In vivo release of high dose vancomycin from loaded cement in patients with periprostheses infection effective bactericidal activity.

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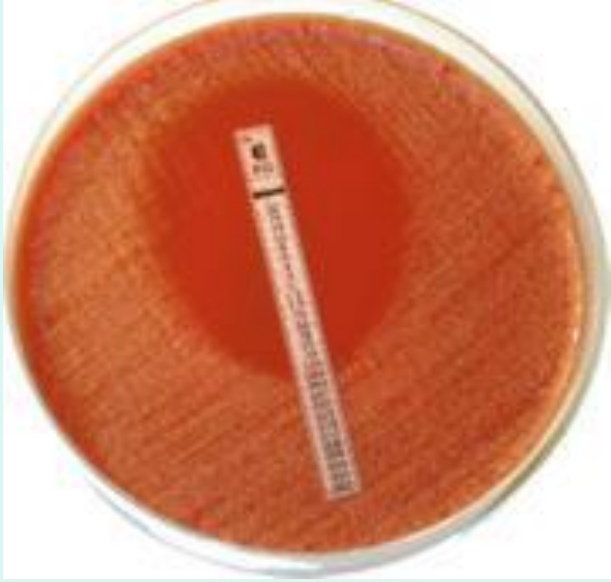
After limb salvage, infection

- is a devastating complication that occurred in **8 to 20% of patients treated** by en bloc resection and prosthetic reconstruction for bone sarcomas.
- Resulting often in **secondary amputation**

Antibiotic loaded cement spacers

- Have been widely used since 1972 to prevent and to treat prosthetic infection
- The delivery of a high concentration of antibiotics in a localized area is thought to be safer than systemic administration of intravenous antibiotics in such doses

the emergence of increased resistance of staphylococcus



- Explains recent less effectiveness of conventionnal antibiotic loaded cement (low dose of antibiotics)
- Plaes for higher doses of antibiotics
- and compells us to consider the antibiotic concentration in the operating field

systemic safety of high dose vancomycin

- The systemic safety of high dose vancomycin loaded spacer has been investigated* but rarely the elution of high vancomycin from cement in vivo.

Systemic Safety of High-Dose Antibiotic-Loaded Cement Spacers after Resection of an Infected Total Knee Arthroplasty *Bryan D. Springer, MD and coll Clin. Orthop.Rel.Desease 2004

The aims of the study

1°)To **confirm the systemic safety** of using high doses of vancomycin in cement

2°)To **evaluate the elution of vancomycin into the site** of the excision arthroplasty to see if effective bactericidal activity can be obtained

Patients and methods

- From 2006 to 2008 , 16 consecutive patients were managed by prosthetic exchange 2 stages procedure using high dose vancomycin loaded cement spacer.
- Patients were males :7 females : 9. Average of age at the time of surgery was 22 years.

Antibiotic-loaded methylmethacrylate cement

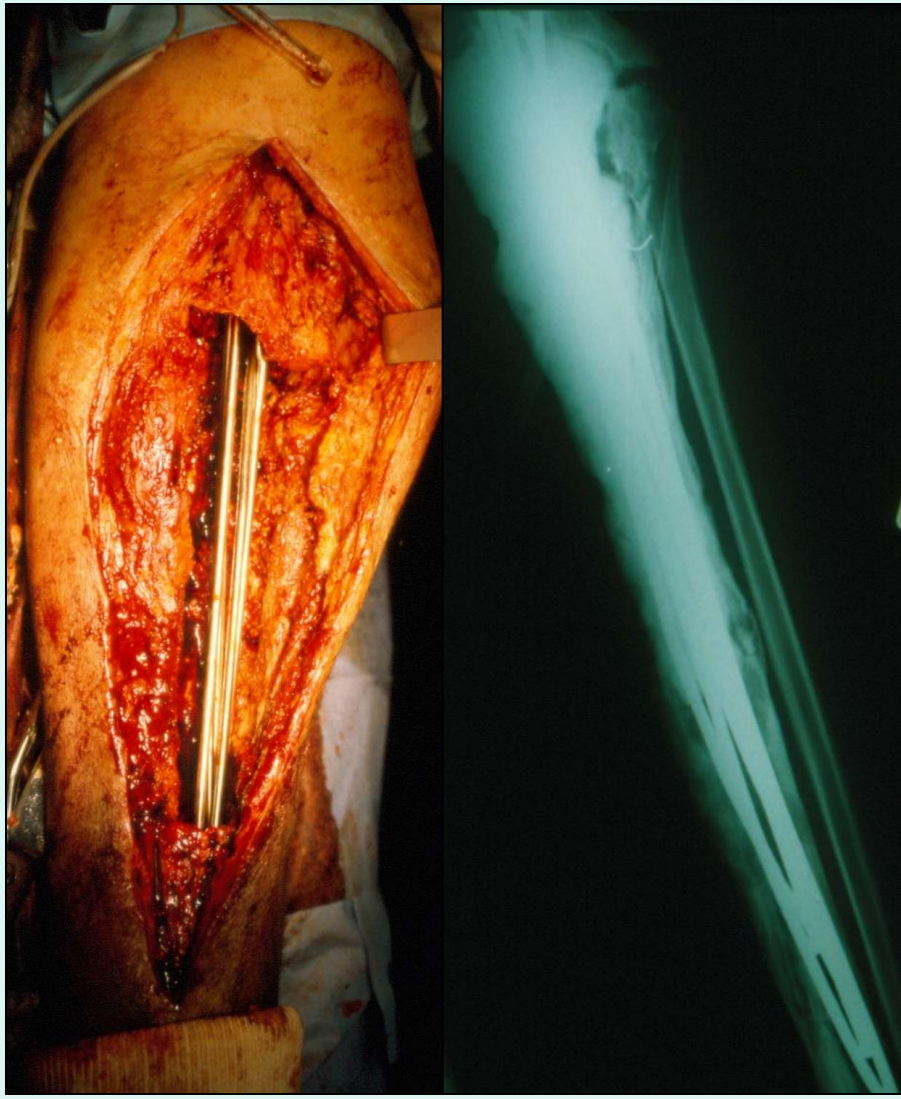
- Cement were prepared by adding **4 g of vancomycin powder to a 40 g pack** of Palacos R cement in the operative room during the operation.

Antibiotic-loaded methylmethacrylate cement

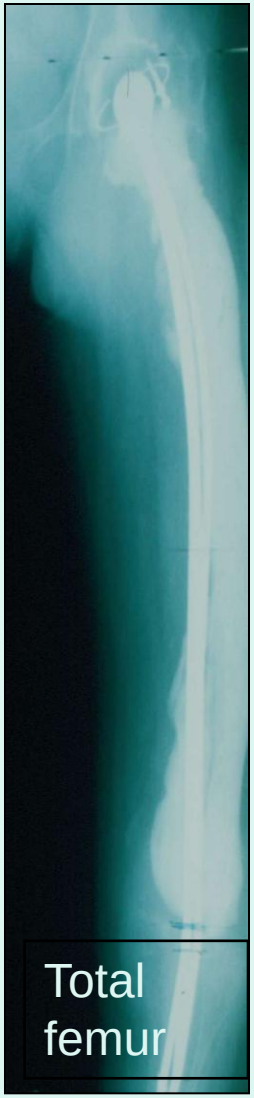
- We generally used **2 to 4 batches of cement in one spacer** depending of the size and length of resection
- The **average dose of implanted vancomycin was 7.5 G (4-14.5).**

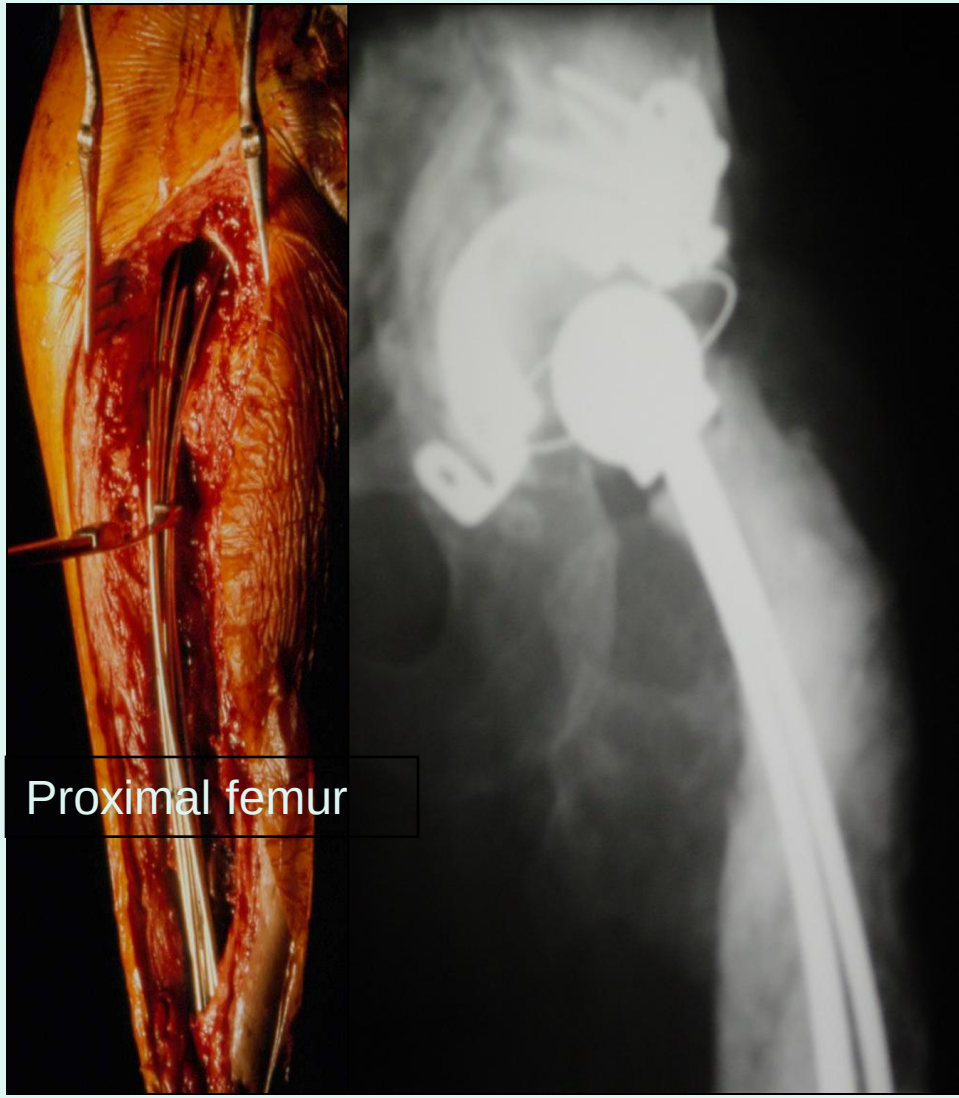
spacer for proximal tibia

- The spacer was composed of metallic rods covered with antibiotic loaded cement
- Gentamycine+
- Vancomycine (4 gr/pack).



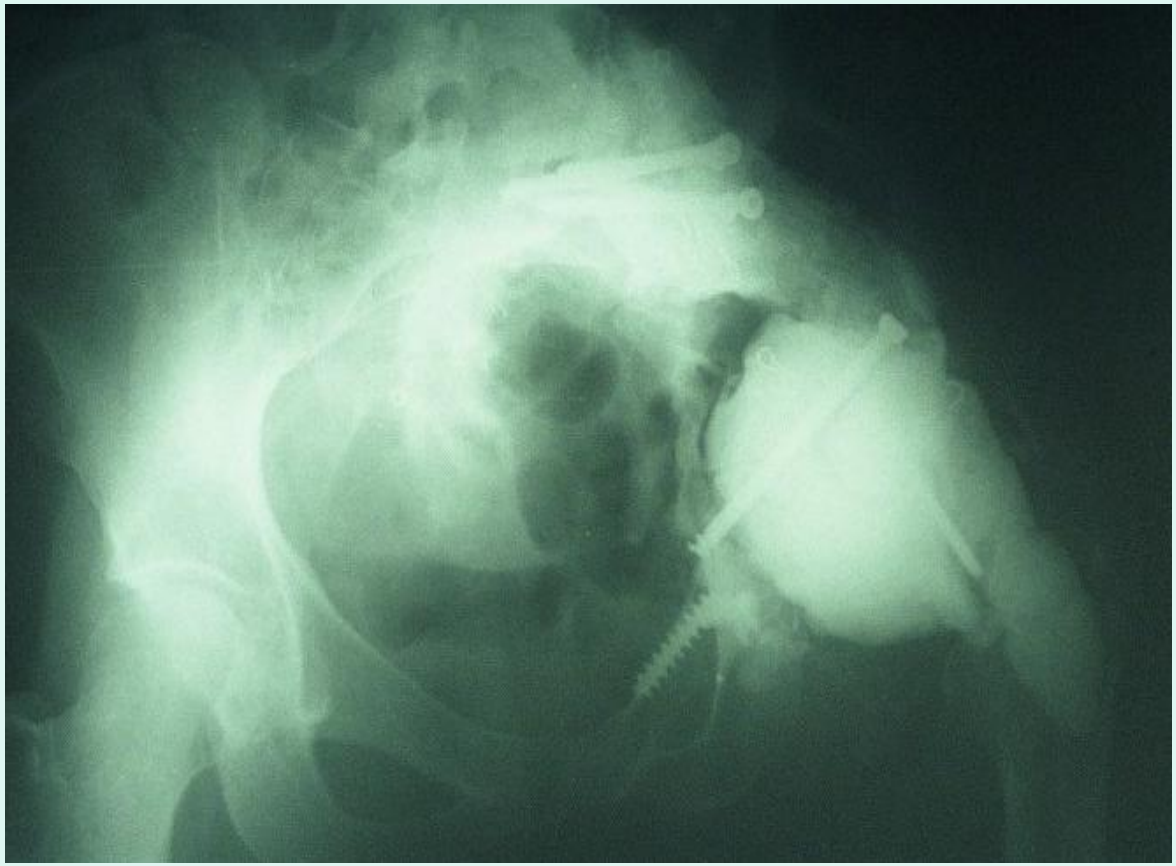
spacers for femur

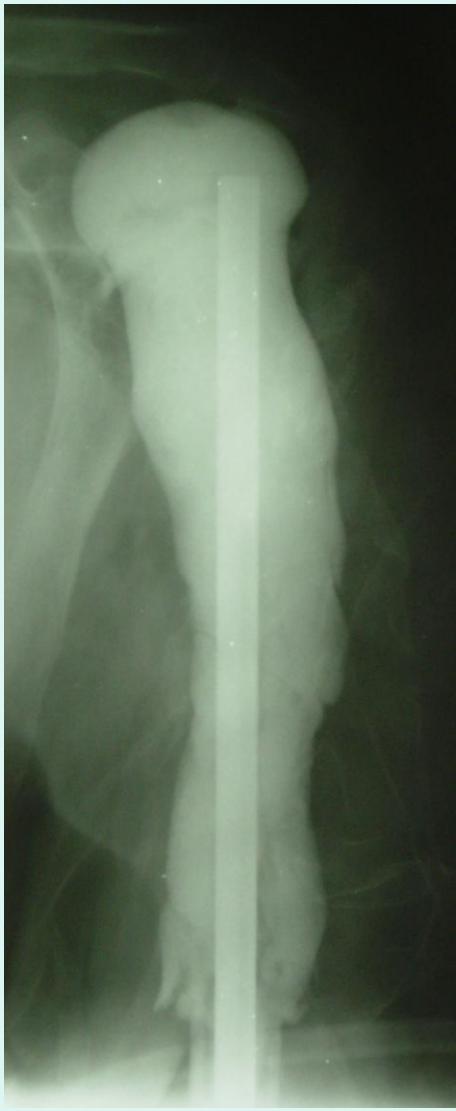




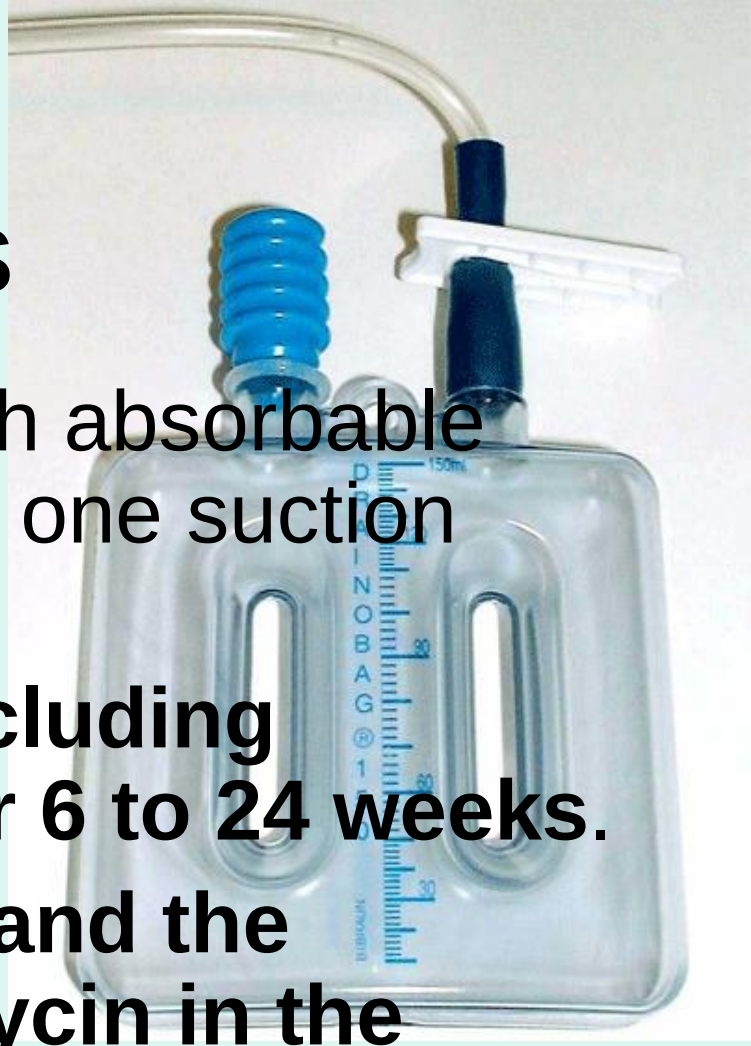
other spacers

Spacers used for proximal humerus or acetabular





Post operative cares



- The wounds were closed with absorbable mono-filaments sutures over one suction drain.
- **Intravenous antibiotics excluding vancomycin were given for 6 to 24 weeks**.
- **Patients biological values and the concentrations of vancomycin in the blood and in the aliquots of suction drainage were checked daily until removal of drain (d10-d15)**.

Results for systemic safety

- **The serum concentration of vancomycin remained under 2 µg/ml in all patients**
- We observed no case of
  - allergy,
  - toxicity
  - or intolerance

Local concentration

- Local concentration of vancomycin depended **of the dose of vancomycin used** and decreased quickly during the first week
- half life :2.25 days.

Local concentration for 10 Grams

	1	2	3	4	5	6	7	8	9	10
12g	750	550	360	270	220	153	120	100	80	66
11g	720	535	250	220	208	125	99	88	68	58
10g	725	515	346	225	190	110	87	70	55	45

- For a dose of 10 G vancomycin , the average concentration from the drain was :d1 :725µg/ml, d2 :510 µg/ ml,d3 :346

Is it bactericidal?

- These results should be compared to the bactericidal concentration of vancomycin **for staphylococcus aureus** :
- **10 to 20 µg/ml for usual** organisms,
- **20 to 40 µg/ml for resistant** organisms .

Conclusion

- high dose vancomycin spacers result in very low serum concentration without risk of systemic toxicity.
- In the operative wound , very high concentration are obtained , 10 to 20 fold bactericidal concentration for staphylococcus aureus.
- Additional studies are needed , with longer follow-up to evaluate the clinical efficacy of this method.