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Epidemiology of Group A Streptococcal Infections—Their Changing Frequency and Severity

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The frequency and severity of streptococcal infections and their sequelae have declined dramatically in the past century, yet the prevalence of streptococcal infections is still high. The reasons for this decline must be intimately related to host resistance, virulence of the agent, and environmental factors, especially crowding. Close examination of these fundamental influences does not reveal any evidence that humans have become less resistant to streptococcal infections, but they react less violently. There is some evidence that the agent may have lost a degree of its virulence. The decline in morbidity and mortality due to streptococcal infections began long before antibiotics, especially penicillin, were available. However, penicillin has proved to be an important factor in prevention of streptococcal infections, especially in rheumatic fever prophylaxis. There are certain indications that repeated streptococcal infections due to similar M types, occurring in young children over the past several decades, have resulted in some degree of immunity as well as the possible evolution of less virulent, but not less infectious, strains of group A streptococci. Also, a decrease in crowding would be expected to result in fewer streptococcal infections. Although there are more people in the world than at any other time in the history of man, urban population density in the western world, at least, is less than in the late 1800s and early 1900s.

INTRODUCTION

There is ample evidence that the incidence and severity of streptococcal diseases have declined markedly during the past several decades in most geographical areas where data are available. At least two contemporary students of the *Streptococcus*, McCarty [1] and Gorrod [2], have commented on this change. In Providence, Rhode Island, where Chapin kept careful records over a 33-year period (1887-1920), mortality rates fell from 40 to 2 per 10,000 and a similar decline occurred in other American cities [3]. Chapin's report [4] on case fatality for scarlet fever during the years 1868-1924 in North America, Europe, and Japan showed dramatically declining rates in each country or city, with the exception of Bulgaria and Leningrad. There were 55,287 deaths from scarlatina in London from 1838 to 1853, and in Sweden from 1864 to 1873 there were 11,630 deaths. In the United States, allowing for limitations in *Sources of Mortality Data*, there has been a profound decrease in the number of deaths and death rates due to scarlet fever and streptococcal sore throat from over 3,000 deaths in 1900 to only 14 in 1976.

The streptococcal picture today varies markedly from the World War I years in army training camps in Texas when the *Streptococcus* was responsible for a highly

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virulent form of pneumonia complicating measles. In World War II the epidemic of streptococcal disease in the U.S. Navy, probably the largest ever recorded, demonstrated that epidemic streptococcal disease can occur under conditions which favor the transmission of serological types of group A streptococci to which susceptible hosts have not previously been exposed. In the U.S. Navy during the four-year period from 1942–1945, there were 58,438 cases of scarlet fever, 43,448 cases of rheumatic fever, a minimum of 223 cases of cellulitis due to group A streptococci, and at least a million cases of streptococcal upper respiratory tract infections [5]. In contrast to the extremely high morbidity, no deaths were recorded [5]. Experiences in the U.S. Army and Air Force with streptococcal infections in World War II were similar to those of the Navy but of lesser magnitude.

Although morbidity and mortality rates for streptococcal disease have declined dramatically, evidence that the *hemolytic Streptococcus* has become less prevalent is lacking. During a 20-year study of children in Nashville, Tennessee, from 1953–1954 through 1973–1974, 32.1 percent of all throat cultures obtained weekly or biweekly were positive for group A streptococci [6]. The significance of positive throat cultures in Nashville school children was evaluated, and it was shown that, among 320 children, the proportion of those with clinical manifestations of an upper respiratory tract infection and throat cultures positive for group A streptococci was approximately the same as that of asymptomatic children [7]. Frequent occurrence of group A streptococci was found in Egypt (1972–1974) where prevalence among families was 19 percent and in school children 25 percent [8].

Not only have streptococcal infections decreased in severity, but so also has one of the sequelae, rheumatic fever. During the first four decades of the twentieth century, entire hospitals and wards were devoted to the care of children with rheumatic fever. Nowadays, acute rheumatic fever is a relatively rare occurrence; medical students may spend four years in medical school without having seen a case. Rheumatic heart disease, however, is still relatively common in developing countries [9] and as a cause of death in older age groups in the United States [10].

The reasons for the decline in morbidity and mortality are not apparent, but certainly must include host resistance, virulence of the agent and their complex interrelationships, and environmental influences. There is no evidence that host resistance to acquisition of streptococcal infections has increased. Children are universally susceptible to infection with group A streptococci. Streptococcal antibodies, evidence of recent or past infection due to group A streptococci, have been demonstrated in populations from such diverse geographical areas as North America, Europe, Pakistan, Thailand, Burma, Mongolia, Algeria, Kenya, Togo, and Nigeria [11]. In none of these areas does streptococcal disease appear to be of a serious nature clinically or a significant cause of death.

Host Factors—Acquisition of Immunity

The acquisition of immunity to different serological types of group A streptococci is an intermittent process throughout childhood, and although some differences have been observed in M protein antibody response after infection by different serotypes [12], there is no question that M protein antibodies are acquired by many children, symptomatic or asymptomatic, who are infected by group A streptococci [7,12]. These antibodies are protective against subsequent infection by the same serotype. A worldwide study showed that less than half of the strains submitted

from 12 laboratories were M typable; among the typable strains, the M types identified most frequently were 1, 3, 4, 5, and 12 [13]. Does this mean that children worldwide are being infected by and acquiring immunity to the same M types?

Host Factors—Clinical Response

None of the foregoing reports explains the decrease in clinical severity of streptococcal infections which has occurred over the past several generations. These changes in severity began long before the availability of any antibiotics which are effective in reducing the severity and duration of streptoccal infections, so that credit can not be assigned to antibiotics for the long-term reduction in mortality or morbidity. Does the gradual acquisition of immunity to serological types in a child's community also result in gradual lessening of the severity of clinical response? Apparently not, because the clinical response of older children, adolescents, and young adults today is more violent than that of infants and younger children four years old or less, and sequelae such as rheumatic fever and nephritis do not begin to occur in significant numbers until children have attained the age of six years or older. These sequelae increase until adolescence or beyond, as in epidemics such as occurred in the U.S. armed force training centers in World War II where the recruits' ages ranged from 18 to 21. Earlier clinicians observed that in scarlet fever, age had marked influence; after puberty, there was a greatly diminished susceptibility compared with earlier life. Likewise mortality was very much higher in children five years of age or less than in older children [14]. Osler observed that the younger the child the greater the danger of death and that the greater proportion of fatal cases occurred in children under six years of age [15].

At the turn of the century, Von Jurgensen was acutely aware of the double significance of the age distribution of scarlet fever and he stated, "there may be indicated a less frequent infection at the corresponding age (after puberty) or there may be a lessened virulence of the infection itself. In the case of scarlatina probably both factors exist side by side" [14]. We now know that immunity to scarlet fever can be acquired by children who have streptococcal infections with or without a rash, but that immunity to scarlet fever does not confer immunity to streptococcal infections. We are confronted with the same dilemma today as Von Jurgensen was some eighty years ago. Certainly streptococcal infections are less frequent after puberty, possibly explained by acquisition of immunity. The lessened virulence of the infections are not explained by the acquisition of immunity or anything else we know about the host at the present time. So we must turn to the agent to seek an explanation.

Agent Factors

Infectivity of group A streptococci would appear to be of a high order, since so many children and adolescents, worldwide, become infected. There is some evidence that microorganisms increase their infectivity during an epidemic [16]. Virulence, on the other hand, would seem to be of a low order, since severity of clinical illness is generally mild and mortality is very low. Data are not available which would allow an appraisal of the property of infectivity of group A streptococci now as compared with fifty or one hundred or more years ago. Several investigators have shown that streptococci residing in the throat of an immune individual or in a person convalescent from a streptococcal infection tend to become less virulent [17,18,19,20]. Could

it be that streptococcal infections, occurring for many generations in children, have resulted in the presence of large numbers of group A streptococci of a lesser order of virulence, and that this property of present-day group A streptococci accounts for the generally mild character of streptococcal disease? Burnet and White [21] observed that for at least two centuries *Streptococcus pyogenes* and *Corynebacterium diphtheriae* persisted as very common, endemic infections of the human throat, producing repeated subclinical infections in childhood with resultant immunity to the effects of the toxin. They speculated that striking fluctuations in virulence of the organisms were presumably the result of changes in the state of lysogenization by toxin-conferring bacteriophages. In regard to rheumatic fever, Stollerman has postulated that there are non-rheumatogenic group A streptococci, or at least some strains have reduced rheumatogenic potentials, and the decline in rheumatic fever may be due to a dilution of the prevalence of the rheumatogenic organisms which previously caused high rheumatic fever attack rates [22]. For whatever reasons, it does appear that virulence of the group A *Streptococcus* has declined. Exactly when the decline began or how long it will last, we do not know, nor do we know the causes other than the few isolated observations mentioned above.

Environmental Factors

Lastly, is there anything about the environment of man which would help to explain the changing incidence and severity of streptococcal infections?

One characteristic of the environment, crowding, at least urban density, was higher in London, New York City, and Paris during the period 1880–1910 than today. Even though the numbers of people in these cities have roughly tripled and similar increases in population have occurred in the metropolitan areas of the western developed world, there are fewer people per land area, fewer people per family by nearly two members, and the living space per family has increased. These aspects of the population and environment would account for less crowding and fewer opportunities for person-to-person spread of infectious respiratory agents such as group A streptococci. Under such environmental conditions, streptococcal diseases among industrialized people have declined in incidence and severity.

The effect of crowding was dramatically apparent during World War II in the military training centers, where large epidemics of streptococcal disease occurred in young men introduced and confined in a crowded environment harboring infected recruits.

When the effect of environment was examined closely as in New Haven, Connecticut, death rates for rheumatic heart disease (a sequela of rheumatic fever, in turn a sequela of streptococcal infection) were highest where crowding was most prevalent and housing and economic status the lowest [23]. Paul wrote extensively on the influence of environmental factors on morbidity and mortality in rheumatic fever and rheumatic heart disease, and concluded that crowding was an important factor contributing to higher rates [24].

The point is often made that modern sanitation, a safe food and milk supply, and adequate bathing and washing facilities have improved such crowded living conditions and minimized the risk of infectious diseases. Yet, there is little or no evidence that adequate sewage and waste disposal, bathing facilities, or a safe water supply minimize group A streptococcal respiratory infections. To be sure, pasteurization of milk has eliminated milk-borne streptococcal infections.

SUMMARY

Consideration of agent, host, and environmental factors leads to the conclusion that we do not know with exact certainty the reasons for the decline in streptococcal morbidity and mortality rates.

However, there are indications that repeated streptococcal infections due to similar M types (worldwide) occurring in young children over many decades (generations) result in immunity and possibly the evolution of less virulent but not less infectious strains of group A streptococci. These factors, along with less crowding among industrialized people, may partially explain the declining severity of streptococcal infections.

Coburn and Young may have been prophetic when they wrote, "Prior to World War II the mildness of streptococcal infections had tended to lull general interest in this bacterium, in spite of its well known cyclic trends of pathogenicity" [5]. Perhaps, someday, if the rates begin to increase again, the reasons for such fluctuations may furnish additional clues to the present decline.

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