Salvage of Infected Pacemakers and Implantable Cardioverter-Defibrillators by Selective, In-situ-targeted Ultra-High Dose Antimicrobial Treatment

The 60th Annual Conference of the Israel Heart Society

Moris Topaz[1],
Mark Kazatsker[1], Gershon Keren[1],
Narin Carmel[2], Guy Topaz[2], Adi Silberman[2], Yoram Oron[2],
Avraham Shotan[1]

1. Hillel Yaffe Medical Centerl, Hadera, Israel 2. Tel Aviv University, Tel Aviv, Israel

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None of the authors have a conflict of interest to report.

Background

- Cardiac device **infections showed an increase**, from 0.94 device infections per 1000 in 1990 to 2.11 device infections per 1000 in 1999
- Exposure and infection of pocket and subcutaneous portion of wires of CIEDs comprise over 52% of the infected devices.
- Exclusive systemic antibiotic treatment of infected CIEDs was reported to be relatively ineffective **(~85% failure rate**).

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Background

- The currently recommended treatment for infected CIEDs is **complete extraction and replacement.**

- Removal and replacement of device may be complicated, is sometimes hazardous and is costly.

Regulated Negative Pressure-Assisted Wound Therapy (RNPT)

- The mechanism of action of RNPT is multifactorial.
- In its basis, the application of computer **regulated negative pressure**, generated by a **pump**, led by tubing to contact the treated surface area by a **sponge mold dressing**.
- The dressing is covered, and is air-tightly sealed by a **drape**.

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The Main Contributing Mechanisms of RNPT in Infected CIEDs:

- The main effects of RNPT application in treatment of CIEDs infection are:
  - Bacterial **isolation** of treated area
  - **Reversal** of lymphatic flow
  - **Containment** of pocket fluid overflow.

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Objectives:

To demonstrate the efficacy and safety of a novel therapy method for salvage of CIEDs with infection limited to their pocket and proximal wiring, reducing the need for extraction by:

1. Trans-cutaneous, continuous, in-situ-targeted, ultra-high dose antibiotics (CITA)
2. Wound isolation under RNPT
3. Combining minimally-invasive surgical procedures

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Methods & Protocol

- We **prospectively** treated **all consecutive** patients diagnosed as infected CIEDs including pocket and/or proximal lead infection, extruded CIEDs and expanding hematomas with dehischarging wounds treated in our center and all patients referred to us during 10.2007 – 12.2012.

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Methods & Protocol

- **Inclusion criteria:**
  - ✓ Infection/exposure of generator and/or proximal wiring of CIEDs
  - ✓ Expanding hematoma of the generator pocket with leak (excluded from this presentation)
- **Exclusion criteria:**
  - ✓ Cardiac vegetation demonstrated by Echo- cardiography (TEE).
  - ✓ Known allergic reaction to vancomycin

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Methods & Protocol

- ✓ **Protocol of Antibiotics – dosage & treatment:**
  - ✓ Initial loading dose of Vancomycin & Gentamicin:

    Maximal daily dose diluted in saline in controlled continuous drip for 24 hours

  - ✓ Daily adjustment of maintenance Abx. Dosage & volume:

    According to serum level, renal function, bacterial susceptibility and patient's general condition.

  - ✓ End of treatment:

    With negative culture results and when clinically indicated.

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Methods & Protocol

- ✓ **Infection of generator and/or proximal wiring of CIEDs were treated prospectively in 34 consecutive patients**
- ✓ **TEE pre- and post-treatment to rule-out intra cardiac infection spread**
- ✓ **Following sampling of multiple cultures CITA-RNPT was initiated.**
- ✓ **Serum antibiotic levels were frequently monitored to adjust for the desired levels and match with pocket levels**
- ✓ **When indicated, minimal manipulation of hardware was performed under local/general anesthesia.**
- ✓ All dressing changes and procedures were performed under **strict sterile conditions** in OR settings

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Methods & Protocol

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Results

- **30/34 (88%)** treated CIEDs were **salvaged with no clinical manifestations of infection following CITA-RNPT treatment.** (**23 (68%)** after 1st course)
  - In 7/34 patients CITA-RNPT was repeated. 4 of them due to mechanical wound closure failure. In all 4 patients CIEDs were salvaged.
- CITA-RNPT average treatment lasted 8 days, (range 3-21 days), followed by a course of up to **4 weeks** of oral antibiotics, as was indicated by clinical condition.
- 16/23 patients were treated under local anesthesia.
- The mean follow up was 25.17 ±11.97 months, (range 6-65 months).
- 20 patients (59%) were followed up for over 1 year.
- 2 patients died, 8 months and 2 years following the end of last treatment with mortality cause unrelated to CIED infection or CITA-RNPT.

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Results

- **Pocket concentrations** of antibiotics were up to three orders of magnitude higher than normal target therapeutic plasma levels.
- **Plasma antibiotic** levels;
  - ✓ Were manipulated within, or below, the normal therapeutic range,
  - ✓ Safe effective trough concentrations with no peak levels
  - ✓ Reflected an apparent first-order pocket-to-plasma delivery.

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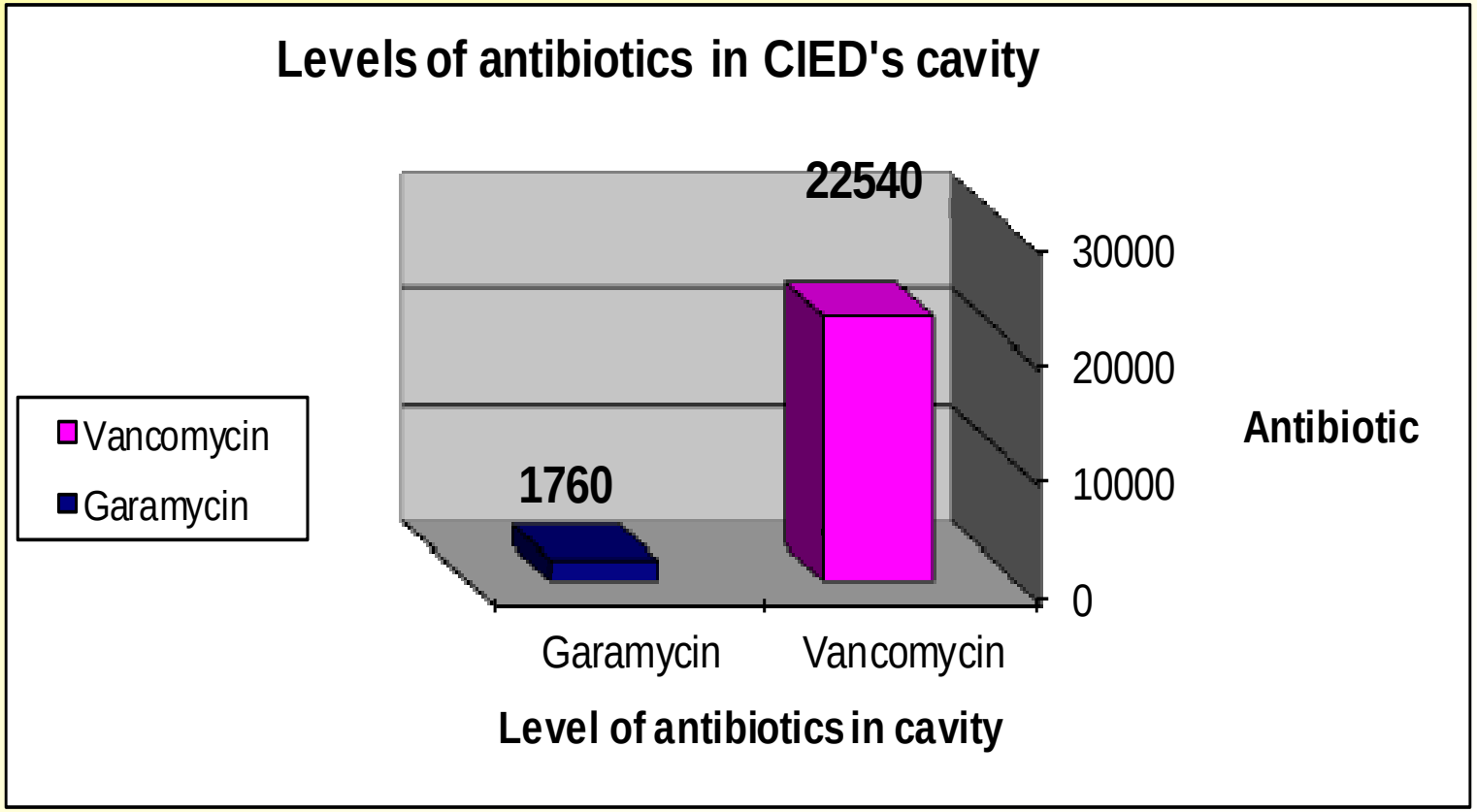
Results

- **Pocket concentrations** of antibiotics were <u>up to three orders of magnitude higher</u> than normal target therapeutic plasma levels



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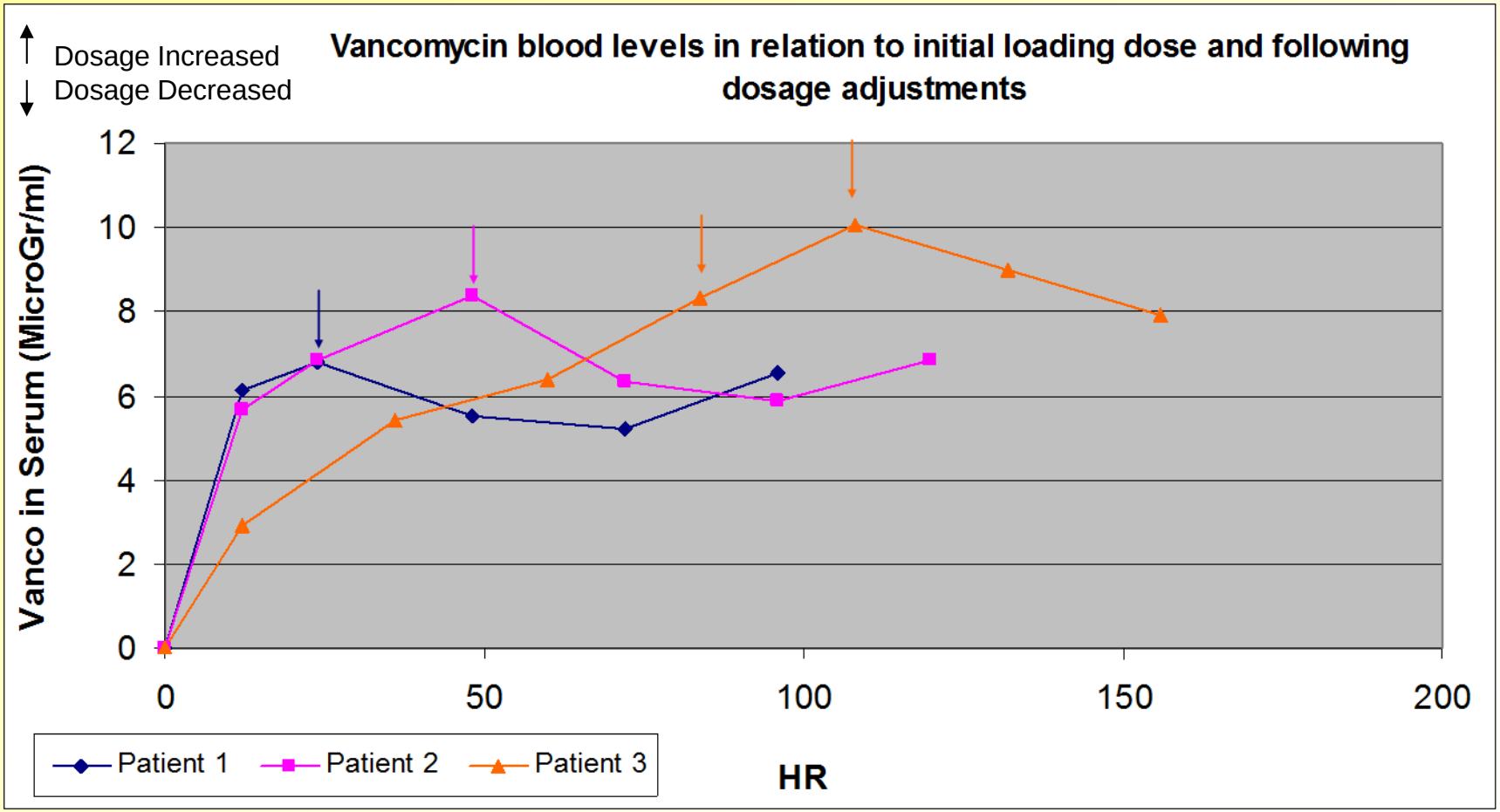
Results – Initiation of treatment*



*Representative graph

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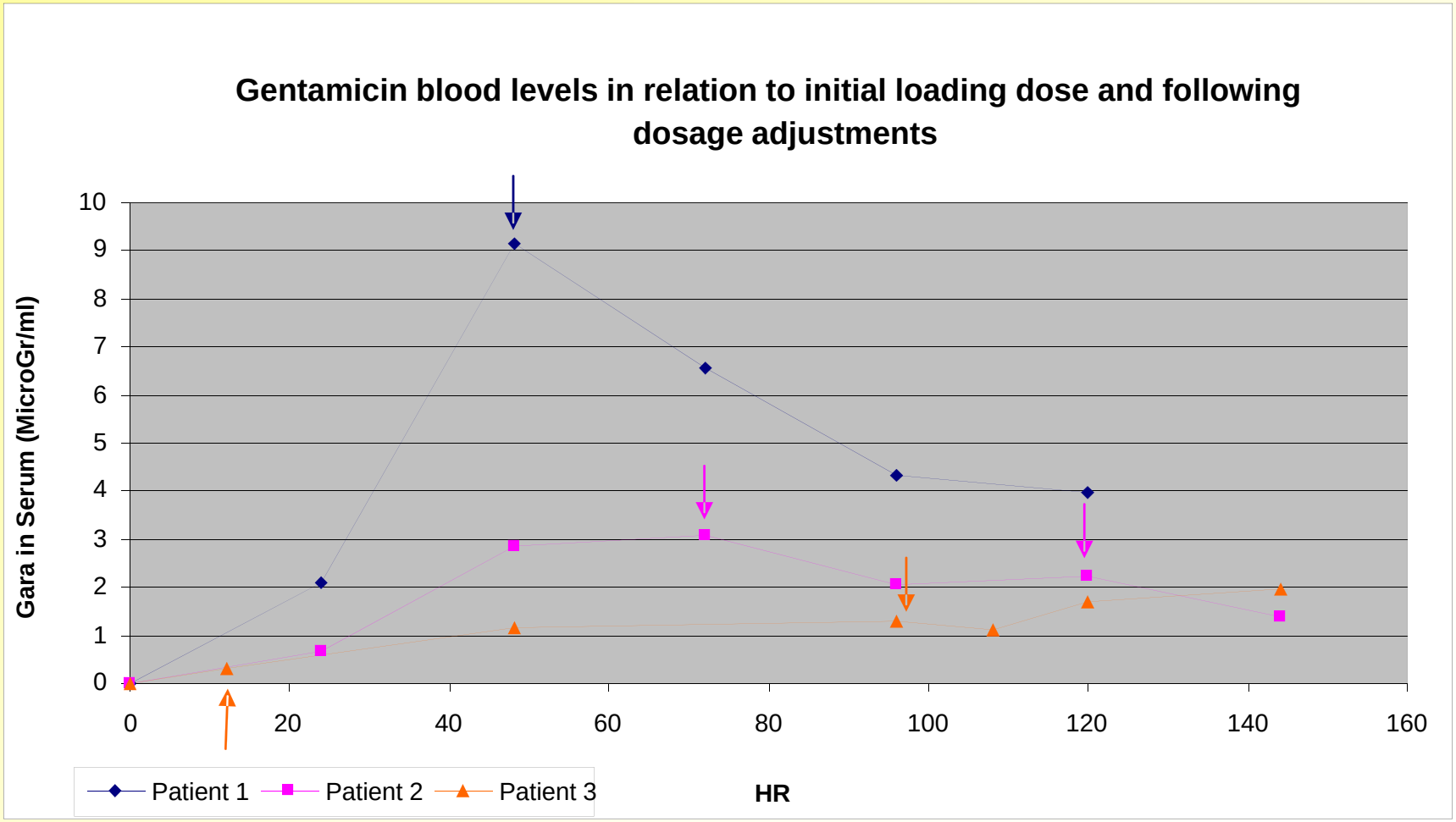
Results – Initiation of treatment*



*Representative graph

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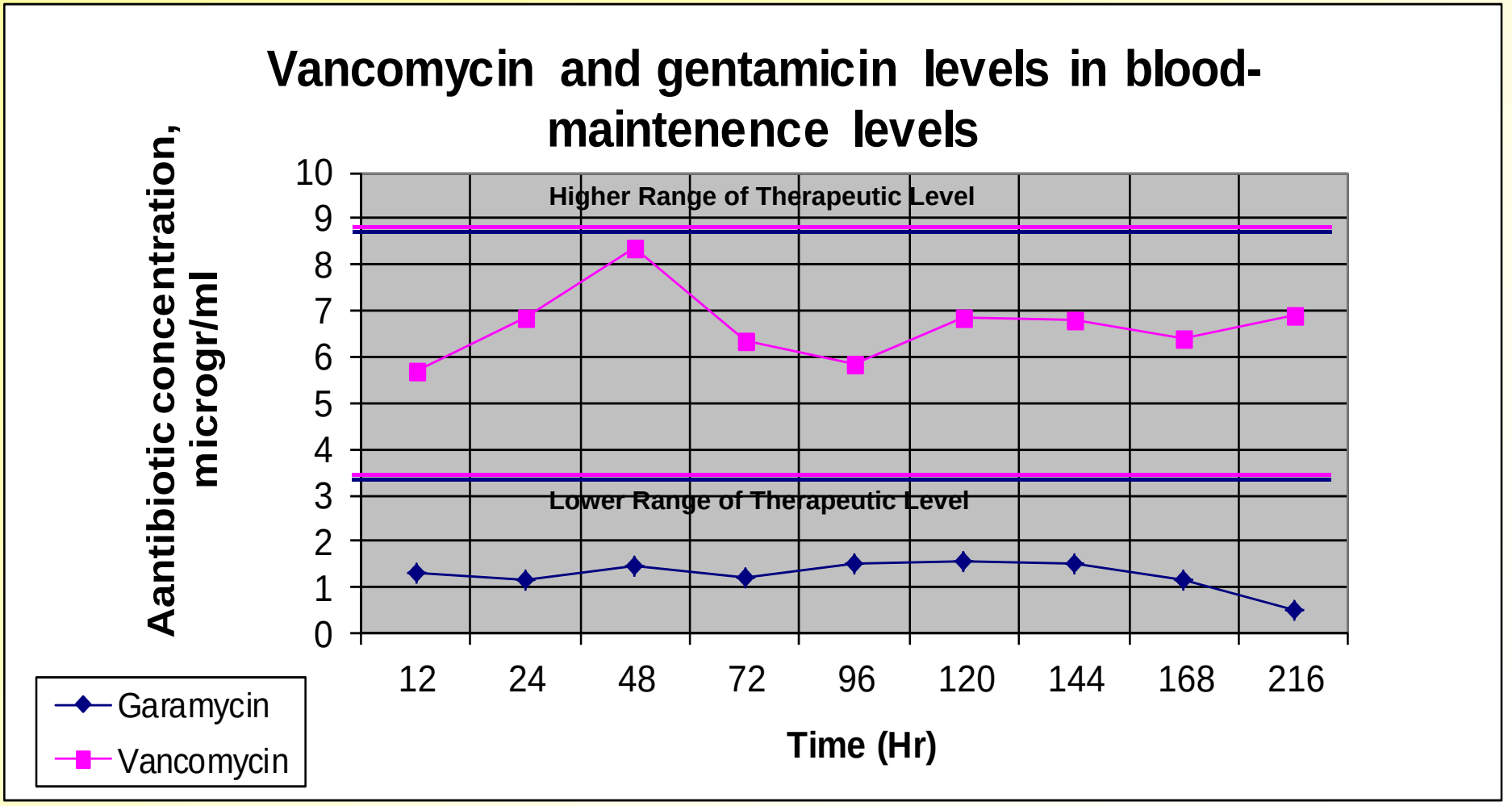
Results – maintenance of treatment*



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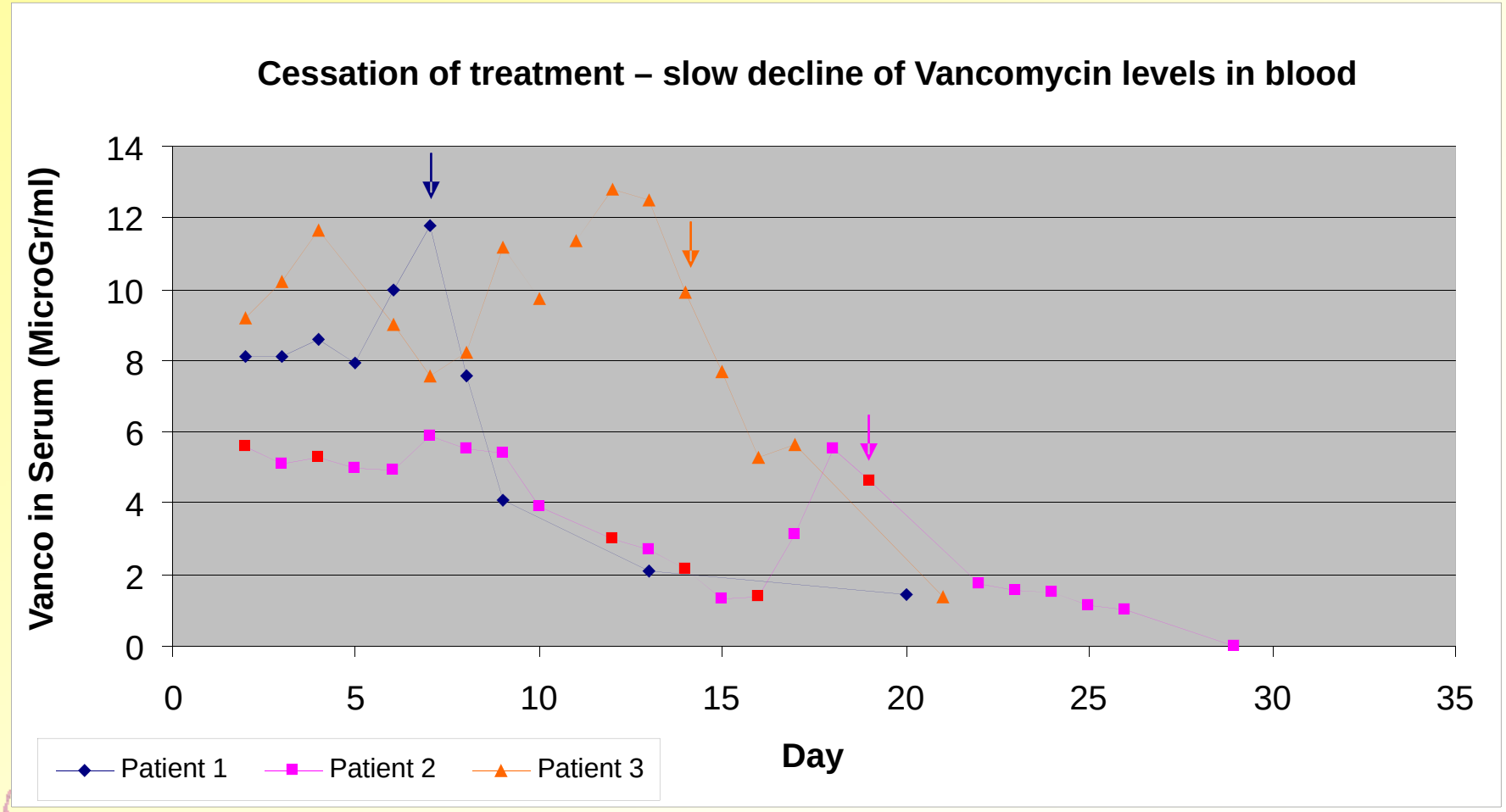
Results – cessation of treatment*



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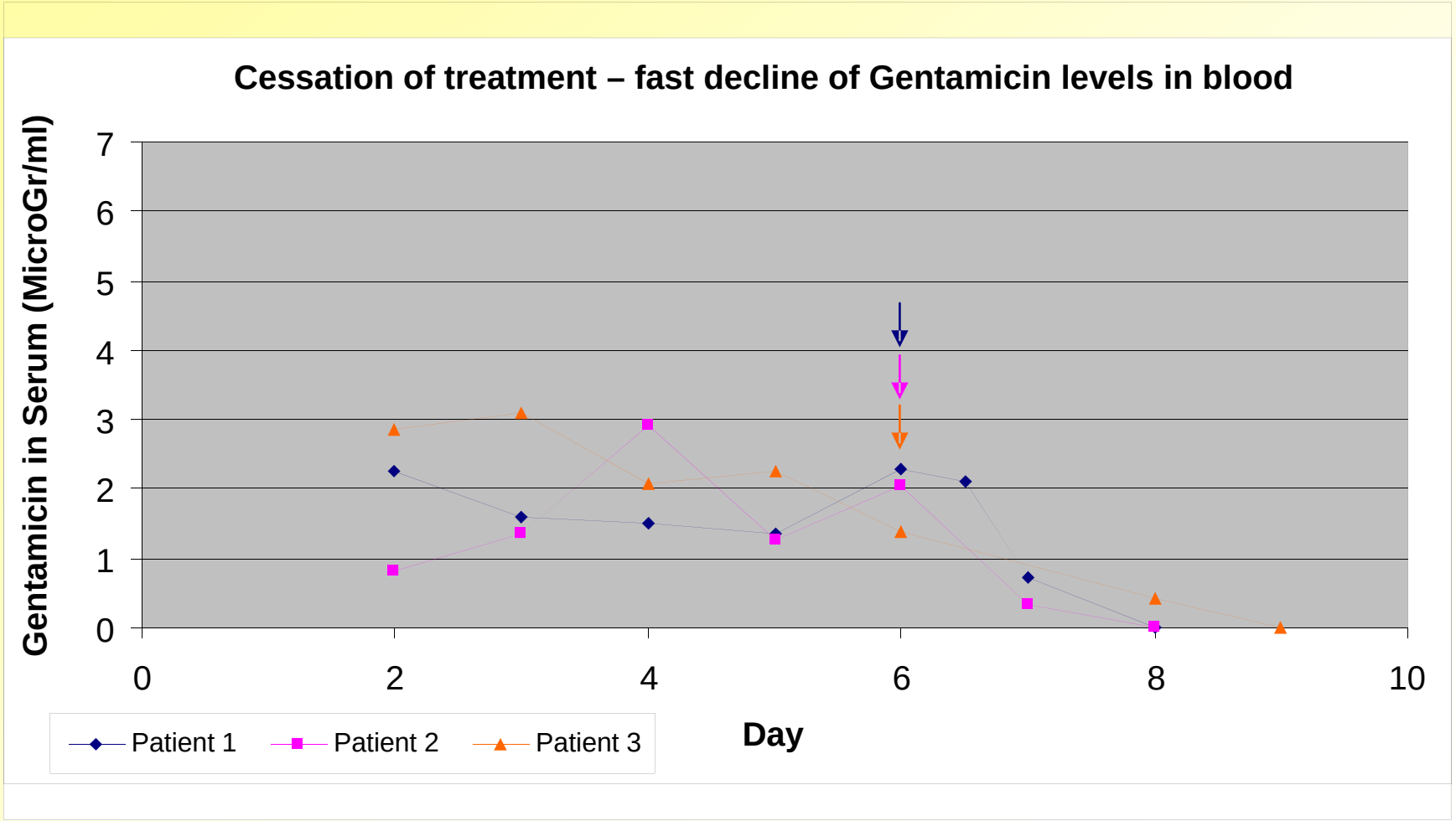
Results – cessation of treatment*



*Representative graph

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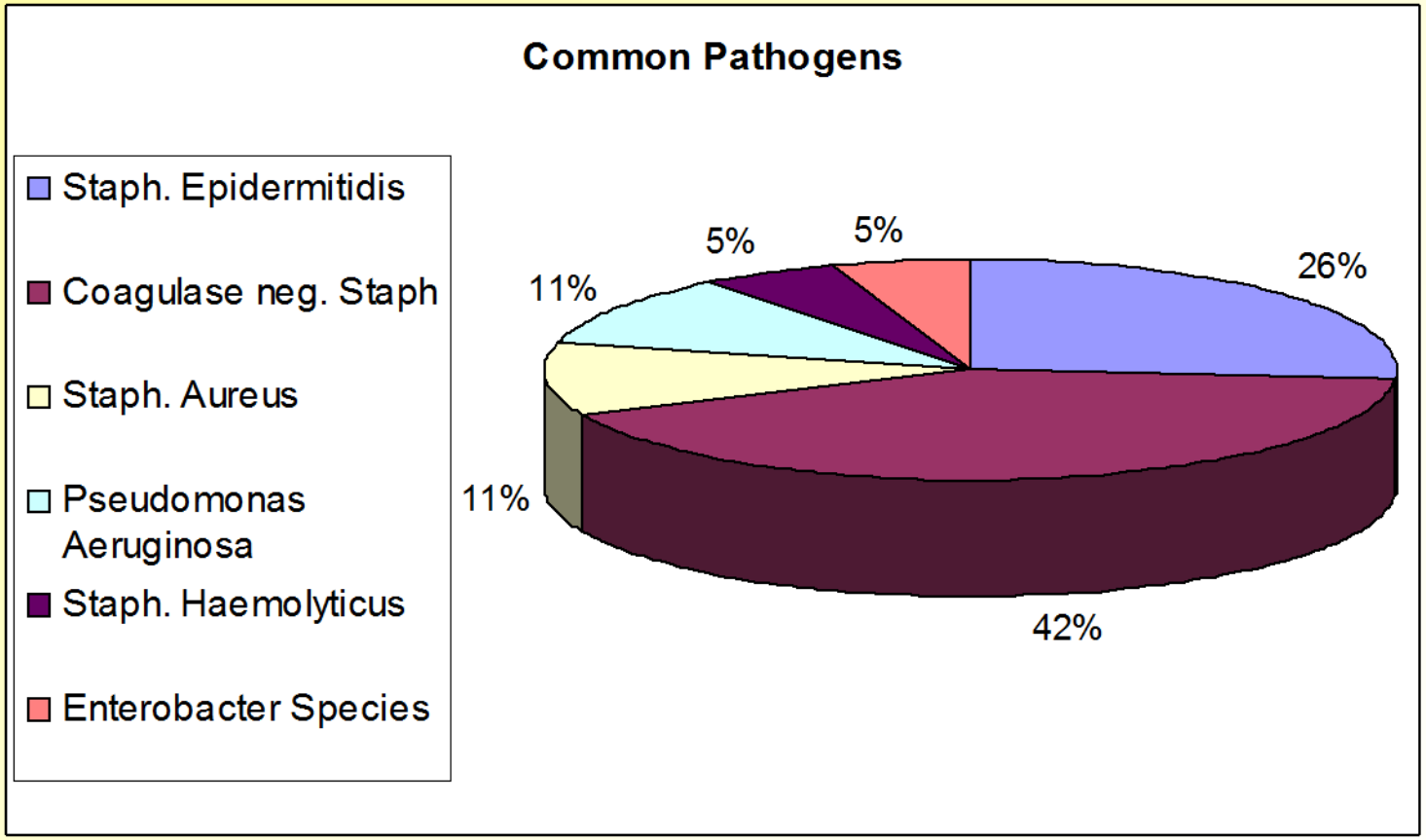
Common pathogens



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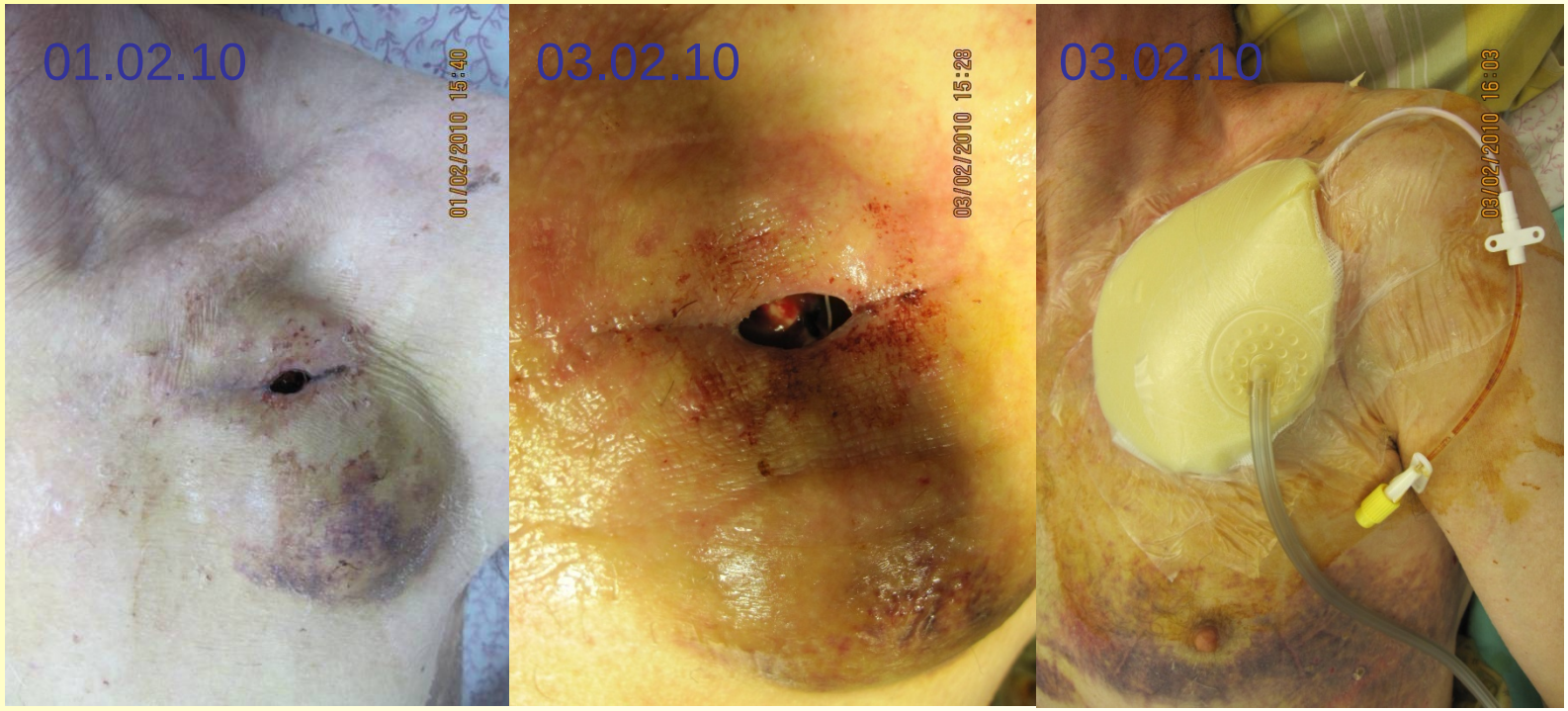
CITA under RNPT in treatment of Infected CIEDs – dehiscence of scar



Primary closure of dehisced wound with hardware exposure

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CITA under RNPT in treatment of Infected CIEDs – Primary closure

Primary closure of dehisced wound with hardware exposure

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CITA under RNPT in treatment of Infected CIEDs – exposure of wiring

07.12.11 **10.12.11**

Long term exposure and infection of hardware. CITA preliminary treatment

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CITA under RNPT in treatment of Infected CIEDs – Exposure of wiring

12.12.2011

Long term exposure and infection of hardware. CITA preliminary treatment

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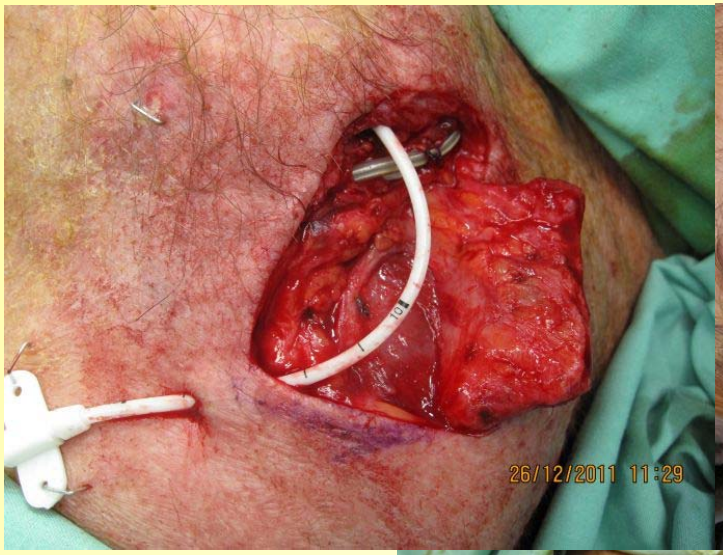
CITA- RNPT of Infected CIED – exposure of lead –

Closure with a flap



26.12.2011

Closure with local flap

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CITA- RNPT of Infected CIED – exposure of lead

22.01.12

11.01.12

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CITA- RNPT of Infected CIED – exposure of lead

Salvage of infected device by CITA-RNPT and coverage by local flap

19.02.12

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Conclusions

Our clinical experience demonstrates that:

- infection of CIED's pocket and/or sub-cutaneous wiring can be efficiently managed (**88% success rate)** by CITA-RNPT, diminishing the need for removal of the device.
- CITA provides a new drug delivery concept of concurrent:
  - ✓ controlled, device targeted & systemic antibiotic therapy,
  - ✓ effective, safe trough concentrations with NO peak levels, adjustable to the patient's clinical needs and restrictions,
  - ✓ reflecting an apparent first-order pocket-to-plasma delivery**.**

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Conclusions

- Pocket concentrations of antibiotics can reach ultra-high levels sufficient to eradicate (biofilm?) infections.
- Vancomycin sensitive organisms need no further oral antibiotic treatment after termination of CITA
- Treatment should be initiated as early as infection is suspected.
- Treatment should be restricted to pocket and proximal subcutaneous portion of hardware.
- Failure of treatment does not impede safe removal of device or deterioration of outcome.
- The **RNPT system** provides an ideal **isolated microenvironment** for pacemaker **pharmaceutical re-sterilization**.

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Thank you