacteria are sterilized. The degree to which the articular cartilage matrix regenerates is not clear. Many clinical reports emphasize the success of early intervention in that in short or intermediate followup joint function appears to return to normal. However, little information is available with long-term followup. The question remains as to whether deficient extracellular matrix or chondrocyte death leads to secondary degenerative arthritis decades later or if the matrix so fragile and so easily degraded can repair itself. Once the matrix collagen is importantly diminished or when cracking appears in the cartilage, there is no data to suggest cartilage repairs itself.

Tissue repair

Inflammatory degeneration of articular cartilage after sepsis is not known to occur, though it has been little studied over any significant period of follow-up. New methods of autologous cartilage cell grafting are not suitable for repairing this type of arthritis. As lower order vertebrates can regrow joints or even whole limbs it is likely that gene therapy will someday be useful in the restoration of some types of postinflammatory arthritides including post septic joints.

Specific goals for the next decade

- Define the principals of effective local antibiotics for prevention and treatment.
- Implement biodegradable time released antibiotics for prevention and treatment.
- Refine clinical regimens of antibiotic therapy with randomized outcome studies.
- Continue to unravel the cellular and molecular events which determine infectivity, host defense mechanisms and pathophysiology.
- Optimize diagnostic tools available to best use magnetic resonance imaging, computerized tomography, radionuclide scans and molecular probes.

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