Resurgence of virulent group A streptococcal infections – the streptococcal toxic shock syndrome

During the past decade we have witnessed a resurgence of infections caused by group A streptococci,\textsuperscript{1,2} including pharyngitis, acute rheumatic fever and severe invasive cutaneous and subcutaneous infections. Several reports have recently been published describing a life-threatening infectious syndrome of alarming rapidity of onset associated with an erythematous generalized rash, shock and progression to a severe multisystem illness. Cone and associates\textsuperscript{3} called attention to two patients with cellulitis of the extremities which progressed in both cases to a severe illness manifested by shock, hypoxemia and renal failure. \textit{Streptococcus pyogenes} was recovered in both cases from wounds but not from blood.

The following year, Bartter\textsuperscript{4} reported three cases of group A streptococcal soft tissue infection associated with multisystem disease which shared most of the features of toxic shock syndrome caused by \textit{Staphylococcus aureus}.\textsuperscript{5} In 1989, Stevens and colleagues\textsuperscript{6} reported on a series of 20 patients seen over a five-year period in the Rocky Mountain area of the United States. The majority of patients had extensive soft tissue infection with necrotizing fascitis with or without myositis being the most common (55%). Most presented with severe hypotension, respiratory failure, confusion, localized swelling and erythema, renal dysfunction, hypoalbuminemia, hypocalcemia and bacteremia. Surgical intervention was of major importance both for establishing a diagnosis and for debriding devitalized tissue. Alarming features of this series were that the majority of patients were younger than 40 years of age without underlying disease, the illness rapidly progressed to severe multisystem organ dysfunction and the mortality rate was 30%. In a recent retrospective review of 24 cases occurring over a four-year period in southern Ontario, the mortality of severe group A streptococcal infections with hypotension was 50% with 58% of the deaths occurring within the first 24 h.\textsuperscript{7}

The reasons for the increase in severe streptococcal infections both in North America and Europe\textsuperscript{6} are not clearly identified. Stollerman\textsuperscript{9} suggested that the reappearance of group A streptococci which cause rheumatic fever is associated with strains with special properties – mucoid, rich in M proteins, high quantities of hyaluronate and resistant to phagocytosis. These more virulent mucoid strains had almost disappeared in developed countries over recent decades but are reappearing in the 1980s and ‘90s coincident with focal epidemics of acute rheumatic fever.\textsuperscript{10} Similarly, there has been an increase in the number of mucoid strains.
recovered from patients with streptococcal toxic shock syndrome, particularly M-1 strains. There has been an increase in the proportion of types 1, 3 and 18 and a decrease in types 4 and 12 in the United States between 1972 and 1988. M types 1, 3 and 18 are currently most often associated with invasive and/or fatal infections.

The reappearance of pyrogenic toxins in group A streptococci has been postulated to be responsible for the recent cases of toxic shock syndrome associated with this organism. Purification and immunological studies of the 'erythrogenic toxin' of group A streptococci, originally thought to be responsible for the characteristic rash of scarlet fever, have found that it is composed of at least three moieties - exotoxins A, B and C, which have important biological properties. Pyrogenic exotoxin A and toxic shock syndrome toxin-1 (TSST-1), elaborated by toxic shock producing strains of Staphylococcus share an extensive homology of molecular structure. Exotoxin A and TSST-1 share many biological properties including pyrogenicity, enhanced susceptibility to endotoxin, cytotoxicity, myocardial depression and suppression of B lymphocyte function. Stevens has suggested that the pyrogenic exotoxin A which has been absent from most strains of group A streptococci over the past few decades has reappeared and we are now seeing the consequences of soft tissue infection due to streptococcal strains with increased toxin producing capability. Stevens found a prevalence of exotoxin A of 80% in the clinical isolates from his series. This finding has been confirmed by Musser and colleagues, who found that 28 of 31 isolates (90%) recovered from patients with streptococcal toxic shock syndrome expressed exotoxin A, whereas only 12 of 45 isolates (27%) associated with less severe invasive streptococcal infections expressed this exotoxin. Furthermore, Cleary and colleagues demonstrated that 90% of strains of group A streptococci from cases of invasive disease possess the genes encoding exotoxin A compared with 54% of strains causing noninvasive disease. It is possible that some cases of 'surgical scarlet fever' occurring during the early part of this century and often associated with a grave prognosis were actually cases of streptococcal toxic shock due to exotoxin A producing strains.

Regardless of the pathogenesis which underlies the recent changes in the epidemiology and frequency of group A streptococcal infections, there are many implications for the practising clinician. A heightened awareness is required for the recognition of not only severe invasive group A streptococcal infections, but also rheumatic fever, as well as a need for an accurate and rapid diagnosis in these cases. At a time when interest has waned with regard to group A streptococcus, the need for prompt recognition and appropriate antibiotic therapy for streptococcal pharyngitis and pyoderma to prevent post-streptococcal sequelae cannot be overemphasized.

REFERENCES
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