PACEMAKER LEAD ENDOCARDITIS (CDR-IE)

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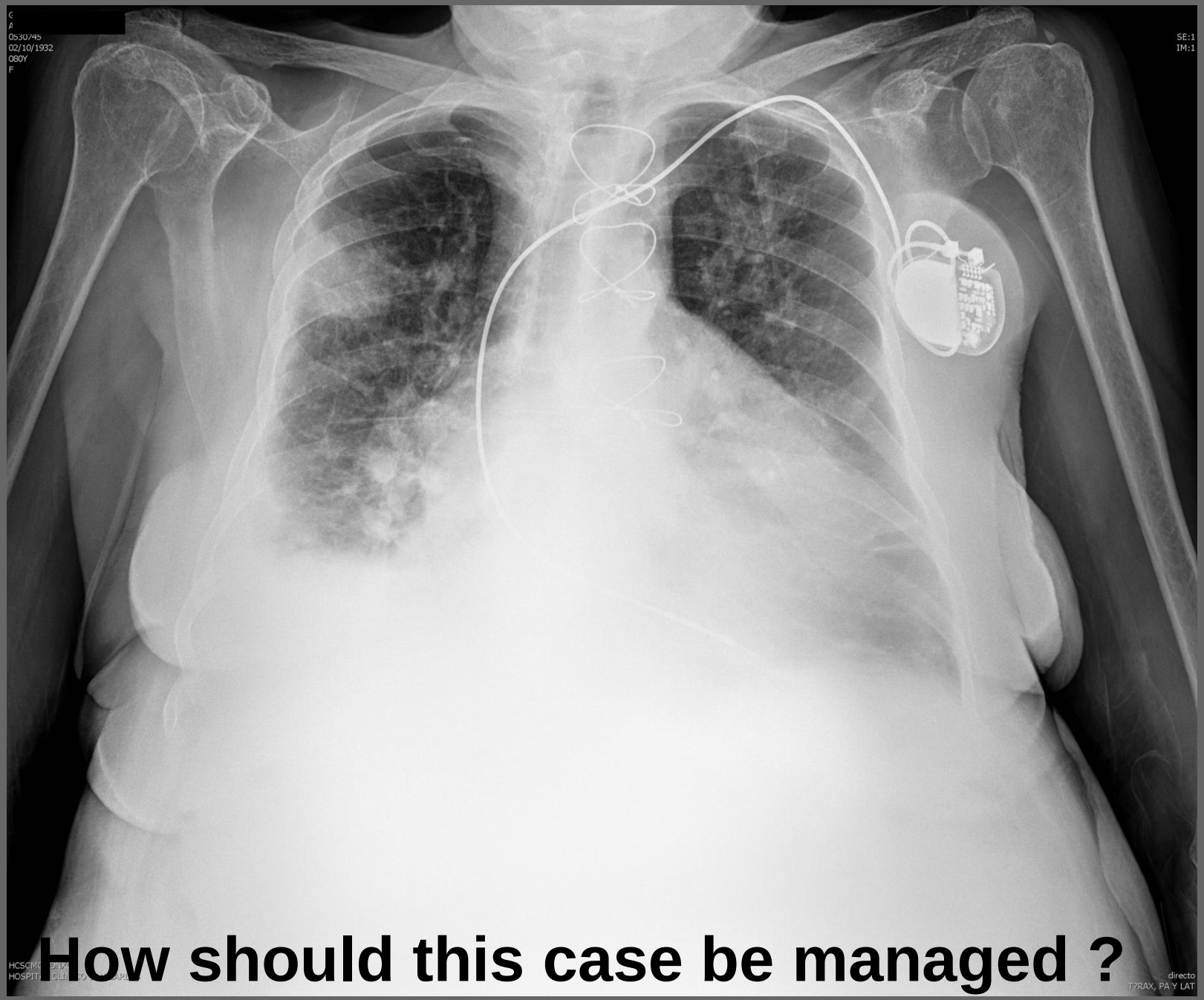
Clinical case

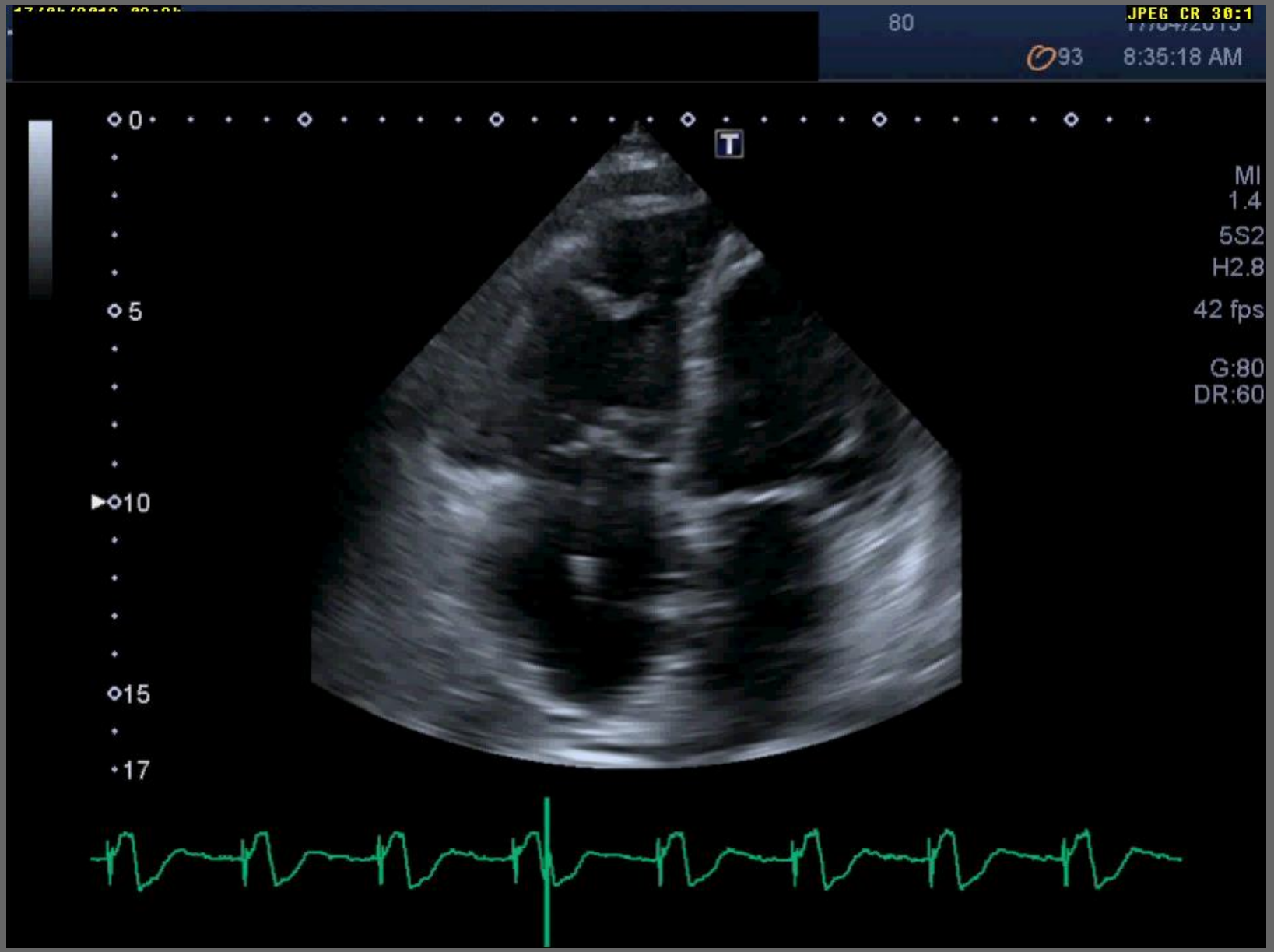
- An 80-year-old obese woman with diabetes, HTN, and **permanent AF** was admitted to the H. for **PM generator replacement**. She had **SOB and fatigue** two weeks before admission.
- **Past history**: LA myxoma surgery in 1988; 2nd heart surgery (myxoma recurrence) in 2000. During postop a **permanent VVI PM** was implanted due to persistent nodal rhythm.
- **Therapy**: **acenocumarol**, digoxin, furosemide, and metformin.
- After the procedure, she developed **progressive heart failure** and was admitted to the CCU.
- Eight days after the procedure she became **febrile (39ºC) and had orthopnea**. A chest X-ray was done.



How should this case be managed ?

Clinical case

- BC were obtained and she was treated with iv. furosemide + antibiotics (vancomycin & gentamicin).
- BC were positive for **MRSA**.
- There were **no signs of infection at the pocket site.**
- **TTE & TEE were performed** to rule-out PM infection.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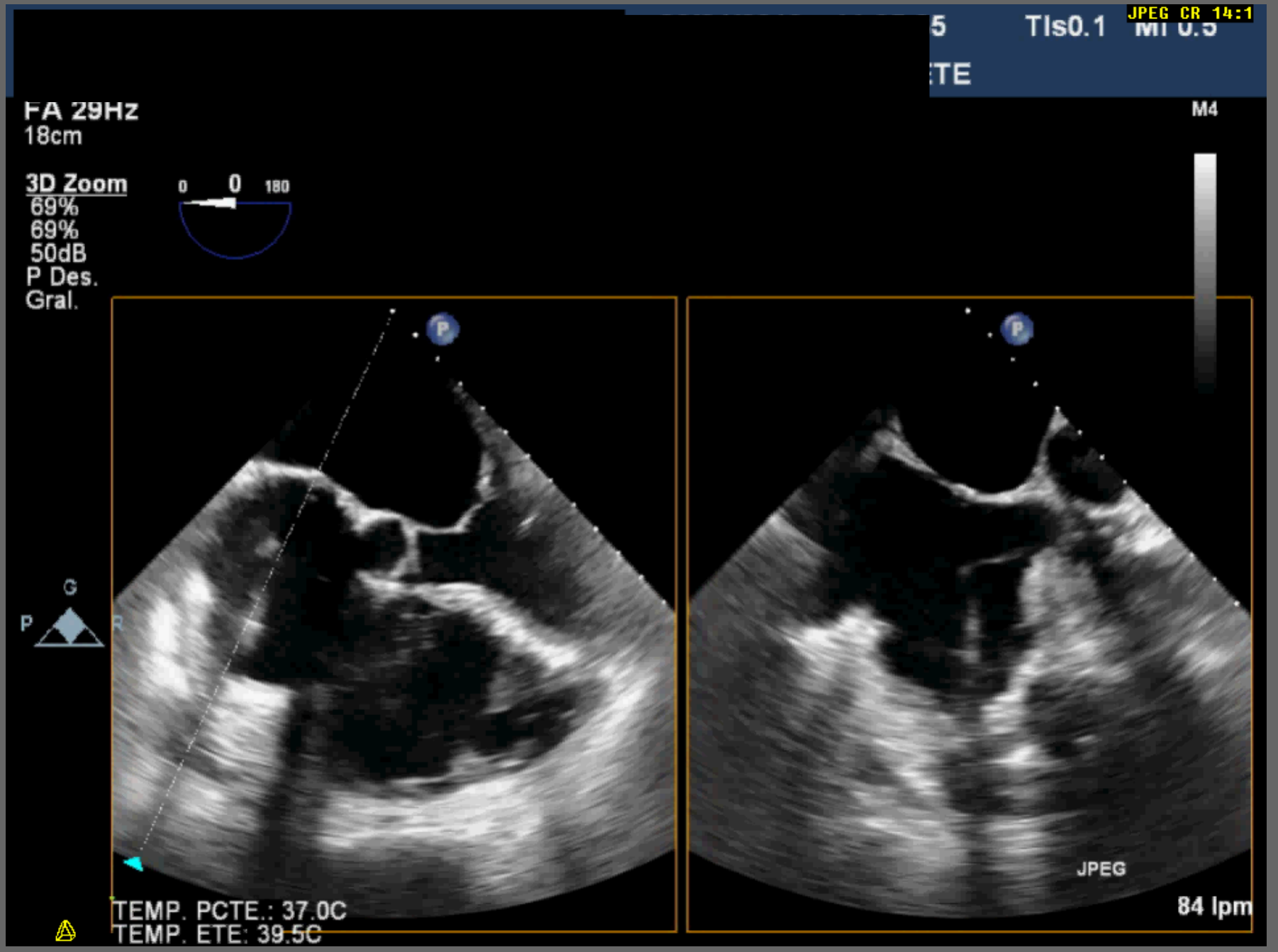
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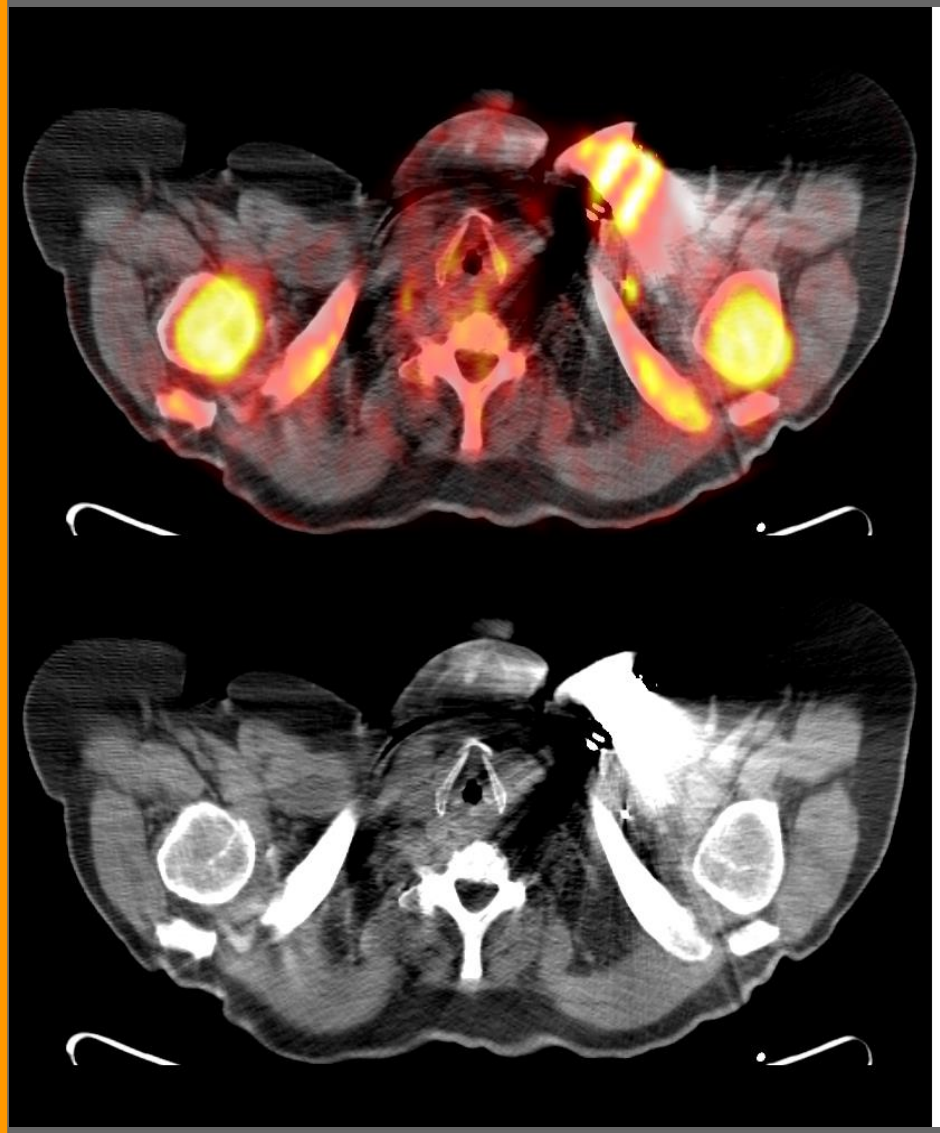
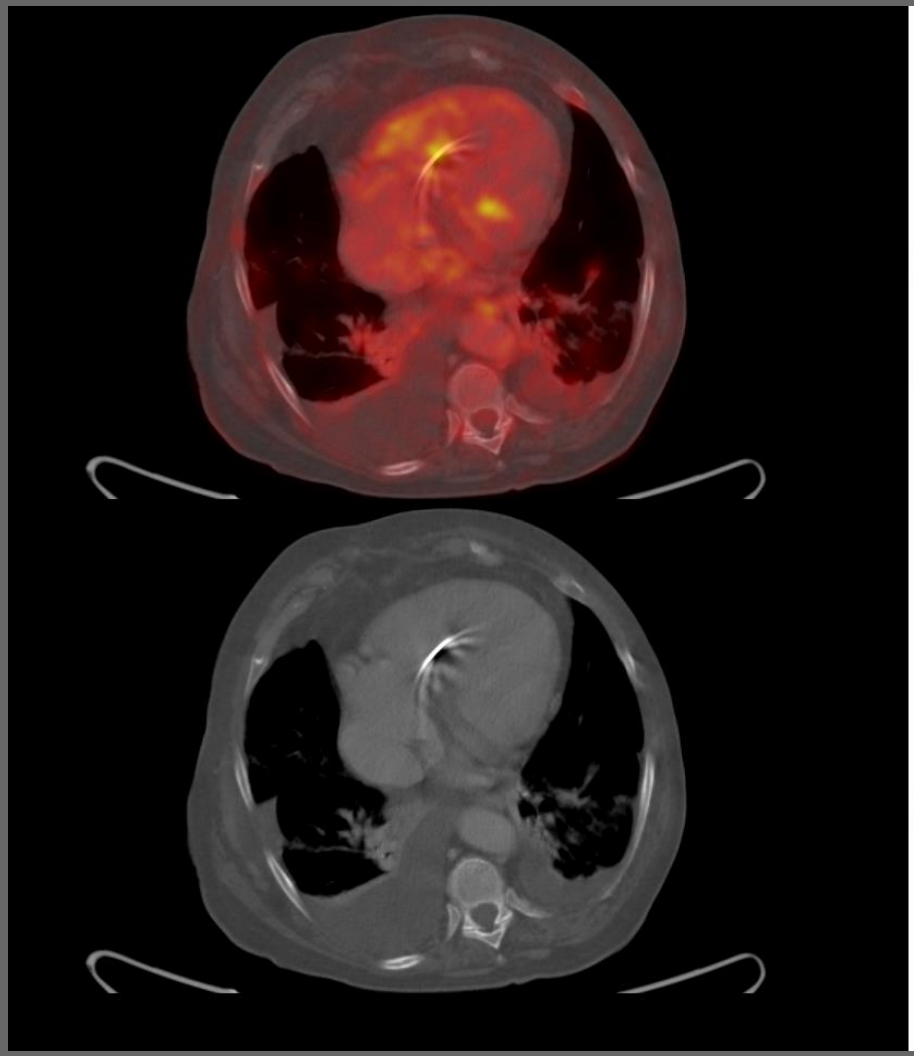
Clinical case

- The patient continued with fever and got worse with hypotension and hypoperfusion. She also complained of mild lumbar pain.
- **Rifampin** was added to the antibiotic regimen.
- **FDG PET/CT** was performed and PM explantation was planned.

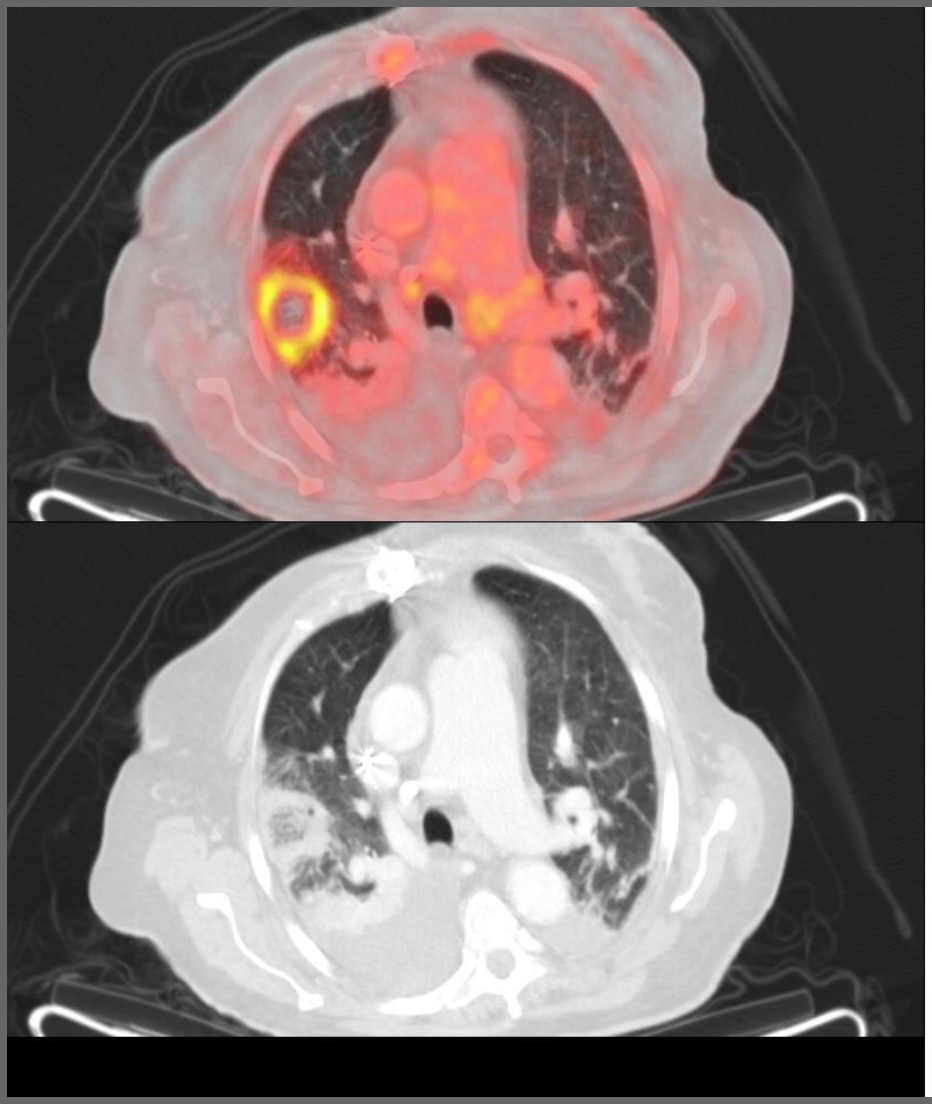
FDG PET/CT & CDR-IE

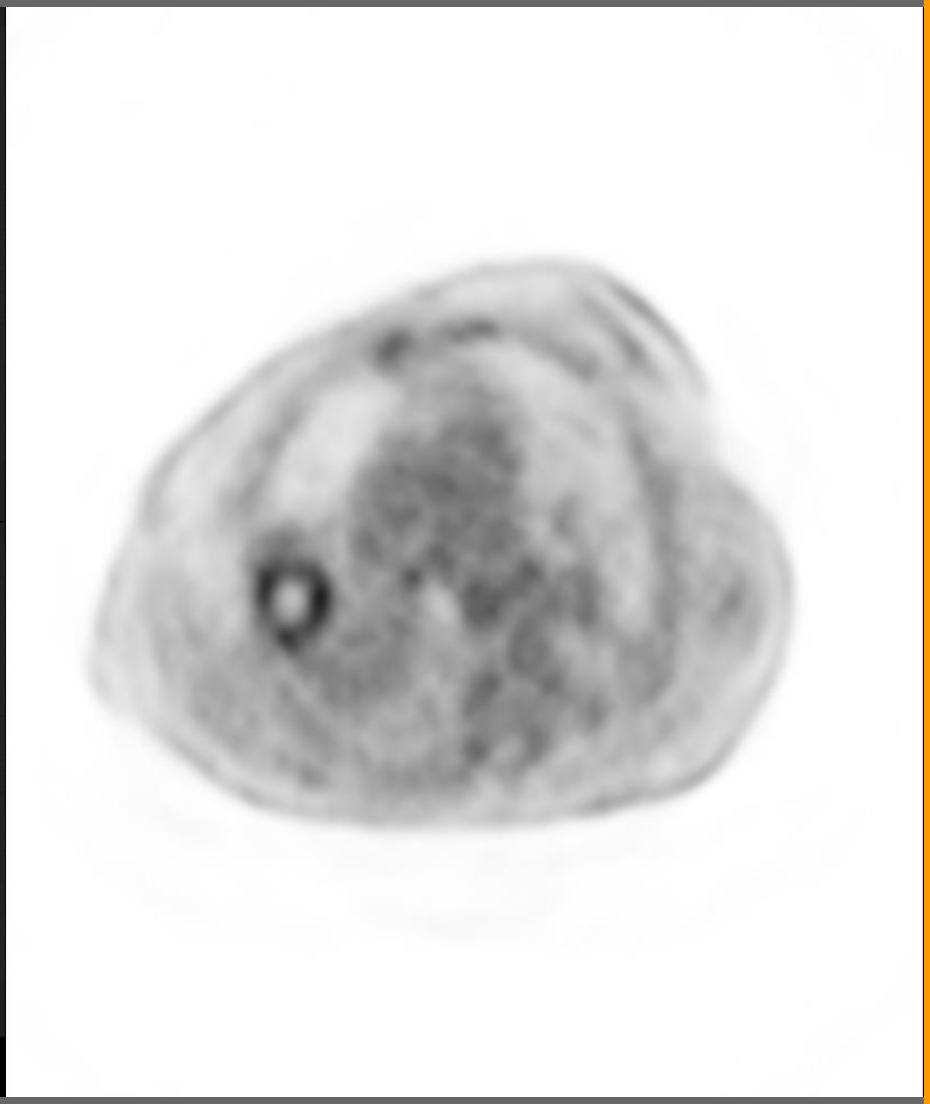


Clinical case

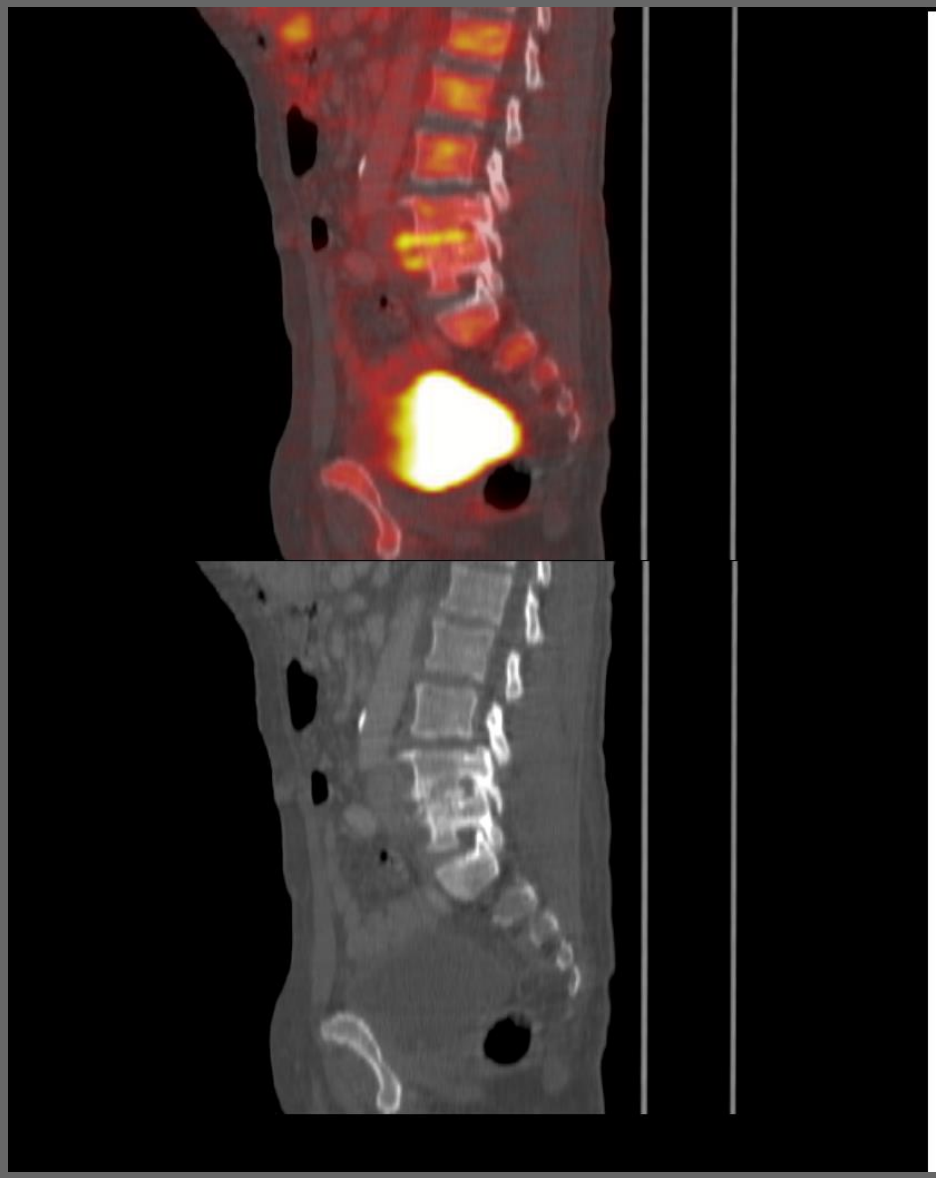


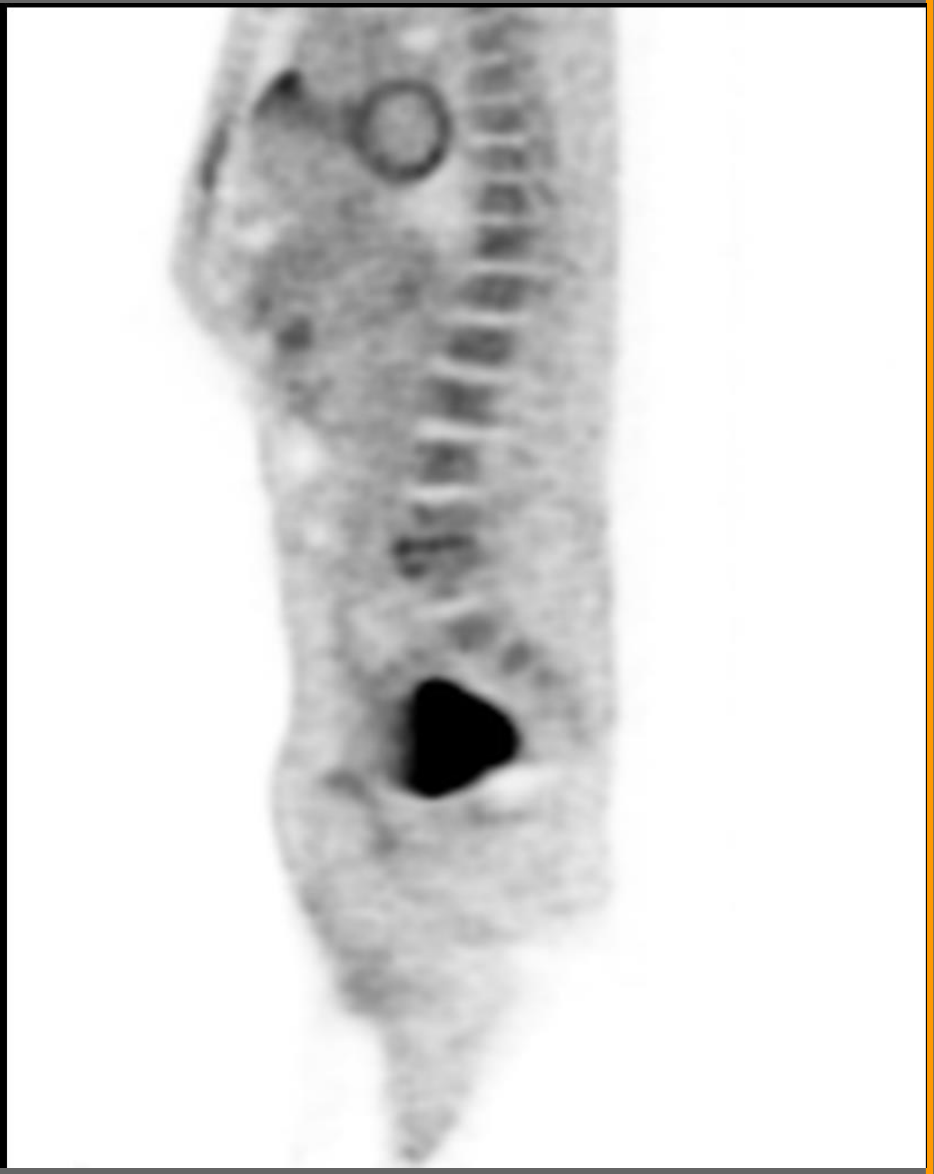
Clinical case





Clinical case





Clinical case

- **Percutaneous removal** of the whole PM system was performed by simple traction. **No vegetations** were seen along the PM lead.
- **Lead tip culture** was positive for MRSA.
- After explantation, the patient was treated with iv antibiotics during 6 weeks and she was discharged with **OST**.
- A **TEE before being discharged** was normal.
- A new PM system was **not necessary**.

CDR-IE-Introduction

- **CIED infection seems to be raising out of proportion** to the increase in device implantation rates.
- Incidence: varies widely among studies: 1,9‰ device-years (1). **Incidence of CDR-IE: 20%-25% of all device related infections**.
- **ICD** are associated with a **greater risk of infection** than are PM. Infection risk in epicardial systems is similar to that of transvenous systems (2).
- Main pathogenic mechanism of CDR-IE: **contamination by local bacteriological** flora at the time of device implantation.

Baddour LM, et al. N Engl J Med 2012; Nof E, Epstein LM. Eur Heart J 2013; (1) Uslan DZ, et al.Arch Intern Med 2007; (2) Silvetti MS, et al. Europace 2006.

Risk factors for CIED infections

- **Patient-related:**
  - Diabetes mellitus.
  - Heart failure.
  - Chronic renal failure.
  - Corticosteroids.
  - Central lines (dialysis).
  - **Anticoagulants**.
  - **Fever** within 24 h of implantation.
- **Procedural factors:**
  - Longer procedure time.
  - Op. inexperience.
  - Temporary pacing leads.
  - Dual or triple-chamber devices.
  - Lack of antibiotic prophylaxis.
  - Pocket **hematoma**

Sohail MR, et al. CID 2007; Bloom H, et al. Pacing Clin Electrophysiol 2006; Kug D, et al. Circulation 1997; Greenspon AJ, et al. JACC 2012; Nery PB, et al. J Cardiovasc Electrophysiol 2010; Johansen JB, et al. Eur Heart J 2011.

CDR-IE; Diagnosis.

1. Three or more sets of blood cultures are recommended before prompt initiation of antimicrobial therapy for CIED infection	I	C
2. Lead-tip culture is indicated when the CIED is explanted	I	C
3. TOE is recommended in patients with suspected CDRIE with positive or negative blood cultures, independent of the results of TTE, to evaluate lead-related endocarditis and heart valve infection	I	C
4. Intracardiac echocardiography may be considered in patients with suspected CDRIE, positive blood cultures and negative TTE and TOE results	IIb	C
5. Radiolabelled leucocyte scintigraphy and ^{18}F-FDG PET/CT scanning may be considered additive tools in patients with suspected CDRIE, positive blood cultures and negative echocardiography	IIb	C

2015 ESC Guidelines.

ECHO-DIAGNOSIS

- **Technique of choice** for detection & sizing of vegetations: TEE.
- Evaluation of the whole infectious lead course (**SVC-RA junction**): TEE.
- Assess (**TTE & TEE**): degree of TR, right chambers dilatation, quantitation of PAP, other valves (left-sided, prosthesis).
- **TTE: poor sensitivity and a low NPV**.
- **TEE: higher sensitivity** & specificity than TTE.

Vilacosta I, et al. Circulation 1994; Klug D, et al. Circulation 1997; Cacoub P, et al. Am J Cardiol 1998; Victor F, et al. Heart 1999. Sohail MR, et al. JACC 2007; Grammes JA, et al. JACC 2010.

CDR-IE-DIAGNOSIS.
Duke criteria

- **Lower sensitivity** of Duke criteria.
- **Modifications proposed**:
  - Local signs of infection.
  - Pulmonary embolism.
- **PET/CT** to assess lead & pocket infection, **presence of pulmonary embolism,** and other extrapulmonary septic foci: should be considered (IIa).

Klug D, et al. Circulation 1997; Massoure P-L, et al. Pacing Clin Electrophysiol 2007; Sohail MR, et al. Mayo Clin Proc 2008.

Conclusions

- CIED infection rate is increasing.
- Main risk factors for CDR-IE include complications at the generator pocket site and device manipulation.
- Staphylococci account for most CDR-IE.
- TEE remains the technique of choice in cases of CDR-IE.
- PET/CT has a complementary role and should be considered (IIa) in the diagnostic work-up.
- Complete removal of the device is strongly recommended, even when signs of infection are limited to the generator pocket site.

Principles of treatment

1. Prolonged (i.e. before and after extraction) antibiotic therapy and complete hardware (device and leads) removal are recommended in definite CDRIE, as well as in presumably isolated pocket infection	I	C
2. Complete hardware removal should be considered on the basis of occult infection without another apparent source of infection	IIa	C
3. In patients with NVE or PVE and an intracardiac device with no evidence of associated device infection, complete hardware extraction may be considered	IIb	C

2015 ESC Guidelines.

Mode of device removal.

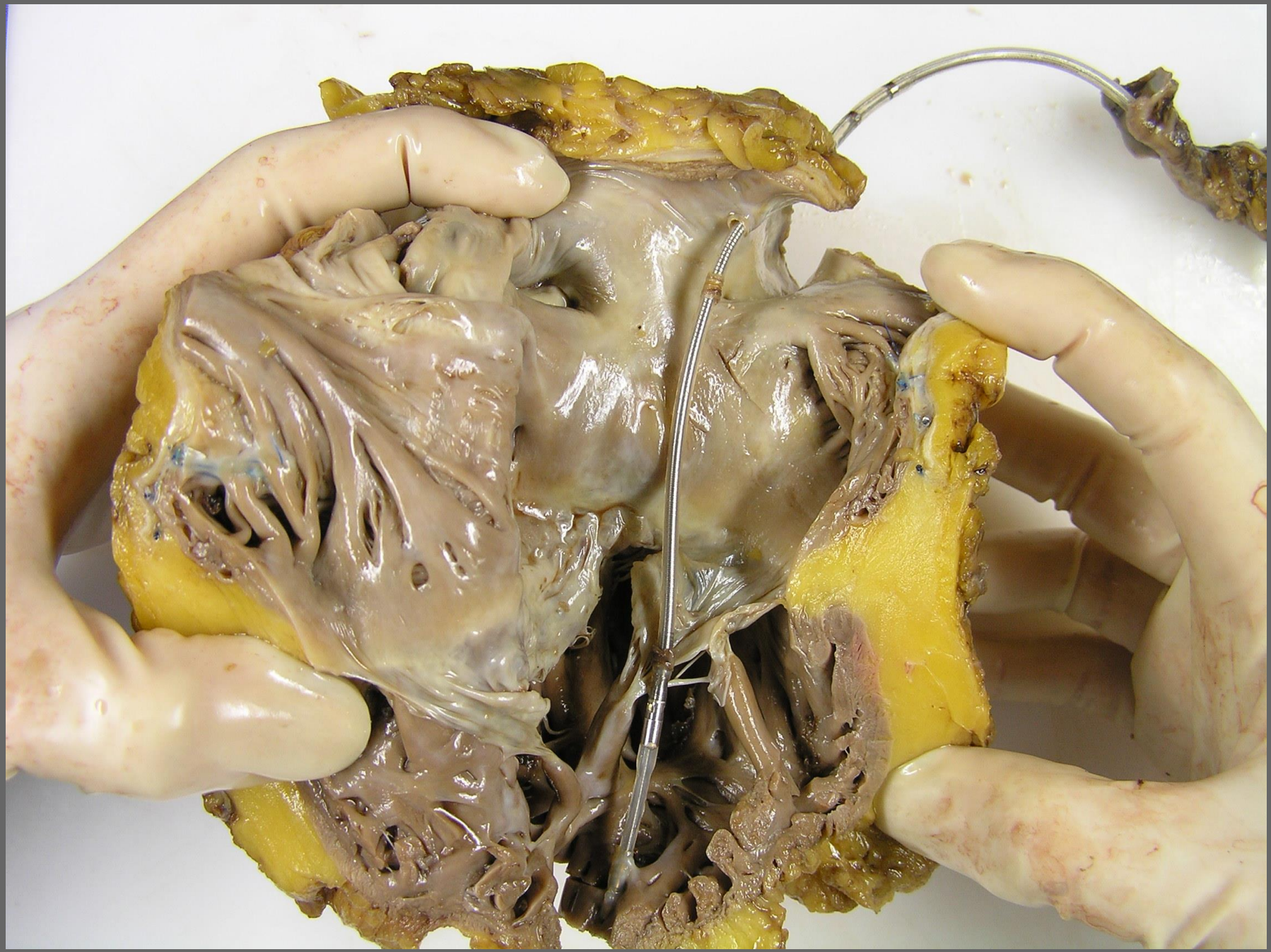
1. Percutaneous extraction is recommended in most patients with CDRIE, even those with vegetations >10 mm	I	B
2. Surgical extraction should be considered if percutaneous extraction is incomplete or impossible or when there is associated severe destructive tricuspid IE	IIa	C
3. Surgical extraction may be considered in patients with large vegetations (>20 mm)	IIb	C

2015 ESC Guidelines.

Percutaneous explantation

- **Percutaneous success rate:** 93-97%.
- **Fibrosis**: in areas of direct contact between the lead and the vasculature and endocardium.
- **Complications**: < 2%.
  - Myocardial avulsion, tricuspid valve lesions, venous lacerations, lead fracture / disruption, tamponade, pulmonary embolism, arrythmias, pneumothorax, death.
- **Team approach** (CT surgeon, etc). OR vs EP lab.
- Several **extraction tools** are available (simple traction, locking stylets, powered sheaths…).

Wilkoff BL, et al. (PLEXES trial). JACC 1999; Byrd CL, et al. Pacing Clin Electrophysiol 1999; Jones SO, et al. Heart Rhythm 2008; Grammes JA, et al. JACC 2010; Rodriguez Y, et al. Intern J Cardiol 2013.



What to do after device removal in CDR-IE ?

- **After extraction of an infected device in patients with CDR-IE:**
  - At least 2 weeks of parenteral therapy.
  - Blood cultures.
  - Chest X-ray (PA & lateral).
  - TEE to rule out RV-RA-**SVC** residual masses (ghost).

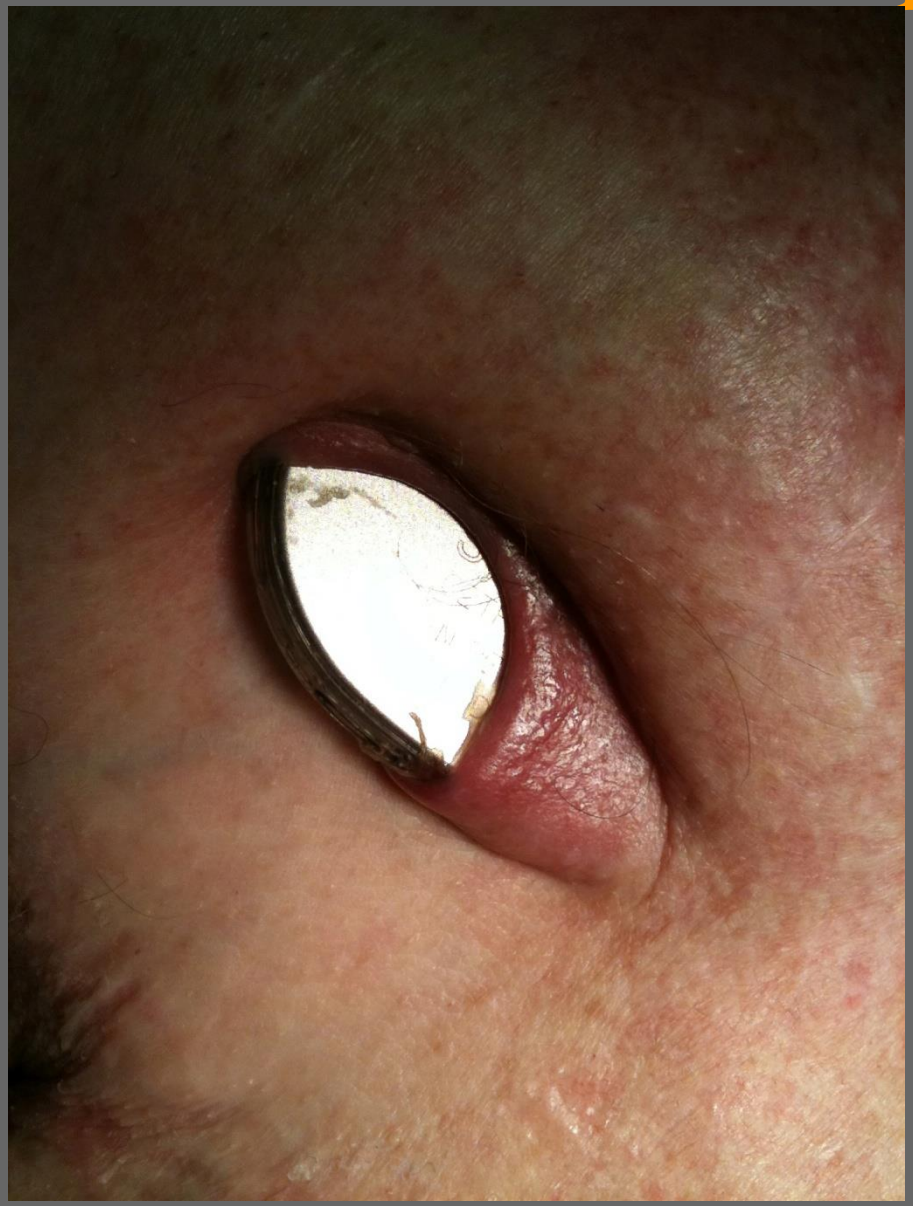
Baddour LM, et al. N Engl J Med 2012; Le Dolley Y, et al. J Am Coll Cardiol Img 2010; Grammes JA, et al. JACC 2010.

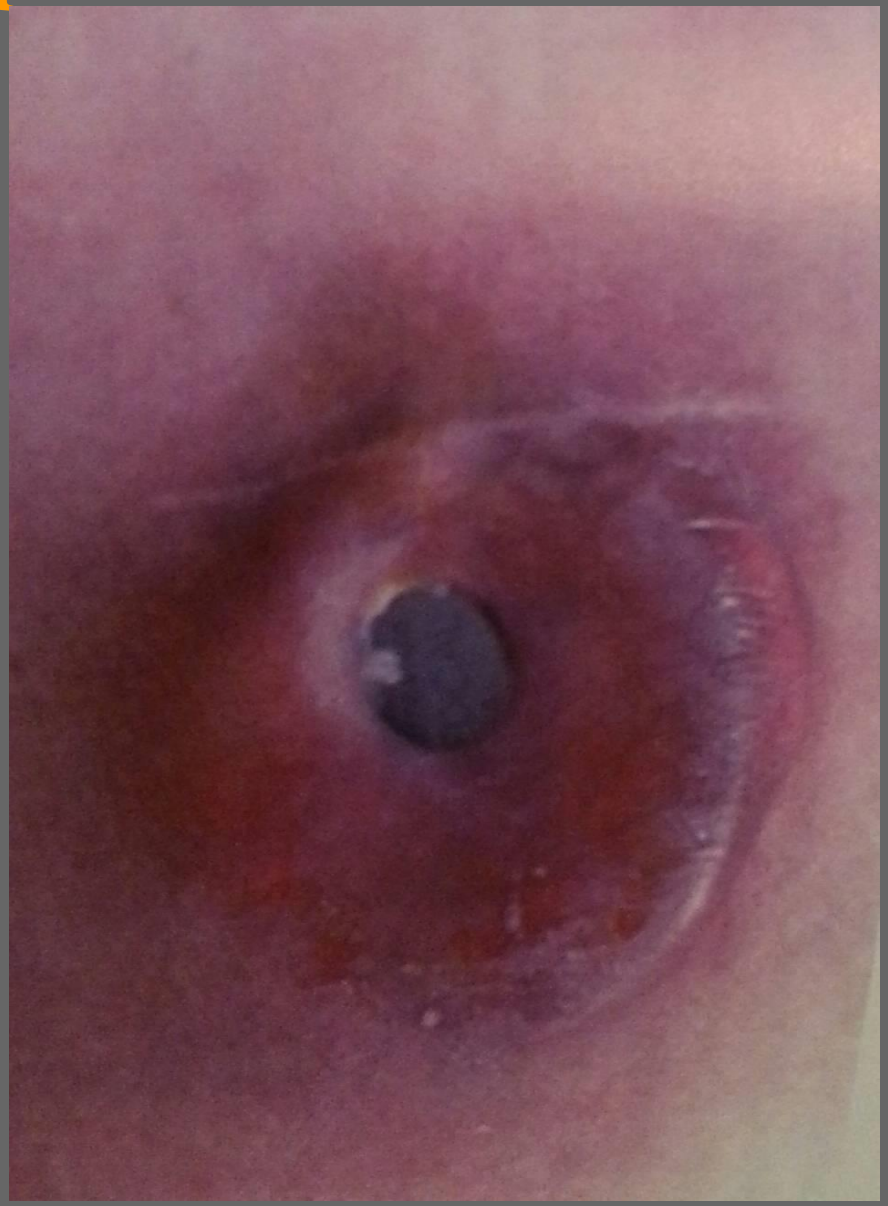
Reimplantation

1. After device extraction, reassessment of the need for reimplantation is recommended	I	C
2. When indicated, definite reimplantation should be postponed if possible, to allow a few days or weeks of antibiotic therapy	IIa	C
3. A 'temporary' ipsilateral active fixation strategy may be considered in pacemaker-dependent patients requiring appropriate antibiotic treatment before reimplantation	IIb	C
4. Temporary pacing is not routinely recommended	III	C

2015 ESC Guidelines.

Generator pocket site





Re-implantation of CIED after device explantation for infection

- **Re-assessment before re-implanting**.
- **Re-implantation** has to be performed **at another site** (contralateral site, epicardial).
- **Avoid immediate reimplantation**.
- **Timing:** on a **case-by-case basis** depending on indication for extraction, urgency, **BC results, pocket infection control,** and clinical status**.**
- Temporary pacing: risk factor for subsequent CD infection.
- **PM-dependent**: "immediate epicardial vs temporary transvenous pacing" not well defined.

Klug, et al. Circulation 2007; ESC Guidelines on IE-2009; ESC Guidelines on CP/CRT-2013; Baddour LM, et al. N Engl J Med 2012.

Diagnosis of CDR-IE

- **Misleading presentation**, with frequent respiratory or rheumathological symptoms, as well as **local signs of infection.**
- CDR-IE must be suspected in any patient with a CD and unexplained fever.
- Echocardiography (TTE & **TEE**) and **BC** are the cornerstone of diagnosis.

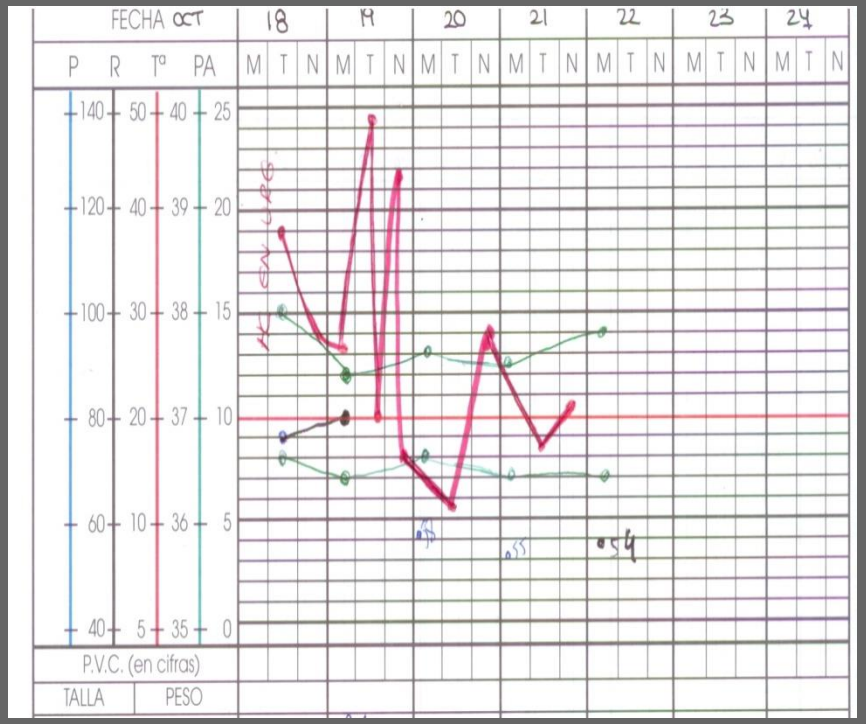
Habib G, et al. Eur Heart J 2009; Baddour LM, et al. N Engl J Med 2012.

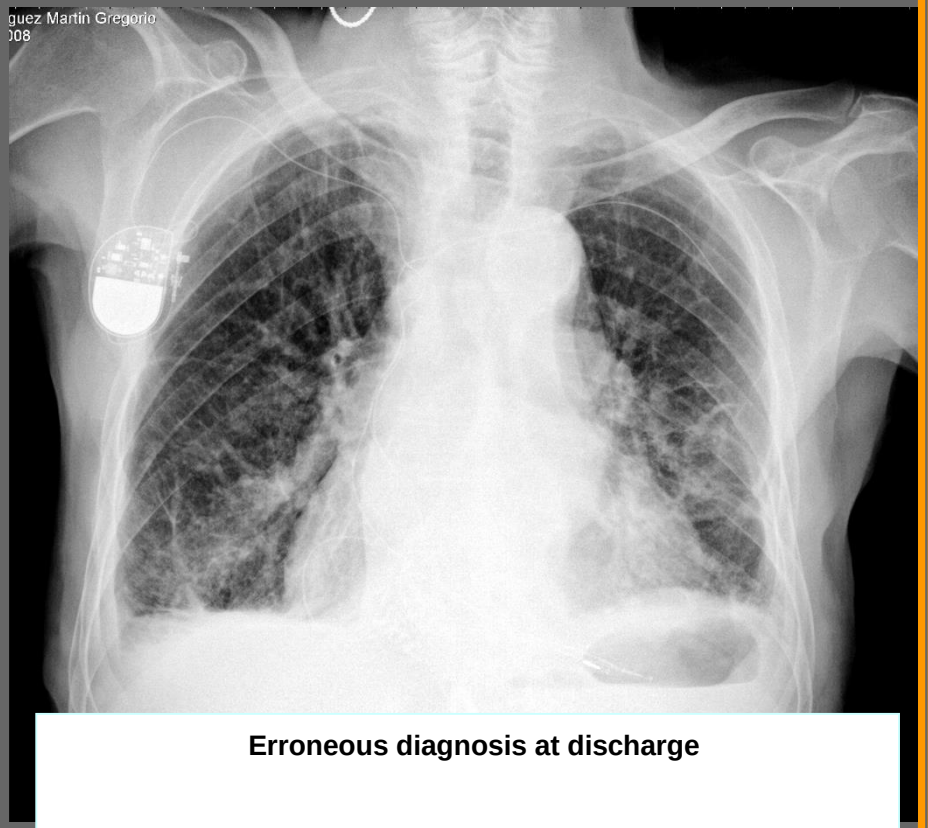
CLINICAL PRESENTATION

- **Varies with the virulence** of the infecting organism.
- Symptoms from **local pocket erosion to full-blown sepsis.**
- **Main symptoms**: fever, chills, malaise, rheumathologic and pulmonary symptoms, and findings at **the generator pocket site**: erythema, pain, swelling, warmth, drainage, and skin and soft-tissue ulceration.
- **Pocket erosion should be treated as pocket infection**.
- The **interval between CIED placement or revision and the** onset of infection varies widely, from days to **years**.

Sohail MR, et al. Mayo Clin Proc 2008; Le KY, et al. Am J Cardiol 2012; Tarakji KG, et al. Heart Rhythm 2010; Baddour LM, et al. N Engl J Med 2012.

Clinical suspicion of CDR-IE





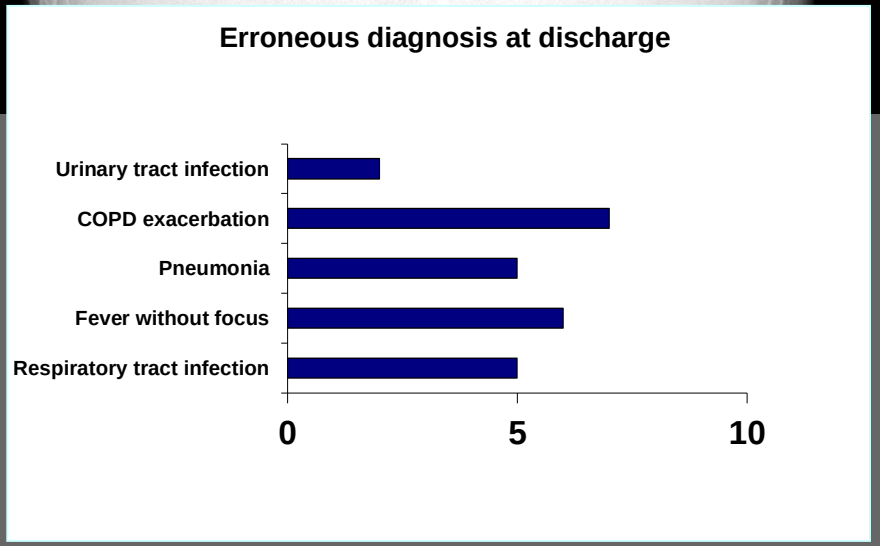
Fever of unknown origin

+

Chills

+

Respiratory symptoms

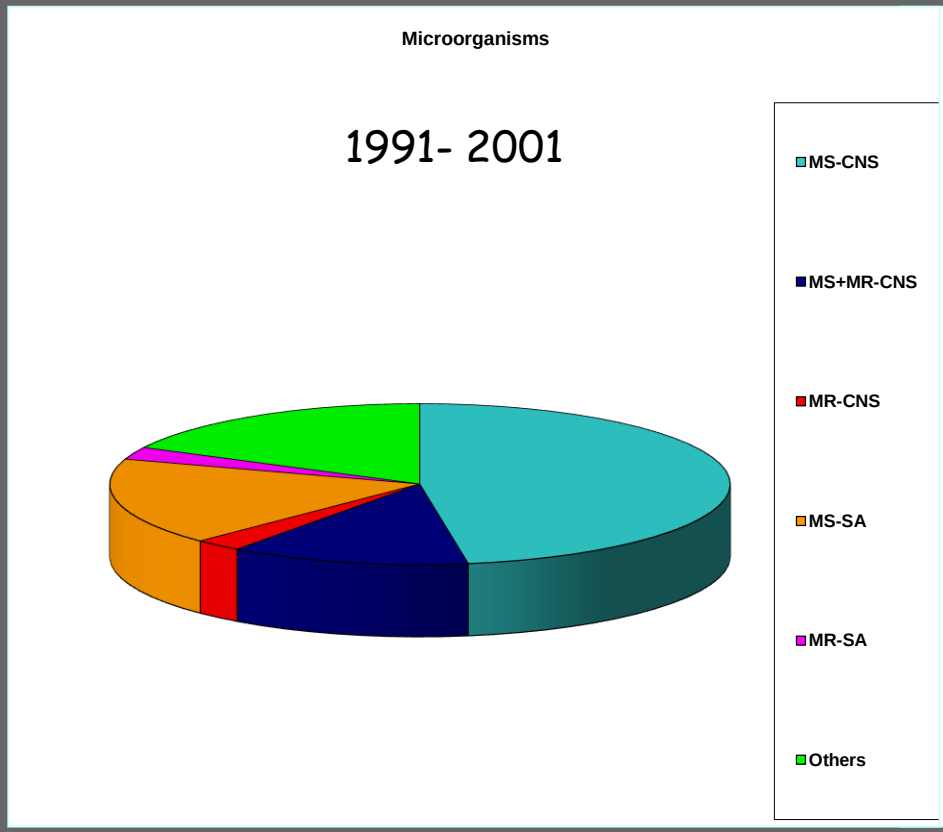


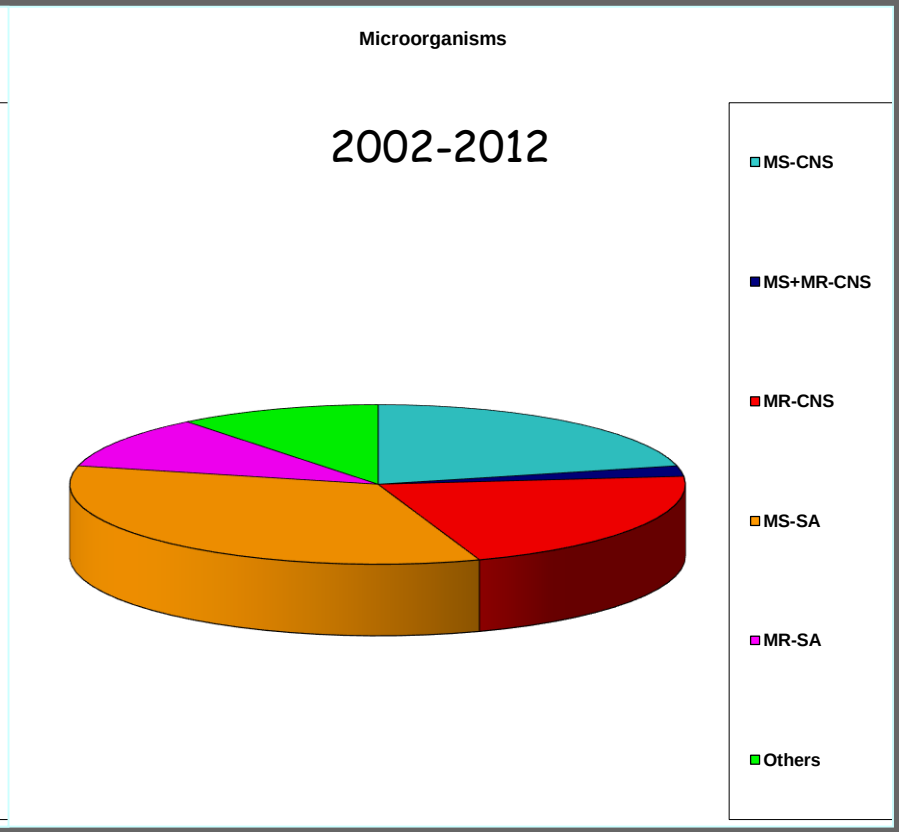
Blood cultures & CDR-IE

- **Blood cultures are recommended in all suspected cases of CIED infection.**
- BC **may be negative** despite CIED infection: local infection or previous antibiotics.
- Positive BC ≠ CDR-IE.
- Likelihood of CIED infection when BC +:
  - ≥ 35% in staphylococcal species.
  - < 20% in nonstaphylococcal or GNB.
- **A single + BC for CoNS: contamination.**
- Multiple + BC for CoNS: CDR-IE.

Baddour LM, et al. N Engl J Med 2012.

Microbiological changing profile





CIED infection-classification (1)

- 1-. **Superficial skin infection**: limited to the skin or suture.
- 2-. **Pocket infection**: local inflammatory or infectious signs or exposure of hardware through the skin.
- 3-. **CDR-IE** (Duke criteria):
  - Definite.
  - Possible.
- * In the presence of a lead vegetation, local device infection was considered a **major criterion** (2).
- * Positive lead culture is a major criterion only in the absence of a pocket infection or when the leads are not removed through the generator pocket.

(1) Baddour LM, et al. Circulation 2010; (2) Sohail MR, et al. Mayo Clin Proc 2008.

Tissue cultures & CDR-IE

- Cultures & gram staining of the **pocket-site tissue** and **lead tips** when device removal.
- **Avoid aspiration of the pocket site**.
- Sensitivity of pocket-site tissue culture higher than that of swab pocket culture.
- **Lead contamination can occur during extraction if a pocket is infected**.

Baddour LM, et al. Circulation 2010

Echocardiography & CDR-IE

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association®

Usefulness of transesophageal echocardiography for diagnosis of infected transvenous permanent pacemakers.

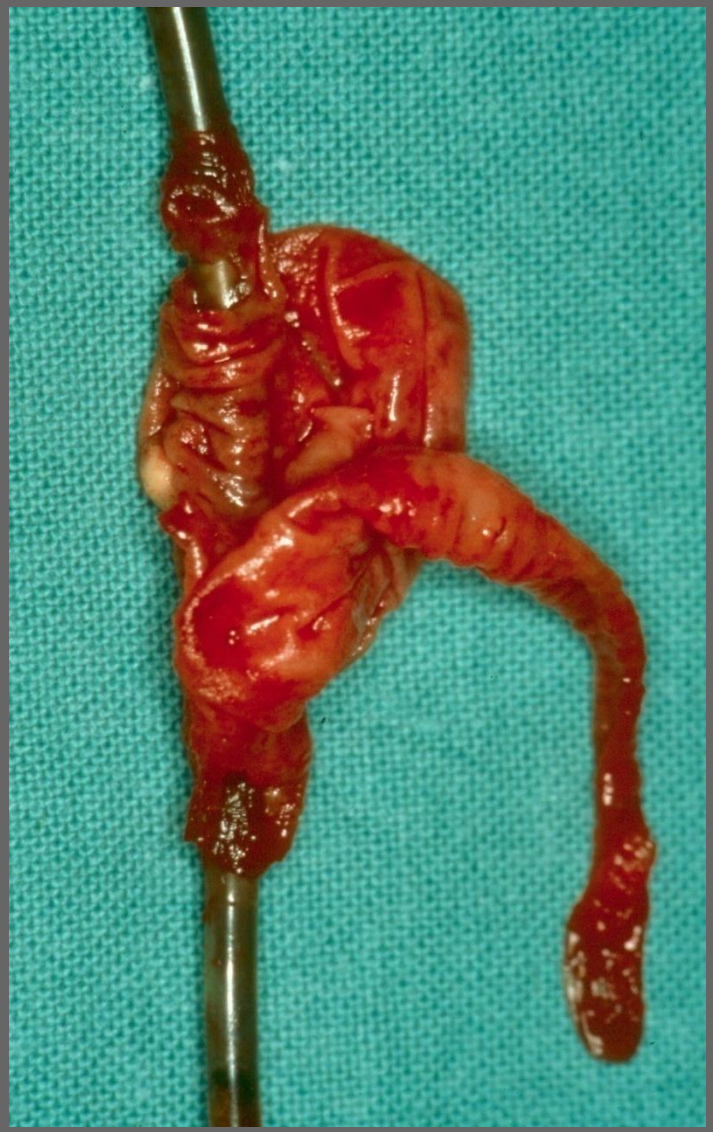
I Vilacosta, C Sarriá, J A San Román, J Jiménez, J A Castillo, E Iturralde, M J Rollán and L Martínez Elbal

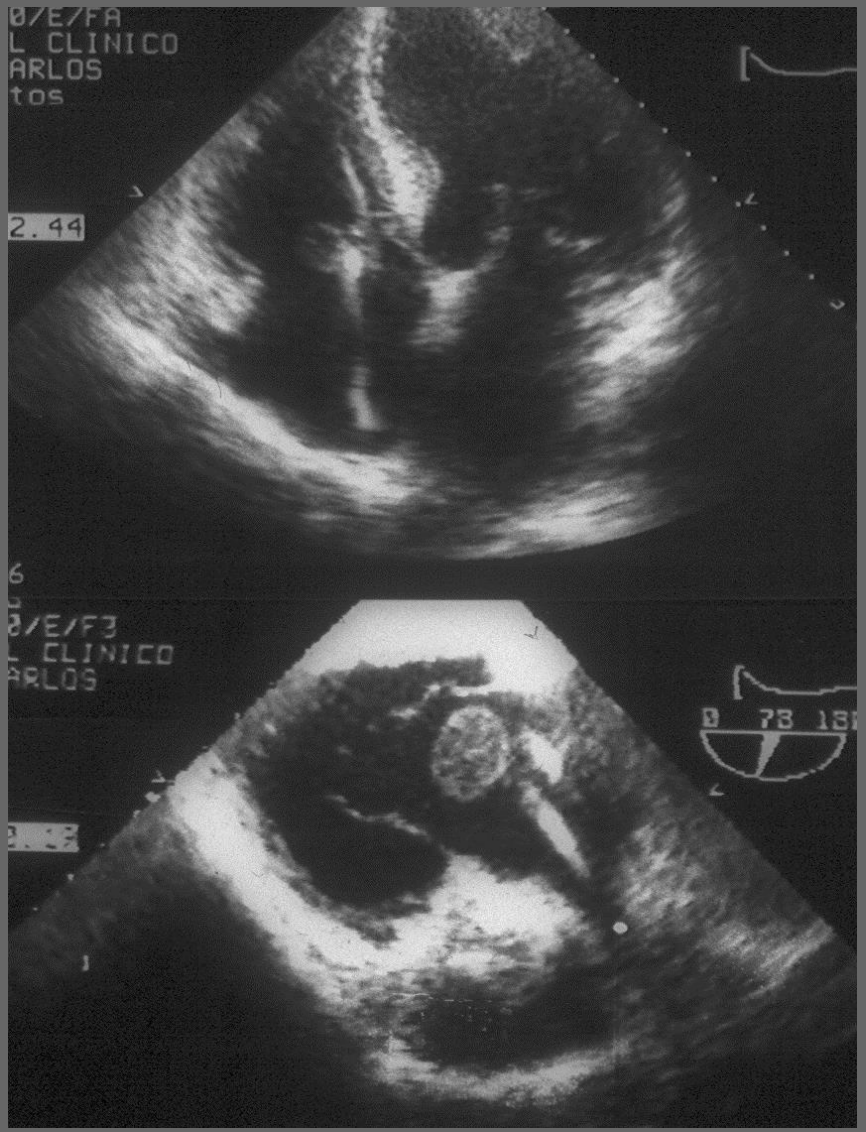
Circulation. 1994;89:2684-2687
doi: 10.1161/01.CIR.89.6.2684
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0009-7322. Online ISSN: 1524-4539

Klug D, et al. Circulation 1997; Cacoub P, et al. Am J Cardiol 1998; Victor F, et al. Heart 1999.

ECHO-DIAGNOSIS





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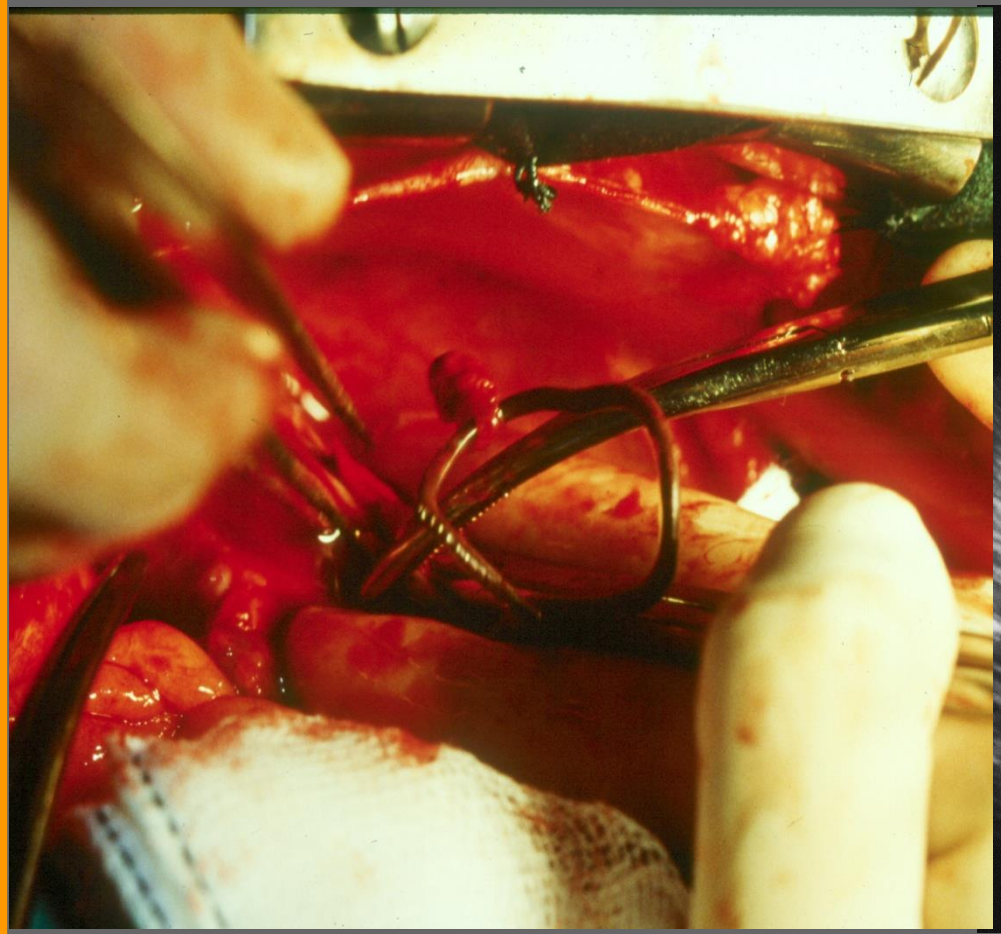
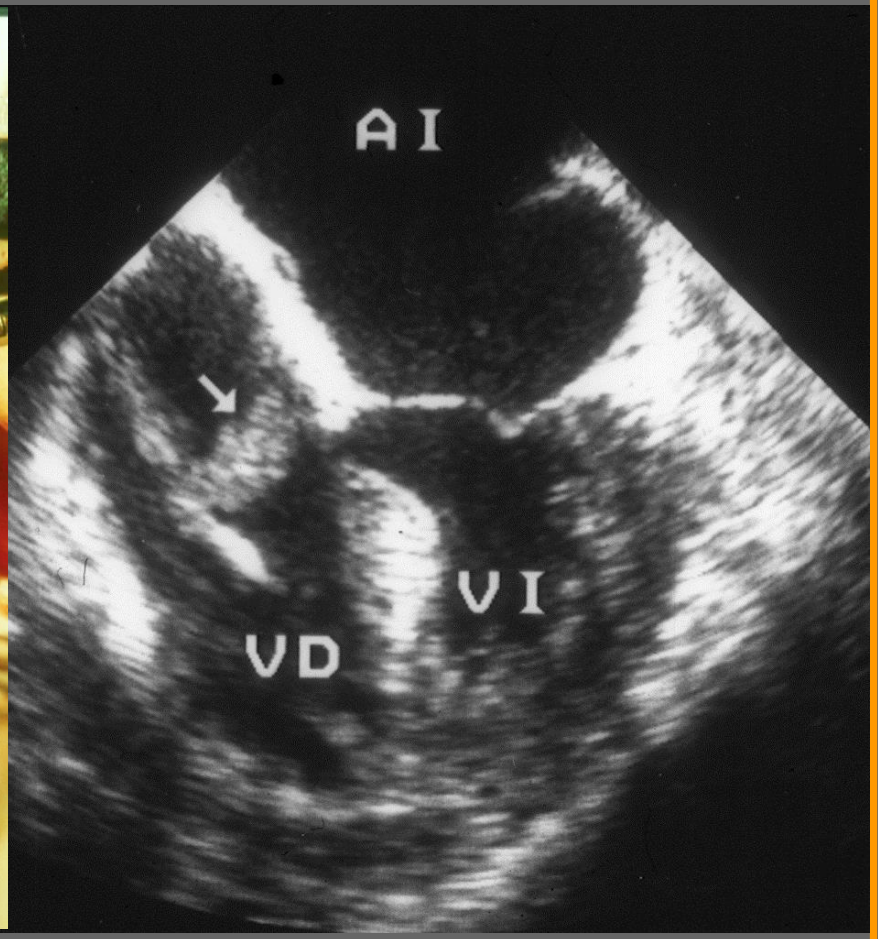
ECHO-DIAGNOSIS





ECHO-DIAGNOSIS

- Why **TTE has difficulties** in CDR-IE?
  - Reverberation lead echoes.
  - Atypical location of vegetations.
  - Inadequate transthoracic window.
- TTE & TEE may be **falsely negative**.
- When clinical suspicion of CDR-IE is high and TEE is negative: **repeat TEE**.
- **Bland clots** on leads have been found on echo exam in 1,4-10 % in CIED recipients without infection. **No possible distinction by echocardiography**.
- **Accretions** on the RA segment of pacing leads (28% by TEE): no effect on mortality.

Lo R, et al. J Invasive Cardiol 2006; Habib G, et al. Eur J Echocardiogr 2010; Downey BC, et al. Pacing Clin Electrophysiol 2011; Dundar C, et al. JASE 2011; Rahbar AS, et al.PACE 2013.

Percutaneous explantation

- **The preferred method** of removal.
- It can be a high-risk procedure if performed in unprepared centres.
- The **sooner the better** for extracting an infected device.
- It is essential to **remove all hardware** to avoid recurrence of infection. In one study (1), 71% of patients with retained material showed recurrence of infection.

(1) Pichlmaier M, et al. J Thorac Cardiovasc Surg 2011; Nof E, et al. Eur Heart J 2013.

RT3D TEE & ICE in CDR-IE

- The utility of **RT3D TEE** in CDR-IE is not well established (1).
- Comparison of the diagnostic yield of **ICE vs TEE** in the detection of ICM in patients undergoing lead extraction (2).
  - **ICE**; sensitivity: 100%, specificity: 82,8%, PPV: 65,6%, NPV: 100%.
  - ICE shows **high diagnostic accuracy** in the detection of ICM among patients with a definite diagnosis of CDR-IE.

(1) Naqvi TZ, et al. JACC Cardiovasc Imag 2010; (2) Narducci ML, et al. JACC 2013.

FDG PET/CT & CDR-IE

- **Purpose**: Assess the diagnostic yield of FDG PET/CT in CIED infection.
- Whole body imaging FDG PET/CT (21):
  - Superficial skin infection (1).
  - **Pocket site infection** (15):
    - Sensitivity: 86,7%.
    - Specificity: 100%.
  - **CDR-IE** (13):7 definite + 6 possible:
    - Sensitivity: 30,8%.
    - Specificity: 62,5%.

Cautela J, et al. Europace 2012.

CDR-IE: ESC treatment guidelines

Recommendations: IE on pacemakers and implantable defibrillators	Class[a]	Level[b]
A - PRINCIPLES OF TREATMENT:		
Prolonged antibiotic therapy and device removal are recommended in definite CDRIE	I	B
Device removal should be considered when CDRIE is suspected on the basis of occult infection without other apparent source of infection	IIa	C
In patients with native or prosthetic valve endocarditis and an intracardiac device with no evidence of associated device infection, device extraction may be considered	IIb	C
B - MODE OF DEVICE REMOVAL:		
Percutaneous extraction is recommended in most patients with CDRIE, even those with large (> 10 mm) vegetations	I	B
Surgical extraction should be considered if percutaneous extraction is incomplete or impossible or when there is associated severe destructive tricuspid IE	IIa	C
Surgical extraction may be considered in patients with very large (> 25 mm) vegetations	IIb	C

Habib G, et al. Eur Heart J 2009

Empirical antibiotic therapy in CDR-IE

Clinical presentation	Main pathogens	Antibiotic therapy
Acute clinical course	*S. Aureus* CoNS	Dapto/Vanco + Gentamicin
Subacute clinical course	CoNS (MS)	Cloxacillin + Gentamicin
Healthcare-associated; severe sepsis.	*S. Aureus* (MR); CoNS (MR); enterococci; GNB.	Dapto/Vanco + Carbapenem + rifampin

Antibiotic therapy in CDR-IE

- **Antimicrobial choice** should be based on **in vitro susceptibility** of the infectious agent.
- **Duration** of antimicrobial therapy:
  - **Non-complicated** infection: 2 weeks.
  - **Complicated** infection: 4-6 weeks.
    - Persistent bacteremia.
    - Thrombophlebitis.
    - Septic metastasis / lung complications.
    - Immunosuppression.
    - Resistant microorganisms.

Baddour LM, et al. Circulation 2010

CDR-IE: AHA guidelines

AHA Scientific Statement

Update on Cardiovascular Implantable Electronic Device Infections and Their Management

A Scientific Statement From the American Heart Association

Endorsed by the Heart Rhythm Society

Larry M. Baddour, MD, FAHA, Chair; Andrew E. Epstein, MD, FAHA, FHRS; Christopher C. Erickson, MD, FAHA; Bradley P. Knight, MD, FHRS; Matthew E. Levison, MD; Peter B. Lockhart, DDS; Frederick A. Masoudi, MD, MSPH; Eric J. Okum, MD; Walter R. Wilson, MD; Lee B. Beerman, MD; Ann F. Bolger, MD, FAHA; N.A. Mark Estes III, MD, FAHA, FHRS; Michael Gewitz, MD, FAHA; Jane W. Newburger, MD, MPH, FAHA; Eleanor B. Schron, PhD, RN, FAHA; Kathryn A. Taubert, PhD, FAHA; on behalf of the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee of the Council on Cardiovascular Disease in the Young; Council on Cardiovascular Surgery and Anesthesia; Council on Cardiovascular Nursing; Council on Clinical Cardiology; and the Interdisciplinary Council on Quality of Care and Outcomes Research

Circulation 2010

CDR-IE: AHA guidelines

Recommendations for Removal of Infected CIED

Class I

1. Complete device and lead removal is recommended for all patients with definite CIED infection, as evidenced by valvular and/or lead endocarditis or sepsis. (*Level of Evidence: A*)
2. Complete device and lead removal is recommended for all patients with CIED pocket infection as evidenced by abscess formation, device erosion, skin adherence, or chronic draining sinus without clinically evident involvement of the transvenous portion of the lead system. (*Level of Evidence: B*)
3. Complete device and lead removal is recommended for all patients with valvular endocarditis without definite involvement of the lead(s) and/or device. (*Level of Evidence: B*)
4. Complete device and lead removal is recommended for patients with occult staphylococcal bacteremia. (*Level of Evidence: B*)

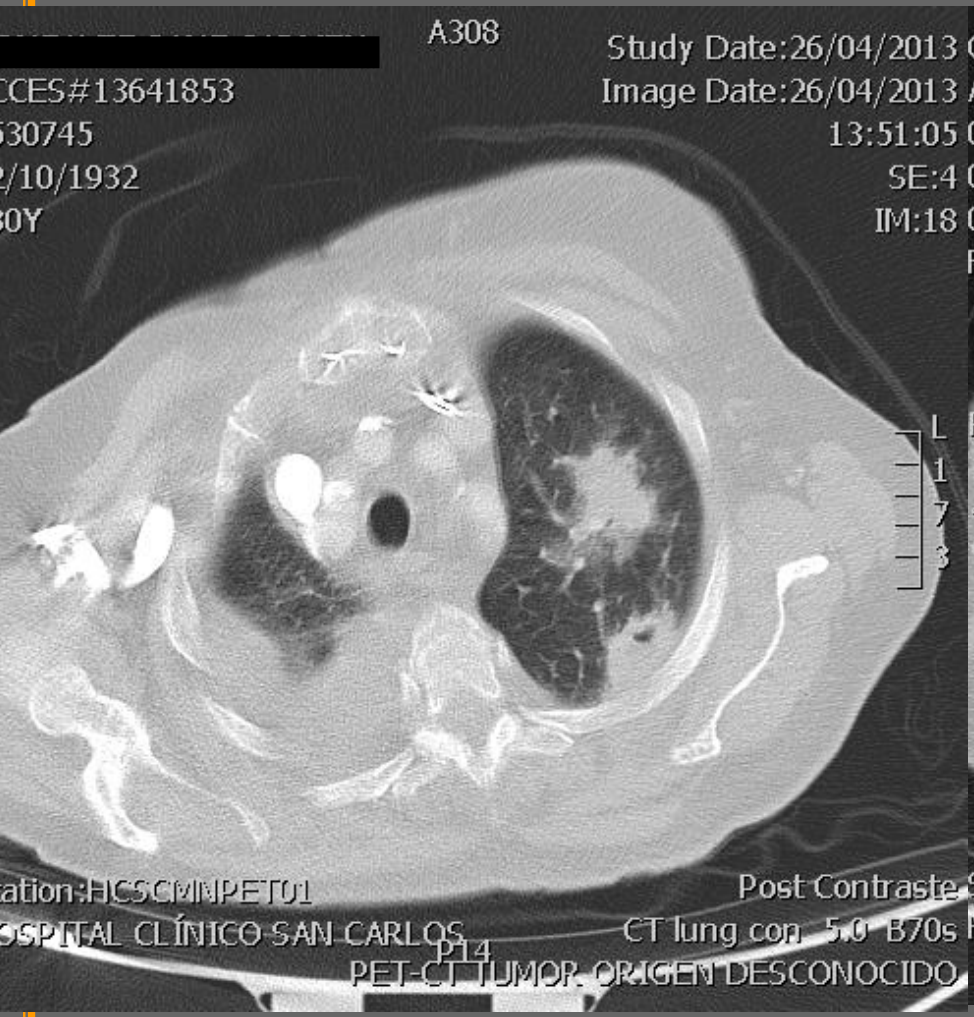
Circulation 2010

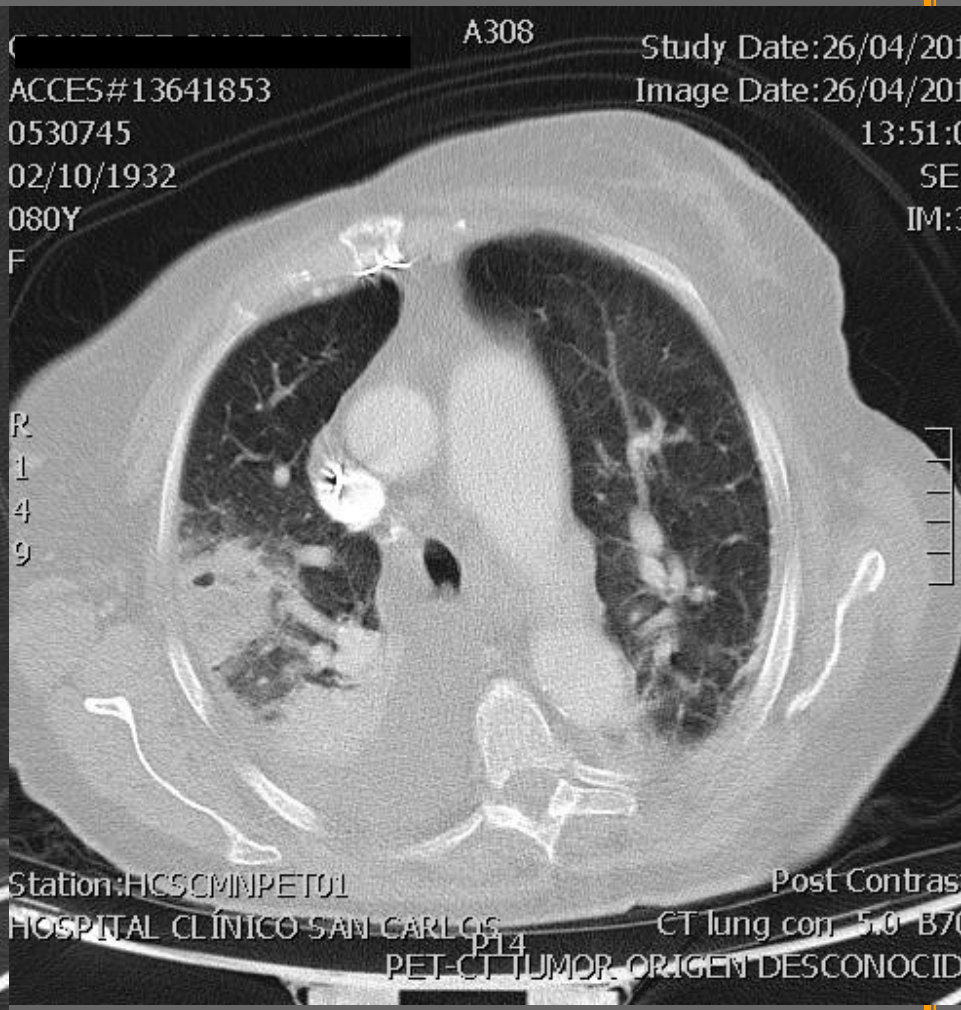
Potential surgical indications

- Vegetation size ≥ 25 mm.
- Extension to mural endocardium, SVC, severe tricuspid valve regurgitation.
- Previous incomplete extraction.
- Large vegetations and PFO /ASD.
- Associated left-sided IE.
- Other surgical reasons (Ao. stenosis).
- Mortality rates: 12,5%-40%.

Baddour L, et al. Circulation 2010; del Rio A, et al. Chest 2003; Verma A, Wilkoff BL. Heart Rhythm 2004.

Clinical case

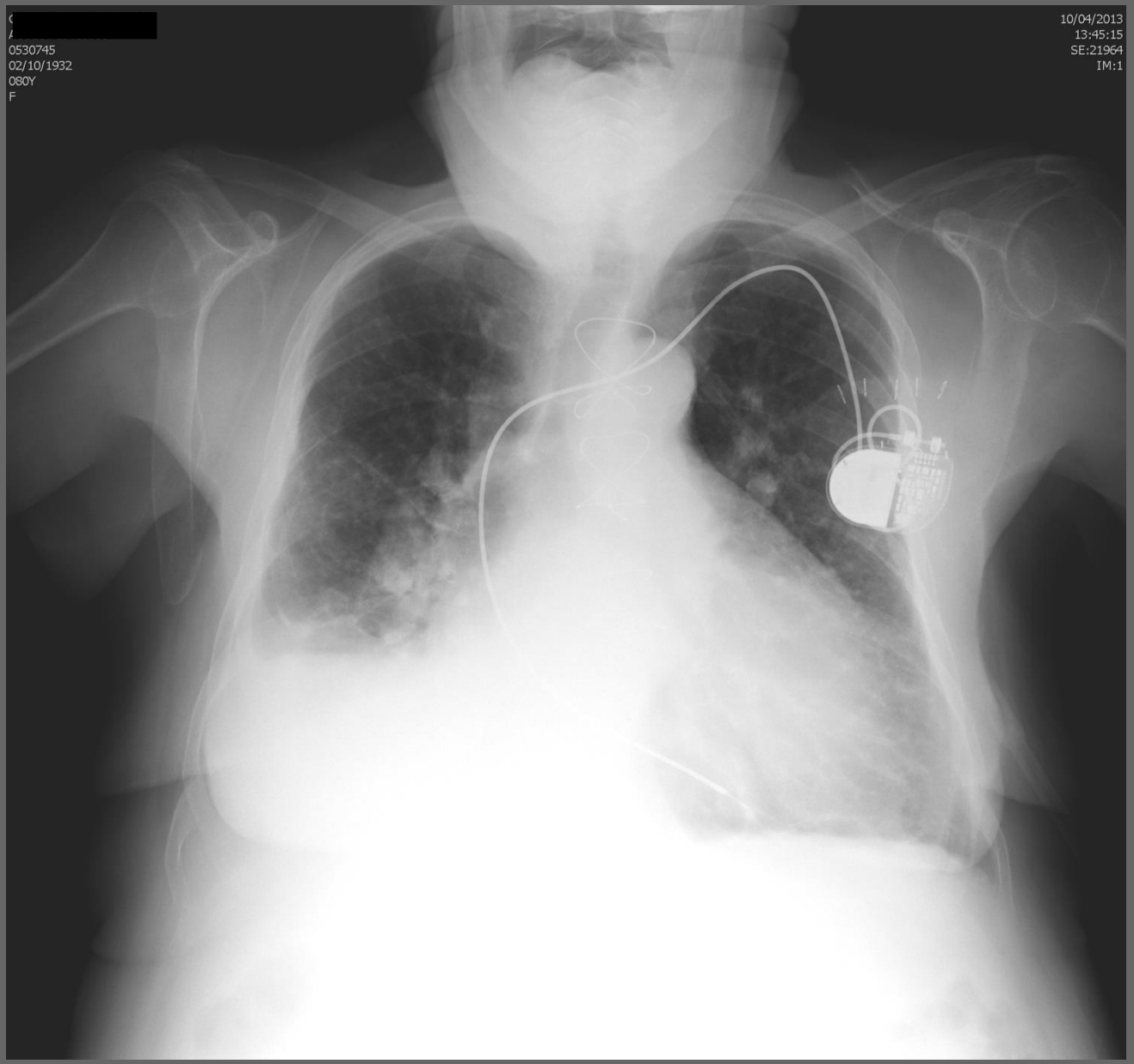




Tissue cultures & CDR-IE

- Cultures & gram staining of the **pocket-site tissue** and **lead tips** when device removal.
- **Avoid aspiration of the pocket site**.
- Sensitivity of pocket-site tissue culture higher than that of swab pocket culture.
- **Lead contamination can occur during extraction if a pocket is infected**.

Baddour LM, et al. Circulation 2010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