The report by Wasserzug et al. [1] in this issue of *Clinical Infectious Diseases* describes 4 outbreaks of group A streptococcal skin infections and their suppurative and nonsuppurative sequelae among Israeli military trainees and reminds us of this organism’s potential for epidemic virulence. The report also emphasizes that one of the favorite target populations for outbreaks of streptococcal infection and their sequelae is military recruits.

One might raise questions about some aspects of the report. For instance, on the basis of the literature, the varied approaches to both antibiotic therapy and prevention that are described might be questioned. Many will be concerned (justifiably, I think) about the authors’ reluctance to adopt the time-tested, effective use of benzathine penicillin G for both prevention and therapy in this military situation. The literature does not support the authors’ concern regarding allergic reactions to penicillin [2]. It would appear from the information presented that the staphylococci were secondary invaders, as has been commented on before [3], which should not be a contraindication for using intramuscular benzathine penicillin G. Without knowing the streptococcal susceptibilities to the macrolides or azalide, the use of azithromycin might be questioned. In some parts of Europe, rates of resistance to azithromycin have approached 40% [4]. Furthermore, in some places, the widespread use of azithromycin has resulted in increased rates of drug resistance [4]. This is not true for penicillin [5]. In apparent contrast with what is practiced in Israel, the long recognized propensity for outbreaks of streptococcal infection among recruits has resulted in a number of military bases in the United States administering benzathine penicillin G to men and women as they enter recruit training.

This report is important in that it again raises the issue of the epidemiology of group A streptococcal infections in dense populations, especially among military recruits. Of special historical and geographical interest is the fact that the M serotype 81 strain was first isolated on 14 April 1978 by Dr. Sonja Bergner-Rabinowitz, who was then Head of the Central Streptococcal Laboratory in Jerusalem, Israel (the strain was later described in a 1978 report by Facklam and Edwards from the Centers for Disease Control and Prevention as SS1173, T nontypable, opacity factor positive, *sof* type 81) [6]. The Centers for Disease Control and Prevention streptococcal laboratory has described this strain as *emm* type 81.0. There are currently 11 *emm* type 81 subtypes in the Centers for Disease Control and Prevention database, so it would be of interest to confirm the *emm* subtype sequencing of the strains from the 4 apparently separate outbreaks [7]. In our streptococcal reference laboratory’s own collection of ~17,000 group A streptococcal strains, we have only 41 M-81 strains. These strains originated from many locations worldwide, including South America, Europe, and India. None of the strains were associated with acute nephritis, but a strain from Chile (submitted to us by Dr. Alan Bisno) was temporarily associated with a patient with rheumatic fever; it is interesting that no rheumatic fever was reported in the Israeli outbreaks.

Efforts to understand streptococcal epidemiology among military personnel have been an important part of the study of infectious diseases in the United States. Because of the magnitude of the streptococcal disease burden during World War II among the American Armed Forces, the US Army Epidemiological Board (later to become known as the Armed Forces Epidemiological Board, and in 2006, renamed the Defense Health Board) authorized the formation of a Commission on Streptococcal Diseases in 1948 [8]. This resulted in the establishment of the Streptococcal Research Laboratory at the Warren Air Force Base in Wyoming, where sentinel epidemiologic and prevention and/or treatment studies involving recruits were performed from 1948 through 1953 by Drs. Charles Rammelkamp, Lewis...
Among the important lessons learned from those unique and intensive investigations were the findings from the “barracks studies.” These findings demonstrated the importance of crowding as a factor in facilitating transmission of streptococci among personnel housed in barracks [9]. The important conclusions from these well-documented observations were not mentioned by the authors of the current report from Israel and are worth reviewing. Crowding and hygiene remain significant problems in military recruit training facilities in many countries, including in some facilities in the United States, where outbreaks of group A streptococcal infections (mainly pharyngitis) still occur. Some such outbreaks still result in sequelae that include morbidity and mortality.

The outbreaks of streptococcal skin infection reported by Wasserzug and colleagues call to mind several still incompletely understood aspects associated with outbreaks of streptococcal infection. One aspect that deserves mention is the fact that, in most countries, military recruits from diverse geographic origins are assigned to centralized recruit training facilities. Israel is geographically a relatively small country; in all branches of the Armed Forces of the United States, recruit training bases represent a melting pot, with recruits from many different geographic regions. One possible explanation for the apparent propensity for an increased risk of epidemic streptococcal infection in recruit facilities is that this likely constitutes a situation similar to the previously described epidemiological phenomenon noted among 12- and 13-year-old students in junior high and middle schools [10, 11]. Reports showing the ages of school children who are at highest risk for group A streptococcal infection indicate that the incidence curve can be bimodal, with a peak between 6 and 9 years of age and another peak at 12 and 13 years of age (i.e., the age of US middle school students). The increase in the incidence of streptococcal infection among children 12 and 13 years of age is consistent with the fact that students from several different elementary schools subsequently attend a single middle school. Children from each individual elementary school have had unique exposures to specific strains and types of group A streptococci but have not had exposure to other M protein types. When students from one school are mixed with students from other elementary schools with different streptococcal populations, one could expect students to be susceptible to infection due to the new M protein types to which they are exposed. This can explain the second peak of the bimodal age-incidence curves. Might not men and women in recruit camps represent the same epidemiologic phenomenon?

The observed propensity for streptococcal infection among recruits also raises very important but incompletely answered questions about ensuing protection after infection, attributable either to the development of type-specific anti–M protein antibody or, perhaps, to antibodies to other, as-yet-unrecognized extracellular or somatic group A streptococcal antigens. This hypothesis regarding subsequent protection from infection due to the same M protein type or strain has been on the minds of those basic scientists and epidemiologists who are attempting to design an effective vaccine against group A streptococci.

Rebecca Lancefield [12] described a patient with type-specific anti–M protein antibody that persisted for 4 decades. We, too, have had the recent opportunity to search for type-specific antibody (and perhaps immunity) in 2 individuals who had documented rheumatic fever during an outbreak in 1960 that was associated with serotype M5 streptococci [13]. We found type-specific anti-M5 antibody to the epidemic M5 strain (which has been kept in our collection) 45 years later, although there appeared to be different “amounts” (measured by the bactericidal test) in the serum samples obtained from the 2 individuals [14]. However, attempts to document the development or presence of type-specific antibody after streptococcal pyoderma (admittedly, not pharyngitis), when compared with pharyngeal colonization, have not been definitive [15].

It seems logical to conclude that type-specific immunity likely has an effect on resulting susceptibility in military recruit camps and perhaps is even a factor in determining whether pharyngeal infection or colonization may progress to serious suppurative sequelae in a given individual. Perhaps the lack of protection leads to what we have termed an epidemiologic “fertile field syndrome” for group A streptococci. There always are many strains entering a population; they have the capacity to seed the fertile field of unprotected recruits [16].

This concept is further supported by 2 independent sets of observations. After the original outbreak of acute poststreptococcal nephritis at Red Lake, Minnesota, in 1953 [17], there was a 13-year hiatus, during which the epidemic M type 49 strain was thought to be essentially absent from that population. In 1966, however, a second Red Lake outbreak of acute glomerulonephritis occurred; this outbreak was also associated with the M type 49 strain [18]. Present in the population in 1966 was a presumably unprotected and, therefore, susceptible group of children who lacked herd immunity to the M type 49 strain. More recently, the same phenomenon appears to have occurred in Utah during a large outbreak of acute rheumatic fever that was presumably associated with M type 18 streptococci [19]. The initial peak of acute rheumatic fever occurred in 1985, when 60 cases were observed. After the peak in 1985, the number of cases of rheumatic fever decreased. Then, in 1998, again 13 years later, a second peak in the incidence of rheumatic fever occurred [20]. The average age of the Utah patients who developed rheumatic fever was be-
tween 9 and 10 years of age. Thus, the patients who developed the nonsuppurative sequel during the second peak, 13 years later, were not even alive in 1985. Can we not conclude that a “fertile field” for infection due to the M type 18 strain and rheumatic fever had evolved?

The present report of outbreaks in the Israeli military is not unique in military populations. However, it does serve to again emphasize a need for a more complete understanding of the as-yet-unsolved epidemiological and immunological issues associated with significant outbreaks of streptococcal infections and their sequelae in densely populated settings, especially in the military. Furthermore, the unresolved questions relating to antibiotic prophylaxis in such populations, to antibiotic treatment in those populations, and especially to the knotty problem of vaccine development remain of practical significance for military and civilian medical and public health authorities, as they do for laboratory basic scientists.

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References

1. Wasserzug O, Valinsky L, Klement E, et al. A cluster of ecthyma outbreaks caused by single clone of invasive and highly infective Strep-