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## **An evaluation of the usefulness of serodiagnosis in clinical practice**

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Abstract: Abstract: The measurement of serum antibodies to S. aureus may be used in the diagnosis of deep seated infection, however, it remains unclear whether such testing is useful in clinical practice. We retrospectively identified results of serum anti-staphylolysin and anti-nuclease titres collected over a three year period. Serological testing was performed on 121 serum samples from 113 individuals between 1st September 2004 and 31st August 2007. Ninety (80%) individuals were managed as suspected or proven deep-seated infection. Serology results indicative of staphylococcal infection were returned in ten (9%) cases, including four where S. aureus was cultured. Serology results which did not indicate staphylococcal infection were returned in 90 (79.5%) cases including seven individuals with positive cultures for S. aureus. There was no evidence in any of the 113 cases that antimicrobial management was altered upon availability of test results. We conclude that staphylococcal serology tests are of no clear benefit in the management of suspected deep-seated infection.

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Expertise in this area (author of paper referenced). Note few recent papers in this area

1                                   **AN EVALUATION OF THE USEFULNESS OF STAPHYLOCOCCUS**  
2                                   **AUREUS SERODIAGNOSIS IN CLINICAL PRACTICE.**  
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27           The measurement of serum antibodies to *S. aureus* has been used in the diagnosis of  
28           individuals with suspected deep seated infection, particularly when culture is difficult  
29           or unproductive. The Health Protection Agency (HPA), UK, currently offers testing to  
30           detect antibodies to alpha haemolysin (staphylolysin) and the nuclease enzyme in  
31           parallel. However, a lack of high specificity and sensitivity of the anti-staphylolysin  
32           test has been demonstrated repeatedly in occult *S. aureus* infections [1-3], whilst there  
33           is little information on the usefulness of the anti-nuclease test. It is understood that  
34           serological tests, even in combination, are an imperfect marker of staphylococcal  
35           infection. It is unclear whether staphylococcal serological testing is useful in clinical  
36           practice.  
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40           We undertook a retrospective evaluation of the use of staphylococcal serodiagnosis in  
41           the Hull and East Yorkshire NHS Trust. Our objectives were to determine the extent  
42           of testing, to identify the clinical context in which tests were requested, to ascertain  
43           whether the results contributed towards patient management, and to inform the  
44           production of local guidelines.  
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47           We retrospectively identified results of serum anti-staphylolysin and anti-nuclease  
48           titres collected from individuals presenting to a 1500-bedded teaching hospital over a  
49           three year period. Information concerning the demographics of the individual, their  
50           relevant hospital and or outpatient attendances, past medical history, clinical  
51           diagnoses, microbiology, antimicrobial and medical management, and outcome was  
52           obtained from their clinical record and the trust pathology database. Test results were  
53           interpreted in accordance with HPA guidance [4]. A positive test was defined as an  
54           antistaphylolysin titre of  $\geq 8$  units/ml and/or an anti-nuclease titre of  $> 32$  units/ml; an  
55           equivocal test (suggestive of staphylococcal infection), an antistaphylolysin titre of 4-  
56           6 units/ml and/or anti-nuclease titre of 32 units/ml; and a negative test (no evidence of  
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1 staphylococcal infection or repeat testing required), an antistaphylolysin titre of  $\leq 2$   
2 units/ml and anti-nuclease titre of  $\leq 16$  units/ml.

3  
4 Serological testing was performed on 121 serum samples collected from 113  
5 individuals between 1st September 2004 and 31st August 2007. 73 (65%) were male;  
6 their median age was 55 years (range 2-90). Testing was performed in both inpatient  
7 (81, 72%) and outpatient (32, 28%) hospital settings. Testing was requested on  
8 individuals managed by a variety of specialties including infectious diseases (78,  
9 70%), orthopaedics (11, 10%), cardiology (3, 2.7%), neurosurgery (3, 2.7%) and the  
10 acute medical admitting teams (16, 14.5%). Ninety (80%) individuals were managed  
11 as suspected or proven deep-seated infection including cases of discitis, (20, 18%),  
12 prosthetic joint (15, 13%) and native (10, 9%) septic arthritis, osteomyelitis (18,  
13 16%), soft tissue infection (15, 13%), infective endocarditis (10, 9%) and with  
14 bacteraemia of uncertain source (2, 1.7%). In the remainder (23, 20%) there was no  
15 evidence of infection. Test results were available a median of 14 days from the time  
16 of the serum sample collection. Repeat serology was performed on only six  
17 individuals.

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19 Serology results indicative of staphylococcal infection were returned in ten (9%)  
20 cases, in four of these, *S. aureus* was cultured during the same hospital admission.  
21 Serology results suggestive of staphylococcal infection (equivocal) were returned in  
22 13 (11.5%) cases; *S. aureus* was cultured from three of these during the hospital  
23 admission, (serum sample was taken within 48 hours of clinical presentation in all  
24 three cases) and an alternative pathogen was isolated in four cases. Serology results  
25 which did not indicate staphylococcal infection were returned in 90 (79.5%) cases  
26 (including seven individuals with positive cultures for *S. aureus*). Most individuals  
27 were treated with an antimicrobial regimen effective against *S. aureus*, unless an  
28 alternative pathogen was isolated (**Figure 1**). There was no evidence in any of the 113  
29 cases that antimicrobial management was altered upon availability of test results.  
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36 In summary, most individuals tested were thought to have deep-seated infection  
37 although inappropriate testing in other clinical situations was observed. Serial  
38 serology was rarely performed. The small number of positive tests included cases  
39 with positive *S. aureus* culture; equivocal test results suggestive of *S. aureus* infection  
40 included cases where an alternative pathogen was isolated; and several 'false  
41 negative' results in individuals with proven deep seated staphylococcal infection were  
42 noted. These results are consistent with the findings of previous studies [1-3]. There  
43 was no evidence that test results influenced clinical decision making in any of the  
44 individuals tested. When alterations in antimicrobial management were observed and  
45 recorded it was noted that these decisions were made on the basis of clinical  
46 judgement supported by basic blood tests including inflammatory markers.  
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50 In clinical practice, the median time from sample collection to receipt of serological  
51 results of two weeks appears important. Antimicrobial therapy is usually initiated near  
52 to the time of the clinical presentation of an individual with deep seated infection, and  
53 response or non-response is likely to be evident clinically and or by serum markers of  
54 inflammation during the first 14 days of therapy. A shorter turnaround time for results  
55 is unlikely to be practical. The value of serological test results known to lack  
56 sensitivity and specificity in the context of a succeeding or failing antimicrobial  
57 regimen is questionable. Whilst serial antibody titres taken at intervals might  
58 potentially be useful in the diagnosis of selected cases of deep-seated infection, the  
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1 same limitations apply and it is therefore unlikely that they would affect clinical  
2 management. Further study is required to inform their use in clinical practice.

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4 Given the known limitations of these tests and our observation that clinical  
5 management was not influenced by test results, we conclude that staphylococcal  
6 serology tests are of no clear benefit in the management of suspected deep-seated  
7 infection. We would suggest that testing should only be performed in highly selected  
8 cases where the degree and duration of suspected infection suggest the results might  
9 contribute.

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Figure 1: Test results



