Policy

Clinical Guideline

Staphylococcus aureus bacteraemia (SAB) management guideline (adult)

Objective file number: 2014-07520
Policy developed by: South Australian Expert Advisory Group on Antibiotic Resistance (SAAGAR)
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Summary The *Staphylococcus aureus* Bacteraemia (SAB) Management Guideline (Adult) provides a flow-diagram to assist in antimicrobial prescribing, recommended investigations, and recommended duration of therapy. A patient information leaflet is available for patients to carry in case of a relapse. Prescribers are given background information around SAB occurrences in Australia and the importance of appropriate treatment to minimise the risk of secondary complications.

Keywords Staphylococcus aureus, bacteraemia, SAB, antibiotics, antimicrobials, SAAGAR, MRSA, MSSA, empiric, patient information, management guideline, clinical guideline

Policy history Is this a new policy? **Y**
Does this policy amend or update an existing policy? **N**
Does this policy replace an existing policy? **N**
If so, which policies?

Applies to All SA Health Portfolio

Staff impact All Clinical, Medical, Nursing, Emergency, Dental, Mental Health, Pathology

PDS reference CG167

Version control and change history

Version	Date from	Date to	Amendment
1.0	14/10/14	current	Original version

Government of South Australia
SA Health

Antimicrobial guidelines
Staphylococcus aureus Bacteraemia (SAB) Management Guideline (Adult)

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Suspected or confirmed *Staphylococcus aureus* bacteraemia

Take and send blood cultures then start

flucloxacillin 2g IV 6 hourly **PLUS vancomycin** 25mg/kg load IV (actual body weight, maximum dose 2g)
See Box 1 and overleaf for maintenance dosing

For non-life threatening (type II-IV) penicillin allergy, INSTEAD of flucloxacillin, use **cephazolin** 2g IV 8 hourly

For immediate / life threatening (type I) penicillin allergy (anaphylaxis, angioedema, urticaria), OMIT flucloxacillin and **use vancomycin alone**

NOT *Staphylococcus aureus* bacteraemia?

- Review microbiology results and modify treatment as appropriate
- Perform investigations as appropriate
- Consult ID/Clinical Microbiologist if necessary

BOX 1: Vancomycin dosing

- Doses require modification based on renal function, weight and trough levels
- Refer to renal adjustment guideline on page 2 or current Therapeutic Guidelines

BOX 2: Non Tertiary Centres

- Transfer to a major metropolitan hospital should be considered for ALL patients with *Staphylococcus aureus* bacteraemia
- Discuss all cases with on-call Clinical Microbiologist
- Contact numbers:
  On-call SA Pathology clinical microbiology consultation:
  08 8222 3000
  Medstar: 13STAR (13 78 27)

Confirmed *Staphylococcus aureus* bacteraemia

- Assess possible focus
- Assess for metastatic infective complications
- Perform investigations
- Remove IV cannula or potentially infected devices
- **Infectious Diseases or Clinical Microbiologist consult strongly recommended**
- **Consider patient transfer (Box 2) and need for TOE (Box 3)**

Check susceptibility of *Staphylococcus aureus* 24-48 hrs after initial isolation

Flucloxacillin **resistant** (MRSA)	Flucloxacillin **sensitive** (MSSA)
Cease flucloxacillin (or cephazolin)	Cease vancomycin (unless type I penicillin allergy)

Obtain blood cultures daily for 72 hours after starting treatment. If still positive at 72 hours, discuss further with ID/Micro

Investigations to be performed:

1) Trans-thoracic echocardiogram (TTE) on **all** patients within 7 days and consider TOE (Box 3)
2) Bone scan +/- MRI if new or worsening back pain, joint or bone pain
3) Ultrasound and joint aspirate if patient has any joint swelling or suspected joint infection
4) Baseline LFT, CXR, CBE and CRP

BOX 3: Who needs a trans-oesophageal echocardiogram (TOE)?

- All patients with a prosthetic valve or permanent pacemaker (PPM)
- Patients with persistently positive blood cultures after 72 hours of antibiotic treatment and a negative Transthoracic Echocardiogram (TTE)
- Patients with clinical features of endocarditis and a negative TTE or who are failing antimicrobial therapy
- Patients with cardiac failure as a complication of endocarditis
- Patients with no obvious primary focus who have metastatic infective complications and a negative TTE
- Community acquired *Staphylococcus aureus* bacteraemia and a negative TTE

Assess duration of therapy based on likelihood of complications

Minimum 2 weeks IV therapy - Uncomplicated catheter related

- Catheter identified as source of infection and promptly removed after diagnosis
- No evidence or symptoms suggestive of metastatic infection
- Fever resolves within 72 hours of antibiotic treatment
- Blood cultures after 72 hours of antibiotic treatment are negative
- No prosthetic material present in intravascular space
- No evidence of valvular abnormality on TTE

Minimum 4 weeks IV therapy - Complicated infections

SEEK ID/ MICROBIOLOGY CONSULTATION FOR THE FOLLOWING:

- Persistent bacteraemia (72 hours) OR slow resolution of fever on treatment
- Prosthetic infection or presence of foreign material/device
- Endocarditis
- Osteomyelitis/septic arthritis
- Internal organ abscess or infarction
- CNS infection including epidural abscess
- Community onset infection

ALL PATIENTS NEED FOLLOW UP FOR RELAPSE

Arrange clinical review 4 weeks following completion of antibiotic therapy
NB. Some infections (e.g. bone & joint) will require ongoing oral therapy after IV treatment completed
Ensure patient receives Information Leaflet (page 7)

Dosing and monitoring of antibiotics in renal impairment

For patients on dialysis please consult Therapeutic Guidelines: Antibiotic or other appropriate renal dosing reference.

ß-lactam[1]

	GFR† > 50 ml/min	GFR† 10-50 ml/min	GFR† <10 ml/min
Flucloxacillin	2g IV 6 hourly	2g IV 6 hourly	1g IV 6 hourly
	GFR† > 40 ml/min	**GFR† 20-40 ml/min**	**GFR† <20 ml/min**
Cephazolin	2g IV 8 hourly	1g IV 8 hourly	1g IV 12 hourly

Vancomycin[2]

	GFR† > 90 ml/min	GFR† 60-90 ml/min	GFR† 20-59 ml/min	GFR† < 20 ml/min
Vancomycin dose	1.5g IV 12 hourly	1g IV 12 hourly	1g IV 24 hourly	1g IV 48hourly
Timing of trough concentration measurement **Target 15-20mg/L**	Before the fourth or fifth dose	Before the fourth or fifth dose	Before the third dose	Before the second dose Re-dose when trough < 15mg/L

† Estimate GFR using Cockroft - Gault formula

Monitor vancomycin trough concentrations every 48-72 hours until stable. Continue to monitor at least weekly thereafter[2]. Trough concentrations <10mg/L may increase development of resistance.[3]

Special populations

Low weight patients: Consider 15mg/kg vancomycin maintenance dosing for patients less than 50kg, appropriately modifying the dose if the patient also has impaired renal function.[4]

Obese patients: The volume of distribution is larger and clearance of vancomycin greater in the obese population. Weight-based dosing using total bodyweight (15mg/kg, maximum 2g per dose) is recommended.[4,5] More frequent dosing (8-hourly or continuous infusion in extremely obese patients) may also be appropriate to compensate for increased clearance.[3, 6-8] Obese patients (>100kg) and those receiving at least 4g/day of vancomycin have been associated with a higher risk of nephrotoxicity and thus warrant regular creatinine clearance monitoring.[8]

General Considerations: It is advisable to seek specialist advice for clinical conditions that alter pharmacokinetic parameters (volume of distribution and clearance), such as pregnancy, burns, critical illness and obesity. These conditions also warrant more frequent vancomycin therapeutic drug monitoring.[4,6]

Follow up post treatment for relapse

Relapse can occur following treatment and all patients with *Staphylococcus aureus* bacteraemia should have a follow-up appointment made one month post completion of antibiotic treatment. Patients should be made aware of the potential for relapse within 3 months of presentation. A patient information leaflet is included with this guideline to assist with detection and management of relapse.

Isolation of *Staphylococcus aureus* in blood cultures should not be regarded as a 'contaminant' – follow-up of positive blood cultures is always required.

Background and importance of adequate management of *Staphylococcus aureus* bacteraemia:

All patients with suspected *Staphylococcus aureus* bacteraemia (SAB) should be evaluated and **isolation of *Staphylococcus aureus* in blood cultures should not be regarded as a 'contaminant'** without proper clinical assessment. On-call infectious diseases physicians or clinical microbiologists are readily available to assist with the interpretation of culture results. It is estimated that only 1.5% of blood cultures positive for *Staphylococcus aureus* are due to contamination.[9]

SAB is a serious and relatively common condition associated with high morbidity and mortality. It is estimated that approximately 6500 cases of SAB occur each year in Australia.[10] Significant complications such as infective endocarditis and metastatic deep tissue infection can result. Treatments need to be commenced promptly with appropriate empirical therapy and clinical investigations as described in this guideline.

Mortality rates in patients with methicillin-susceptible *Staphylococcus aureus* (MSSA) infection are higher if treated with vancomycin instead of an appropriate ß-lactam such as flucloxacillin.[9,10] However, if the isolate is methicillin resistant (MRSA), appropriate antibiotic cover is required from outset.

It is therefore suggested that dual therapy be commenced empirically, reducing therapy to a single agent when sensitivities are determined (usually within 48 hours after initial isolation).

- Cease vancomycin if the *Staphylococcus aureus* is methicillin sensitive (MSSA)
- Cease flucloxacillin or cephazolin if *Staphylococcus aureus* is methicillin resistant (MRSA)

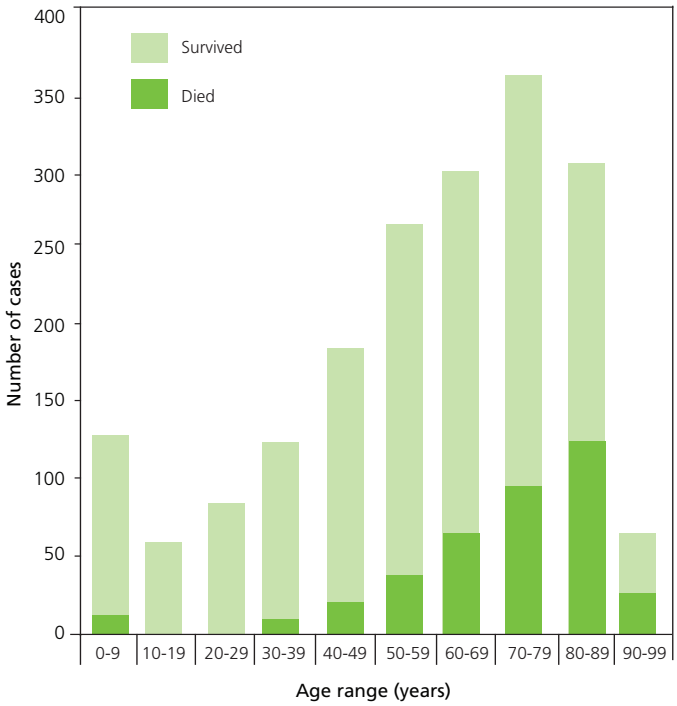
Published mortality rates due to SAB vary significantly (2.5%-40%)[10], however a patient's age, clinical manifestation and comorbidities are contributors. Age has been shown to be the strongest predictor of SAB associated mortality, the risk increasing with each decade[10]. Mortality rates reported by ASSOP 2013 show a significantly higher rate of mortality associated with MRSA- than MSSA- SAB (20.1% vs 13%).[11]

Complications such as left-sided endocarditis, device infection with a secondary focus, pneumonia/empyema and sepsis syndrome also result in increased mortality. A prospective study of Australian and New Zealand patients from June 2007 to May 2008 showed 20.8% all-cause mortality for *Staphylococcus aureus* bacteraemia at 30 days.[10] For hospital acquired SAB in South Australia, the estimated additional cost, in 1998, was AUD$22,000 per case.[12]

Infections can stem from community or hospital origin, with an Australian/New Zealand study suggesting 61% of cases were contracted in the community environment.[10] A recent Australian report (ASSOP 2013) stated that only 28.4% of cases were of community onset, from a pool of 26 Australian hospitals.[11]

This latter report determined that methicillin resistant (MRSA) strains of *Staphylococcus aureus* were found in 19.1% of all SAB cases.[11] This is slightly lower than the 24.1% of all cases reported in the Australian/New Zealand 2007-8 study, of which 17.8% were community-onset and 33.8% hospital-onset infections.[10] Another Australian study completed in 2002 showed MRSA was responsible for 12% of community-onset and 40% of hospital-onset cases.[12] This supports the use of dual empiric therapy until sensitivities are determined.

Figure 1#: Number of cases of *Staphylococcus aureus* bacteraemia and patient survival, by age*



*Data not shown for one patient aged 100 years who survived.

#Figure 1: Turnidge JD, Kotsanas D, et al. *Staphylococcus aureus* bacteraemia: a major cause of mortality in Australia and New Zealand. Med J Aust 2009; 191 (7):368-373.

Vascular lines are a known potential source of bacteraemia, and the use of these devices in community/outpatient settings is increasing. Many SAB episodes defined as "community acquired" may be better described as "non-inpatient healthcare associated" episodes. It is estimated that approximately one third of Australian "community onset" episodes were associated with healthcare or medical procedures, yet would not be classified as "hospital acquired" as patients were not an inpatient for at least 48 hours. Importance must therefore be placed on procedures to reduce numbers of all healthcare-associated infections (inpatient, outpatient and community healthcare).[12]

Removal of foci/detection of metastatic complications:

The potential source of infection should be actively sought and the removal or drainage of infectious foci should be undertaken whenever possible. Retention of an infected intravenous catheter has been shown to be the strongest independent risk factor for a relapse of SAB. Removal of infected prosthetic heart valves, prosthetic joints, permanent pacemakers or implantable cardiac defibrillators improves outcomes.[9, 13] Common sites of metastatic infection include heart valves, bone and joints (particularly when prosthetic material is present), intervertebral discs, the epidural space, and intra-abdominal sites such as kidneys, liver and spleen.[5]

Deep seated infections such as vertebral osteomyelitis or deep tissue abscess are likely to relapse if therapy duration is insufficient. Further investigations (based on clinical signs and symptoms) may include MRI of the spine (pain or tenderness of spine), bone scan (bone/joint or muscular pain), CT of brain or abdomen (focal neurology, seizures, abdominal pain) and ultrasound-guided aspiration of swollen, tender joints.

All patients should receive investigatory echocardiogram. A trans-thoracic echocardiogram (TTE) is a rapid, non-invasive test with good specificity but poor sensitivity for detecting cardiac vegetations. A trans-oesophageal echocardiogram (TOE) is superior in quality and improves sensitivity, however is more invasive and is not readily available at some sites.[14,15] Investigations via TOE should be used in specific patient subgroups – see Box 3 of guideline.

Duration of therapy

The duration of IV therapy for SAB should be at least 14 days. Continued review is essential to detect relapse or metastatic infection. Complicated infections (e.g. positive follow up blood cultures, community acquired infection, fever for more than 72hrs[16] – see table on page 1) will require longer courses of antibiotic treatment. In staphylococcal endocarditis, antibiotics should be continued intravenously for the total duration of therapy. In osteomyelitis, oral therapy may need to continue for many months.[2] It is strongly recommended that advice is sought from an infectious diseases physician or on-call clinical microbiologist to assist in choosing antibiotic duration and treatment plan.

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Patient information leaflet

Important information for patients diagnosed with *Staphylococcus aureus* bacteraemia

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Patient Details:

Name: _____

UR Number: _____

Date of Birth: _____

You were recently diagnosed and treated for a blood stream infection caused by the bacterium *Staphylococcus aureus*.

Staphylococcus aureus is a bacterium (germ) that is frequently found on the skin as one of the normal resident bacteria. Usually it causes no medical problems, but occasionally this bacterium can enter the body and cause a serious infection. Most of the time, the *Staphylococcus* bacteria gets into the body through a break in the skin. Common infections that are caused by *Staphylococcus aureus* include cellulitis (infection of the skin), abscesses or boils. Less common but more serious infections caused by *Staphylococcus aureus* include blood stream infections, septic arthritis (an infection of a joint) and infection of the heart valves (known as endocarditis).

While the intensive treatment you received normally cures the infection, there is a small risk that the infection can return within THREE months following completion of antibiotics.

You are asked to see your General Practitioner (GP) if you have any of the following symptoms:

1) Fever (a recorded temperature greater than or equal to 38^{o}C), chills or shakes
2) Unusual backache or pain
3) Chest pain and/or shortness of breath
4) Headache, dizziness, nausea and/or vomiting

If you are very unwell you should arrange to go directly to the nearest hospital.

This information sheet will provide useful information to the medical staff, so take it with you if you can. Blood tests taken **before** restarting antibiotics (especially a blood culture test) will be helpful in your treatment.

Any concerns should be discussed with your doctor prior to discharge or completion of therapy. For further information go to www.sahealth.sa.gov.au and search *Staphylococcus aureus*.

For completion by home team prior to discharge:

Hospital treatment details

Doctor's name (print)_____ **Treatment Hospital** _____

Home Team _____ **Phone/Pager** _____

Type of *S. aureus* bacteraemia: MRSA / MSSA (clinician please circle)

Date of initial infection _____/_____ /_____

MRSA: Methicillin Resistant *Staphylococcus aureus*. MSSA: Methicillin Sensitive *Staphylococcus aureus*.

Useful contact numbers (patient to complete)

GP _____ **Local Hospital** _____