Infected endocarditis clinician information

General information and early medical management of suspected infected endocarditis cases for medical practitioners.

Infected endocarditis Queensland management group (IEQMG)

https://medicine-program.uq.edu.au/school-clinical-medicine/research/infected-endocarditis-qld

Infected Endocarditis (IE) is a relatively uncommon condition in general practice and can be challenging to diagnose with highly variable illness presentation and common, vague symptoms. This condition affects dozens of Queenslanders per year, many requiring open-heart surgery. At least 1 in 10 Queenslanders with this disease will die from it and many will have strokes or gangrene because of this illness. This information brochure has been developed to assist you in recognising IE in your patients and guide you in your care and treatment of the suspected IE patient.

What is IE?

IE is an inflammation of the inner lining of the heart or the ‘endocardium’ and regularly involves the valves in the heart. IE develops in 3 stages:

1. Bacteremia: Microorganisms are present in the blood. These microorganisms may originate from distant infected sites (e.g., abscess, inflamed or infected gums, urinary tract infection) or obvious portals of entry such as an intravenous drug injection site.
2. Adhesion: The microorganism adheres to abnormal or damaged endothelium.
3. Colonisation: Proliferation of the organism together with inflammation, leading to the growth of a vegetation.

Image reference: By Bruce Blaus - Own work, CC BY-SA 4.0, https://commons.wikimedia.org/w/index.php?curid=57340203

Patient presentation

Clinical presentation

- IE is not always clinically obvious.
- The presentation may vary from acute (abrupt severe symptoms of only a few days) to sub-acute (gradual increase of initially mild symptoms over weeks or months).
- Up to 90% of patients present with a fever, which is often associated with systemic symptoms of chills, poor appetite, and weight loss.
- Heart murmurs are found in up to 85% of patients.
- Vasculitis signs such as splinter haemorrhages, glomerulonephritis and retinal haemorrhages are increasingly uncommon as the diagnosis is being made earlier.
- Emboli to brain, lung, spleen or extremities occur in up to 30% of patients and can be the presenting feature.
- Patients with known valvular or intra-cardiac abnormalities/prostheses including permanent pacemakers or implantable cardioverter-defibrillator are often identified as ‘at endocarditis risk’.
Patient complaints
Patients may present complaining of the following symptoms:

- Fever and chills
- Lethargy
- Anorexia
- Diffuse ache
- Dyspnoea and non-productive cough
- Pleuritic chest pain

Unusual risks and bacterial causes
Domestic and native wildlife
Patients involved with domestic animals (especially cattle, sheep and goats), can acquire Q Fever. Whilst Cattle, sheep and goats are the main sources of infection, a wide range of animals including domestic and feral dogs and cats, feral pigs, horses, rabbits, rodents, alpacas, camels, llamas, foxes, and Australian native wildlife (including kangaroos, wallabies and bandicoots) can also be sources of infection.

Q fever is caused by inhaling or being in contact with *Coxiella burnetii* bacteria from an infected animal or infected animal placentas (the highest risk). Spores from these organisms may persist in soil for years. Infection may be acquired from soil, abattoirs, live stock sale-yards and in very rare cases, may presumably result from breathing in spores from a cattle-transporter that has passed by. Landscape gardeners are becoming the leading occupation risk in regions of Queensland. Most people with acute Q fever have no long-term problems, although a small proportion, especially those with ‘endocarditis risk heart’ may develop IE, usually within the first 2 years after exposure. Acute Q fever typically presents as a “flu-like illness” with fevers, ‘drenching’ sweats, chills, anorexia and malaise. There may also be signs of pneumonia or jaundice. Most people with acute Q fever have no long-term problems, although a small proportion, especially those with “endocarditis risk heart” may develop endocarditis, usually within the first 2 years of exposure.

Q fever vaccination may be considered in some individuals at risk. We currently recommend all individuals with acute Q fever undergo a transthoracic echocardiography (TTE) to stratify risk based on pre-existing intra-cardiac abnormalities. If there are no pre-existing cardiac abnormalities on TTE, the patient is generally stratified as ‘low Q fever endocarditis risk’. In both high and low risk cases we also recommend following with serial serology which may also aid in predicting progression to chronic Q fever/IE. We suggest notifying all cases of acute Q fever promptly (by telephone) to your local infectious disease (ID) service for further advice.

Cats
*Bartonella henselae* is often found on cat claws and can be transmitted to humans by cat scratches or bites. Acute Bartonellosis caused by cat scratches usually presents with fevers, headache and tender lymph glands near the bite/scratch-site. In rare cases it can develop into IE over several months.

Gardening
*Legionella longbeachiae* can be found in soil and potting mix. Gardeners with an ‘endocarditis risk heart’ should garden with gloves and wear a face mask, especially when using potting mix. Infection symptoms can include fever, cough and chest pain.

Feral Pigs
Feral pigs in Queensland or NSW are often infected with *Brucella suis* which can cause bacteraemias and occasionally endocarditis. Patients can be infected by eating uncooked feral pig meat or by cuts/scratches from live or dead feral pigs. Acute symptoms of infection are fevers, abdominal pains and anorexia /lethargy which may be profound.

Parrots
Parrots can be infected with bacteria called *Chlamydia psittaci* which can occasionally cause IE. If your patient is exposed to an infected parrot, they may require a course of doxycycline. Acute symptoms of infection are usually fever, cough (usually dry) which may be profound and may persist for months, and rarely evolve into IE.
Open Heart Surgery

*Mycobacterium chimaera* has been associated with contaminated faulty heart/lung bypass machines used in open heart surgery. Incubation can be up to 5 years. Patients with this infection usually only have chronic sweats and weight loss as symptoms. The incidence in Australia is low and declining since most implicated bypass machines have been removed from service.

Investigations – Blood Cultures (BCs)

- BCs are the best method for identification of the microorganisms causing IE.
- BCs are positive in about 90% of cases but may be negative in cases of fastidious pathogens or after previous antibiotic treatment commenced. **Performing blood cultures before any antibiotic treatment is thus mandatory when IE is suspected.**
- Blood collection must be a minimum 7mls of blood per bottle in adults (preferably 10mls to maximize sensitivity).
- If there are problems with blood collection volume, anaerobic bottles can be omitted (as < 1% of IE is due to strict anaerobes.)
- **DO NOT use Paediatric (1ml) bottles in adults** as the sensitivity is only ~10%.
- Paediatric bottles are only to be used in paediatric cases (with exact volume related to age/weight).
- Pathology request form must note;
  - time/site (anatomical + peripheral or IVC) of collection
  - “pre-antibiotics” or “on antibiotics” and a description of antibiotics and doses administered
- One set of BCs are to be **recollected daily if a pathogen found** until confirmed sterilized (no growth). The duration of positivity impacts on treatment and prognosis. Often only one bottle is necessary per draw if only to demonstrate sterilisation.
- BCs are not required if antibiotics are being administered only as prophylaxis prior to procedures such as dental work or Endoscopy.

‘At endocarditis risk’ patient presenting with fever or suspected bacterial infection, but IE felt unlikely to be diagnosis

- These patients should have 2 sets of BCs drawn (preferably at least 20 minutes apart) before antibiotics commenced to identify whether a bacteraemia is taking place.
- Antibiotics can be commenced the instant BCs have been drawn. No further draws are necessary unless clinically indicated.
- **Commencing antibiotics** (either oral or parenteral) **prior to drawing BCs may mask potential pathogens**, potentially leading to a misdiagnosis/delayed diagnosis or unnecessary adverse drug reactions.

Patient presenting with suspected IE

- If a patient suspected to have IE (illness with possible embolic features OR no clear source OR cardiac manifestations **even if no known ‘endocarditis risk factors’**), at least 3 sets of BCs must be drawn prior to antibiotic administration.
- BCs to be preferably drawn over at least 12 hours if the patient is clinically stable. If treatment cannot be stalled send 3 sets promptly from different peripheral blood sites.
- **Avoid Intravenous cannula collections** (IVC), if possible, even if the IVC has just been inserted, as contaminants are common, and can possibly lead to mis-diagnosis.
- IVC collections may be acceptable if;
  
  a) Catheter Associated Blood Stream infections (CA-BSI) is suspected. Simultaneous blood collection from IVC and peripheral stab collections should occur with bottles and pathology request form clearly noting BCs source site and time specimens collected. CA-BSI is confirmed if IVC BCs flags at least 2 hours faster than peripheral BCs.
  
  b) Unable to source blood (for example with Intravenous Drug Users patient cohort), in which case each BCs must be from a separate (and clearly noted on the bottles and pathology request form) site.
Avoid commencing antibiotics until appropriate BCs have been collected unless;

- The patient is too unwell to delay therapy
- BCs bottles are not available within 30 minutes

What to do when the BCs are negative

- BCs are negative in approximately 10% of cases of IE, which can lead to delay in diagnosis and treatment commencement which can have a profound impact on clinical outcome.
- Blood culture negative endocarditis (BCNE) are most commonly related to the previous administration of antibiotics.
- BCNE may be associated with fastidious organisms, including
  
  a. *Legionella, Coxiella, Bartonella, Brucella, T. whippelie, rarely Mycoplasma or Chlamydia*. Serology is useful for diagnosis of these organisms.
  
  b. *Fungi such as Candida, Histoplasma and Aspergillus species*. Serology is useful for diagnosis of Histoplasma infection.
  
  c. *Muranic (non-infective IE) may mimic IE.*
- Histological examination may also be useful when infected tissue is available from cardiac surgery or retrieved embolic material. Culture, microscopy and if indicated PCR may also be useful in diagnosis.
- Polymerase Chain Reaction (PCR) can be useful when negative cultures are caused by previous administration of antibiotics or the presence of a fastidious organism. 16s (pan bacteria) PCR and 18s (pan fungal) PCR are generally performed only on tissue. If PCR positive, an attempt is made to identify the organisms by sequencing. Targeted PCR’s may be sued on either blood or tissue and include Q fever and Bartonella although other primers may (often experimentally) be used on occasion.
- Further investigations such as echocardiography may be required to confirm IE.

Echocardiography

- TTE is the initial technique of choice for radiological investigations of IE and is used to confirm that endocarditis is unlikely and suggests investigations should be directed elsewhere in low “at endocarditis risk” patients.
- TOE, with its higher sensitivity and specificity, may be required if the TTE is normal and suspicion of IE remains high in those patients deemed “at endocarditis risk”.
- TOE is the imaging modality of choice if prosthetic valve endocarditis is suspected.
- TOE may be preferred also if TTE images are suboptimal (obesity or emphysema) especially for left sided valves and is superior for detecting aortic root abscess.
- Sometimes, although TOE is preferred, it is not possible to perform (patient unwilling, unable to travel or not appropriate (patient not a candidate for open heart surgery if IE confirmed).

Other imaging modalities

Sometimes other imaging modalities can diagnose endocarditis, either by demonstrating abnormalities in the cardiac architecture or by demonstrating embolic lesions. These imaging modalities may include computed tomography (CT) scans, Magnetic resonance imaging (MRI), white cell (WC) scans or positron emission tomography (PET) scans.

Antimicrobial therapy and expert advice

- Antibiotics are to be administered as per Electronic Therapeutic Guidelines (eTG)
  
  

- Contact your local Infectious Diseases (ID) unit for information/guidance (this is preferred in all suspected IE cases prior to commencing Antibiotics during business hours and even if therapy for presumed IE has already commenced, and all hours if a complicated patient.)

- Some patients may be recruited for IE Biobank/database. Please liaise with local ID unit. Early referral in centres recruiting is encouraged.
• If the patient is being transferred to a Cardio-thoracic surgery hospital, please include documentation of all relevant prior pathology, radiology and clinical findings if available.
• If Q fever, Bartonella or another atypical pathogen is suspected, additional blood in an EDTA tube for PCR test, or serum tube for antibody detection may be requested by the local ID unit.

Diagnostic criteria
• The Duke criteria have been developed to assist in stratifying patients suspected of having IE. Whilst it does not replace clinical judgement, it helps in sorting patients into ‘endocarditis definite’, endocarditis possible’ and ‘endocarditis unlikely’ categories.
• Many online calculators have been published for rapid clinician assessment; for example https://reference.medscape.com/calculator/endocarditis-diagnostic-criteria-duke
• The criteria are sensitive for disease detection and have a high negative predictive value, however rarely IE can occur without fulfilling Duke criteria. (refer over to attached Duke criteria table for further information).

---

**Important points for consideration**

• Any *bacteraemic process may result in IE in ‘at endocarditis risk’ patients."
• Advise ‘at endocarditis risk‘ patients to seek medical advice promptly if unwell.
• Do not commence any therapeutic antibiotics (prophylactic antibiotics are exempt) in ‘at endocarditis risk’ patients without obtaining blood cultures first. Initial dose of antibiotics can commence the moment blood cultures have been collected. This will reduce the complications due to a mis-diagnosis or inappropriate therapy of a BCNE.
• If the patient likely has IE, contact your local ID service for advice as soon as possible.
• If eTGT antibiotic suggestions are not appropriate, please contact your local ID service as soon as possible.
**Pathological criteria**

- Positive histology or microbiology of pathological material obtained at autopsy or cardiac surgery (valve tissue, vegetations, embolic fragments, or intracardiac abscess content)

**Major criteria**

- Two positive blood cultures showing typical organisms consistent with infective endocarditis, such as Streptococcus viridans and the HACEK group OR
- Persistent bacteraemia from two blood cultures taken > 12 hours apart or three or more positive blood cultures where the pathogen is less specific, such as Staphylococcus aureus and Staph epidermidis OR
- Positive serology for Coxiella burnetti, Bartonella species, or Chlamydia psittaci OR
- Positive molecular assays for specific gene targets
- Positive echocardiogram showing oscillating structures, abscess formation, new valvular regurgitation, or dehiscence of prosthetic valves

**Minor criteria**

- Predisposing heart disease
- Fever > 38°C
- Immunological phenomena such as glomerulonephritis, Osler’s nodes, Roth spots, or positive rheumatoid factor
- Microbiological evidence not fitting major criteria
- Elevated C reactive protein or erythrocyte sedimentation rate
- Vascular phenomena such as major emboli, splenomegaly, clubbing, splinter haemorrhages, petechiae, or purpura

**Definite infective endocarditis**

- Pathological criteria positive OR
- Two major criteria OR
- One major and two minor criteria OR
- Five minor criteria

Reference - https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4632890/

For further information please contact:

infective endocarditis Queensland [ieQ]

Email: ieq@health.qld.gov.au

Website: https://medicine-program.uq.edu.au/school-clinical-medicine/research/infective-endocarditis-qld