Audit of Anti Streptolysin O (ASOT) testing in RVL in 2015

1.0 Name of audit

Audit of ASOT testing in RVL 2015

2.0 Personnel involved

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Thanks to Mark McDonald BHSCT for downloading data from Pathmanager

3.0 Date of audit

This is a retrospective audit of ASOT testing in 2015.

4.0 Type of clinical audit (e.g. national, individual discipline etc)

Regional Virus Laboratory – Clinical Utility of an assay.

5.0 Background to audit

Group A streptococcus (GAS) is a Gram positive, β-haemolytic bacterium that can cause both acute suppurative and non-suppurative complications in humans. The primary site of infection is the skin or the throat, acute GAS infection may also present as scarlet fever\(^1\). Non-suppurative complications of GAS include acute rheumatic fever, rheumatic heart disease, post streptococcal glomerulonephritis, post streptococcal reactive arthritis and paediatric autoimmune neuropsychiatric disorder associated with streptococcal infection. The pathogenesis of these conditions is thought to arise from shared epitopes on antigens from GAS and the host resulting in an autoimmune response. These complications often arise several weeks after an acute infection when symptoms may have resolved. Diagnosis of non-suppurative complications requires evidence of preceding streptococcal infection using serological tests such as antistreptolysin O titre (ASOT)\(^1\).
RVL uses the BioKit Rheumajet ASO rapid test for the qualitative and semi-quantitative determination of the anti streptolysin O titre in serum by agglutination of latex particles on a slide. Whilst the test is relatively inexpensive and easy to perform the interpretation of the result is often unclear and there are no interpretative comments added to ASOT tests authorised by the duty virologist for this reason. A number of specimens per year are also referred to Bristol PHE for ASOT and anti-DNase testing.

A previous audit on Monospot testing within RVL has highlighted that ASOT requests are often seen as a dual request with a monospot. Clinical details are frequently not provided with these requests but the inference is that the patient is suffering from acute pharyngitis, which would not be an appropriate use of ASO testing.

### 6.0 Objectives of audit

1. To determine how many ASOT tests were carried out in 2015 by RVL and the appropriateness of testing based on the current recommendations, requesting locations and clinical context.

2. To determine how many specimens are referred to Bristol PHE for ASOT and anti-DNase testing in 2015 and the criteria for sending these requests.

3. To make recommendations to maintain ASOT testing within the right clinical context, avoiding the risk of inappropriate tests, requests and results interpretation.
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7.0 Standards

NICE Clinical Knowledge Summary [http://cks.nice.org.uk/scarlet-fever](http://cks.nice.org.uk/scarlet-fever)

- Throat swabs and rapid antigen tests are not routinely indicated for the diagnosis of scarlet fever.
- Anti-streptococcal antibody titres are not useful in acute infection but may be helpful in the diagnosis of complications such as acute rheumatic fever or glomerulonephritis.


- Use ASOT when clinical suspicion of post-streptococcal complications e.g. glomerulonephritis, rheumatic heart disease. Anti-streptococcal antibody titers are not recommended in the routine diagnosis of acute pharyngitis as they reflect past but not current events.

- For acute pharyngitis, WHO recommends a throat swab or rapid antigen test, however, neither of these tests will be able to distinguish between true GAS infection and carrier status with a viral pharyngitis.

- All available serum samples from a patient should be examined simultaneously to minimize possible errors inherent in comparing results from several independent determinations.

- Single lower titres do not exclude the possibility of streptococcal infection; since their comparison with a “normal value” may not be valid it is therefore preferable to undertake acute and convalescent determinations. A negative ASO alone cannot be used to rule out ARF.
or other streptococcal sequelae, additional antibody tests (e.g. anti-DNase) may be required.

- ASO antibodies are usually long lasting and a single increased titre is not an indication of a current infection. Only a fourfold or greater rise in titre on successive serum samples taken 10-14 days apart should be considered indicative of recent infection.

- The definition of elevated ASOT should be made by comparison with age-matched controls in the same geographical location.

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- Serological diagnosis of scarlet fever can be made by anti-hyaluronidase testing with acute and convalescent sera.


- Throat culture, rapid antigen testing or Centor Clinical scoring system is useful in targeting antibiotic use. ASOT and anti-DNase B are not recommended

IDSA Guideline for GAS pharyngitis. CID 2012

- Throat culture or rapid antigen test for GAS pharyngitis
- Anti streptococcal antibody titres are not recommended in routine diagnosis of acute pharyngitis as they reflect past but not current events.
8.0 Data collection

The laboratory computer system “Labcentre”, the relational database management system “Paradox Version 4.5”, and “Clinisys PathManager” were used to collate the data for this audit retrospectively.

9.0 Results

Figure 1 2564 specimens were tested for ASOT in 2015, an average of 49 specimens per week. For the majority of these requests no clinical details were available. Collated clinical details include the following: - sore throat/joint pain, Q croup, haematuria, tired/weight loss, purpuric lesions, fatigue/swollen glands, hand blisters, bilateral knee swell, Q Glandular fever, rash/pain, Ataxia, Q PANDAS, cervical LA, PUO, Q Post strep, tonsillitis, severe tonsillitis, Q Kawasaki, Q encephalitis, Farmer PUO, Psoriasis, Deranged LFT’s, neck swelling, Crohns, 10 wks pregnant b19, recurrent sore throats.

The source of these requests is illustrated below.
Figure 2a 1447 (56%) specimens were from BHSCT (including GP requests). The biggest volume of requests came from GPs (33.9%) followed by RBHSC A&E (24.6%)

Figure 2b  % requests from source BHSCT
Figure 3 25.8% of requests from BHSCT were dual Monospot/ASOT requests within 7 days inferring acute sore throat at time of request.

![Pie chart showing 25.8% dual Monospot/ASOT requests within 7 days.]

Figure 4 3.2% of requests from BHSCT were dual Monospot/ASOT requests from the same patient > 7 days inferring recurrent sore throat.

![Pie chart showing 3.2% dual Monospot/ASOT requests > 7 days.]

Figure 5 Age range ASOT/MONO dual requests.

![Bar chart showing age range ASOT/MONO dual requests.]

Figure 6 ASOT requests received per patient. Only 3.92% of patients had more than one ASOT requested indicating that single ASOT measurements are being used for patient management.

![Pie chart showing ASOT requests per patient.]

3.92% 2 specimens
96.08% single specimen
Figure 7 41 specimens were referred for ASOT/anti-DNase testing in 2015. Source of these requests is summarised below. These appear to have been direct requests for anti-DNase testing from the requestor. Collated clinical details include; - haematuria, uveitis, nephritis, involuntary movements, Sydenham’s chorea.

10.0 Length of audit

1 year

11.0 Outcomes/recommendations/actions taken

Outcomes

96% of specimens received for ASOT testing are single test requests with no follow up. This is not in line with the WHO recommendation that two assays are performed 10-14 days apart. It has been documented in the literature that there are several reasons why use of a single ASOT measurement and ULN threshold is liable to misdiagnosis of a preceding GAS infection¹.

30% or requests received in 2015 were in relation to management of acute pharyngitis, this was inferred by the dual request with a monospot test. ASO
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Titres begin to rise in the first week following GAS infection and peak 3-6 weeks after onset. For this reason, the utility of this test is in demonstrating preceding and not current infection therefore these requests are inappropriate and contradict current guidance. The majority of these dual requests come from GP’s (71%) followed by RBHSC A&E (8%).

Clinical details were not provided with the majority of requests received and whilst some requests were obviously appropriate e.g. Q post strep, Sydenham’s chorea, nephritis, a lot of requests would seem to be inappropriate based on clinical details e.g. sore throat, swollen glands, recurrent sore throat etc. and indicate the need to educate clinical users.

**Recommendations**

Testing of ASOT should not be performed unless there is clear indication that a non-suppurative post streptococcal complication is suspected. If there are no clinical details or inappropriate testing indications the specimen should be held for three weeks as per normal lab policy for specimens with no test request. An educational laboratory comment (refer to Actions) will be reported to the requestor asking them to contact the duty virologist if post streptococcal complications are suspected.

A second streptococcal serological marker such as anti-DNase B to be tested with ASOT is recommended to improve sensitivity\(^1\). There are three options;

1. Introduce anti-DNase testing to be performed alongside ASOT in RVL or
2. Refer specimens to Bristol PHE where both ASOT and Anti-DNase are currently performed, or
3. Maintain status quo and perform ASOT only in RVL but gate the tests performed by only testing those specimens which are clinically relevant.
It is envisaged that the number of clinically relevant test requests for ASOT should reduce substantially when RVL introduces gating measures. Numbers will be small and so the effort to introduce and validate a new test as well as the lack of expertise in interpretation of these results would suggest that referral to a reference laboratory may be the preferred option. We also currently pay for an external quality control scheme in Finland which is expensive, difficult to manage and would not be needed if samples were referred to Bristol. This option should be explored by a trial of gating measures to estimate specimen numbers.

Testing of a single sample by ASOT is not recommended. If ASOT testing is to remain in RVL without the additional introduction of anti-DNase and there is a relevant clinical indication for testing, a second serum should be requested and both acute and convalescent sera tested in parallel using ASOT.

**Actions**

- RVL will share the findings of this audit with users especially the main requestors which are GPs and RBHSC A&E. There appears to be a lack of understanding in the clinical setting re the utility of the ASOT test, we will aim to educate users via educational interpretative comments.

- The current ASOT testing algorithm would appear to be sub optimal. Proposed options for improving this need to be discussed and implemented. Gating measures to reduce inappropriate testing will be implemented and ASOT testing re- audited after 3-6 months.

**Proposed comment for holding specimens requesting ASOT**

Anti-streptococcal antibody titres are not recommended in the routine diagnosis of acute pharyngitis as they reflect past but not current infection. This specimen will be held for 3 weeks. If you clinically suspect post
streptococcal complications e.g. glomerulonephritis or rheumatic heart disease, please contact the duty virologist on 07889086946 to discuss testing.

The Centor clinical scoring system can help to identify patients who have a higher likelihood of Group A streptococcal throat infection and is helpful in targeting antibiotic use. A useful resource is the ESCMID 2012 guideline for management of acute sore throat.

**Proposed comment for reporting with ASOT results for specimens that are tested.**

ASO antibodies are usually long lasting and a single increased titre is not an indication of a current infection. Only a fourfold or greater rise in titre on successive serum samples taken 10-14 days apart should be considered indicative of recent infection.

**References**

2. NICE Clinical Knowledge Summary [http://cks.nice.org.uk/scarlet-fever](http://cks.nice.org.uk/scarlet-fever)
5. PHE Investigation of red rash Clinical Guidance | G 7 | Issue no: 2.1 | Issue date: 04.03.14
7. IDSA Guideline for GAS pharyngitis. CID 2012

**12.0 Proposed re-audit**

- A reaudit will be performed 3-6 months after introduction of new ASOT testing policy
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