Bone and joint infections

CHAIRPERSON
TJ LOUIE, MD, FRCPC

AN OVERVIEW OF MICROBIOLOGICAL AND CLINICAL ASPECTS of bone and joint infections was presented by Dr T Louie. The essential characteristics of osteomyelitis include adhesive colonization of damaged bone, tissue substrate or biomaterials, eg, prosthetic orthopedic devices (1-3). Chronic persistent infection where microbes are protected from host defenses and antimicrobial intervention by bacterial biofilms, devitalized tissue and foreign body effect become a formidable medical-surgical management problem (4-6).

Animal models of osteomyelitis have partially clarified pathogenesis. However, bone infection is generally difficult to initiate without concurrent tissue damage, introduction of sclerotic chemicals or foreign bodies (7-8). Animal models have shown that microbial synergy may be important in promoting infection in situations where polymicrobial contamination of bone occurs. Therapeutic studies of animal models of osteomyelitis have shown that beta-lactam antibiotics and vancomycin treatment, even for four weeks, does not result in sterilization of the infected site. Less conventional treatment options such as clindamycin, beta-lactams in combination with rifampin or rifampin plus a quinolone antimicrobial agent merit serious consideration in well designed clinical trials (9,10).

The committee reviewed clinical trial options and concluded that management of the infected total hip and total knee prostheses, as well as other infected orthopedic devices, was of major clinical interest to infectious disease clinicians across Canada. Committee members indicated that the infected total hip replacement was the most common difficult to manage infectious disease problem facing both infectious disease clinicians, internists and orthopedic surgeons. The infected total hip replacement is ideally suited to a multi-

centre clinical trial approach since each medical centre, independently, will have only five to 20 cases per year. These are insufficient numbers to allow single medical centres to evaluate diagnostic and therapeutic approaches in a reasonable time frame of two to three years. It was proposed that the Canadian Infectious Disease Society in conjunction with the Canadian Orthopedic Association develop a clinical trial network to address outstanding infectious disease/orthopedic problems. Specifically with respect to the total hip replacement, the role of hospital infection control units should be examined as a clinical trials resource since procedure-related infection rates are monitored across Canada.

Diagnostic and therapeutic approaches to the management of infected total hip replacement in a clinical trials setting were discussed.

DIAGNOSIS

Diagnostic approaches to separate mechanical loosening versus infection or both were reviewed (11,12). Combinations of preoperative aspiration culture, multiple-site intraoperative cultures, the erythrocyte sedimentation rate, plain x-rays, technetium⁹⁹ bone scans, gallium scans, ¹¹¹indium-labelled white blood cell scans, indium-labelled polyclonal IgG scans, computed tomography scans and magnetic resonance imaging scans have been investigated. It was concluded that no single test is both highly sensitive and specific for total hip replacement infection (13). However, several combinations and a decision tree approach are recommended (11). While laboratory tests are helpful in guiding management, clinical observation over time in conjunction with adequate cultures are essential.

THERAPY

An observational study to monitor current therapy in Canadian hospitals was suggested. The proportion of patients managed by debridement and antibiotics or by one- and two-stage revisions would be tabulated. Outcomes would be used to identify problems and potential solutions to total hip replacement infection problems.

Workshop participants: K Buchan, N Christou, K Forward, C Frenette, O Hammerberg, G Harding, J Langley, J Leblanc, C Lee, A Martel, L Nicolle, O Rotstein, R Zoutman

Correspondence: Dr TJ Louie, Department of Internal Medicine, Calgary General Hospital, 841 Centre Avenue, Calgary Alberta T2E 0A1

Previous studies have shown that antibiotic treatment and suppression along with debridement without prosthesis removal results in effective suppression of infection in the minority of patients (14).

One- and two-stage revision surgery, in conjunction with varying lengths of intravenous antibiotic therapy have shown that progressively superior results of reconstruction surgery are attained with a combination of prosthetic removal and debridement plus six weeks of aggressive intravenous antibiotic therapy followed by prosthetic insertion. With certain pathogens, such as *Pseudomonas aeruginosa* and other Gram-negative bacilli, some investigators have recommended extended durations of observation following antibiotic treatment prior to prosthetic insertion (17).

Clinical trials on the most appropriate antimicrobials, eg. beta-lactams versus other antimicrobial classes, eg. macrolides for Gram-positive infecting pathogens, combinations of antibiotics, or the investigation of new antimicrobials should be developed. Combinations which show promise in animal models should be considered (8-10).

PREVENTION

Most committee members felt that a prophylaxis trial would be too difficult to conduct because of the large number of patients required to show significant differences between antimicrobial agents. Currently, in-

fection rates are approximately 1% in Canadian hospitals. Other variables including HEPA-filtered operating room air, antimicrobial containing wound irrigants, age, co-existing infection at other sites and underlying disease need to be considered in prophylaxis trials. Finally, the use of different bone cements which harden at varying temperatures should be investigated as an infection variable. Currently, the most commonly used bone cement hardens at 70°C a temperature that may compromise host defenses.

The role of antibiotic-containing bone cements in orthopedic surgery should also be investigated. Different clinical trials each with small numbers of patients have shown that two-stage revisions with and without gentamicin-containing bone cement have yielded similar outcomes (13,15,16,18,19). Comparative trials with larger numbers of patients would be of practical interest.

Other bone and joint infections including acute hematogenous osteomyelitis, the diabetic foot, chronic osteomyelitis and fracture-associated infections were considered for purposes of clinical trials. However, the infected hip prosthesis, while low in number, is a long term medical problem which disproportionately consumes health care resources and creates significant deterioration in quality of life. It is hoped that some of the above issues can be addressed by multicentre clinical trial(s) in the near future.

REFERENCES

1. Gristina AG, Naylor PT, Myrvik QN. Mechanisms of musculoskeletal sepsis. *Orthop Clin North Am* 1991;22:363.
2. Christensen GD, Simpson WA, Bisno AL, et al. Experimental foreign body infection in mice challenged with slime-producing *S epidermidis*. *Infect Immun* 1983;40:407.
3. Costerton JW, Cheng K-J, Geesey GG, et al. Bacterial biofilms in nature and disease. *Ann Rev Microbiol* 1987;41:435-64.
4. Nichols WW, Evans JJ, Slack MPE, et al. The penetration of antibiotics into aggregates of mucoid and non-mucoid *Pseudomonas aeruginosa*. *J Gen Microbiol* 1989;135:1291.
5. Voytek A, Gristina AG, Barth F, et al. Staphylococcal adhesion to collagen in intra-articular sepsis. *Biomaterials* 1988;9:107-10.
6. Falcieri F, Vaudaux P, Huggler E, et al. Role of bacterial exopolymers and host factors on adherence and phagocytosis of *S aureus* foreign body infection. *J Infect Dis* 1987;155:524.
7. Rissing JP. Animal models of osteomyelitis. *Infect Dis Clin North Am* 1990;4:377-90.
8. Norden CW. Lessons learned from animal models of osteomyelitis. *Rev Infect Dis* 1988;10:103.
9. Norden CW. Experimental chronic staphylococcal osteomyelitis in rabbits: Treatment with rifampin alone and in combination with other antimicrobial agents. *Rev Infect Dis* 1983;5:S491.
10. Norden CW, Shinnors E, Niederreiter K. Clindamycin treatment of experimental chronic osteomyelitis due to *S aureus*. *J Infect Dis* 1986;153:956.
11. Schauwecker DR, Braunstein EM, Wheat JL. Diagnostic imaging of osteomyelitis. *Infect Dis Clin North Am* 1990;4:441.
12. Wegener WA, Alavi A. Diagnostic imaging in musculoskeletal infections. *Orthop Clin North Am* 1991;22:401.
13. Cuckler JM, Star AM, Alavi A, Noto RB. Diagnosis and management of the infected total joint arthroplasty. *Orthop Clin North Am* 1991;22:523.
14. Goulet JA, Pellici PM, Brause BD, et al. Prolonged suppression of infection in total hip arthroplasty. *J Arthroplasty* 1988;3:109.
15. Sanzen L, Carlsson AK, Josefsson G, et al. Revision operations in infected total hip arthroplasties. Two to nine year follow-up study. *Clin Orthop Rel Res* 1988;229:165.
16. Hope PG, Kristinsson KG, Norman P, et al. Deep infection of cemented total hip arthroplasties caused by coagulase-negative staphylococci. *J Bone Joint Surg* 1989;71:851.
17. Fitzgerald RH Jr, Jones DR. The infected implant: Treatment with resection arthroplasty and late total hip replacement. *Am J Med* 1985;78:225.
18. Fitzgerald RH Jr. Indirect exchange of the infected hip implant. *Orthop Transplant* 1981;5:372.
19. Salvali EA, Chekofsky KM, Brause RO, et al. Reimplantation in infection: A 12 year experience. *Clin Orthop Rel Res* 1982;170:62.