Infected cardiac-implantable electronic devices:

diagnosis, and treatment

- The incidence of infection following implantation of cardiac implantable electronic devices (CIEDs) is increasing at a faster rate than that of device implantation. Patients with a CIED infection usually require hospitalisation and complete device and lead removal. A significant proportion die from their infection.
- Causes for this trend are uncertain, but likely relate to increasing proportion of implantable cardioverter defibrillator (ICD) and cardiac resynchronization therapy (CRT) devices implanted, coupled to implantations in ‘higher risk’ candidates, that is, patients with heart failure, diabetes, and renal failure.

Incidence of cardiac implantable electronic device infection

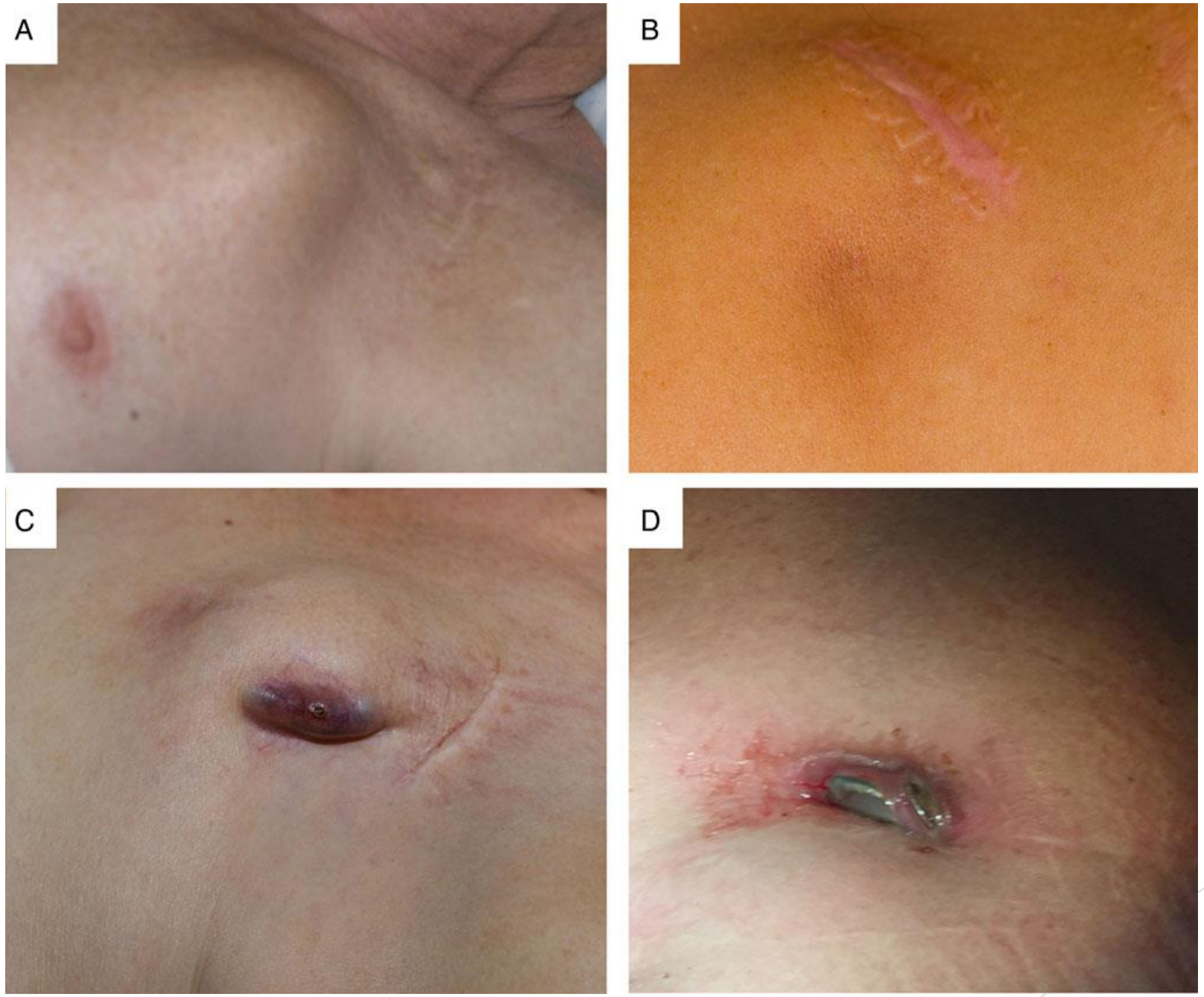
- In a large cohort of pacemaker recipients, estimated incidence was 4.82/1000 device-years and higher within the first 12 months. Infection risk after pacemaker implant is 0.5–1% within the first 6–12 months
- Risk is higher with ICDs, recently estimated 1.7% within 6 months among 200 000 ICD recipients
- even higher in CRT-recipients, 9.5% over 2 years and among these highest with defibrillators (CRT-D).
- Infection risk is higher for devices implanted at thoracotomy and may be
- 2–4× greater after device replacement and upgrades

Pathogenesis and presentation

- Breach of the skin barrier introduces bacteria into the pocket. These may colonize and not always cause clinically relevant infection.
- biofilm formation on device surfaces, described as ‘a structured community of bacterial cells enclosed in a self-produced polymeric matrix and adherent to an inert or living surface’.
- Cultures are negative in 15%.
- Pocket infection is the most common presentation of CIED infection.
- infection commonly tracks along leads and/or causes secondary blood-stream infection and endocarditis.
- Less commonly, the mechanism of blood-stream infection is haematogenous spread of bacteria from another infection site with secondary involvement of intravascular CIED parts.

Diagnosis of cardiac implantable electronic device infection

- Diagnosis may be difficult and a high index of clinical suspicion is warranted.
- from subtle complaints of mild pain without pocket abnormalities, device migration occurring years after implant, erosion, to a hot, red pocket, and septic shock.
- CIED infection commonly presents as local infection around the device. Such pocket infection usually occurs within 12 months post-implant,but may occur later.
- Blood-stream infection is less common, may appear with or without concomitant pocket infection, and with or without valve endocarditis.
- Transoesophageal imaging more accurately visualizes leads, valvular involvement, and vegetation.
- Recently, fluorine-18 marked fluorodesoxyglucose (18F-FDG) positron emission tomography and computed tomography was found useful for differentiating patients with CIED infection from those without.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Which individuals are of greater risk of developing CIED infection?

- •Among patient-related factors, chronic steroid therapy, anticoagulation with warfarin (predisposing patients to post-implantation pocket hematoma), diabetes mellitus, heart failure, active malignancy, immunosuppressive therapy, or presence of a central venous catheter (risk factor for bacteremia and subsequent device seeding) are the most significant predisposing conditions.
- •Device characteristics that increase the risk of infection include abdominal generator placement, use of epicardial leads, more than two transvenous leads, multiple device revisions, and previous history of CIED infection.
- •Implantation procedure-related factors that predispose to subsequent infection include use of temporary pacing leads before permanent device implantation, failure to administer prophylactic antibiotics before implantation, operator inexperience, fever within 24 hours of implantation, and post-operative hematoma at the pocket site.

Beware: there are other diseases that can mimic disease CIED infection:

- pocket hematoma
- bacteremia without any inflammatory signs at the device pocket
- echocardiography cannot discriminate infective vegetation from non-infected thrombotic or fibrous masses
- Occasionally, septic jugular thrombophlebitis can mimic device-related endovascular infection, and CT or MRI is needed to exclude this possibility.

What laboratory studies should you order and what should you expect to find?

- •All patients with suspected CIED infection should have Peripheral white blood cell (WBC) with differential, electrolytes, serum creatinine, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), chest x-ray, and two sets of blood cultures drawn at admission.
- •Patients with CIED pocket infection frequently have normal lab studies.
- •All patients with positive blood cultures should undergo transesophageal echocardiography (TEE) to identify or exclude device-related endocarditis.
- •CT scan of the chest may be considered in cases in which pulmonary emboli are suspected.
- •If the decision is made to explant the device, pocket swabs and tissue specimens should be submitted for bacterial cultures.
- •Fungal or mycobacterial stains and cultures should be considered in cases of chronic or recurrent infection in which bacterial cultures are negative and when the patient is immunocompromised.

What laboratory studies should you order and what should you expect to find?

- •CIED pocket infection is essentially a clinical diagnosis. Microbiologic confirmation can be obtained by swab or tissue cultures from the generator pocket and is helpful to choose appropriate antimicrobial therapy.
- •Diagnosis of device-related endovascular infection requires confirmation by positive blood cultures.
- •TEE is necessary to identify or exclude device-related endocarditis.

Treatment of cardiac implantable electronic device infection

1.Complete removal of infected device including all leads

2. Appropriate antimicrobial therapy for causative pathogen

3. Implantation of a new device once acute infection has cleared

Removal of infected device

- •Complete removal of the infected device, including generator and epicardial or transvenous leads, is a requisite for curing acute infection and preventing relapse.
- •Percutaneous extraction is generally considered safe, even in cases in which a large vegetation (>1 cm) is attached to the device leads.
- •Cardiac surgery should be consulted in cases in which infection is complicated by valvular endocarditis, intracardiac abscess formation, perforation, or dehiscence of native or prosthetic valves and cases in which percutaneous extraction fails or poses significant risk to the patient.

Choice and duration of anti-infective therapy

- •In cases in which infection is limited to the device pocket, 10-14 days of anti-infective therapy is adequate. Patients can be switched to an oral agent at discharge from the hospital if the organism is susceptible.
- •Patients with device-related bloodstream infection (without evidence of endocarditis on TEE) should be treated with 2 weeks of parenteral anti-infective therapy based on identification and susceptibility of the causative pathogen. Therapy may be extended to 4 weeks in cases of S. aureus bacteremia.
- •Device-related endocarditis should be treated with 4-6 weeks of parenteral antibiotic therapy .

Organism	Antibiotic	Dose	Alternative
S. aureus and coagulase-negative staphylococcus (methicillin-susceptible)	Nafcillin Oxacillin IV Cefazolin	2 g q4 2 g q4 1-2 g q8h	Vancomycin or Daptomycin (see below for dosing)
S. aureus and coagulase-negative staphylococcus (methicillin-resistant)	Vancomycin	15-20 mg/kg q12h (monitor serum levels)	Daptomycin: 6 mg/kg q24h (4 mg/kg q24h for pocket infection only)
Enterococcus	Vancomycin (for pocket infection or Penicllin-resistant organisms) --- Ampicillin plus Gentamicin (Amp+Gent combination preffered for device related endocarditis)	15-20 mg/kg q12h (monitor serum levels) --- 12 g/24h IV in 6 equally divided doses plus 3 mg/kg/24h IV or IM in 3 equally divided doses	Daptomycin (dose as above) OR Linezolid (IV or PO): 600 mg q12h --- Ampicillin (12 g/d in 6 divided doses) plus Ceftriaxone 4 gm/d in 2 divided doses) (for device related endocarditis)
Pseudomonas aeruginosa	Cefepime Meropenem Imepenem	1-2 g IV q12h 500 mg IV q6h 500 mg IV q6h	Ciprofloxacin (IV): 400 mg q12h OR piperacillin/tazobactam:3.375 g q6h OR Aztreonam: 1-2 g q8hr

Timing of implantation of new device

- •A new device can be placed on the contra-lateral side once the infected device has been removed and blood cultures obtained after device removal are negative for at least 72 hours.
- •Implantation of a new device should be delayed 14 days (from the first negative blood culture) in cases in which device infection was complicated by valvular endocarditis.

What complications could arise as a consequence of CIED infection?
What should you tell the family about the patient's prognosis?

Complication resulting from CIED infection: These include lead or valvular endocarditis, septic thrombosis or metastatic seeding to other organs.

2.Lead extraction complications: Most transvenous leads are removed percutaneously. Potential complications of percutaneous extraction include damage to tricuspid valve, subclavian vein laceration, pneumo- or hemothorax, or myocardial rupture. Moreover, infected vegetations can detach from transvenous leads during percutaneous extraction and result in septic pulmonary emboli.

•Most patients with CIED pocket infection do well, provided there are no significant complications during device lead extraction.

•Device-related endovascular infection (bacteremia with or without endocarditis) is associated with significant in-hospital mortality ranging from 10 to 20%.

•Risk factors for poor outcome include symptomatic heart failure at presentation, chronic steroid use, renal failure, metastatic malignancy, device-related endocarditis, and infection with S. aureus.