Orthopaedic Heresy: Fact and Fiction in the Care of Chronic Osteomyelitis

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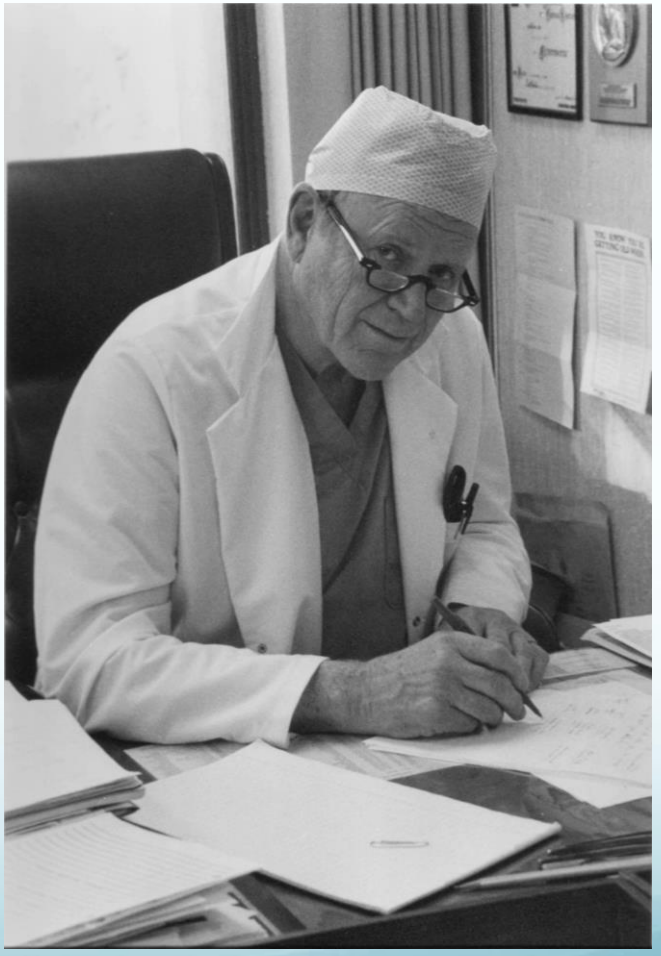
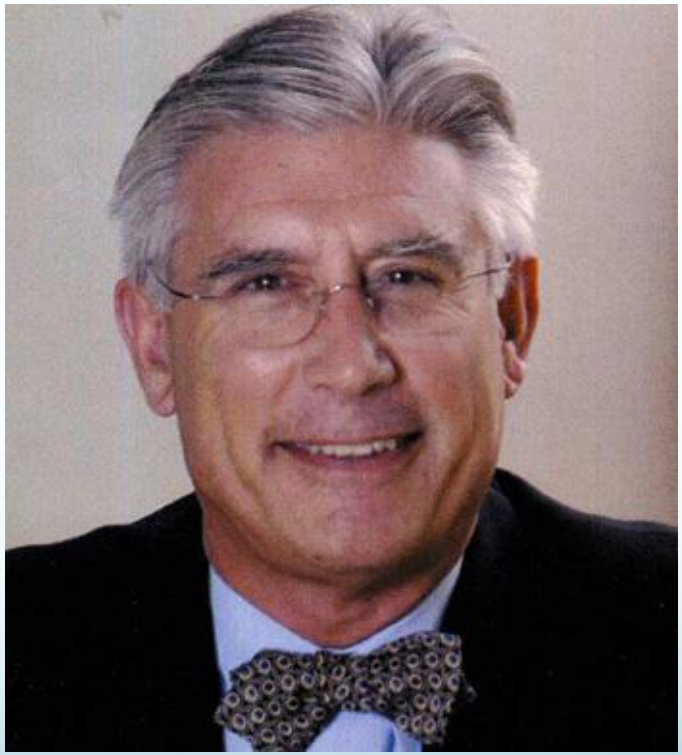
Dr. Harry J. Buncke (1922 – 2008)

"The Father of Microsurgery"

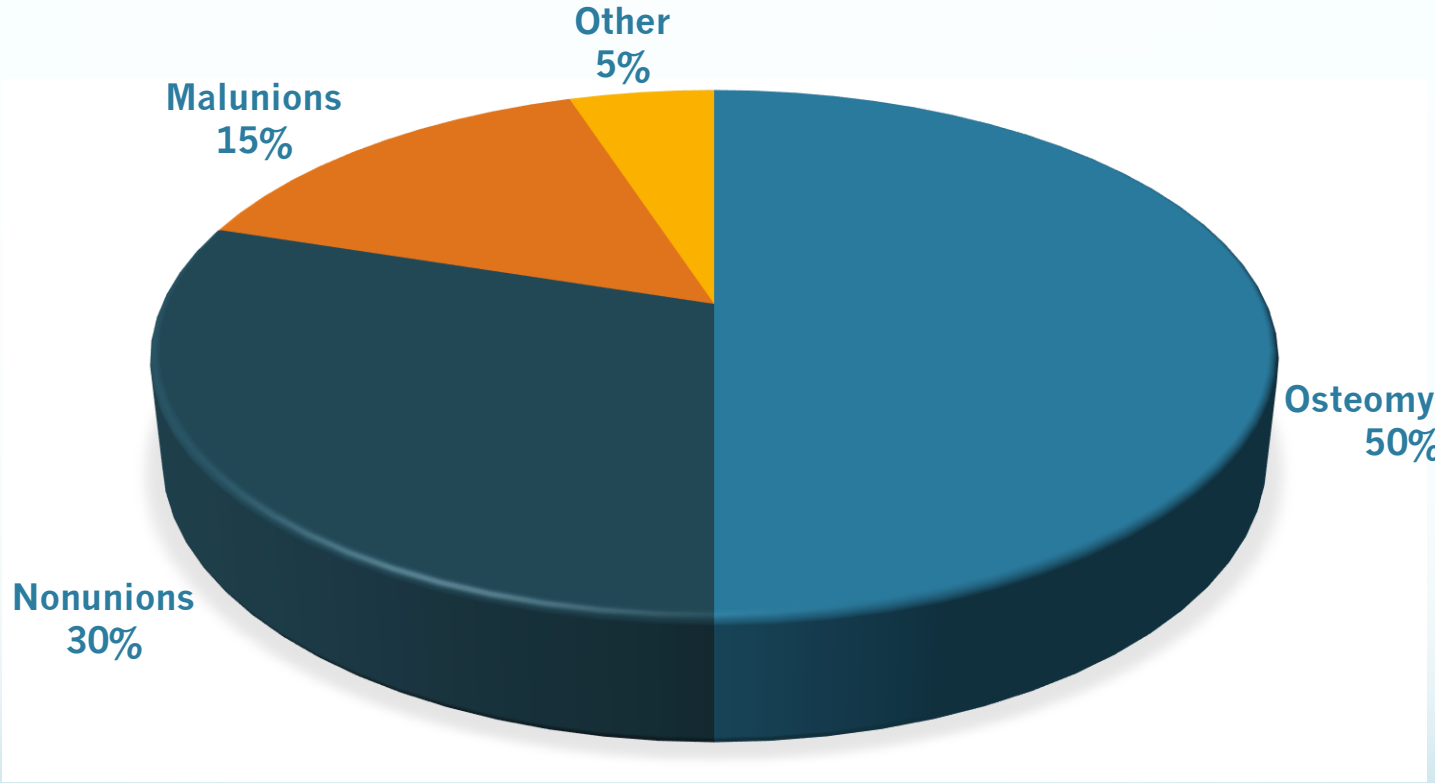


Dr. George Cierny, III (1947 – 2013)

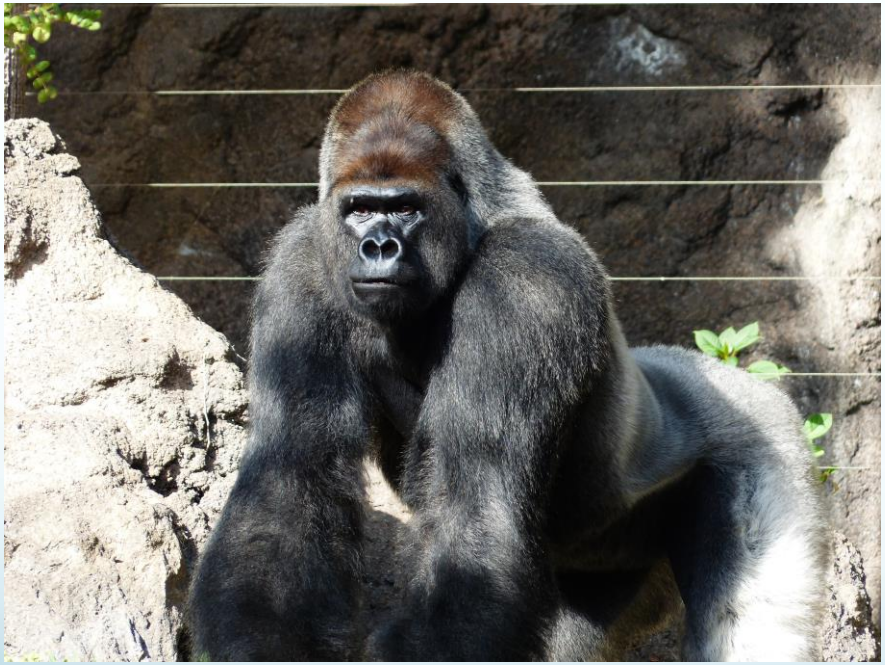
"The Father of Osteomyelitis Surgery"



Breakdown of My Practice



Intravenous Antibiotics



- What is their role in the treatment of chronic osteomyelitis?
- What is the data backing their prolonged usage?
- Do they then work?

What % of Patients at your Institution are Discharged with a PICC Line for Treatment of an Infected Nonunion/Osteomyelitis

- 100%
- 75 – 99%
- 50 – 74%
- 25 – 49%
- <25%

Intravenous Antibiotics

- Historically, Chronic Osteomyelitis had an ~12% cure rate.
- Level IV data on the treatment of ***Acute Osteomyelitis in the pediatric population*** showed good results with a 6 week course of intravenous antibiotics +/- subsequent oral regimen.
- There were literally no other reasonable options.

The Battle

- ***Prokaryotes***

vs.

Eukaryotes

Ratio of cell types in our "Biosphere"

Prokaryotes : Eucaryotes

- ***10 to 1***

Viruses : Prokaryotes

- ***10 to 1***

Viral particles : Us = 100 to 1

400 microbial genes for each human gene in the body

“To beat microbes we first must learn to think like microbes”

Understanding the Language

- ***Planktonic Cells***: This refers to bacteria upon initial inoculation. They are "young" and have rapid turnover. They are non-adherent and float freely in the environment they have colonized, like ***plankton***.

Understanding the Language

- ***Sessile Cell Phase***: This represents the phase of the life cycle when the bacteria has established colonization in a biofilm. It represents a slow growth cycle, and ***almost*** a spore form of life. Metabolic turnover is markedly reduced.

Understanding the Language

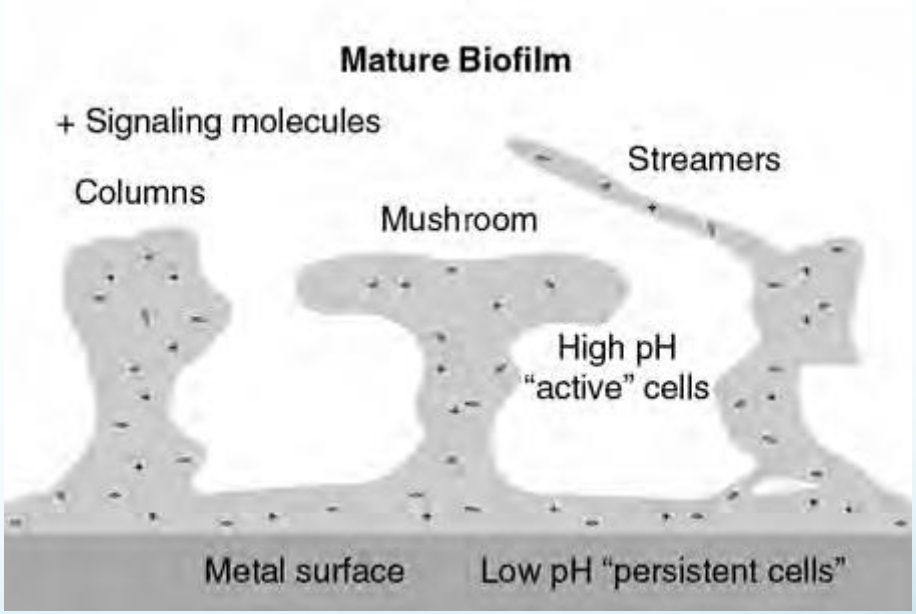
- ***Biofilm***: An organized polymeric matrix composed of bacterial cellular debris (DNA, proteins, & polysaccharides).

  This represents the shielded ***hydrophobic*** environment the bacteria produce so they can go into a semi-dormant (sessile) state.

Within the biofilm biosphere microbes behave as a multicellular organism

Establishment of Infection

- *Biofilm* occurs due to the organized cell death of the first waves of bacterial invasion on a host site ("death of the privates, corporals, and sergeants.")



McPherson, EJ, Peters, CL: Musculoskeletal Infection, *in Orthopaedic Knowledge Update 10, American Academy of Orthopaedic Surgeons, Rosemont, IL, 2011.*

How long does it take for a biofilm to evolve into maturity?

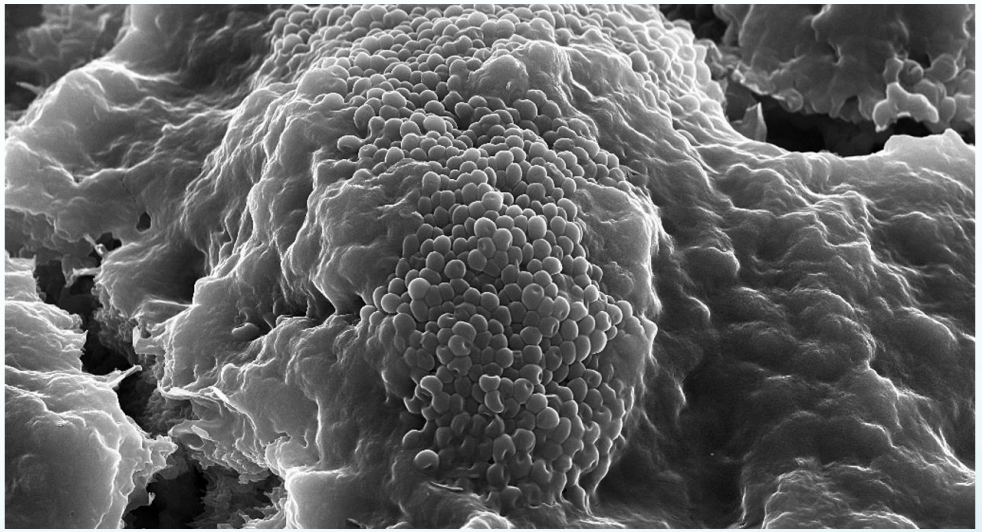
- A. 5 – 7 days.
- B. 8-10 days.
- C. 11 -15 days.
- D. > 15 days.
- E. Nobody knows.

Biofilm Maturation

- A very difficult question, as it does **not** seem in the lab that the construction of the biofilm and the bacterial cell phase progress in a ***"co-similar" linear relationship***.
- The vast majority of biofilm studies in the literature involve an ***in vitro*** model.
- ***HERESY:*** We have little if any understanding of a mature biofilm colony.

The Battle

- ***Prokaryotic cell phase of growth.***
- ***Is there a mature biofilm.***



Importance of Bacterial "Phase" in the Host

Planktonic

- This represents the initial innoculum phase.
- The bacteria have a high metabolic rate.
- They are "free floating".

Biofilm

- This represents the semi-dormant bacterial phase where the microbe is "trying" to live in a symbiotic state.
- Low metabolic rate.
- Adherent to the biofilm.
- 10^3 times less sensitive to most antibiotics.

Intravenous Antibiotics

- ***What is their role in chronic osteomyelitis?***

Comparison of Short Term vs. Long Term I.V. Antibiotics

- George Cierny
- A Retrospective/Prospective Study of < 2 weeks of i.v. antibiotics vs. 6 weeks of antibiotics treated surgically by a single surgeon.
- > 400 patients in each treatment arm.

Comparison of Short Term vs. Long Term I.V. Antibiotics

- ***No Difference in Outcome.***

Infectious Disease Physicians

- ***We need to work collaboratively and educate each other***

Injury, Int. J. Care Injured 50S (2019) S56–S61

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

Newer perspectives in the treatment of chronic osteomyelitis: A preliminary outcome report

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Retrospective Review of Chronic Osteomyelitis Treated

- October 2012 through October 2017
  (Not including Type C Hosts with no intervention)
- **164 Cases**
  - ***Exclusions:*** *4 cases coccidiomycosis*
    17patients with failed TKA who underwent knee pseudofusions
    7 cases poor follow up, lost to follow up
    9 cases in para and quadriplegics

Study Total: 127 Patients

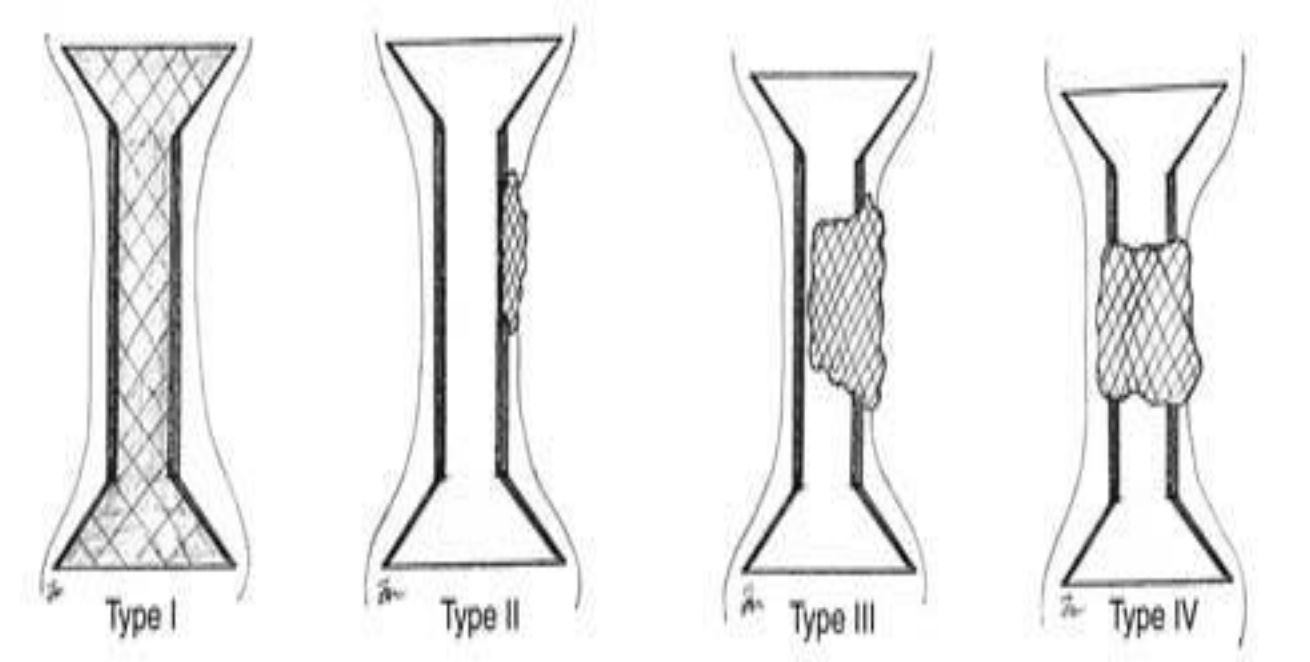
Patient Demographics

- Male = 89 (70%) Female = 37 (30%)

- Age: Mean = 54

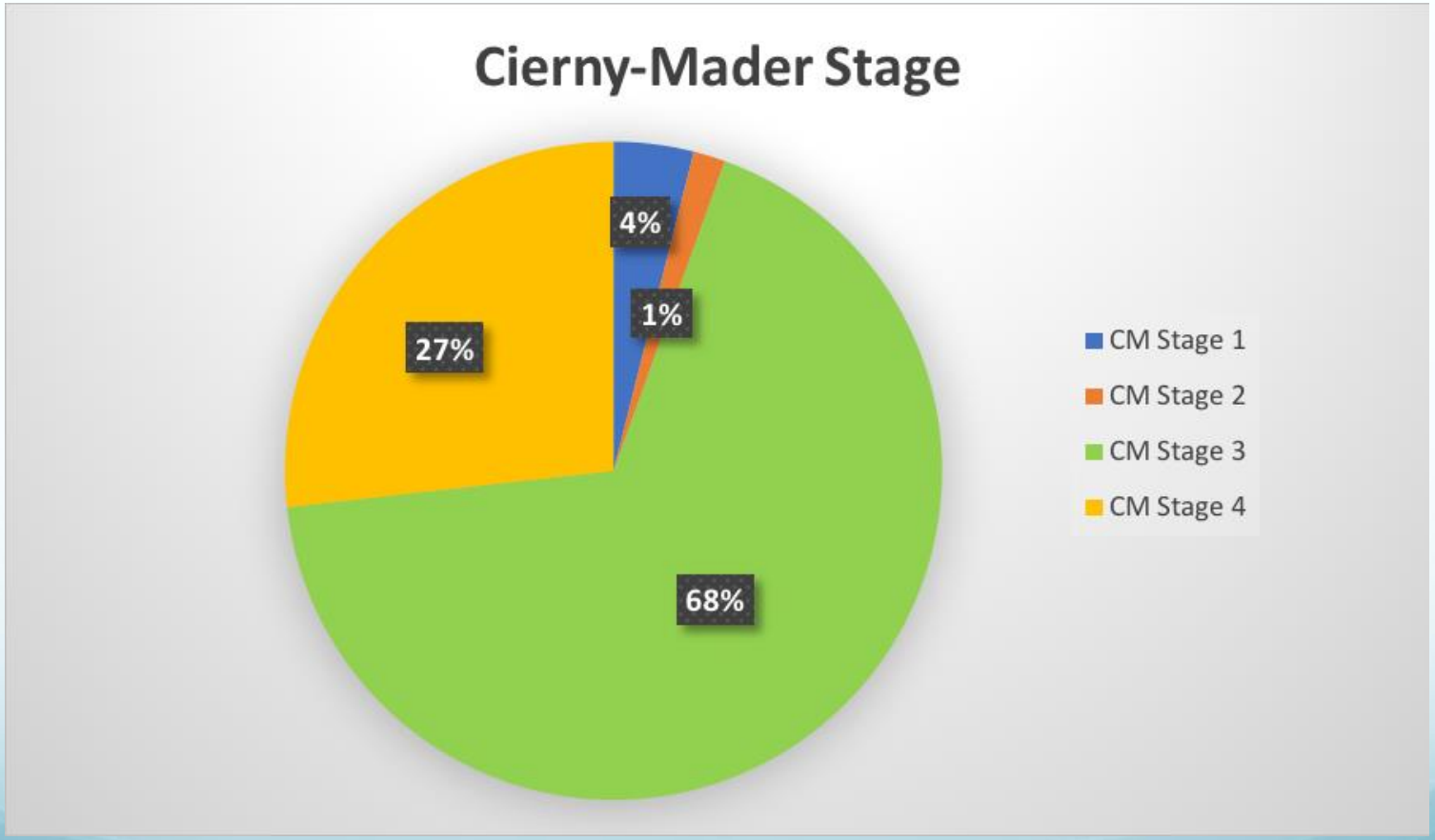
  Median = 53

Cierny-Mader Classification

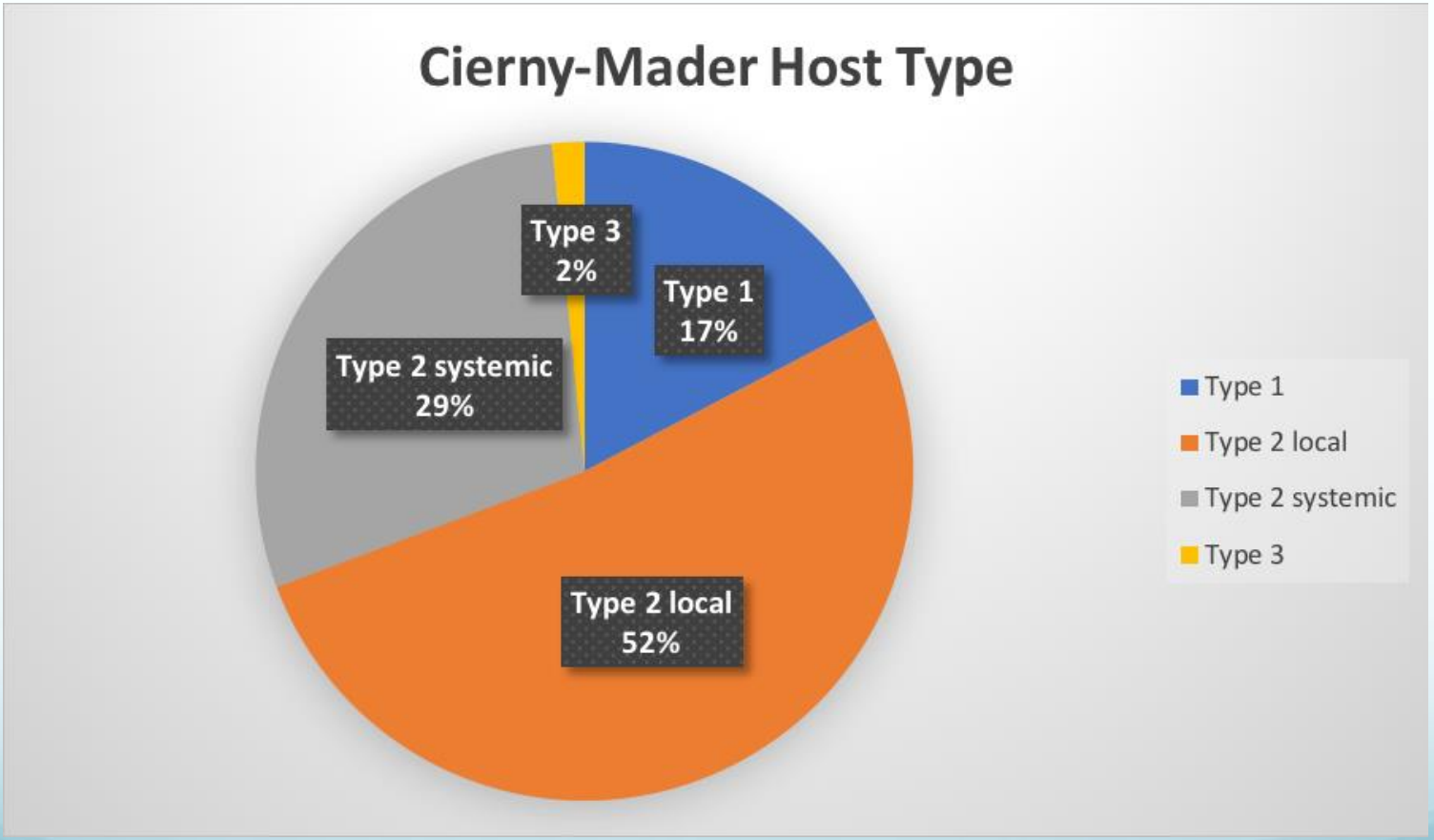


(Reproduced from Ziran BH, Rao N: Infections, in Baumgaertener MR, Tornetta P III [eds]: Orthopaedic Knowledge Update: Trauma 3. American Academy of Orthopaedic Surgeons, Rosemont, IL, 2005, p 132.)

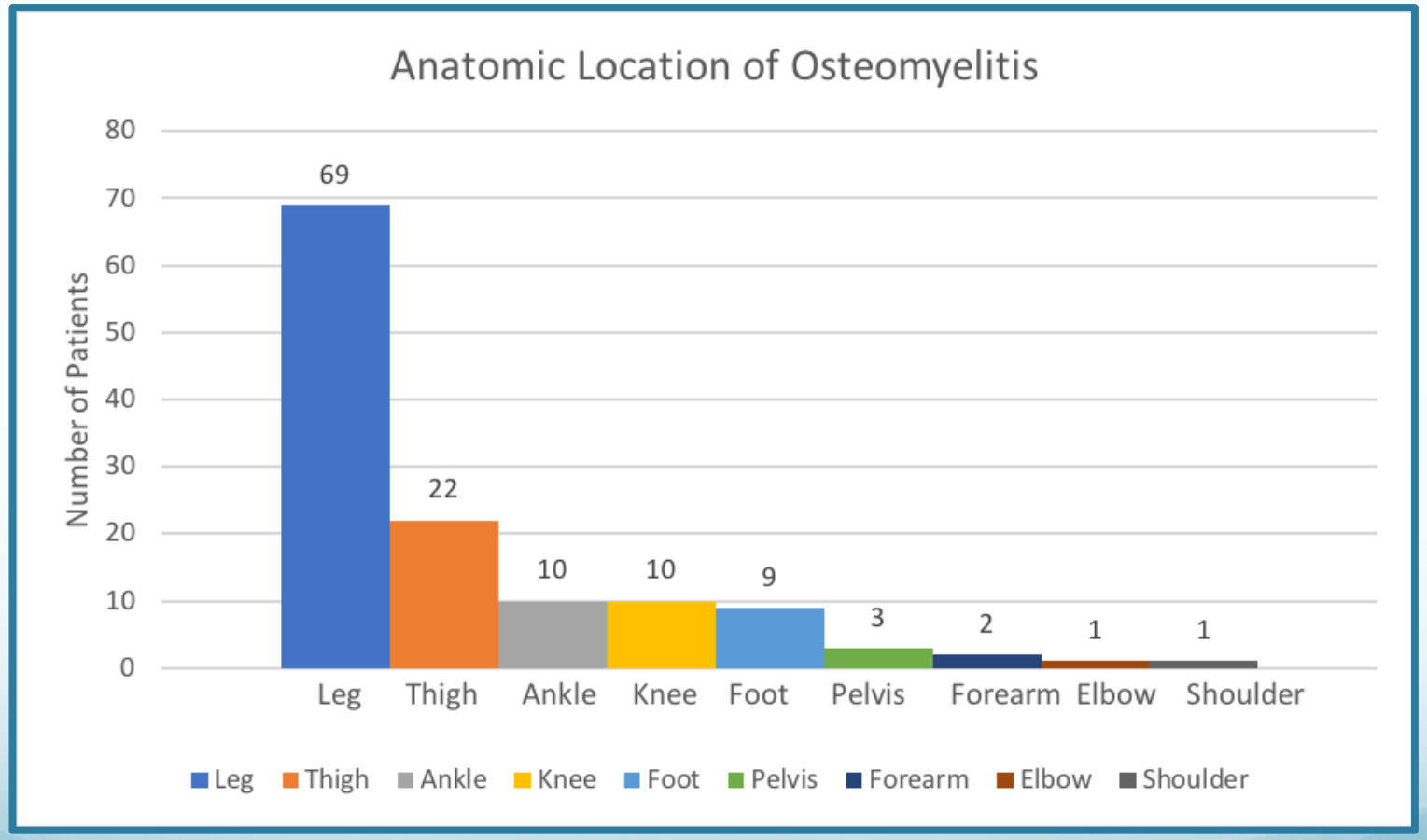
Cierny-Mader Stage



Cierny-Mader Host Type



Site of Chronic Osteomyelitis



Treatment

Temporal Order	Reconstruction Step Performed
1	Excise ***ALL*** devitalized/infected bone and soft tissue.
2	Manage the dead space.
3	Obtain a healed soft tissue envelope.
4	Reconstruct the bone defect.

Liberal use of free tissue transfers for soft tissue envelope reconstruction.

Treatment

- 38 Patients **(30%)** did receive free tissue transfer.

RESULTS

- ***7 Patients (5.5%) placed on outpatient IV antibiotics.***
- 94.5% of patients received only 1 to 6 days IV antibiotics while hospitalized with some receiving accompanying < 10 day course of oral antibioitic at discharge.

Decision for Extended IV Antibiotics

- 5 Patients with Autoimmune Disease (Lupus, Still's Disease, R.A.) with systemic immune suppression.
- 2 Patients with severe systemic disease (cancer, cirrhosis).

RESULTS

- **2 Recurrences (1.6%)**
  - One patient with C-M Stage 4 tibia mistakenly treated as Stage 3; with recurrence under flap. Treated with en bloc resection and transport with cure.
  - One patient with C-M Stage 4 femoral shaft with recurrently infected TKA treated as Stage 3 with recurrences. A C-M Type 3 Host, and not a candidate for bone transport, underwent AKA.

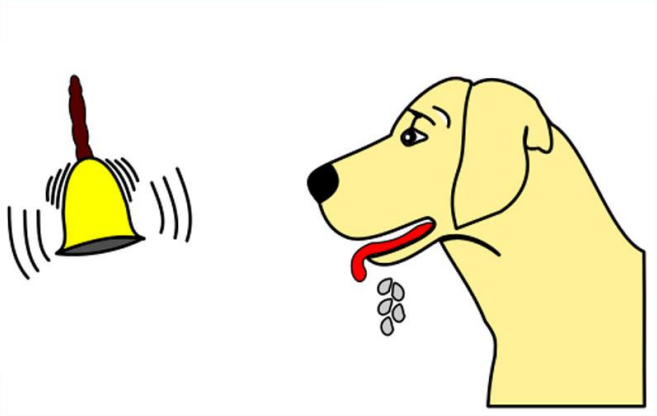
97.6% disease free at mean 3 year follow up

So What Happens When Systemic Antibiotics are Given in a Biofilm State?

PAVLOVIAN RESPONSE

- The ***subtherapeutic*** serum level of antibiotic simply teaches the Biofilm to:

1. Cease the shedding of Planktonic Cells.
2. Utilize its defenses ("Distributed Genome", etc.) to ***pursue further resistance***.



Heresy

- ***THE SPECIFICS OF THE MICROBE ARE LESS IMPORTANT THAN THE SPECIFICS OR CONDITION OF THE HOST.***

Timing of Wound Closure in Open Fractures Based on Cultures Obtained After Debridement

Lenarz, CJ, Watson, JT, Moed, BR, Israel, H, Mullen, JD, MacDonald, JB
J Bone Joint Surg Am. 2010;92:1921-6

- Deep Infection Rate:

  G&A Type II = 4%

  G&A Type IIIA = 1.8%

  G&A Type IIIB = 10.6%

  G&A Type IIIC = 20%

- Higher infection rate in diabetics and ↑ BMI.
- *Trend of ↑ in infection when protocol not followed.*

Timing of Wound Closure in Open Fractures Based on Cultures Obtained After Debridement

Lenarz, CJ, Watson, JT, Moed, BR, Israel, H, Mullen, JD, MacDonald, JB
J Bone Joint Surg Am. 2010;92:1921-6

- BOTTOM LINE:

Wash, Debride, & Culture

Cultures negative ➔ Close Wound
(irrespective of the organisms that were cultured)

Type	Infection Status	Perpetuating Factors	Treatment
A	Normal physiologic response	Little or no systemic or local compromise	No contraindications to surgical treatment
B (local)	Locally active Impairment of response	Prior trauma, or surgery to area; chronic sinus; free flap; impaired local vascular supply	Consider healing potential of soft tissues and bone, consider adjunctive measures
B (systemic)	Systemically active Impairment of response	Diabetes, immunosuppression, vascular, or metabolic disease	Treat correctable metabolic/nutritional abnormalities first
C	Severe infection	Severe systemic compromise and stressors	Suppressive treatment or amputation

Treatment of Chronic Musculoskeletal Infections

HERESY

- **The 3 Microbe Theorem:**

A treatment algorithm based solely on 3 pieces of data.

Prokaryote

Mycobacterium

Fungus

As per best Microbiologists's estimates, what % of bacteria can we currently culture on earth?

- A. ~50%.
- B. ~25%.
- C. ~15%.
- D. ~7%.
- E. ~1%.

HERESY: Hyperbaric O_2

Shandley, S, Matthews, KP, Cox, J, Romano, D, Abplanalp, A, Kalns, J; J Orthop Res, Feb;30(2), 203-8, 2012.

- ***I think we have finally put the nail in the coffin.***
- No efficacy found in the treatment of implant-associated osteomyelitis for methicillin-resistant Staphylococcus aureus and Pseudomonas aeruginosa in an animal model.

Treatment of Chronic Musculoskeletal Infections

What Works

- Thorough debridement with dead space management, local antibiotic delivery to eradicate remaining planktonic organisms.
- Possibly vaccine regimens *(future)*.
- Maybe Phage Therapy *(future)*.

What Doesn't

- I.V. antibiotics alone.
- Hyperbaric oxygen.
- Wound care centers.
- Most other crap.

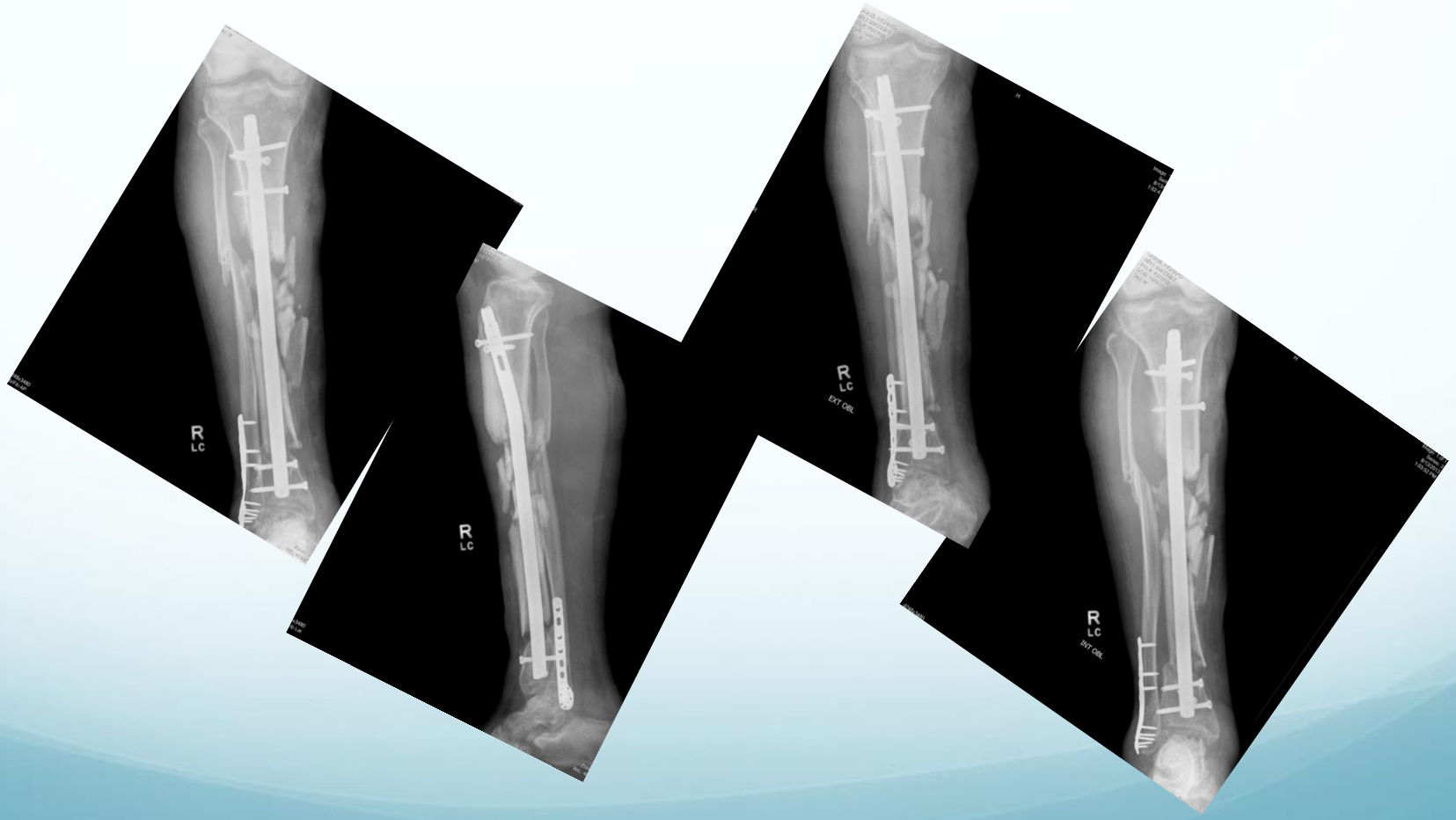
RL: 38 y/o M s/p MCA

- Sustained isolated right closed segmental open tibia and fibula fracture.
- Underwent washout, closure of wounds and IM rodding.
- Developed multiple draining sites and was told this was normal and doing well for 6 months duration.

RL: 38 y/o M s/p MCA

- Treating surgeon by 8 months decided patient might have a bone infection.
- Referred him to the world expert on the treatment of osteomyelitis on 6/26/13.
- Only one problem ..... he passed away on 6/24/2013.
- Patient then presented one month later for care.

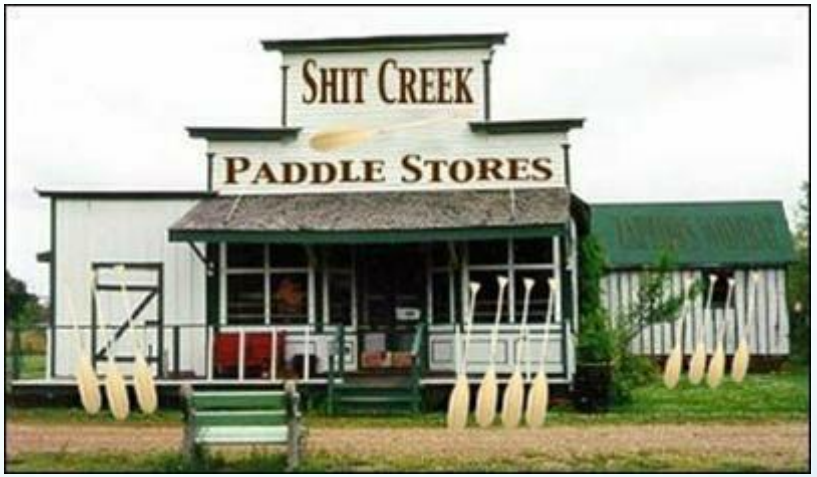
Segmental Nonunions with Draining Sinus Tracts



Multiple Sinus Tracts and Degloving of Soft Tissue Envelope

What Do You Do??

- Amputation
- Re-rodding
- Masquelet procedure
- Limb Salvage

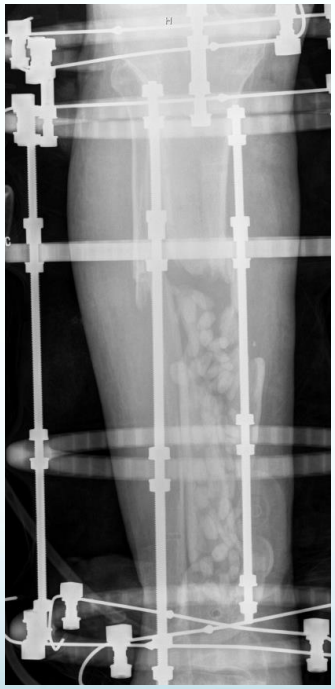


Basic Principles of Osteomyelitis Surgery

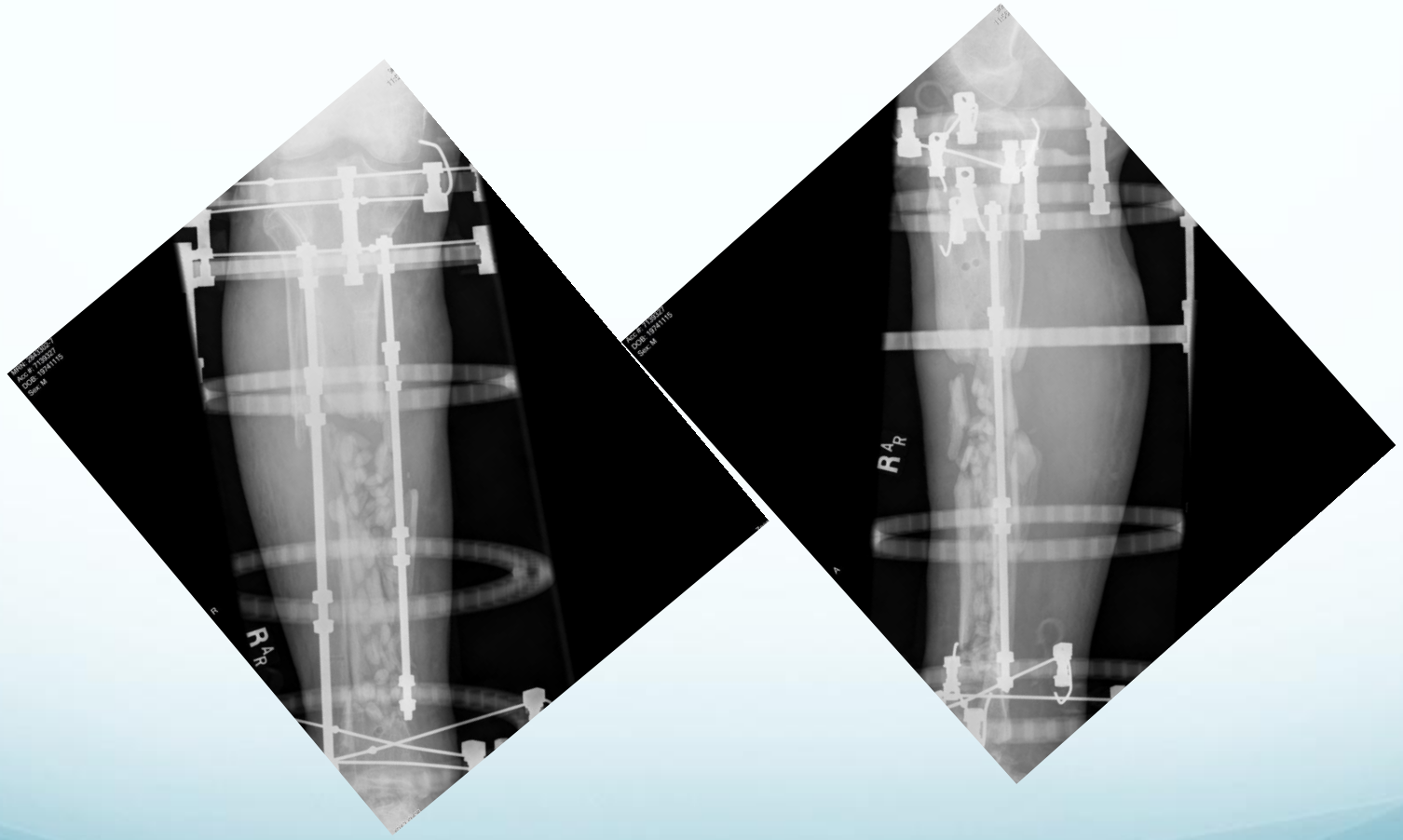
1. Excise ***ALL*** devitalized/infected bone and soft tissue.
2. Manage the dead space.
3. Obtain a healed soft tissue envelope.
4. Reconstruct the bone defect.

"Climb the Nonunion Ladder"

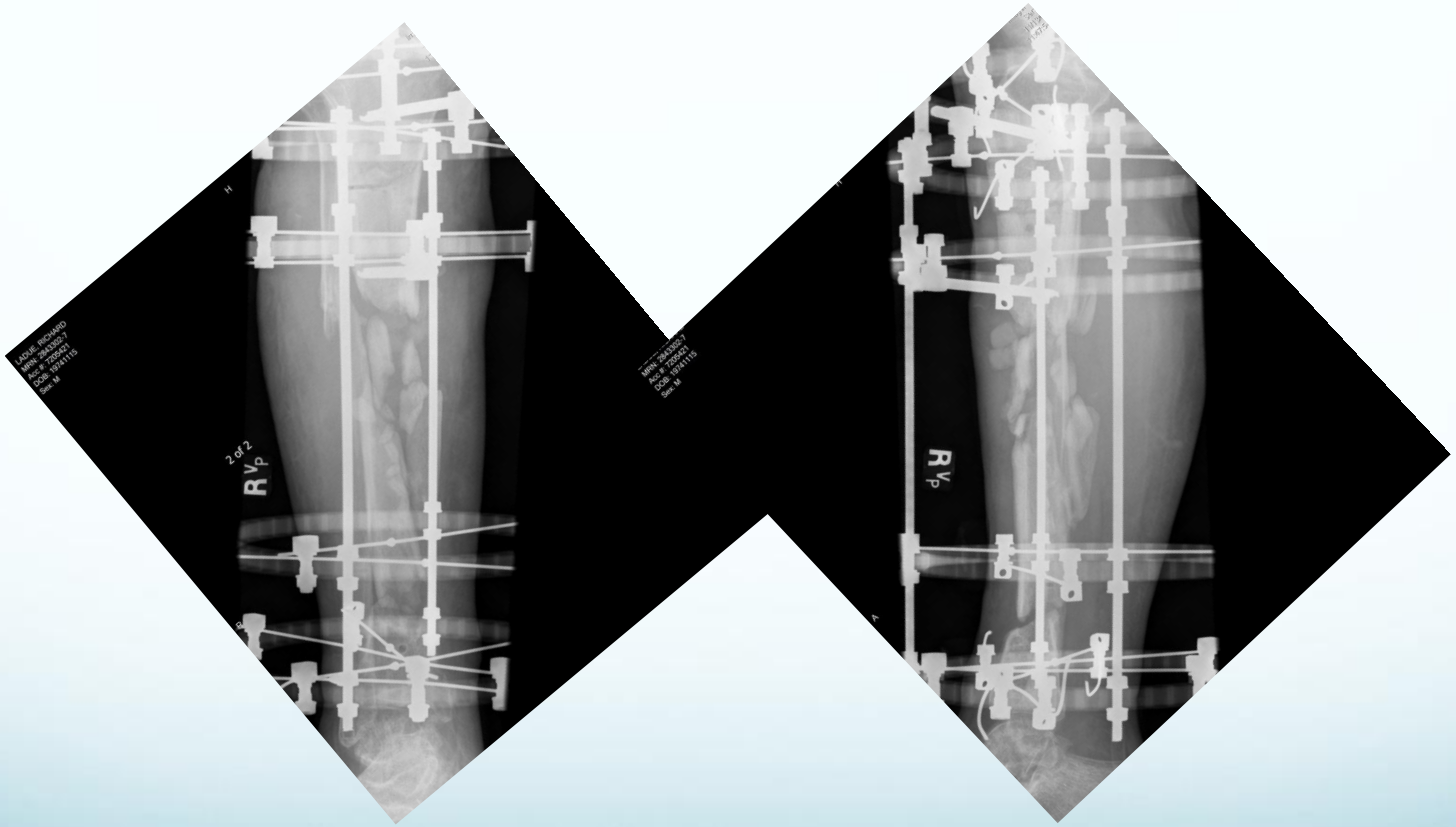
Eradicate regions of Cierny-Mader Type 1, 3, and 4 osteomyelitis



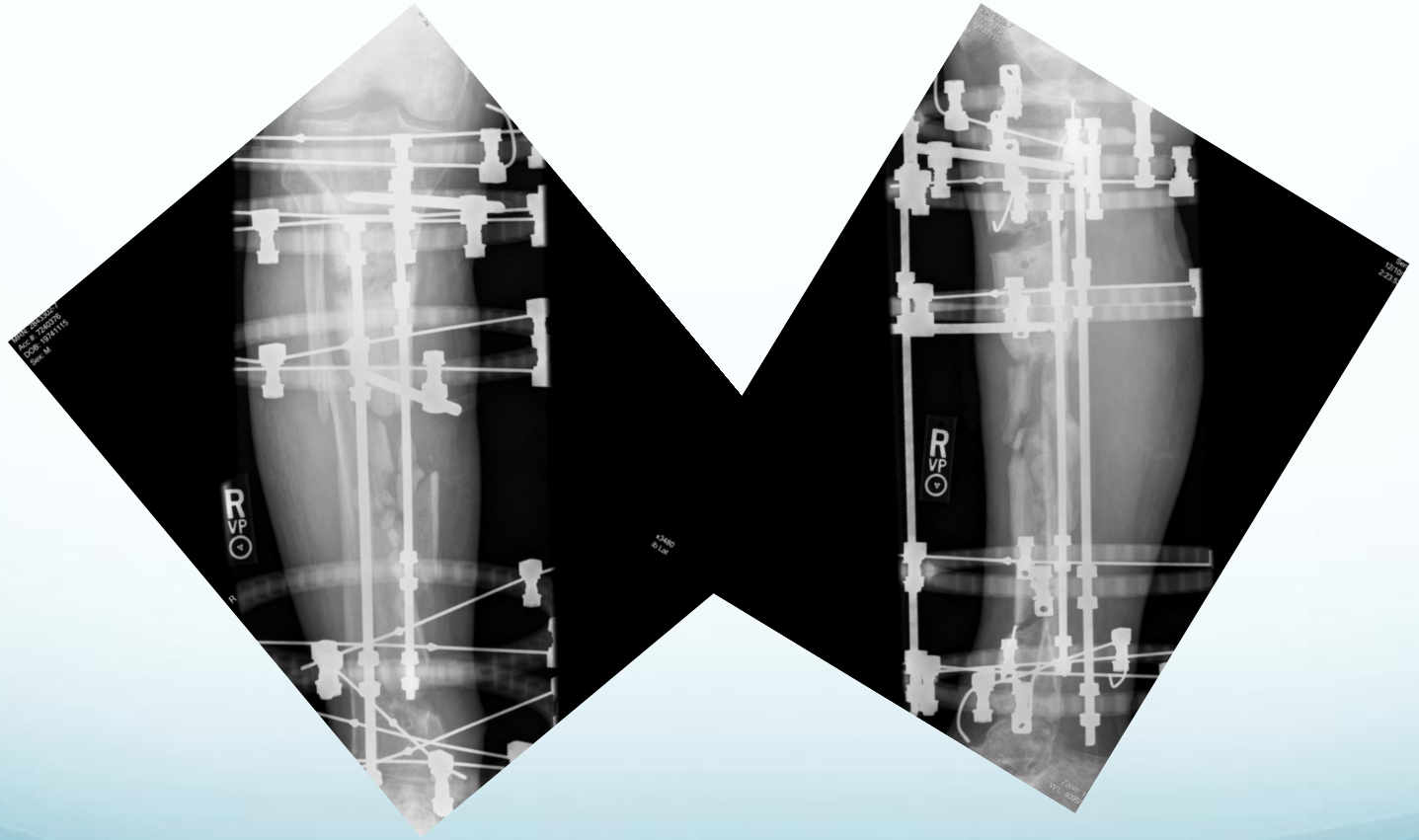
RL: Following Debridement and Stabilization



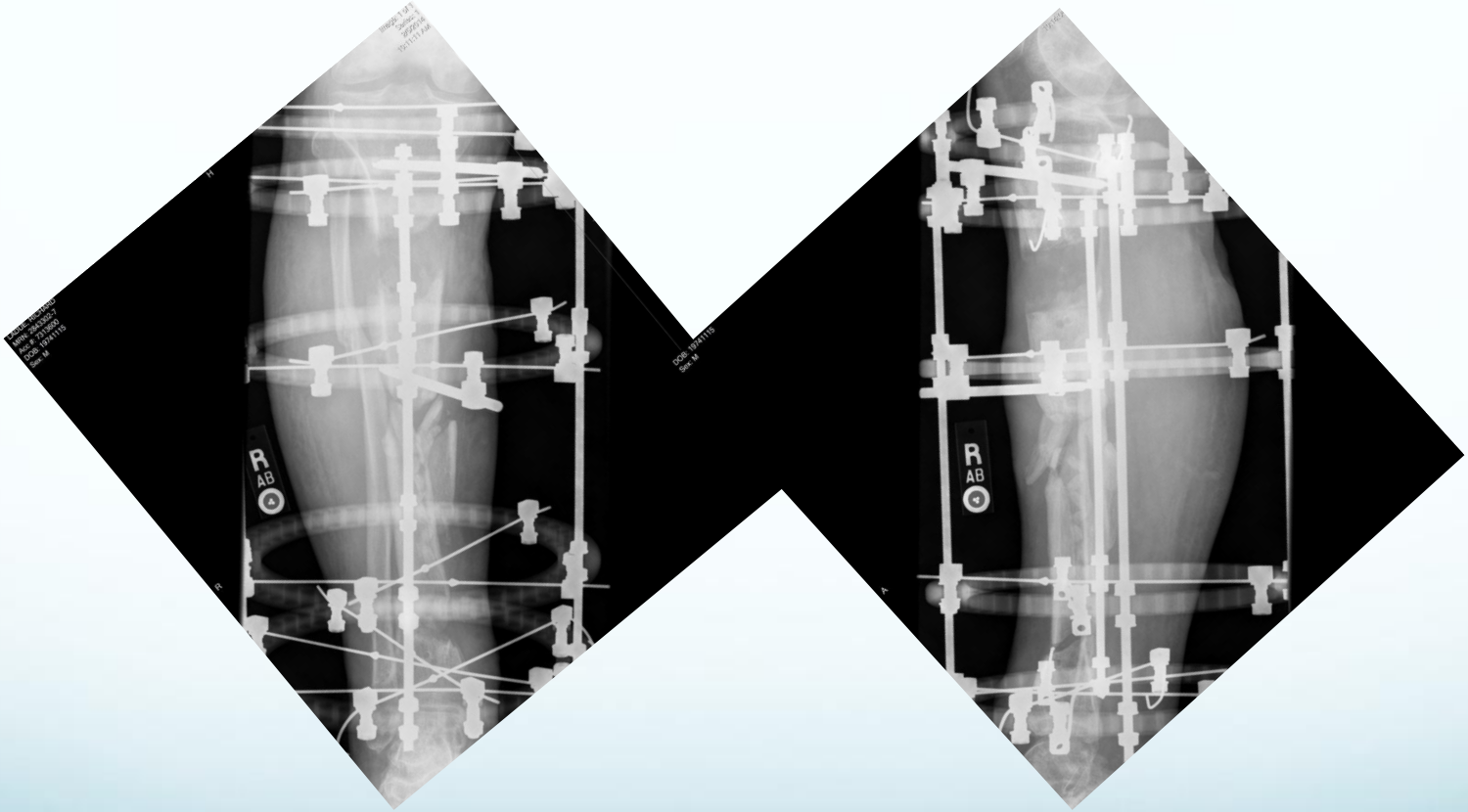
RL: Remove Proximal Beads, Begin Bone Transport



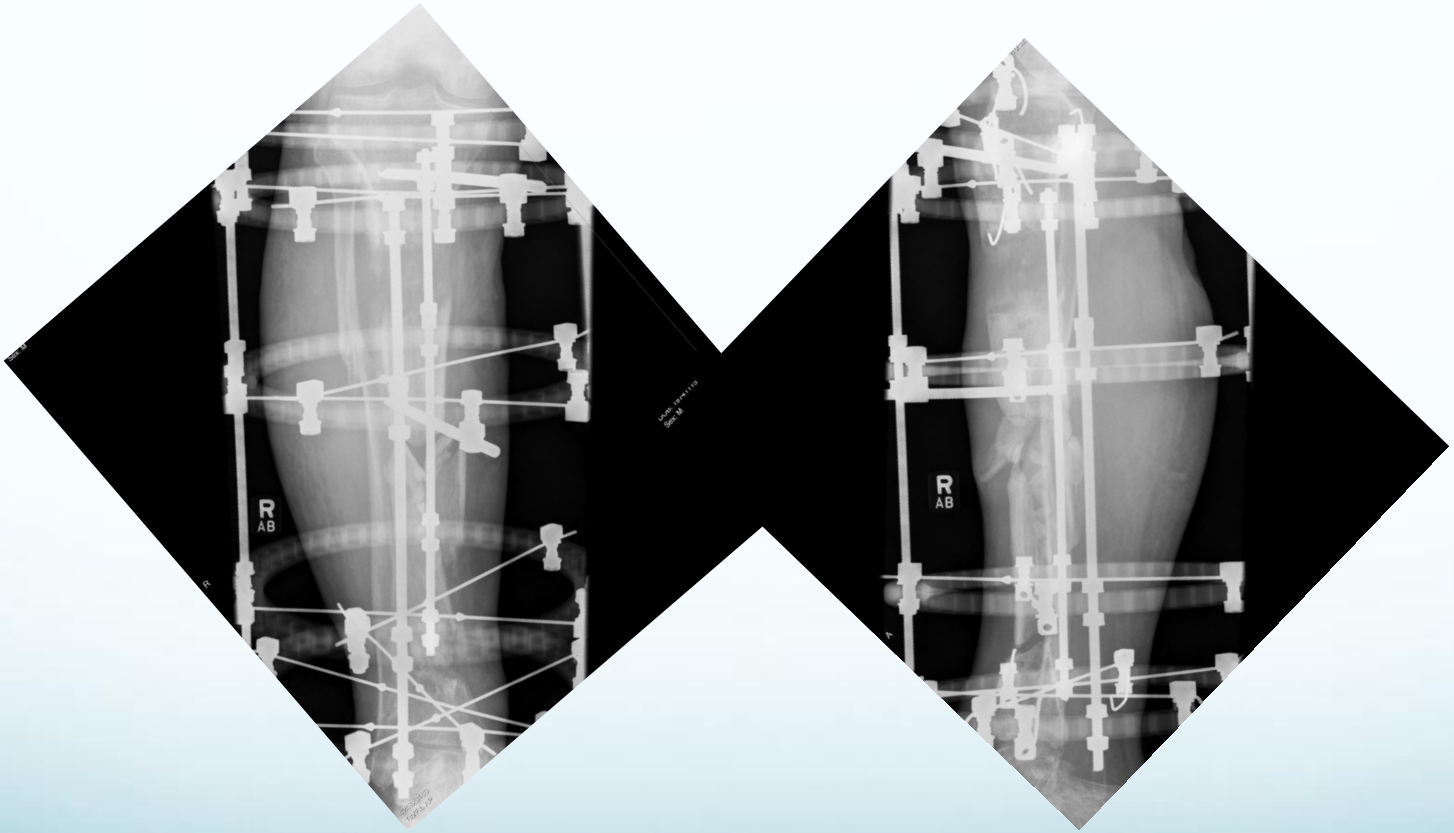
Begin Bone Transport



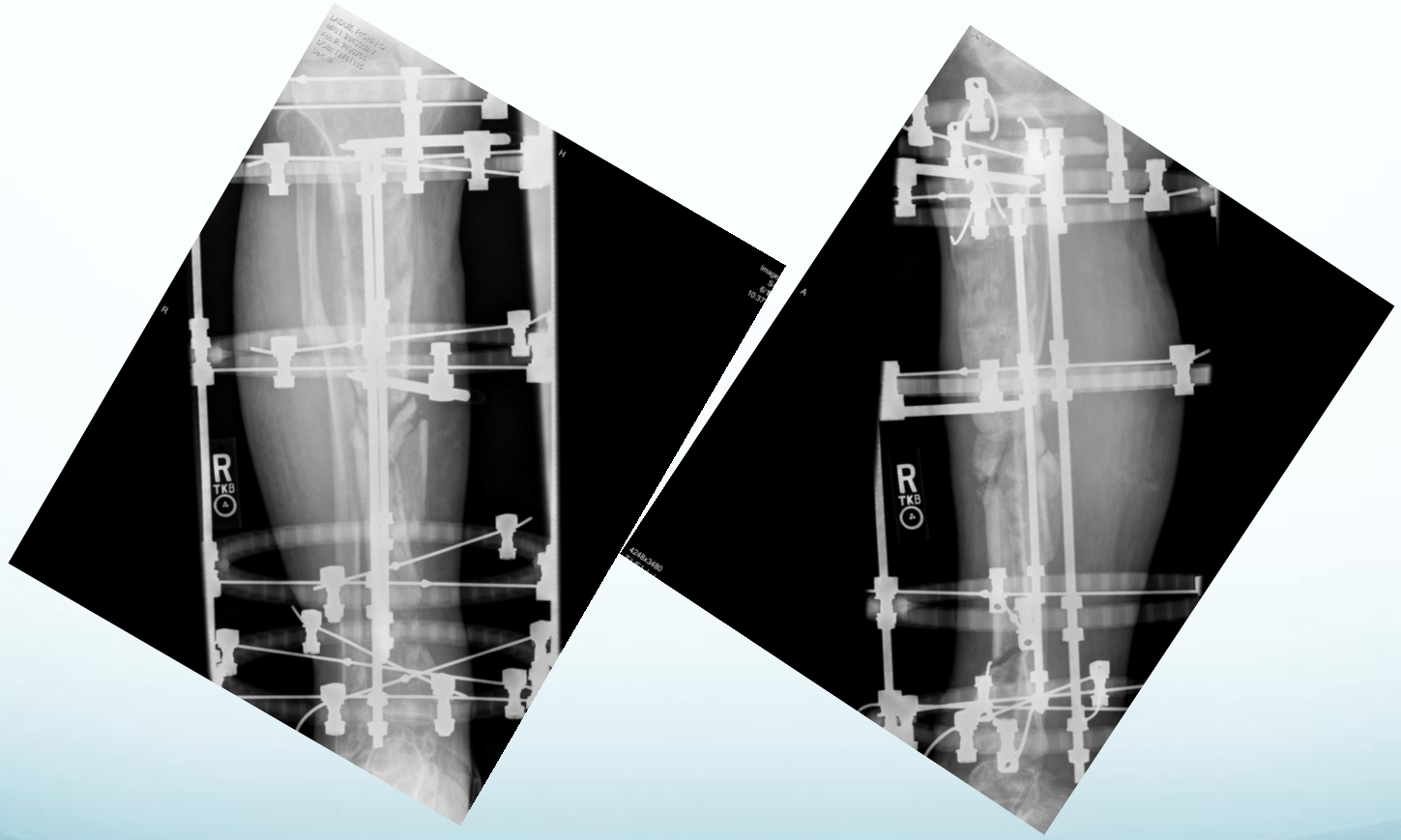
Bone Transport



End of Bone Transport

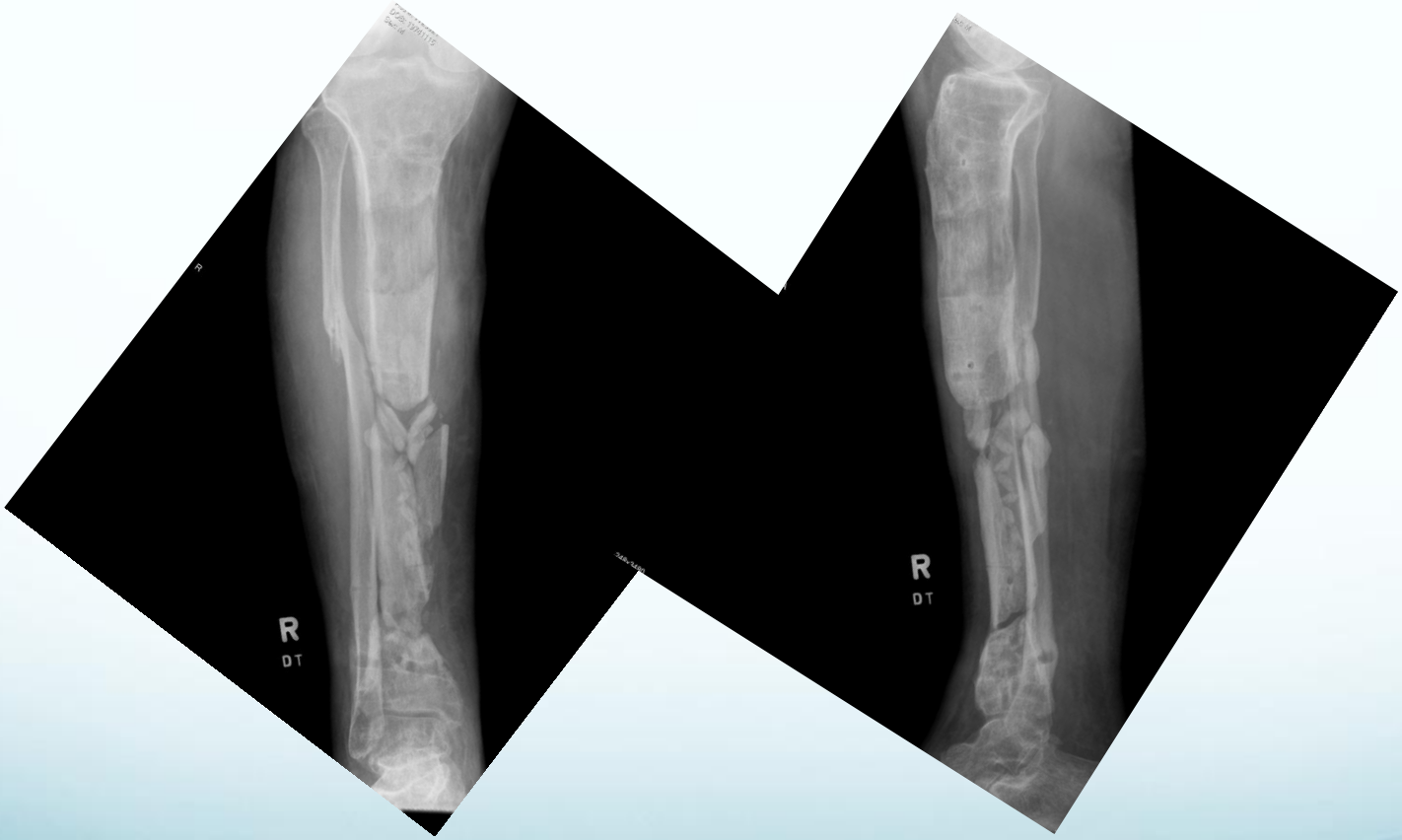


Bone Maturation



Bone Maturation

Following Frame Removal

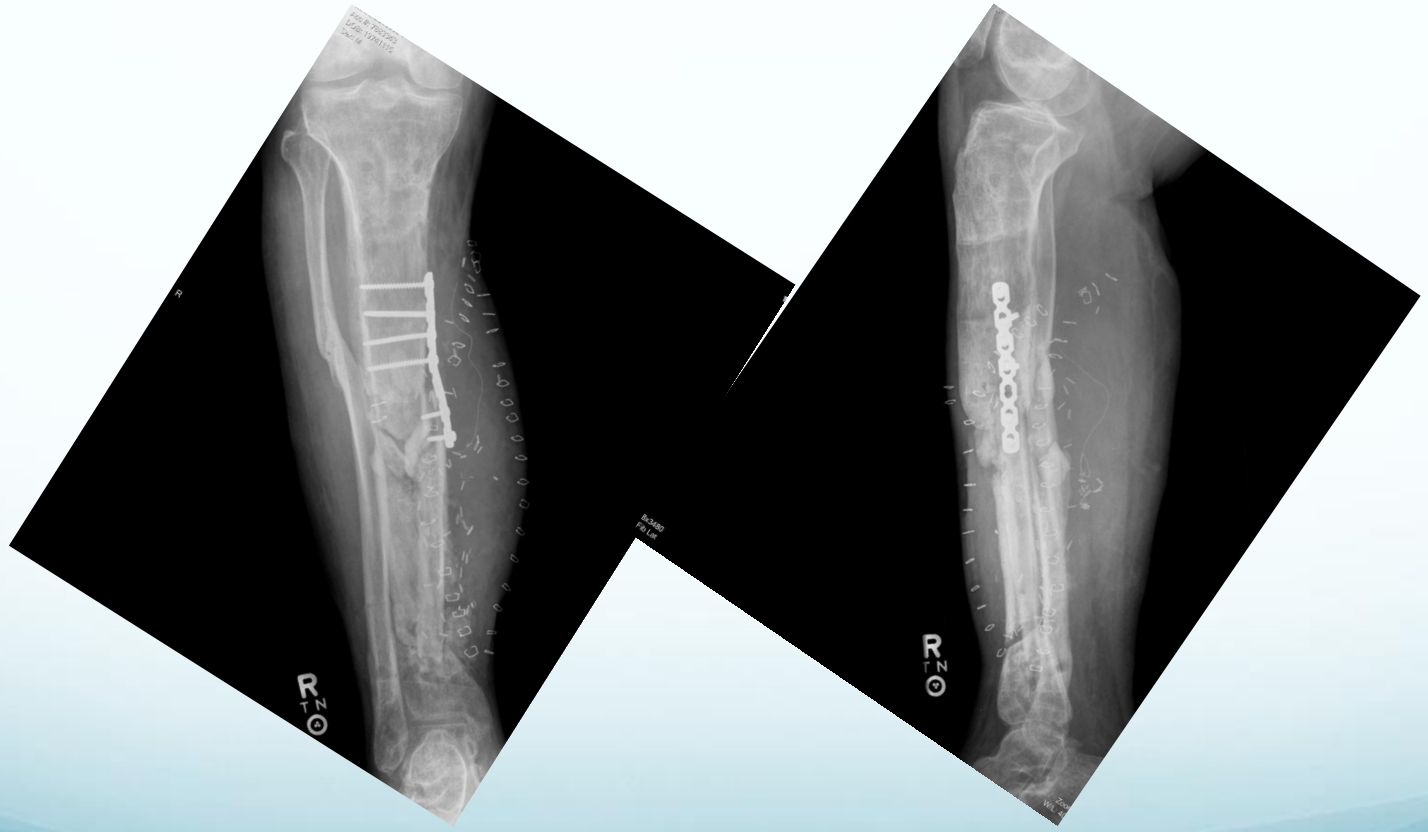


Now What??

- Living bone
- Improved soft tissue envelope
- Segmental noninfected nonunion

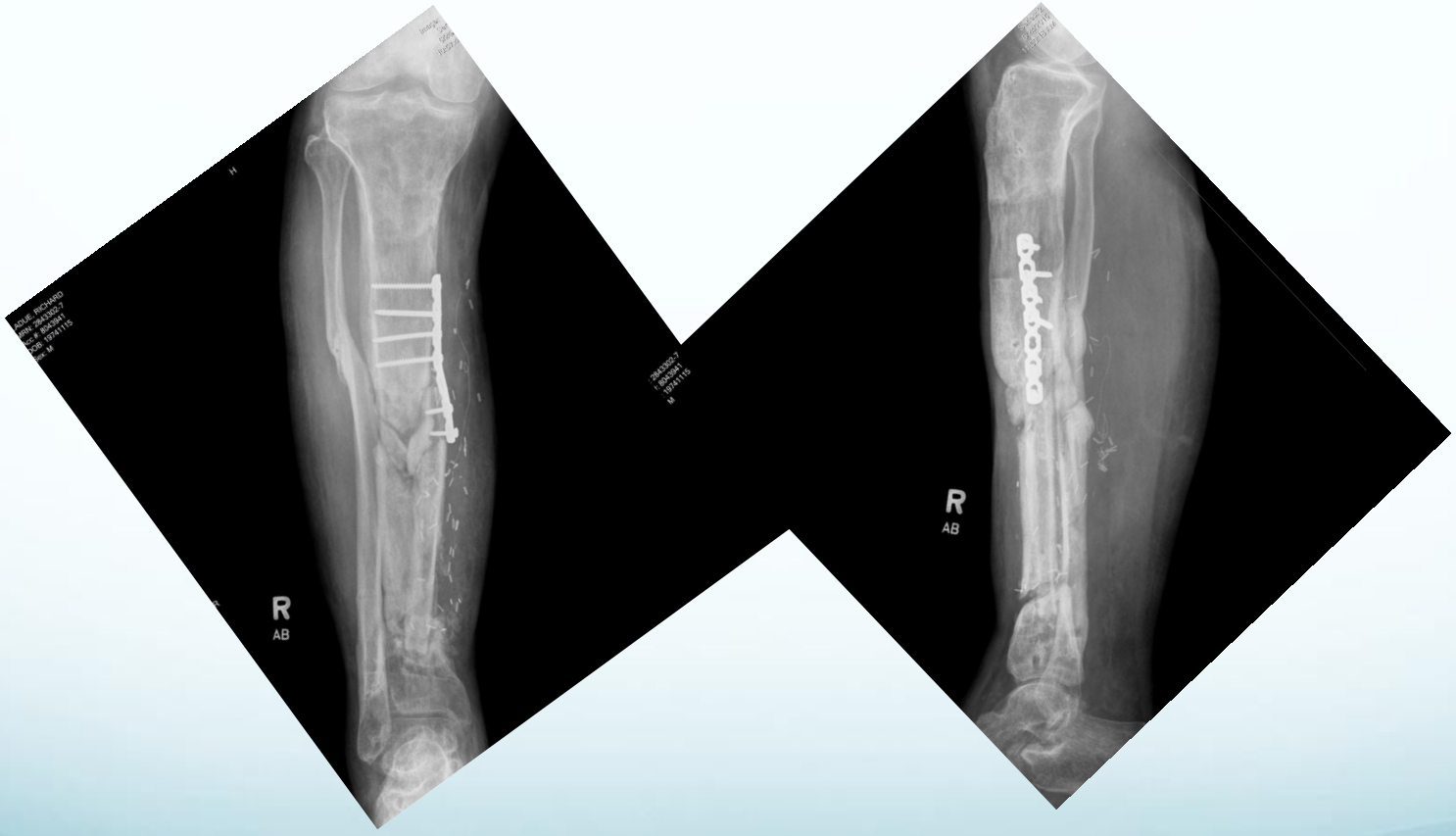
Climbing the Ladder

ICBG with inlay Free Fibula

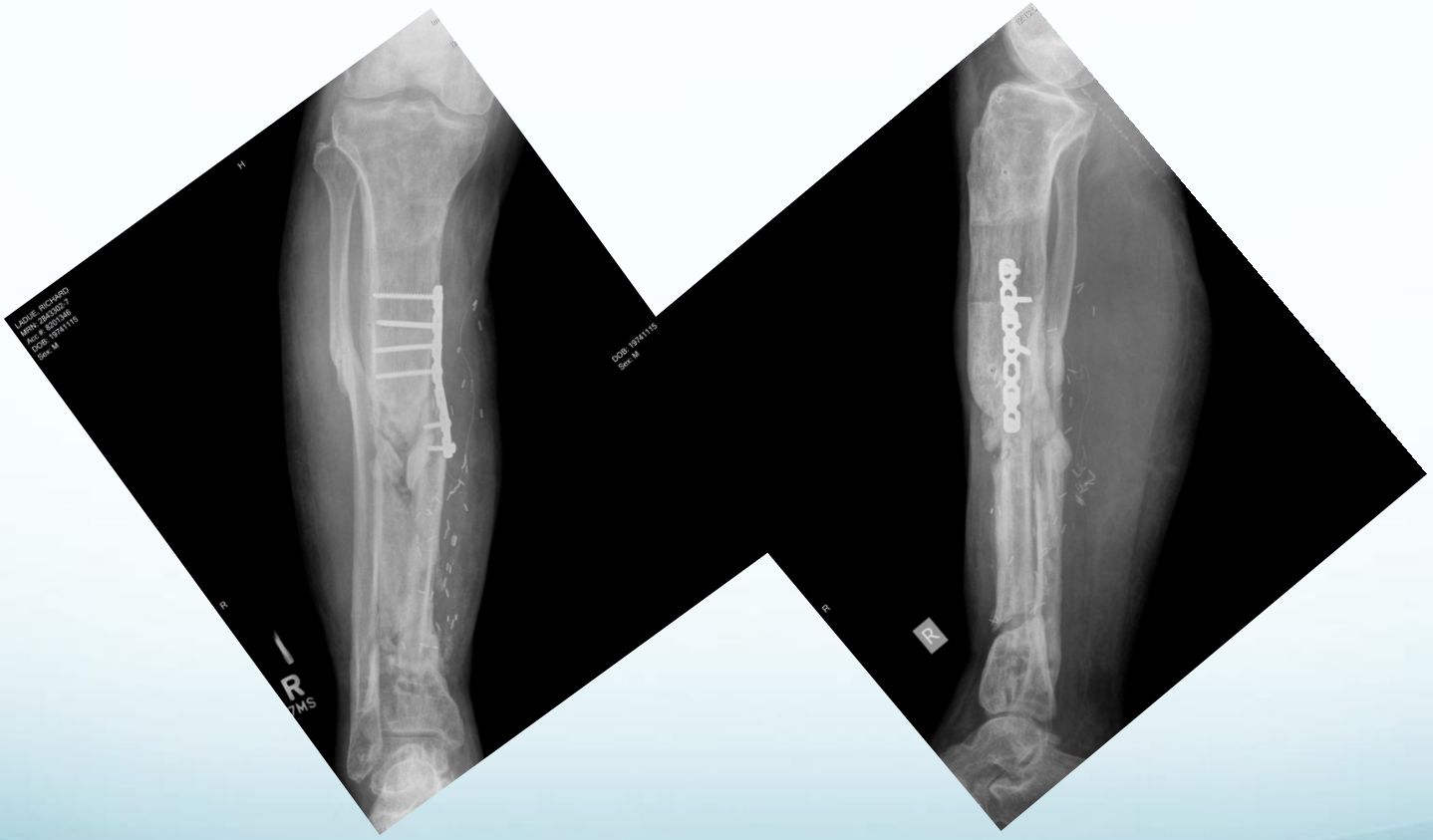


1 month following ICBG & Free Fibula

3 months following Free Fibula



6 month following free fibula, walking normally

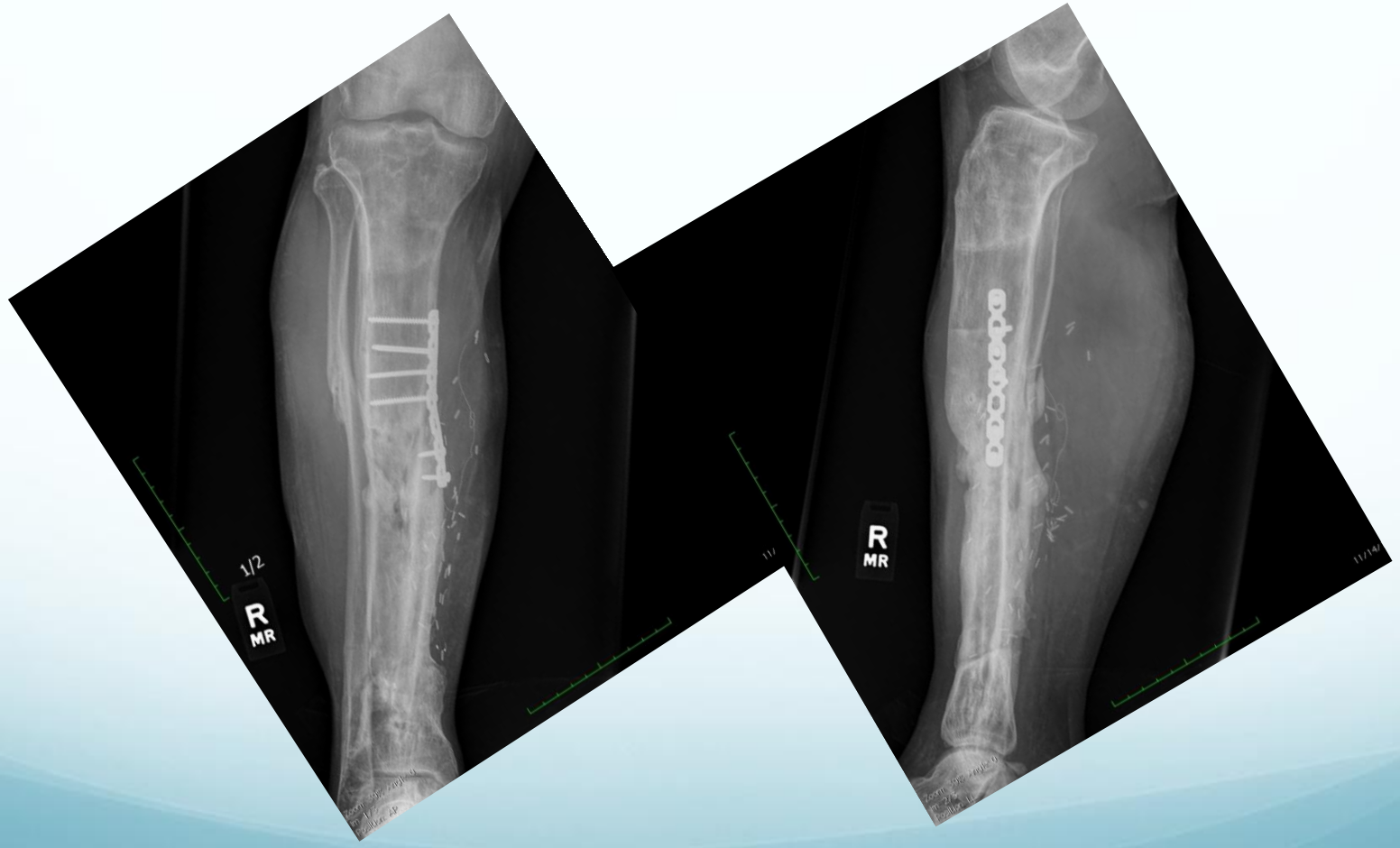


No pain, walking independently

10 months following distal site ICBG

10 months following free fibula/ICBG

3 years following free fibula, no limitations, working 50 hours/week as a trucker



Pictures of leg 3 years s/p free fibula & grafting

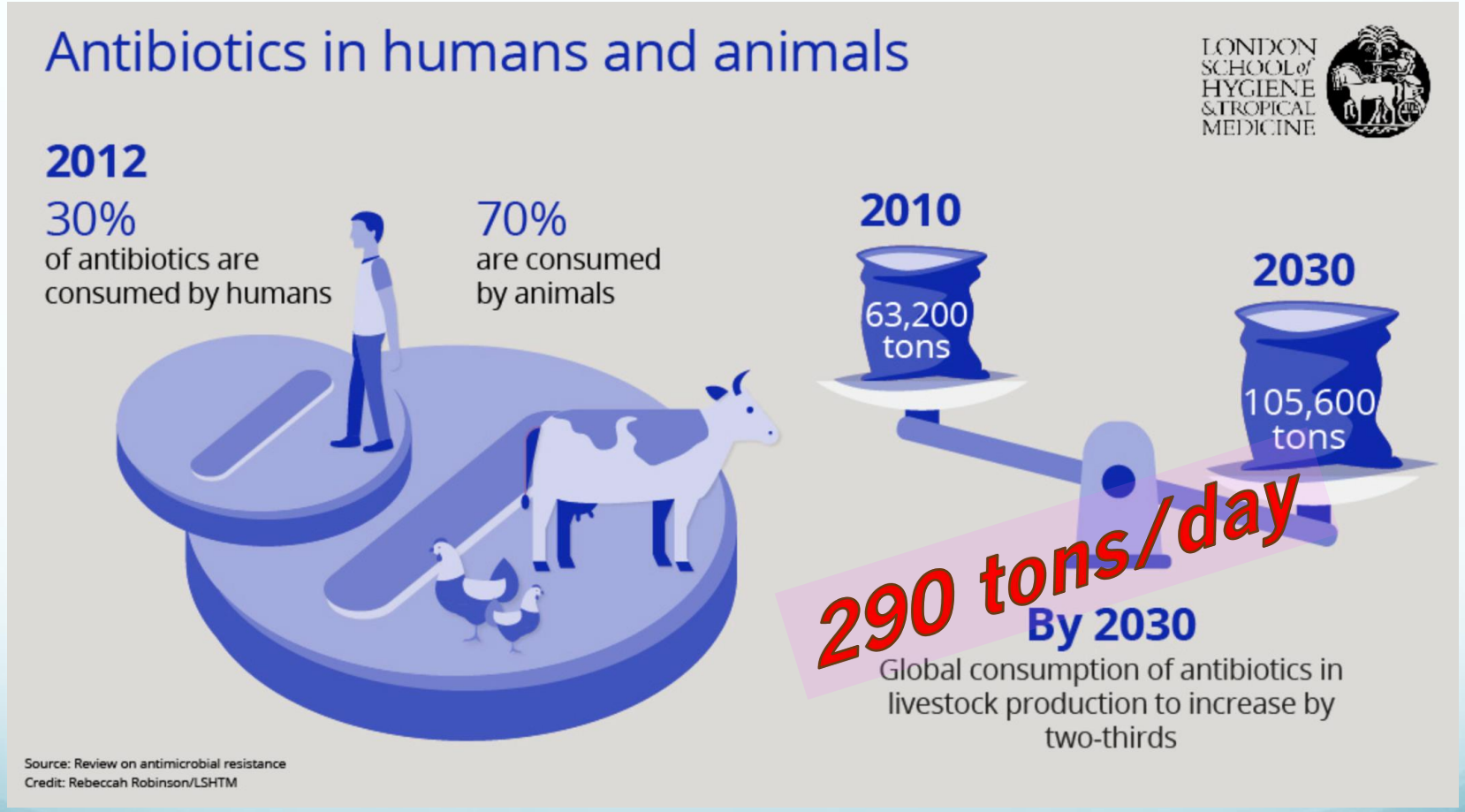
6 years post free fibula

- Talked to by phone, “Doc, I’m fine and can do everything. Got a new motorcycle. I don’t need to see you.”
- He remains working full time as a short-haul trucker. No real limitations by his description.

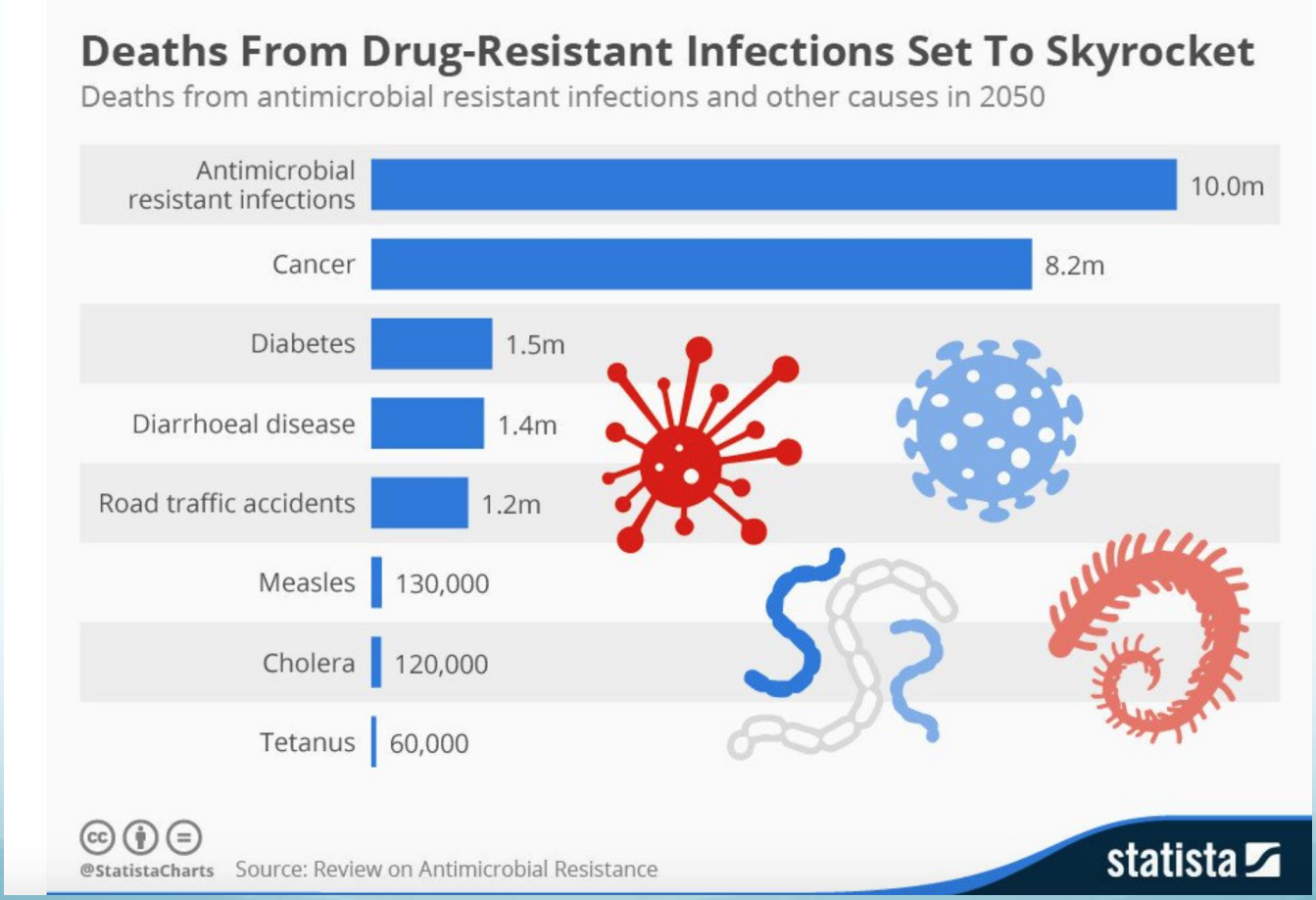
How much antibiotic is “consumed” in the U.S. ?

- A. 5 tons a day.
- B. 19 tons a year.
- C. 41 tons a year.
- D. 51 tons a year.
- E. 51 tons a day.

Projected Antibiotic Usage



Projected deaths as compared to other causes



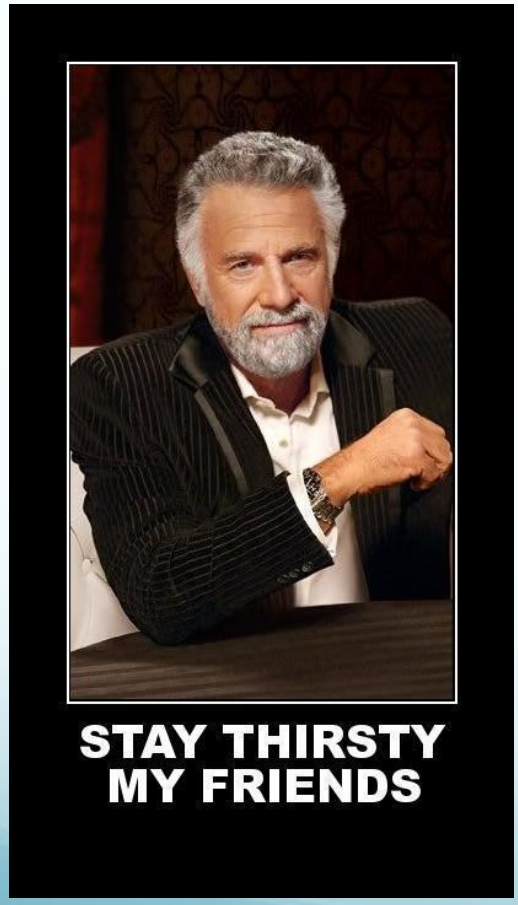
Diagnostic Technologies ..... What is New & Better

- DNA/RNA Sequencing
  - Involves some component of PCR with sequencing.
  - Most focus on the ”constrained/constant” 16S ribosome.
  - Undoubtedly the future.
  - Seems to be a problem with sampling technique ..... Fluid vs. Tissue.
  - ***All are not equal.***
  - ***We are definitely not there yet.***

Infection Following ORIF ..... Hardware Retention vs. Removal

- Early vs. Late ..... Is the biofilm/sessile growth phase present.
- Chronic
  - Cierny-Mader Stage 1 or 2: Retention is reasonable with suppression until healing.
  - Cierny-Mader Stage 3 or 4: Will predictably fail; ***"don't kick the can down the road".***

Thanks to those before me



My Mentors & Teachers

- Robert B. Gordon, MD
- Harry J. Buncke, MD
- George Cierny, MD
- Steven Mathes, MD
- Leonel Saenz, MD
- Richard Maurer, MD
- William Murray, MD
- James O. Johnston, MD
- Michael W. Chapman, MD
- Lorraine Day, MD