Group A Streptococcal Carrier versus Acute Infection: The Continuing Dilemma

Harry R. Hill
Departments of Pathology, Pediatrics, and Medicine, University of Utah School of Medicine, and the ARUP Institute for Clinical and Experimental Pathology, Salt Lake City, Utah

(See the article by Johnson et al, on pages 481–90.)

An age old question reappears in the article by Johnson et al in this issue of Clinical Infectious Diseases [1]. Defining what is an acute infection due to group A streptococci versus the carrier state of this very common pathogen is of considerable significance because nonsuppurative sequelae, such as acute rheumatic fever and acute glomerulonephritis, are said to only follow acute disease. Moreover, transmission of group A streptococci and the development of invasive disease are felt to be associated more often, if not exclusively, with a new acquisition and acute infection rather than the carrier state. The problem, of course, is that as much as 20%–25% of the school-age population may be positive for group A streptococci during the late winter and spring months, even extending into June here in Utah. Intercurrent, viral infection may result in the patient being seen and tested by antigen detection or group A streptococcal culture for this very common pathogen. A positive result for streptococci will likely result in antimicrobial therapy being administered for 5–10 days, depending on the antimicrobial agent selected, because such therapy has been shown to markedly decrease the incidence (90%) of acute rheumatic fever, decrease acute glomerulonephritis by perhaps 50%, and aid in preventing invasive disease and further spread. Numerous authors, including these same investigators at the University of Minnesota, have pointed out that serologic studies targeting nonspecific streptococcal extracellular products, such as streptolysin O and DNase B, may be useful in differentiating the carrier state of group A streptococci from acute infection. Longitudinal analysis of group A streptococcal culture results combined with sequential serologic studies have confirmed what Zimmerman et al [2] reported years ago in patients and families they followed in 3 Colorado communities. This group reported that certain families acquired a new streptococcal M or T type that often persisted in individual patients and the family for extended periods of time, up to 2–3 years in some cases. These “carriers” often developed significantly elevated nonspecific streptococcal antibody responses but almost never seem to develop nonsuppurative sequelae. The present studies by Johnson et al [1] certainly confirm those findings. As one who has observed the streptococcal world for the past ∼40 years, including working with the group at the Fort Collins Centers for Disease Control and Prevention Streptococcal Disease Laboratory and with the streptococcal group at the University of Minnesota, I am struck by how often important observations in medicine have to continue to be remade to affect the current status of medical care. Our memory may be too short or perhaps we just need to refocus our attention to what we may already know and make use of it in medical decision making.

As one who directs a large clinical immunology laboratory at the University of Utah–owned Associated Regional and University Laboratories as well as being a clinician, I can only agree with the findings and comments of Johnson and colleagues on the inadequacy of using a single serologic result to try to predict the presences of acute infection versus chronic carriage of an organism. In my experience, a single serologic response, especially to something as common and nonspecific as streptolysin O and DNase B, should never be used to distinguish between acute infection and the carrier state or even the response to vaccination. One has to look at acute and convalescence responses to determine whether there is a new exposure to a particular pathogen. The overall concentration of that antibody in the “acute sample” likely depends on past exposure to that or similar pathogens, vaccination,
cross-reacting microbes, or even the individual immunologic responsiveness or characteristics of decay of the antibody response in the patient. Comparison to normal values obtained from healthy, age-matched controls, in my opinion, has little role in defining the presences of acute infection or vaccine responses to an individual pathogen or one of its components. One must have serologic sampling over time to rationally use such data.

This brings up another question about the clinical usefulness of the excellent data contained in the article by Johnson et al [1], especially to the practicing clinician. These data suggest that serologic studies performed on at least 2 occasions, 2–4 weeks apart, can perhaps separate the patient with acute group A streptococcal pharyngitis from the chronic carrier of this pathogen. Currently, the busy pediatrician or family practitioner or perhaps even the local mini-clinic’s physician’s assistant or nurse practitioner has only time to collect a swab for antigen detection for group A streptococci, which hopefully is followed by culture for this organism if the result is negative (because such rapid tests are only 80%–90% sensitive). To prevent acute rheumatic fever, recommendations are for 10 days of antimicrobial therapy (shorter courses with a 6-pack of antibiotics, such as azithromycin, has not always prevented acute rheumatic fever in our experience here in Utah; L.G. Veasy and H.R.H., unpublished observations) initiated shortly after the detection of the organism. Very early therapy is also needed to show any benefit in preventing acute glomerulonephritis, and only very early treatment has been demonstrated to shorten the clinical course of streptococcal pharyngitis. Waiting 2–4 weeks for a serologic response is simply unacceptable as routine criteria for detecting acute infection versus the carrier state in the practicing clinician’s setting. Could early antibody responses or even T cell responses (such as cytokines) to specific or nonspecific streptococcal antigens be detectable at the time of acute infection? Perhaps this possibility needs to be explored in the future.

The above comments should not be misconstrued as indicating that the study by Johnson and colleagues is not of real value in understanding group A streptococcal infections and their nonsuppurative sequelae. Just by pointing out that a single elevated group A streptococcal serologic antibody determination cannot always indicate that an observed clinical disorder is ascribable to a past or present group A streptococcal infection, the authors have done a great service. If one were to demand that such sequential serologic and culture-based data be present to confirm the streptococcal etiology of certain syndromes, it is likely that a causative agent or event would still be sought for PANDAS (Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococci) and obsessive/compulsive disorders. Perhaps Dr Kaplan’s group, as indicated, will address this question in a future study.

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References