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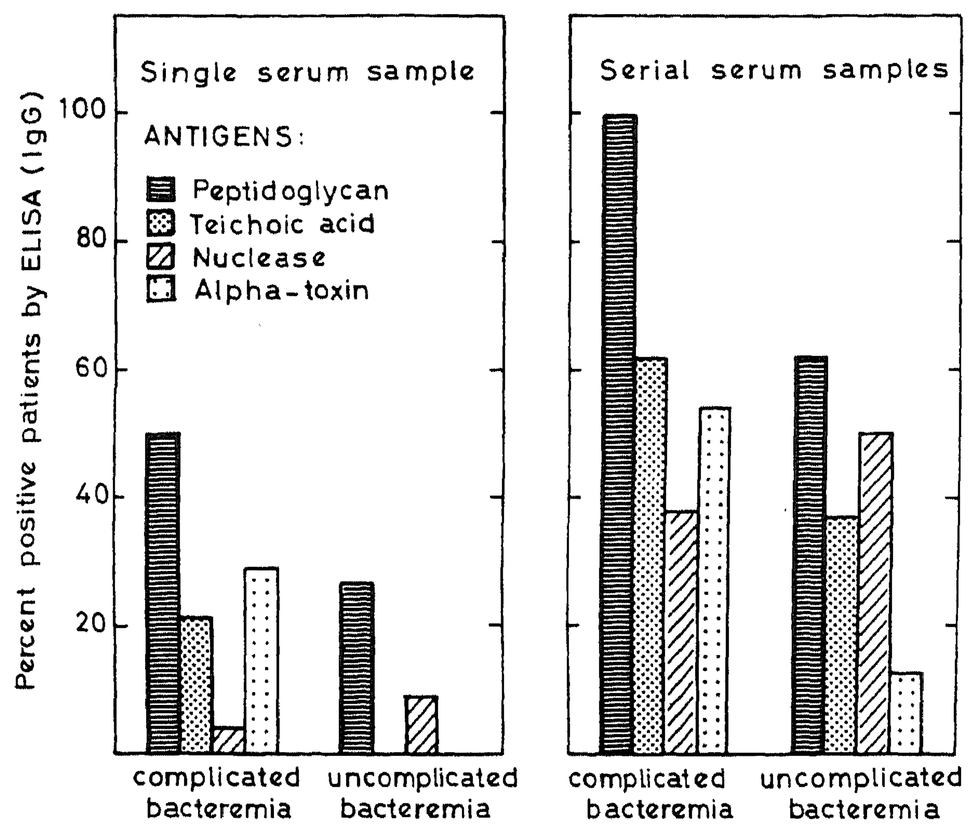
Serology of *Staphylococcus aureus* Infections Using Multiple Antigens and Serial Serum Samples



Legend. Percentage of patients with bacteremia due to *Staphylococcus aureus* whose sera showed a significant IgG antibody response to four staphylococcal antigens. Of 37 patients, 26 had complicated bacteremia (18 had infective endocarditis and eight had other deep foci of infection) and 11 had uncomplicated bacteremic episodes (six of which were iv catheter related). Serial serum samples were obtained starting from one to 30 days (mean, 11.1 days) after the first positive blood culture. *S aureus* peptidoglycan and teichoic acid antigens were prepared as previously described [2], α-toxin was provided by Dr Curtis G. Gemmell (University of Glasgow, Scotland), and purified nuclease was obtained commercially (Worthington Biochemical Corp, Freehold, NJ). IgG antibodies to these antigens were determined by a polyvinyl microtiter-plate ELISA that has been previously described [2]. All serum samples were fully titrated in duplicate. A positive result was indicated in the case of a single serum sample (*left*) when the final OD at a serum dilution of 1:2,000 was >2 SD above the mean OD of similarly tested serum samples from 56 healthy donors; a positive result was indicated in the case of serial serum samples (*right*) when the titer of antigen-specific IgG antibody increased twofold or more.

Summary

The detection of antibody to *S aureus* in human serum can aid in the management of staphylococcal diseases [1]. RIAs and ELISAs can detect low levels of antibody and demonstrate increased antibody production during serious staphylococcal infections [2, 3]. We compared four *S aureus* constituents—cell-wall peptidoglycan and teichoic acid, and extracellular α-toxin and nuclease—as antigens in a sensitive ELISA. The value of testing more than a single serum sample was also determined. Elevated IgG antibody to peptidoglycan, present in one or more serum samples of 13 (50%) of 26 patients with complicated bacteremia, was found to be the most sensitive test. All 26 patients had a significant IgG antibody response to peptidoglycan. Three (27%) of 11 patients with uncomplicated bacteremia had elevated levels of antibody to peptidoglycan in their serum, and seven (64%) showed a significant change in titer when serial serum samples were tested. Maximum detection rates for the other antigens in complicated and uncomplicated bacteremia were, respectively, 62% and 37% for teichoic acid, 38% and 37% for nuclease, and 54% and 13% for α-toxin. In single serum samples, the detection rate for all four antigens marginally improved the results, with detection rates of 62% and 36% for complicated and uncomplicated bacteremia, respectively. Cross-reactive antibody to peptidoglycan but not to the other three antigens was present in six (75%) of eight patients with long-standing subacute bacterial endocarditis due to either viridans streptococci or *Staphylococcus epidermidis* (data not shown). Thus, simultaneous measurement of antibodies to peptidoglycan and teichoic acid in serial serum samples may be the most reliable method of detecting significant humoral immune responses during *S aureus* infections. Single serum tests may fail to detect increases in antibody titer. It remains doubtful whether serologic tests alone can identify bacteremia patients who will have a clinically complicated course. However, a complete absence of an antibody response to peptidoglycan and teichoic acid would argue against the presence of a complicated bacteremic episode.

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