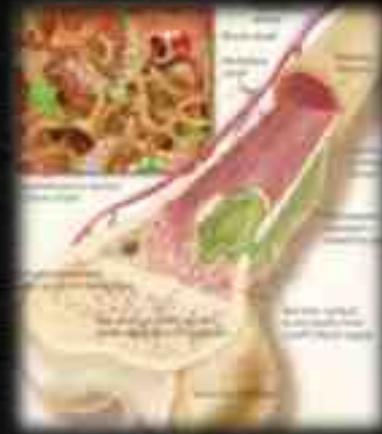


# CHRONIC OSTEOMYELITIS IN CHILDREN

## EVALUATION AND MANAGEMENT



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# INTRODUCTION

- Chronic osteomyelitis
  - A daunting challenge to orthopaedic surgeons
  - Often described as a disease that can never truly be cured
- 10 to 30% of acute haematogenous osteomyelitis → chronic osteomyelitis
- Socio-economically underdeveloped regions → high incidence of osteomyelitis in childhood.

Immunosuppression,

Malnutrition

High incidence of  
trauma

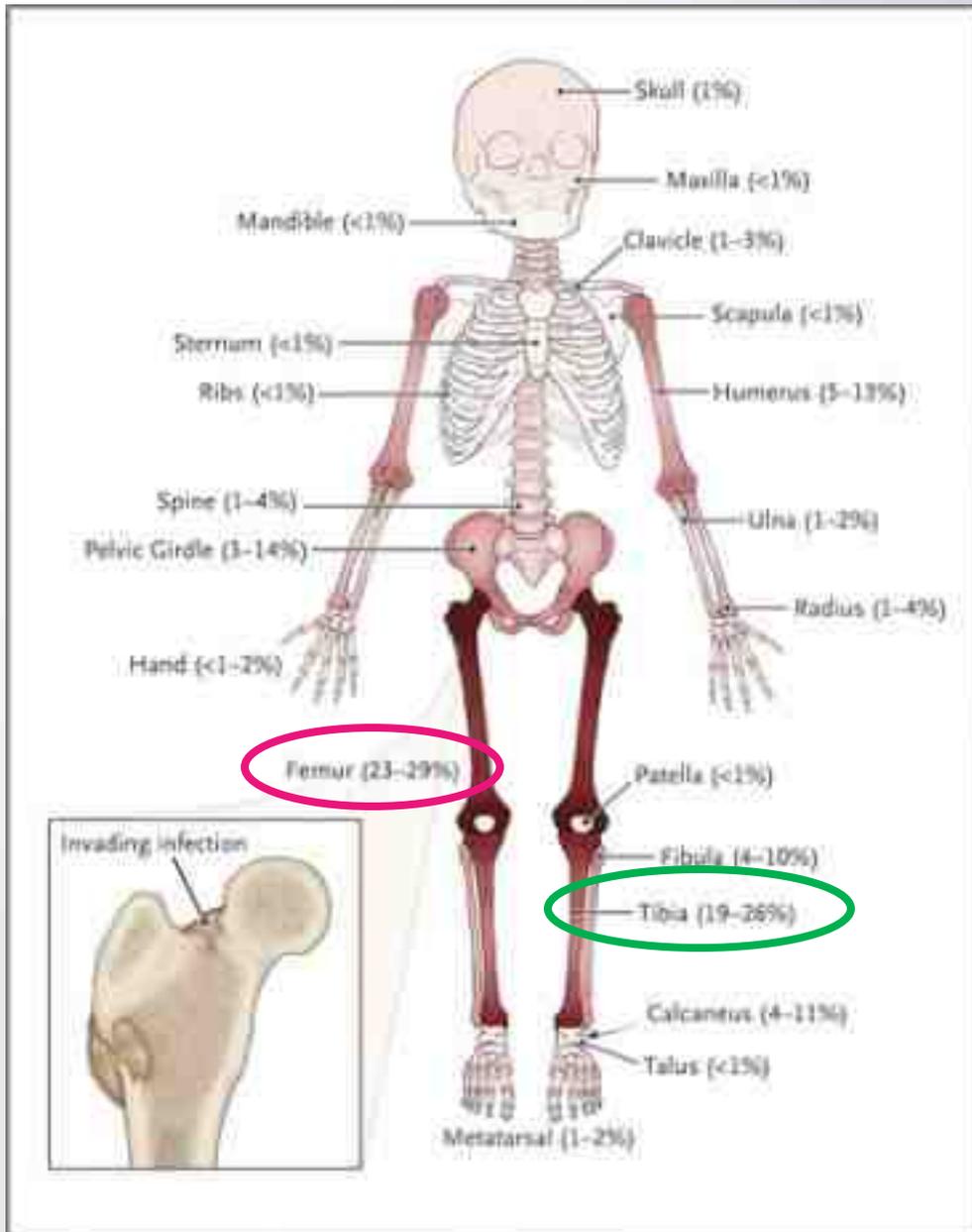
# EPI DEMI OLOGY



- Open Fracture
- Surgical treatment of CF
- Infection post arthroplasty
- Revision
- Second revision
- Overall implantation

- Open fractures (3–50%)
- The surgical management of closed fractures may (1–5%)
- Primary hip or knee replacement (0.5–2%)
- Revision surgery (5%)
- Second stage revision for periprosthetic infection (20%)
- Overall complication of orthopaedic cases during the life-time of the prosthesis or implant (5%)

# EPIDEMIOLOGY



# DEFINITION

## Chronic osteomyelitis

- Long-standing infection of the bone characterized by persistence of microorganisms, presence of sequestrum, low-grade inflammation, and fistulae

- This definition originated from

Observation acute  
haematogenous  
osteomyelitis

Left untreated

Formation of  
necrotic segments  
of bone

a source of on-  
going or chronic  
infection

# Pathophysiology

Inadequately treated hematogenous acute osteomyelitis or more commonly from a contiguous source of infection

Inflammatory process causes obliteration and compression of the vascular channels.

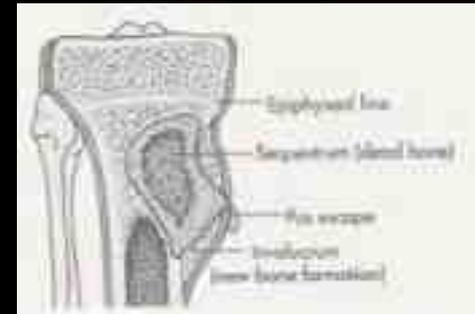
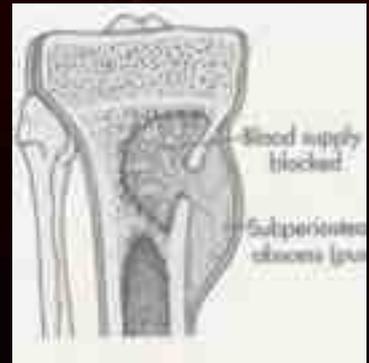
Part of the bone undergoes necrosis → sequestrum

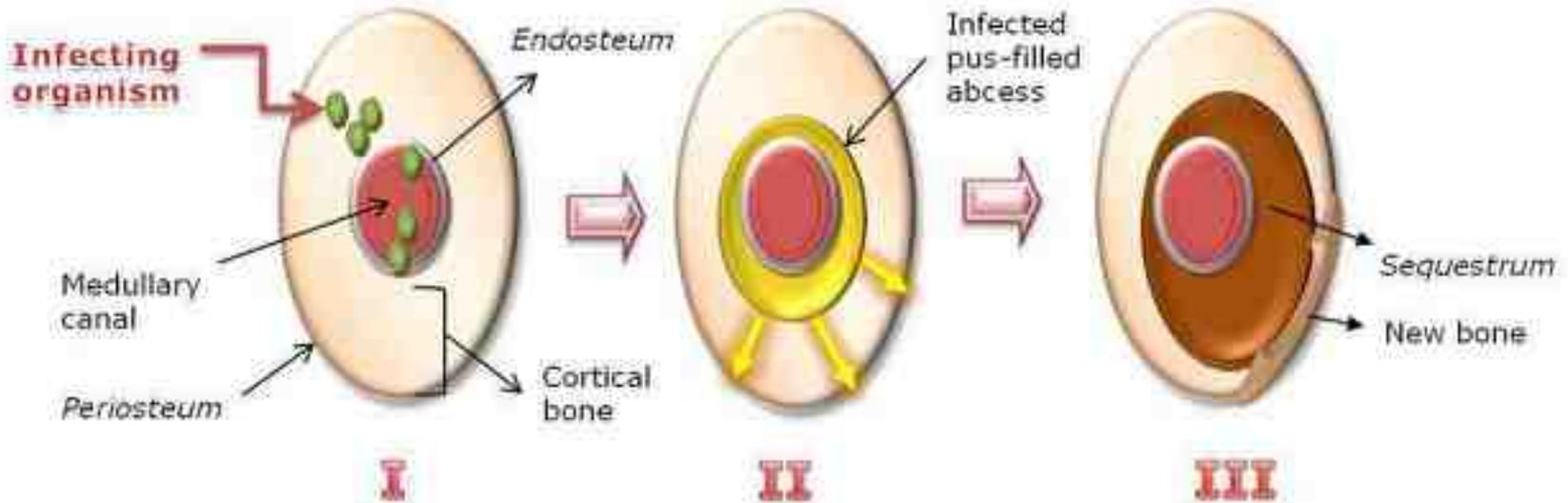
Destruction of bone, and microorganisms propagate within the destroyed bone.

New bone is formed around the sequestrum from the intact periosteum and endosteum → involucrum.

The involucrum is perforated by openings known as cloacae

Chronic Osteomyelitis

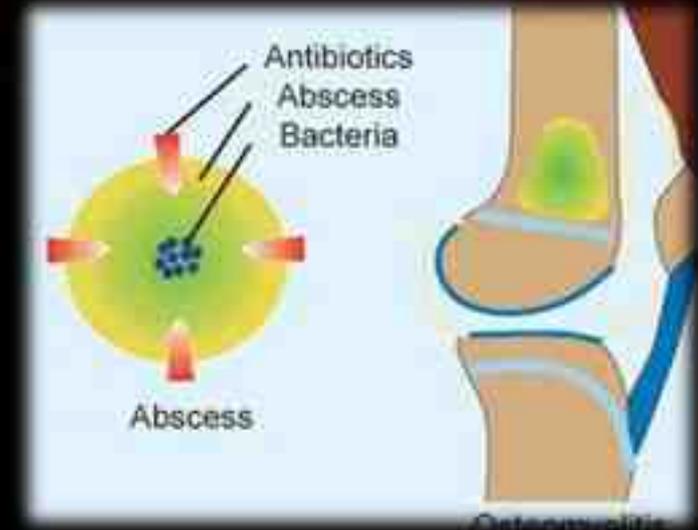
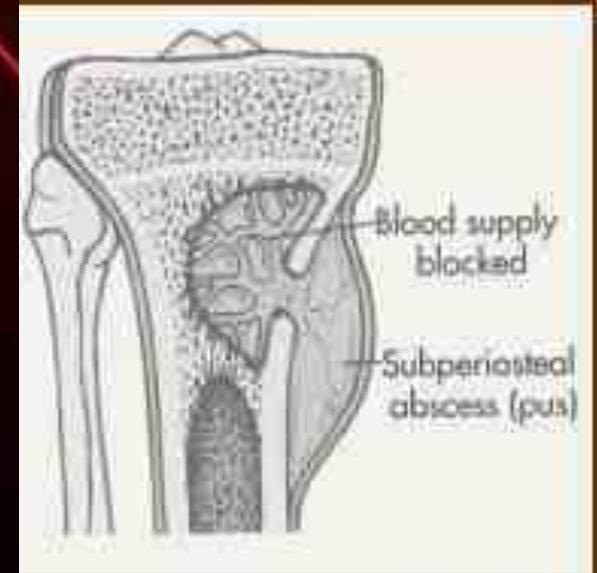




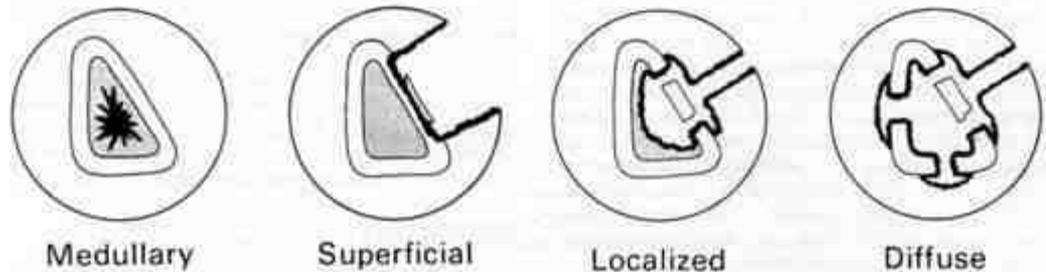
- I - A large inoculum of bacteria reaches the medular channel
- II - (Acute state) Pus resulting from inflammatory response spreads into vascular channels
- III - (Chronic state) Vascular channels are compressed and obliterated by the inflammatory process, and the resulting ischaemia also contributes to bone necrosis

# What are the causes of chronic osteomyelitis?

- **Decreased blood flow** as a result of initial insult or operative procedure diminishes the healing capacity
- **Antibiotics cannot penetrate** though the infected and necrotic area and **sequestrum** produces an area of lowered vascularity
- **Resistance of organisms to antibiotics.** Organism forms a biofilm around the sequestrum or implant
- **Inadequate surgical debridement.**



# Classification



**Table 1** Cierny-Mader staging for long-bone osteomyelitis<sup>21</sup>

Stage	Anatomic type	Description	Causation	Recommended treatment
1	Medullary		Infection following intramedullary nailing	Removal of infected implant and intramedullary debridement
2	Superficial	Medullary canal and full thickness of cortex not involved	Chronic wound with colonization and focal involvement of underlying bone	Removal of affected bone till viable vascular bone
3	Localized	Full-thickness cortical involvement, medullary spread, stable uninvolved segment of cortex at same level	Following direct trauma with devascularization and seeding of bone	Excision of infected tissue without compromising stability of bone
4	Diffuse	Involvement of entire axial segment leading to segmental defect on excision	Major devascularization with colonization	Resection with reconstruction of defect

**Table 2** Physiologic class of host

Type	Status	Underlying factors	Treatment recommendation
A	Normal physiologic response	Minimal or none, local or systemic factors	Surgery as appropriate
B (local)	Local impairment	Cellulitis, prior trauma, surgery, presence of scar, or sinus	Address healing potential of local tissue
B (systemic)	Systemic factors	Coexistent diseases like diabetes, immunocompromise, vascular disease, hypoproteinemia	Treatment of correctable metabolic and nutritional abnormality
C	Severe infection	Severe systemic and local compromise	Treatment worse than disease, may need amputation

# ANATOMIC CLASSIFICATION OF CHRONIC OSTEOMYELITIS IN CHILDREN WITH TREATMENT RECOMMENDATIONS

Penny JN. Children's Orthopaedic Surgery and Rehabilitation in Africa. AAOS ICL 228; 2004.

## Diaphyseal Osteomyelitis

- **Type I** : *"typical" osteomyelitis,*
- Type II : *"atrophic"*
- **Type III** : *"sclerotic"*
- Type IV : *"cortical"*
- Type V : *"multiple walled-off abscesses"*
- Type VI : *"multiple microabscesses"*



## Metaphyseal Osteomyelitis

- appears as a single, or multiple, walled-off abscesses with or without a sclerotic margin. Sequestra are uncommon
- a limited saucerization and curettage should be sufficient



# Diphyseal Osteomyelitis

## Type I “*typical*” osteomyelitis

- A well-defined sequestrum and an involucrum
- → sequestrectomy/ debridement followed by protection of the limb until the bone has been reconstituted

## Type II “*atrophic*”

- Failure of the involucrum to form
- → Waiting at least 3 to 6 months to see if the periosteum will respond. If there is no response, then plans can be made for reconstruction, whether by grafting or bone transport.



# Diaphyseal Osteomyelitis

## Type III “sclerotic”

- Fusiform, dense sclerotic healing reaction generated by the periosteum
- → Debridement through a cortical window

## Type IV “cortical”

- Localized sequestrum within the cortex of the involved bone
- → Sequestrectomy through a localized cortical window



# Diaphyseal Osteomyelitis

## Type V *"multiple walled-off abscesses"*

- *involves one or more well-defined lucencies within the involucrum*
- → explored and debrided through a cortical window

## Type VI *"multiple microabscesses"*

- *Similar to type V based on both appearance and proposed etiology, but smaller and more numerous lucencies within the involucrum.*
- → a longitudinal partial diaphysectomy with debridement



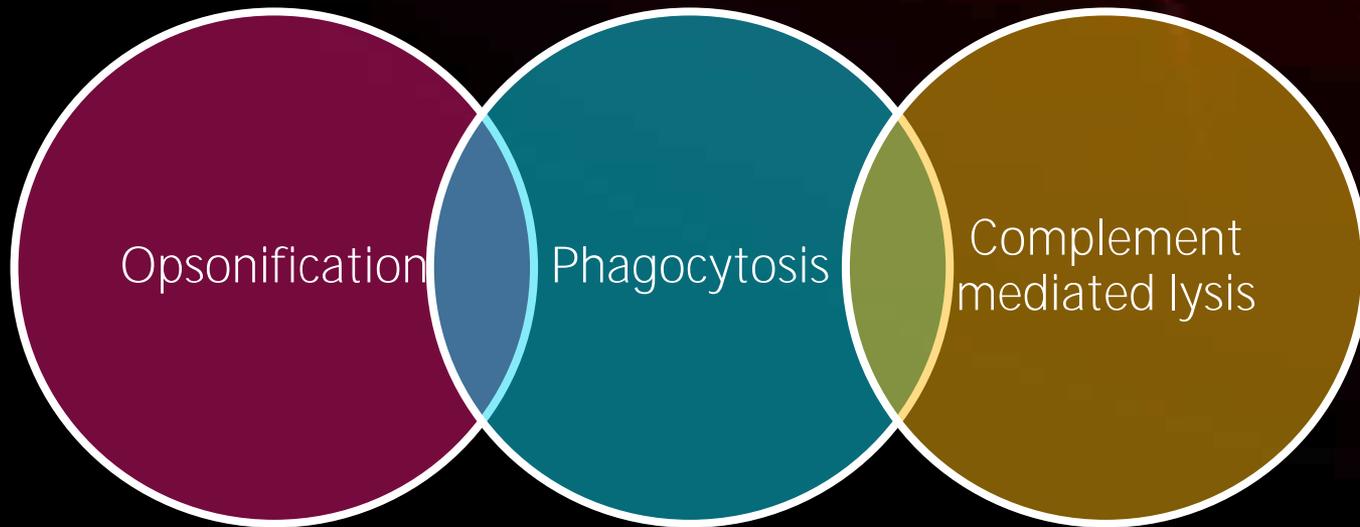
# Most common isolated microorganisms in osteomyelitis are related to age and susceptibility factors

Age	Etiology
Newborn babies	<i>S. aureus</i> , <i>Enterobacter</i> spp., <i>Streptococcus</i> (group A and B)
Children	<i>S. aureus</i> , <i>Enterobacter</i> spp., <i>Streptococcus</i> (group B), <i>Haemophilus influenzae</i>
Adults	<i>S. aureus</i>
Susceptibility factors	Etiology
Injectable drug users	<i>S. aureus</i> , <i>P. aeruginosa</i> , <i>Serratia marcescens</i> , <i>Candida</i> spp.
Immunocompromised	<i>S. aureus</i> , <i>Bartonella henselae</i> , <i>Aspergillus</i> spp., <i>Mycobacterium avium</i> complex, <i>Candida albicans</i>
Urinary infection	<i>P. aeruginosa</i> , <i>Enterococcus</i> spp.
Spinal column surgery	<i>S. aureus</i> , coagulase-negative staphylococci, aerobic gram-negative bacilli
Orthopedic fixation devices	<i>S. aureus</i> , coagulase-negative staphylococci, <i>Propionibacterium</i> spp.
Hospitalization (nosocomial source)	Enterobacteriaceae, <i>P. aeruginosa</i> , <i>Candida</i> spp.
Diabetes mellitus, vascular insufficiency, contaminated open fracture	Polimicrobial: <i>S. aureus</i> , Staphylococci coagulase negative, <i>Streptococcus</i> spp., <i>Enterococcus</i> spp., Gram-negative bacilli, anaerobes

- adapted from Lew, Waldvogel, 2004; Brook, 2008; McNally, Nagarajah, 2010; Chihara, Segreti, 2010; Jorge *et al.*, 2010; Zimmerli, 2010; Eid, Berbari 2012

# Defence Mechanism

- The host protective cellular layer with functional defence mechanisms

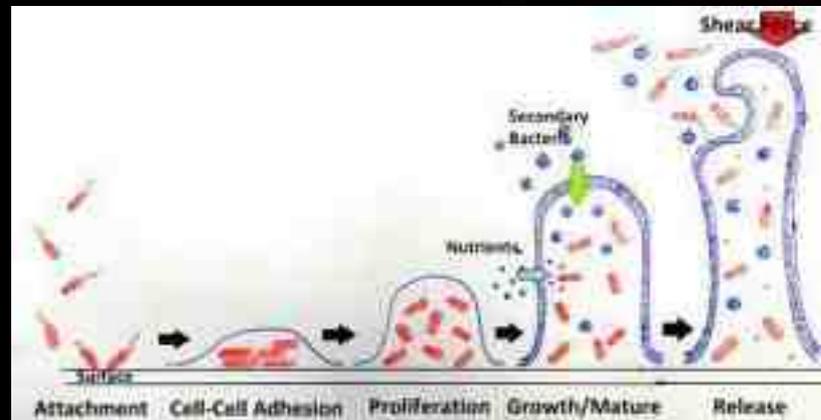
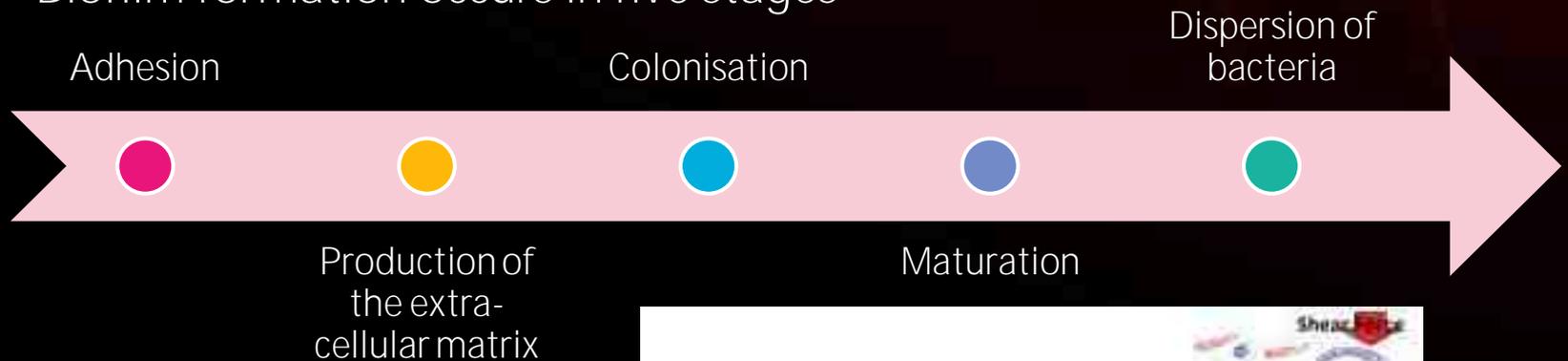


# Biofilm Formation

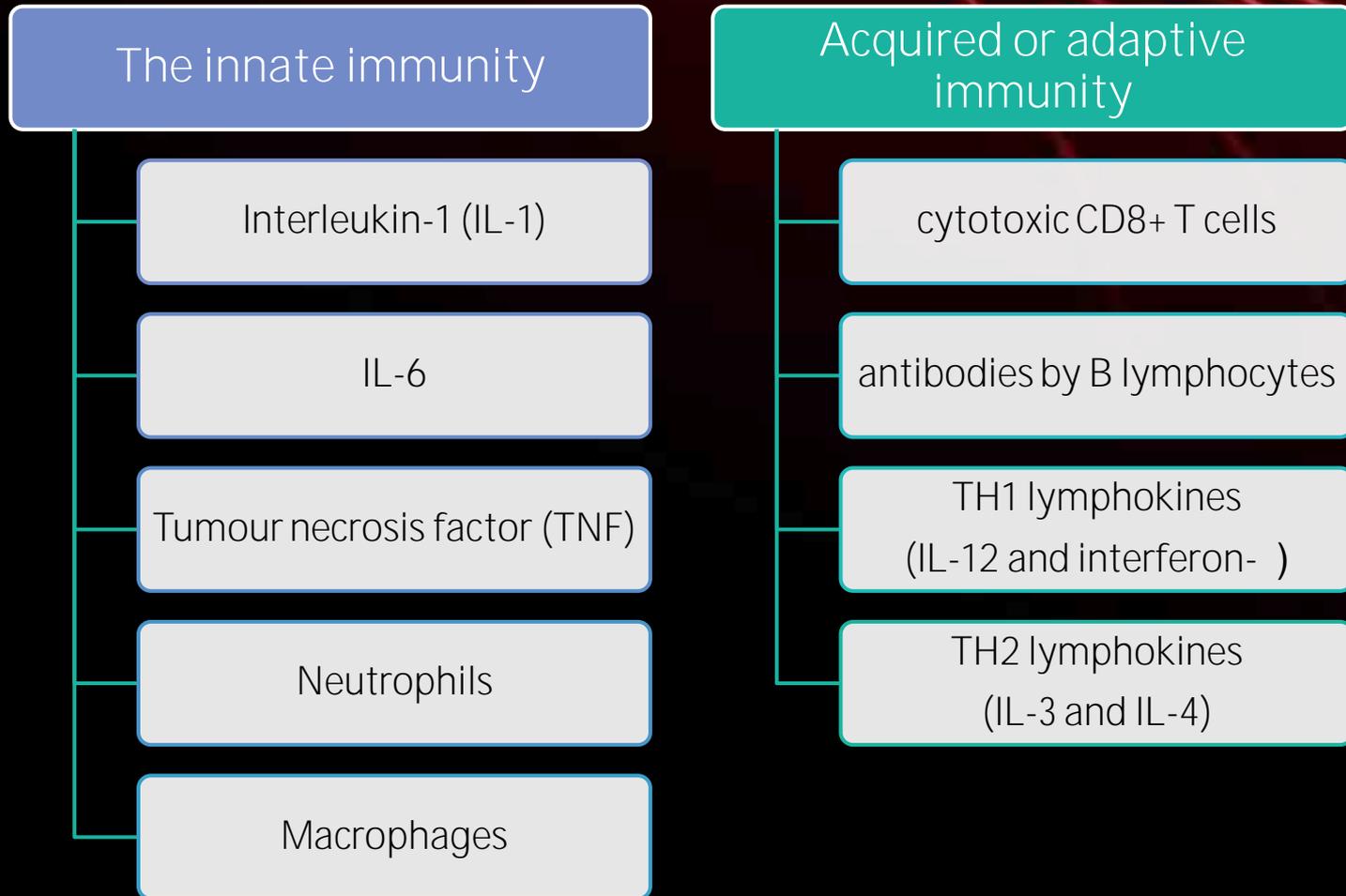
- The invading bacteria enter their default growth pattern and establish a biofilm.

A layer-like aggregation of microbial cells and extracellular polymeric substances attached to a substrate which provides an environment for the exchange of genetic material between bacterial cells

- Biofilm formation occurs in five stages

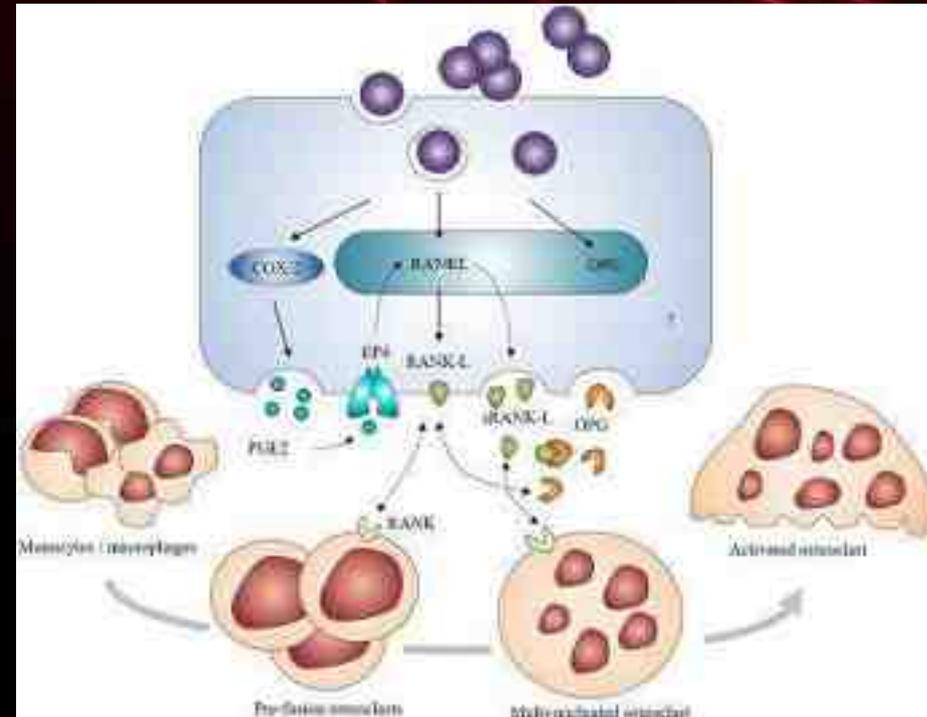


# The Host Response

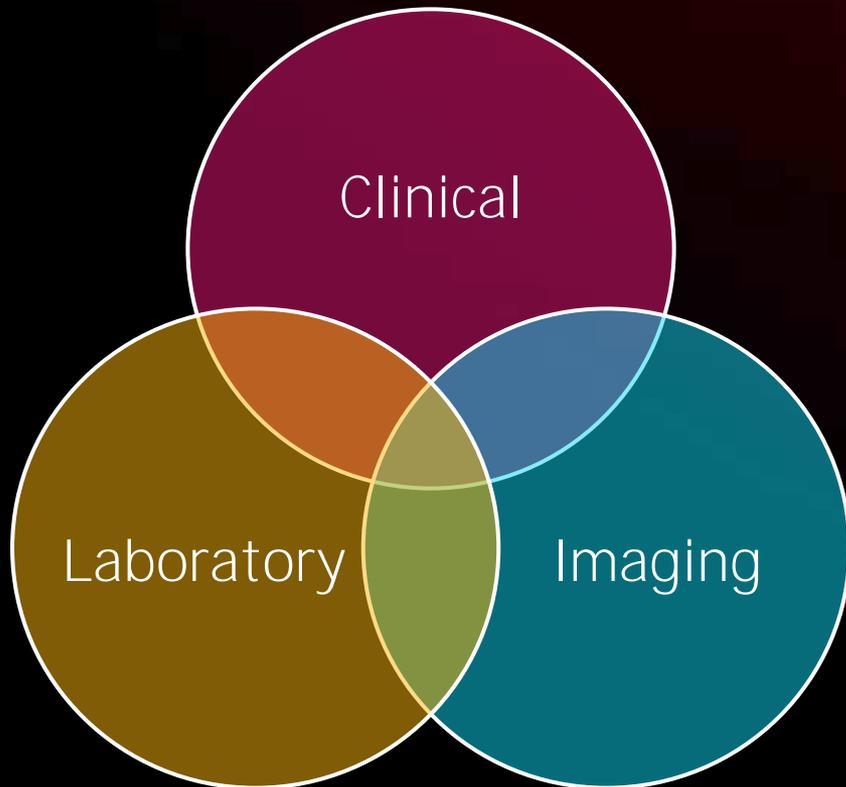


# The Role Of Osteoclasts

- Receptor activator of nuclear factor kappa-B ligand (RANKL) is a potent activator of osteoclasts and is produced by bone marrow stromal cells under normal conditions.
- In osteomyelitis certain bacterial components, such as lipopolysaccharide (LPS), result in the production of RANKL by a variety of cells (including activated T-cells) ultimately causing abnormal bone loss



# Diagnosti c



## Clinical signs

- Exposed bone
- Persistent sinus tract
- Tissue necrosis overlying bone
- Chronic wound overlying surgical hardware
- Chronic wound overlying fracture

Imaging studies (e.g., plain radiography, magnetic resonance imaging, bone scintigraphy) demonstrating contiguous soft tissue infection or bony destruction

## Laboratory evaluation

- Positive blood cultures
- Elevated C-reactive protein level
- Elevated erythrocyte sedimentation rate

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*NOTE: Items listed in order of decreasing diagnostic ability for osteomyelitis. If osteomyelitis is suspected, a bone biopsy with bacterial culture should be considered for definitive diagnosis.*

# Clinical evaluation

## ■ History

- ▣ Main complaint
- ▣ associated problems
- ▣ medical history
- ▣ Previous surgical history
- ▣ Prior therapeutic interventions

## ● Examination

- Local Pathology
  - sinus tracts
  - exposed bone
- Skeletal stability
- Condition of soft tissue
  - chronic wound over a fracture site or surgical implant
  - tissue necrosis overlying bone
- Vascularization
- Neurological status



# CHRONIC OSTEOMYELITIS

is often associated with

Angular or rotational deformity

Deformities of the adjacent joints.

Limb length discrepancy (LLD)

A deep cavity in the bone

A big sequestrum, which creates a big gap



# Imaging

## Ultrasound

- the presence of periosteal reaction or purulent collections.
- as a guide during deep aspiration of fluid collections for culture and sensitivity



## X-rays and CT

- useful in localising sequestra or cloacae and
- aid in the assessment of skeletal integrity and stability



## Sinography

- contrast material is injected into the sinus opening to ascertain the course and extent of the sinus and its communication with deeper tissues



# Imaging

## MRI

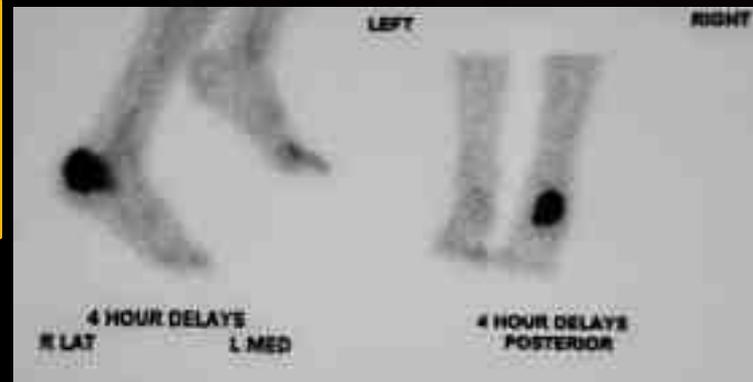
- provides the most accurate information on extent of disease in bone and soft tissue
- Useful when planning a marginal or wide resection
- Sensitivity 83% Specificity 62%,

## Positron emission tomography (PET)

- the most sensitive (96%) and specific (91%) imaging modality to diagnose the presence of infection



Figure 2. X-ray and MRI images indicating osteomyelitis in the metaphysis of the distal femur



# Laboratory investigations

Full blood count

Infection markers

- WBC, ESR, CRP, Procalcitonin

Pro-inflammatory cytokine

- IL-1, IL-6, IL-8, TNF

Renal and liver function tests

Electrolyte

Nutritional profile

Aim

- To ascertain the degree of systemic compromise
- As a diagnostic tool in the confirmation of the presence of sepsis.

# Pathogen identification

## Cierny recommendation

- an attempt be made to identify the pathogen prior to the first surgical debridement through biopsy of deep granulation tissue
- In cases **without significant** local or systemic septic complications, pathogen detection may be **delayed** after the primary debridement procedure
- **Pre-operative ('neo-adjuvant') antibiotics** may be mandatory, for example in patients with
  - **Significant local compromise** (cellulitis in the region of the incision) **or**
  - **Systemic compromise** (systemic sepsis or septic shock).

→ open biopsy or deep aspiration under ultrasound guidance, prior to definitive surgery.

# Pathogen identification

- Swab culture from a sinus may offer some diagnostic benefit.
  - Identification of methicillin-resistant *S. aureus* (MRSA) or vancomycin-resistant enterococcus necessitates the implementation of stringent infection control measures during hospitalization.
  - Isolation of *S. aureus* from a superficial culture has a high degree of correlation with deep cultures
- In cases without significant local or systemic septic complications, pathogen detection may be delayed to after the primary debridement procedure

# Treatment

- Multidisciplinary effort is needed for successful treatment.
- The team should consist of
  - Surgeons (orthopedic and reconstructive surgery)
  - Infectious disease specialist
  - Specialist to advise on nutrition
  - Psychologist if needed

# Management strategies

## Aim

Eradication of infection and limb reconstruction

A wide array of surgical procedures and techniques in terms of debridement

Dead space management

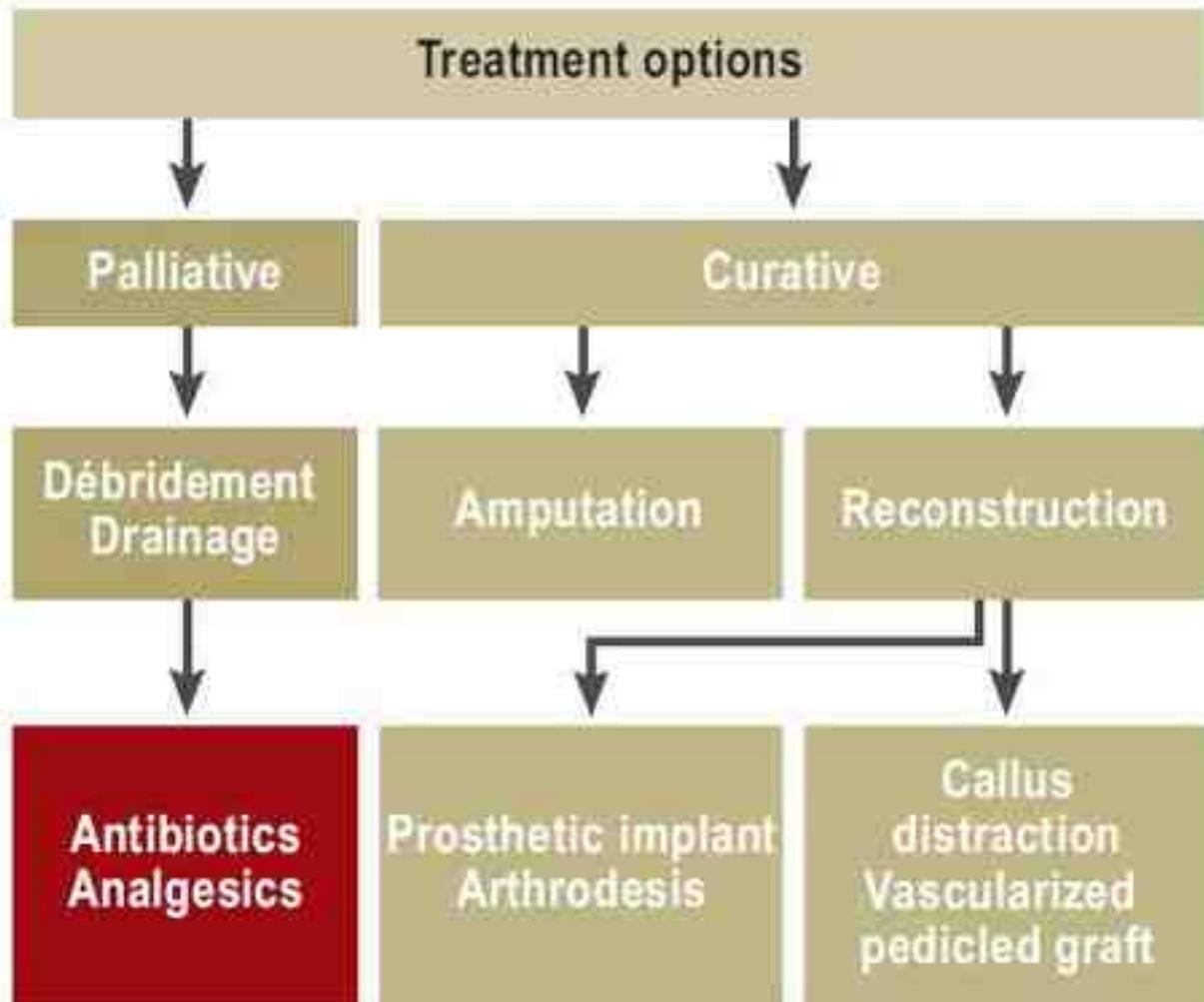
Soft tissue cover

Skeletal reconstruction

Healing of bone segment

Preservation of limb length and function

# Treatment options for chronic osteomyelitis



Walter G, Kemmerer M, Kappler C, Hoffmann R: Treatment algorithms for chronic osteomyelitis. Dtsch Arztebl Int 2012; 109(14): 257–64.

# Management strategies

## ■ Approach

### Curative

- multiple surgical procedures

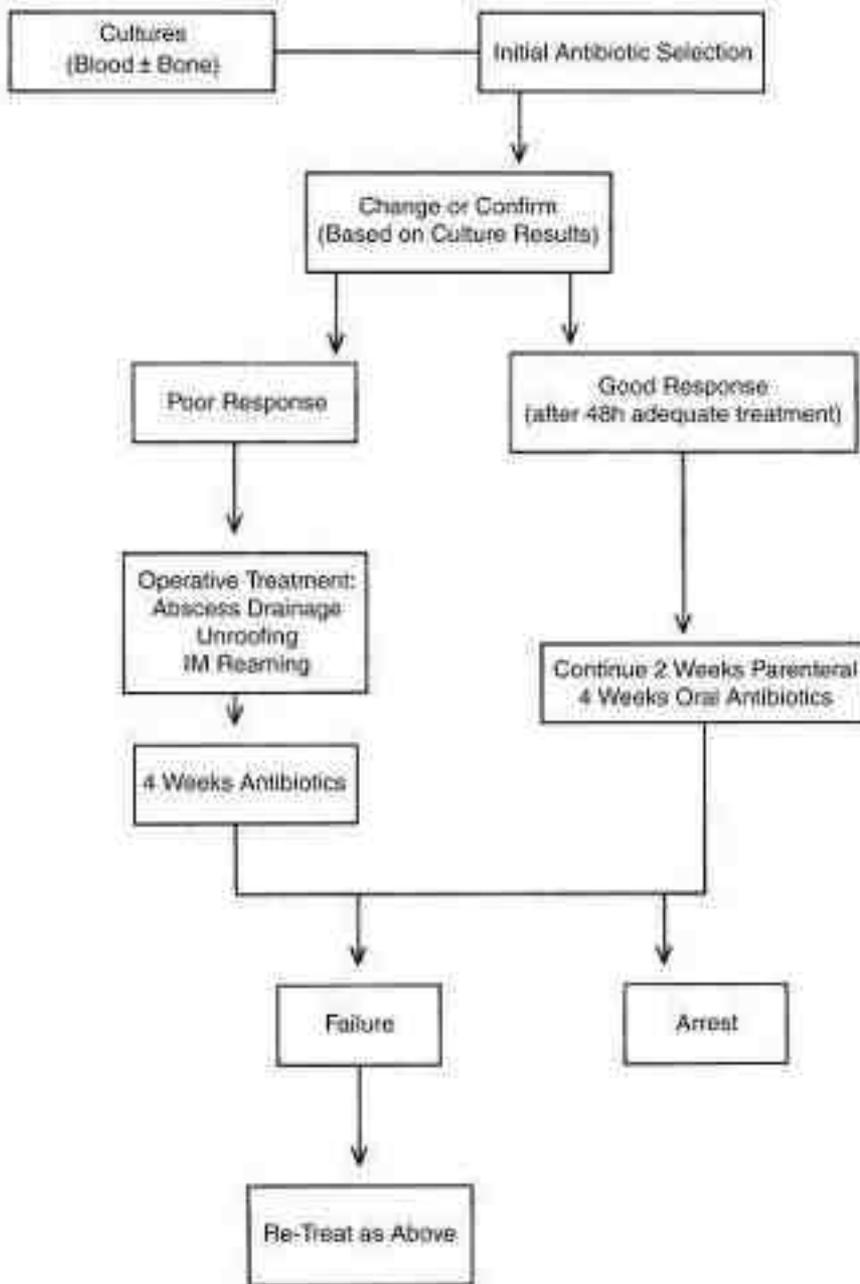
### Palliative

- Less invasive and typically involve the use of chronic suppressive antibiotic therapy
- incision and drainage, oral antibiotics, ambulatory aides, and pain medication

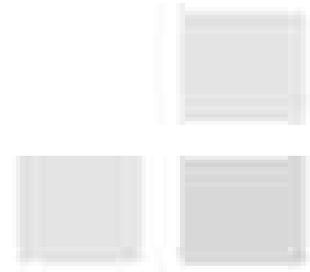
- This decision consideration as described by Cierny
  - C-host should be palliated
  - A- and B-hosts may be considered for a curative treatment protocol

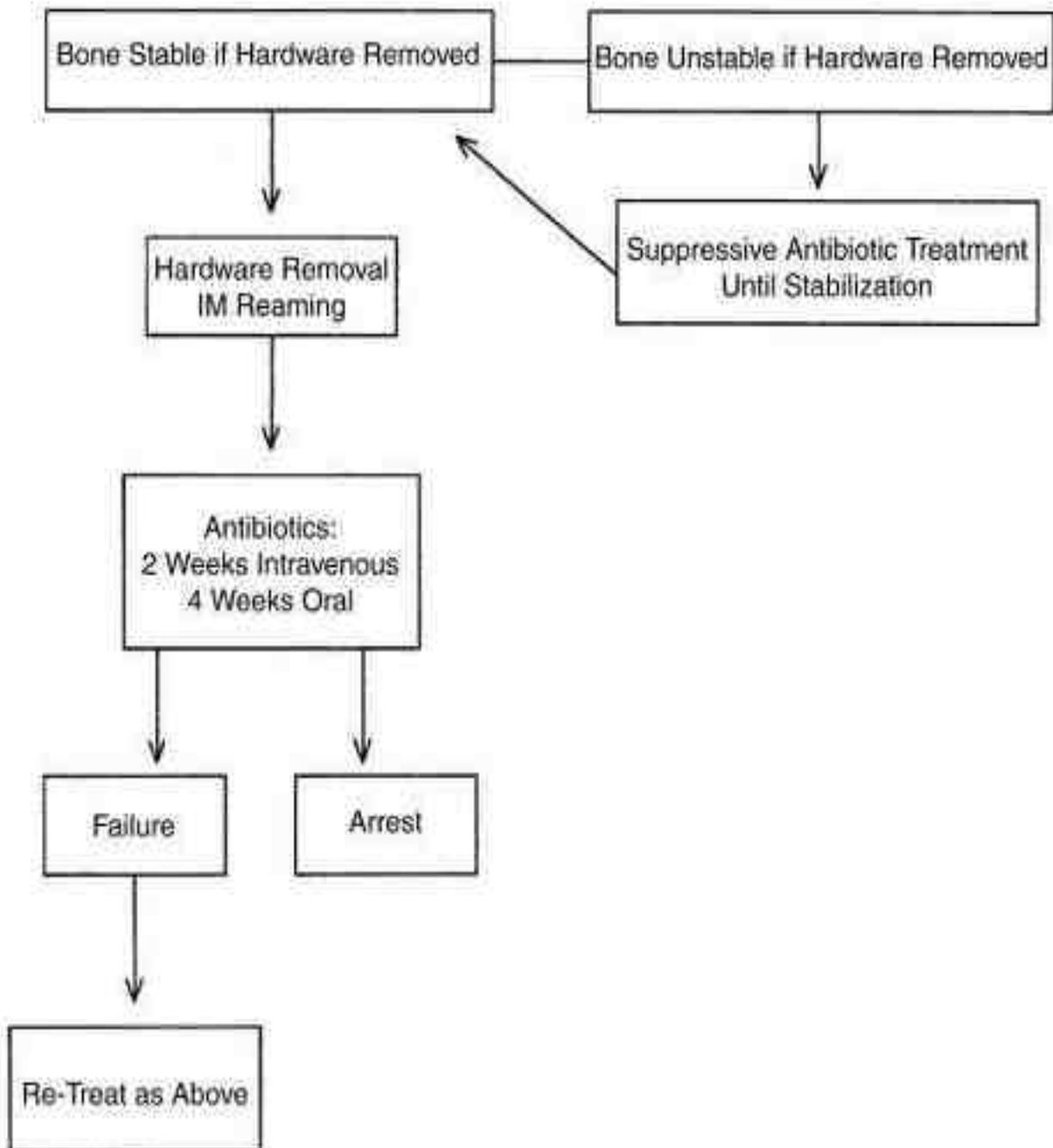
### Physiologic class

A host	Normal
B host	
Bs	Systemic compromise
Bl	Local compromise
Bls	Systemic and local compromise
C host	Treatment worse than the disease



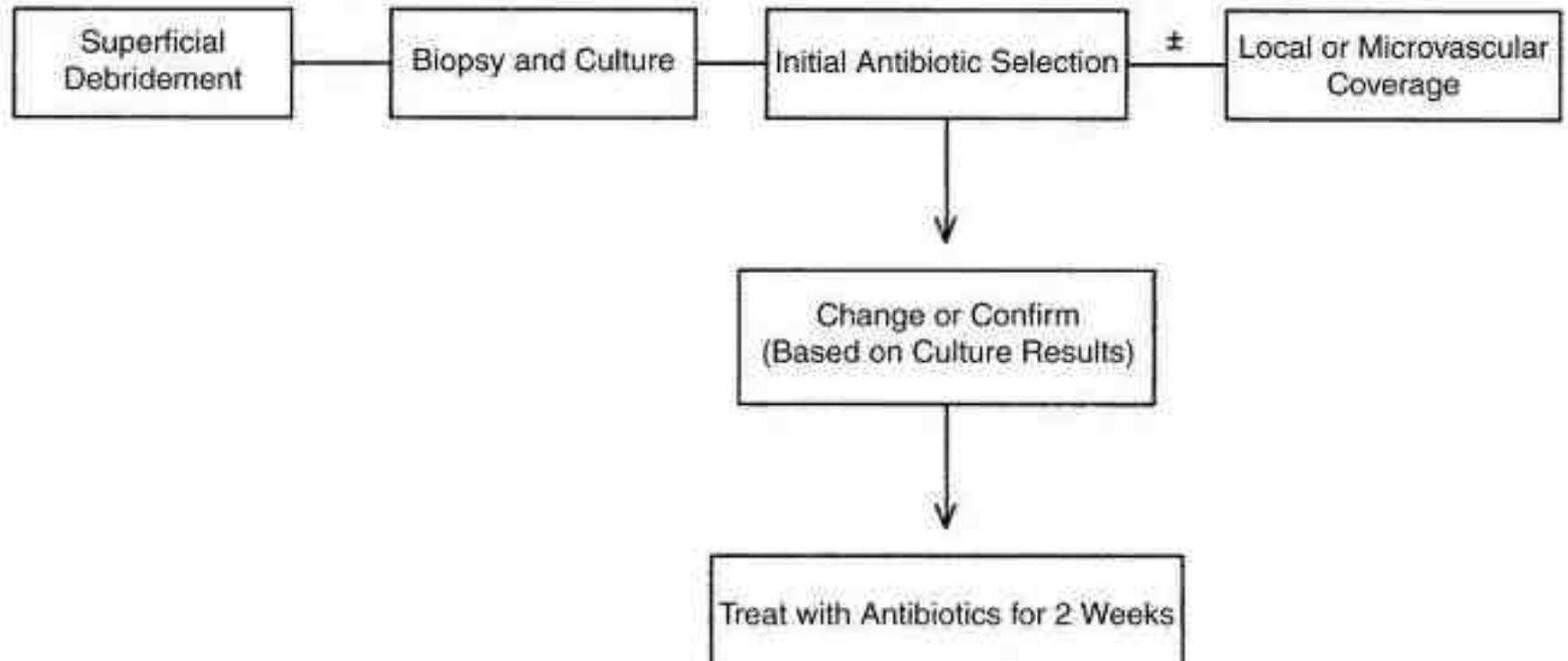
TREATMENT  
ALGORITHM OF  
CIERNY-MADER  
STAGE-1,  
OR  
HEMATOGENOUS,  
LONG-BONE  
OSTEOMYELITIS



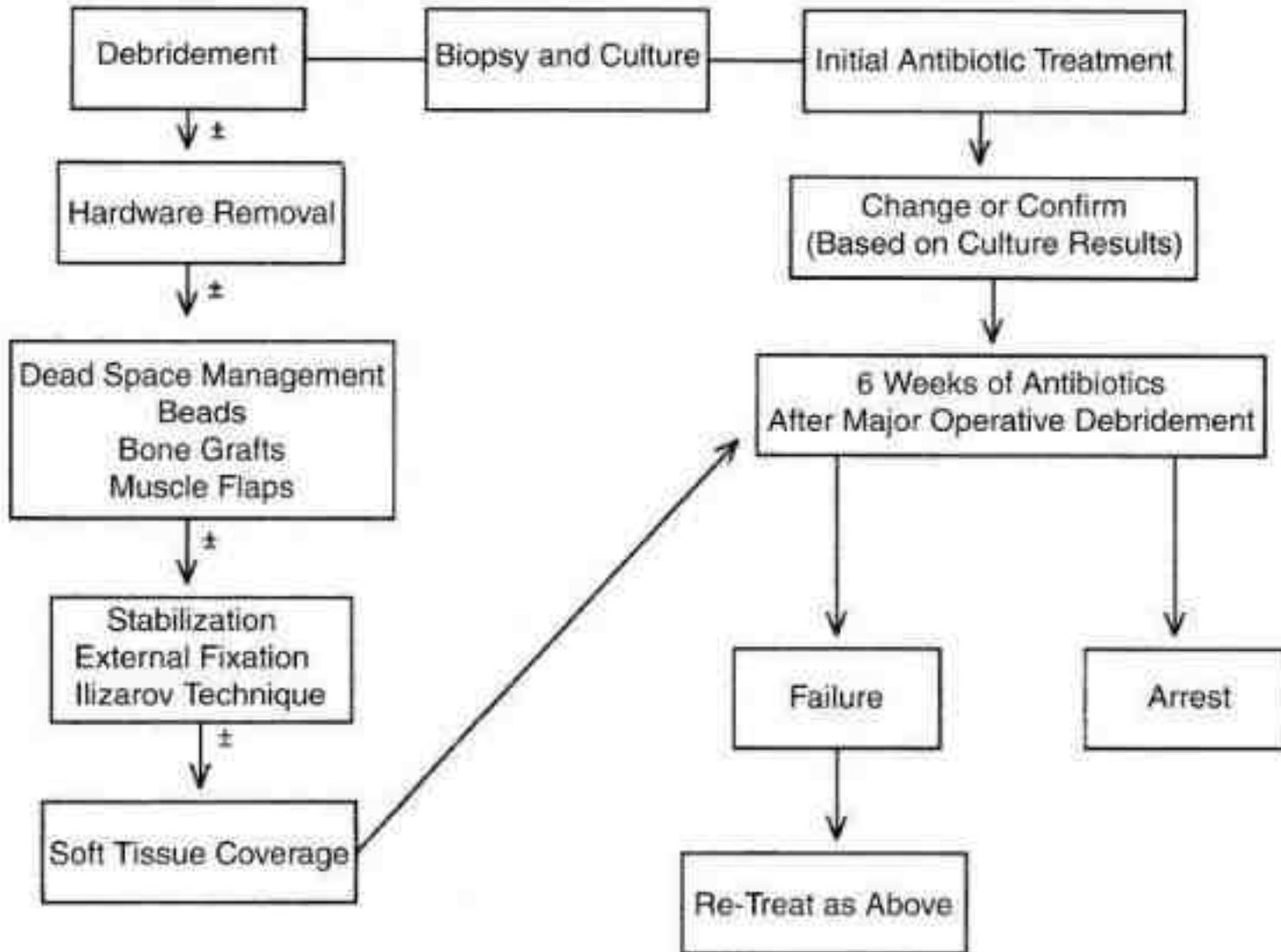


TREATMENT  
ALGORITHM OF  
CIERNY-MADER  
STAGE-1 LONG-  
BONE  
OSTEOMYELITIS  
ASSOCIATED  
WITH INFECTION  
AT THE SITE OF  
HARDWARE

# TREATMENT ALGORITHM OF CIERNY-MADER STAGE-2 LONG-BONE OSTEOMYELITIS



# TREATMENT ALGORITHM OF CIERNY-MADER STAGES-3 AND 4 LONG-BONE OSTEOMYELITIS





# ANTIBIOTIC THERAPY

- Antibiotic-therapy regimen is vital
  - This should be based on the identification of the infective organism and its susceptibility
- The challenges for successful antibiotic therapy
  - The presence of devitalized, avascular tissue
  - Biofilm formation
  - Chemical environment at the site of infection
- Effective treatment of chronic osteomyelitis requires prolonged antimicrobial therapy



# ADVANTAGES AND DISADVANTAGES OF PARENTERAL, ORAL AND LOCAL ANTI BIOTIC THERAPY

Therapy Type	Advantages	Disadvantages
Parenteral	<ul style="list-style-type: none"> <li>- Delivery of antibiotic to areas that cannot be reached with oral therapy</li> <li>- Choice of a large set of agents</li> <li>- Arrest or eradication of infection in most cases (in conjunction with surgical debridement)</li> </ul>	<ul style="list-style-type: none"> <li>- Often requires hospitalization</li> <li>- Lack of patient compliance</li> <li>- Systemic drug toxicity</li> <li>- Even with prolonged intravenous antibiotic therapy relapse of bone infection is not uncommon</li> <li>- Expensive</li> </ul>
Oral	<ul style="list-style-type: none"> <li>- Ease of administration</li> <li>- Reduced duration of hospitalization and health care costs</li> </ul>	<ul style="list-style-type: none"> <li>- Therapeutically unpredictable</li> <li>- Capacity for replace the prolonged courses of parenteral therapy is controversial</li> <li>- Limited choice of agents</li> </ul>
Local	<ul style="list-style-type: none"> <li>- Avoid high serum concentrations of the antibiotic</li> <li>- Deliver antibiotic directly to the infection site</li> <li>- Reduced duration of hospitalization and health care costs</li> </ul>	<ul style="list-style-type: none"> <li>- Lack of proven efficacy in good randomized clinical trials</li> </ul>

- adapted from Gitelis, Brebach, 2002; Ambrose *et al.*, 2003; Lazzarini *et al.*, 2005

# CONTROVERSIAL ISSUE

- A review of studies on antibiotic therapy for osteomyelitis published between 1968 and 2000 concluded that there is **inadequate evidence** to recommend the **best agent, route of administration, or duration of therapy**

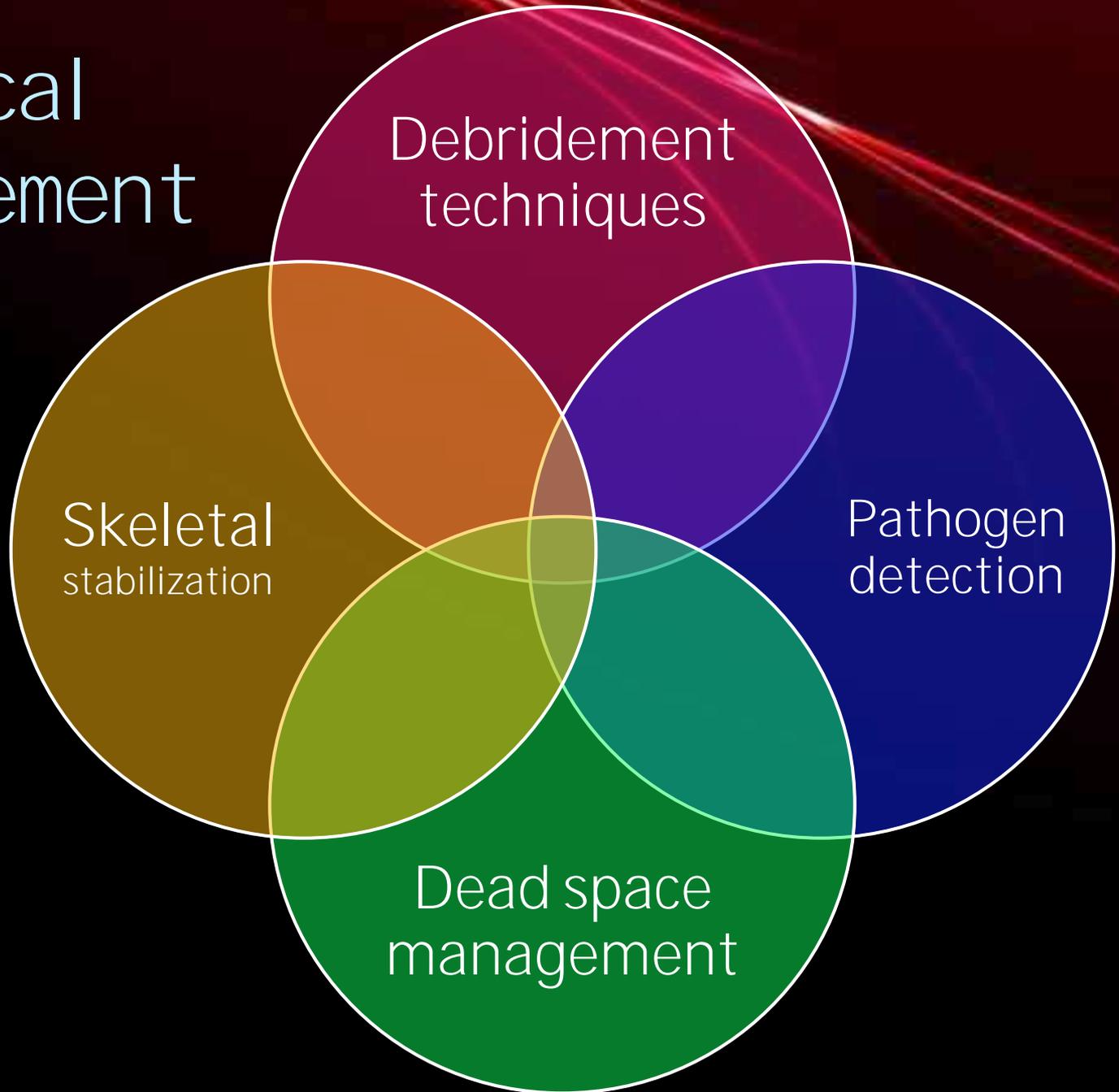


- **The duration of antibiotic therapy ???**
  - The standard recommendation of use of **antibiotics for 4–6 weeks** is based on animal studies on time taken for revascularization of bone

- Spellberg and Lipsky, 2012 reviewed publications from 1970 to 2011
  1. Oral antibiotic therapy with agents that have high bioavailability is comparable with parenteral therapy
  2. Improved cure rates with addition of rifampicin
  3. The duration of antibiotic therapy should be individualized based on clinical, hematological, and radiological response, and patients should be monitored after completion of therapy
  4. The cure rate of chronic osteomyelitis is increased with surgical resection of infected and devitalized tissue in conjunction with antibiotic therapy

Spellberg B, Lipsky BA. Systemic antibiotic therapy for chronic osteomyelitis in adults. *Clin Infect Dis*. 2012;54:393–407.

# Surgical management



# Debridement techniques

All necrotic or ischaemic tissues should be excised

All foreign bodies and surgical implants need to be removed

- Except of early infection following osteosynthesis where union is expected to occur

Soft tissues, and scar tissue

- should be resected to a supple, well-perfused margin

Bony debridement technique

- Simple sequestrectomy
- Intra-medullary reaming (indirect unroofing)
- Tangential excision (direct unroofing)
- Segmental resection and amputation

# Problem

## Compromised hosts

- Theoretically best treated with a wide resection of all infected tissues and subsequent **limb reconstruction**
- The reconstruction procedures required → involving **bone transport** or extensive **bone grafts**
- Fraught with **danger in the poor host** and failure frequently **results in the amputation** of the limb

# Pathogen detection

- Routine microscopy, culture and sensitivity (MCS) of tissue, bone and exudates taken **under aseptic condition** in the **absence of antibiotic therapy** in the preceding **10 days**
- **Multiple samples** should be acquired early in the procedure from fluid collections, soft tissue, bone and foreign materials or sequestra
- Samples should undergo **aerobic and anaerobic incubation** for prolonged periods, **at least 7 days**, in order to increase detection of fastidious organisms

# Pathogen detection

- Molecular methods have grown rapidly as the method of choice in pathogen detection

## Polymerase chain reaction (PCR)

- Pyrosequencing is currently the most popular technique
- It can be performed on any specimen
- Able to reliably identify the micro-organism involved, irrespective of its phenotype (culturability), prior antibiotic therapy or metabolic state

# Dead space management

Gentamycin-impregnated polymethylmethacrylate (PMMA) beads

- useful in type III lesions

Lautenbach irrigation systems

- commonly utilised in type I lesion

Antibiotic-impregnated PMMA spacers or intramedullary nails or antibiotic-loaded calcium sulphate pellets

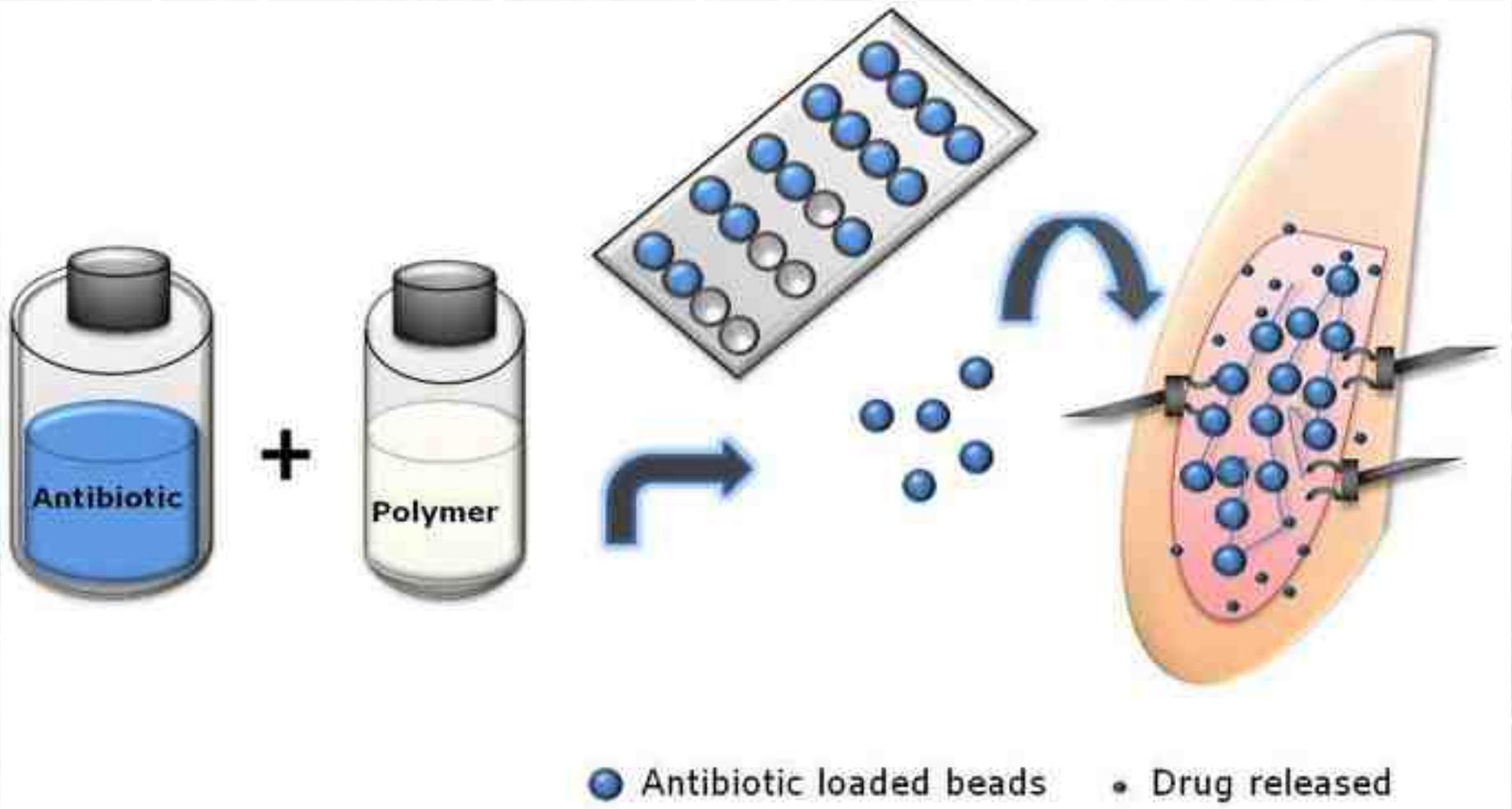
- May be used in type I infections
- Especially in the setting of post-operative sepsis

Local or free soft tissue transfer procedures

- microvascular free-muscle transfer is considered the gold standard
- type II lesions



*Figure 3.  
Antibiotic-impregnated  
spacer following a wide  
resection. Stability was  
achieved with the aid of  
a circular external fixator.*



- The in situ implantation of antibiotic-impregnated beads
  - As a local antibiotic delivery system
  - Obliterate bacteria in the area
  - Reduce the dead space in the bone

# Gentamycin-impregnated polymethyl methacrylate (PMMA) beads

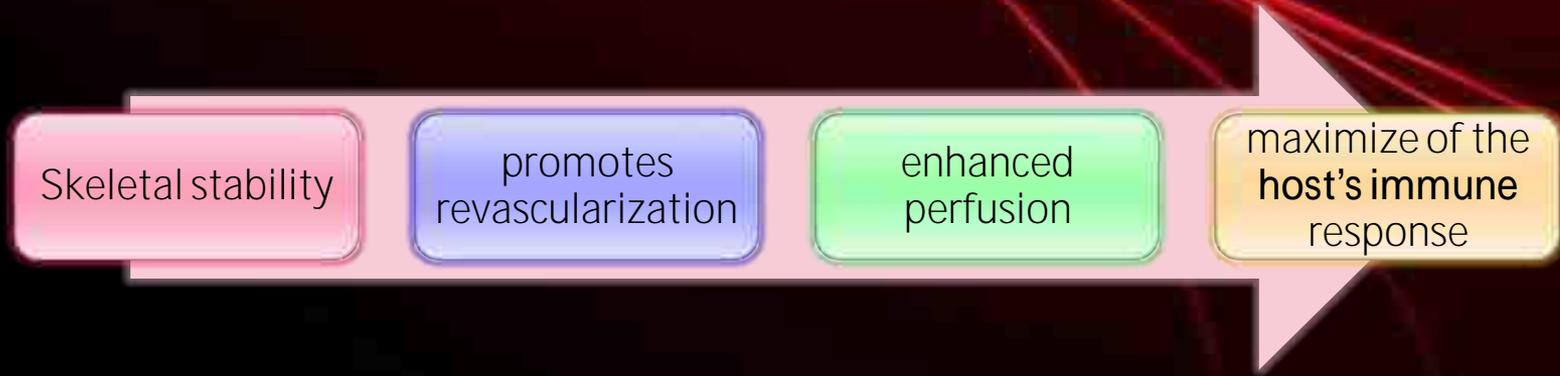
## Gentamicin/vancomycin-loaded spacers

- Most effective against *S. epidermidis* and MRSA

## Gentamicin/teicoplanin-combination spacer

- Best results against *E. faecalis* and *S. aureus*
- Proportional weights of up to approximately 5 weight/weight % (2 g vancomycin per 40 g cement powder) have a negligible influence on the mechanical strength of the cement

# Skeletal stabilization



- Skeletal stabilization is needed for **all stage 4 and some stage 3** lesions following excision of the devitalized bone
- **A variety of fixation options**

External fixation	<ul style="list-style-type: none"><li>• generally preferred</li></ul>
Intramedullary PMMA nails	<ul style="list-style-type: none"><li>• Provide some stability</li><li>• But cannot achieve the level of stability provided by external fixation</li></ul>
Circular external fixators	<ul style="list-style-type: none"><li>• Good modularity</li><li>• Minimally invasive nature</li><li>• Ability to effect bone transport and deformity correction</li></ul>

## **Surgical interventions in chronic osteomyelitis**

Shrestha BK<sup>1</sup>, Rajbhandary T<sup>2</sup>, Bijukachhe B<sup>2</sup>, Banskota AK<sup>3</sup>

<sup>1</sup>Associate Professor, <sup>2</sup>Senior Registrar, <sup>3</sup>Professor & Perceptor, Kathmandu University Medical School

- 
- Ninety children (60 boys, 30 girls) were included in this study
  - The commonest site involved (50%) followed by tibia (45%).
  - A total of 112 surgical procedures were carried out in 90 patients.
    - Sequestrectomy (59.8%)
    - Ilizarov external fixator application (13.4%)
    - Saucerization (10.7%)

### Conclusion

- Repeated debridements may be necessary to eradicate or control infection
- The ring fixator has been shown to be a useful tool to address pathological fracture, diaphyseal bone gaps, nonunions and stiffness and deformity

## Treatment of Chronic Osteomyelitis in Children by Ilizarov Technique

Bari MM, Shahidul I, Mahfuzer R, Shetu NH, Golam M, et al. (2015) Treatment of Chronic Osteomyelitis in Children by Ilizarov Technique. MOJ Orthop Rheumatol 2(4): 00054

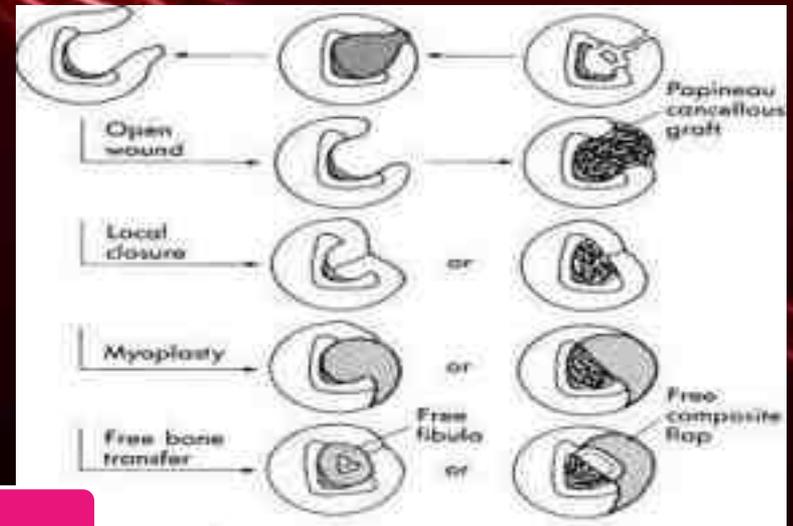
### Ilizarov technique

- To create a **mechanical condition** necessary for the development of distraction & compression.
- To **store the new bone forming cells** developed during lengthening and deposited along the line of stress and tension.
- **Increase blood circulation** for increased metabolic transformation of local tissue.
- Most importantly **the medullary and the periosteal blood supply** is not disturbed.

# Surgical technique



# Papineau Technique



Radical debridement

Bone grafting in stages

Delayed soft-tissue closure

Wound allowed to granulate naturally  
or with skin grafting

- Stage 3 infections are best suited for this technique, as bone grafts do not provide the necessary stability.

# The Belfast technique

- Proposed by McNally et al
- The reported a cure rate of 92% with this technique

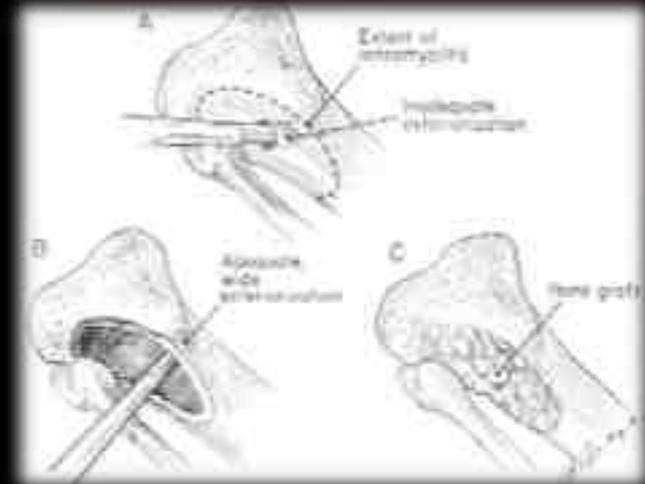
Radical  
debridement



Delayed bone  
grafting

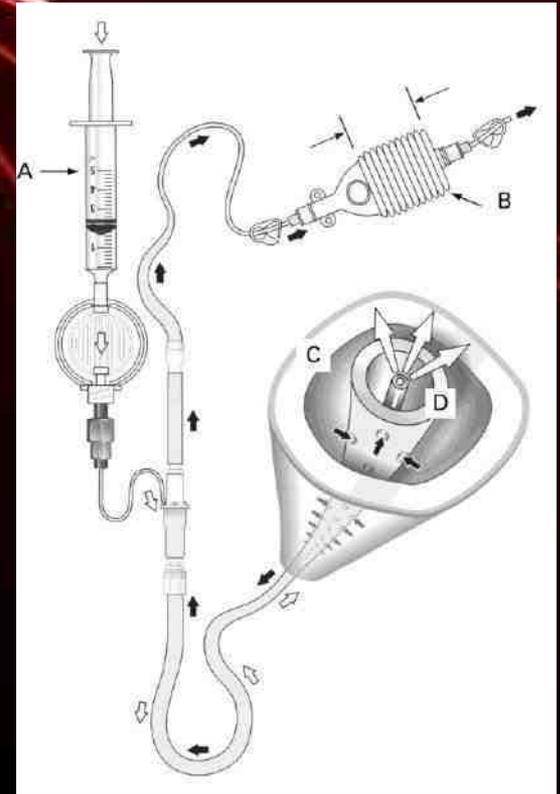


Early soft-tissue  
cover for  
elimination of dead  
space



# Lautenbach technique

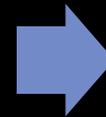
- First described for infected total hip arthroplasty
- It is useful for cases with persistent infection after debridement and parenteral or oral antibiotic therapy.



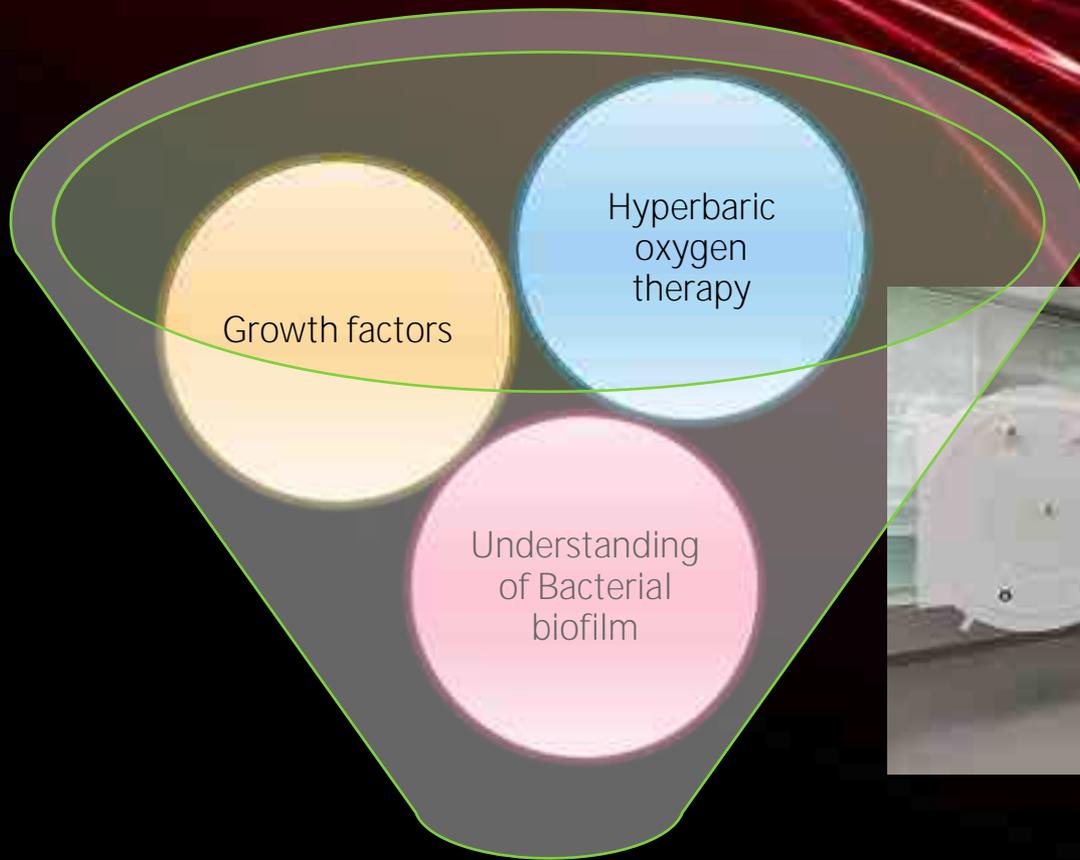
Using a closed irrigation system



Antibiotics are delivered locally



It is possible to obtain frequent samples for culture



Adjunctive therapies

# Hyperbaric oxygen therapy

Providing oxygen at high concentration and pressure in diseased tissues that are hypoxic

Improves the bactericidal ability of the neutrophils

Helps neutralize collagen synthesis and osteogenesis

Inducing angiogenesis

Suppressing anaerobic organisms

Enhancing antibiotic activity

Promoting oxygen-dependent osteoclastic resorption of necrotic bone

- There is a **lack of guidelines** for use as well as high-quality clinical trials for hyperbaric oxygen in chronic osteomyelitis.
- The available literature however **suggests great potential** for this modality

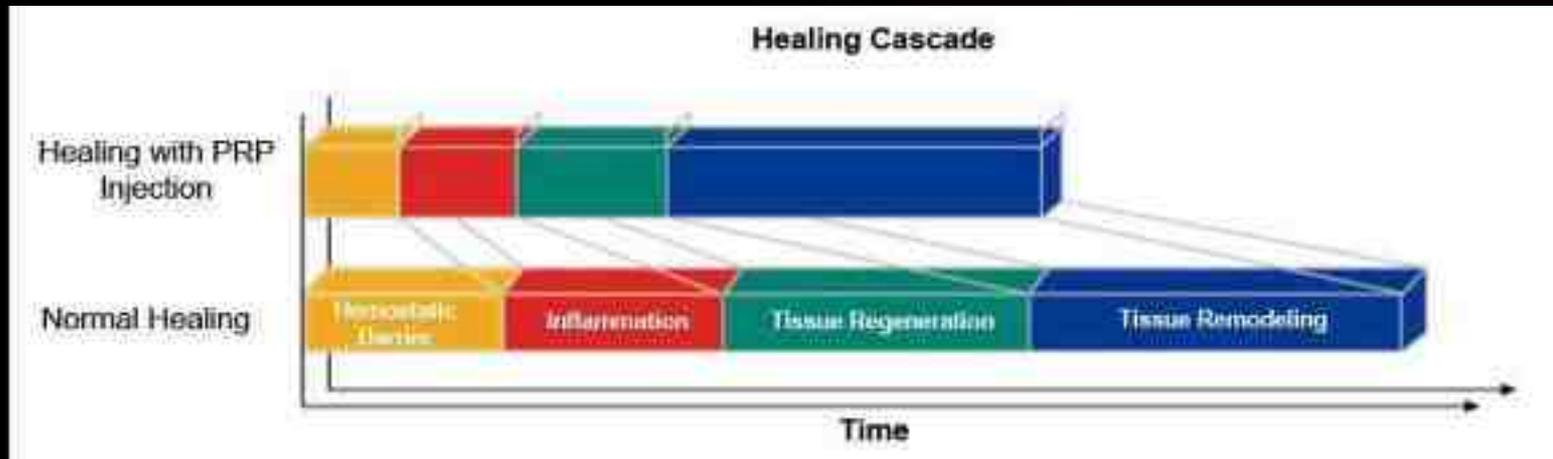
# Growth Factors

## Bone morphogenetic protein

- Accelerate osteogenesis and bone healing

## Platelet-rich plasma

- Promote bone and soft-tissue healing



# Bacterial biofilm

- The formation of biofilm is an important pathogenic factor for bacterial resistance and persistence of infection in chronic osteomyelitis
- The alternative strategies resulting from understanding of the role of biofilm in chronic infection include
  - quorum-sensing inhibitors
  - bacteriophages
  - interspecies interaction
  - biofilm disruptors (sonication)
  - specific antibiofilm molecules

# COMPLICATIONS

- Pathologic fracture
- Septic arthritis with joint destruction
- Physeal damage
- Nonunion or segmental bone loss
- Leg length discrepancy (shortening or overgrowth)

# Concl usi on

- Management of chronic osteomyelitis is challenging and prolonged
- Proper staging and identification of causative organism remains vital to the success of treatment.
- Newer treatment modalities are being developed to address the role of biofilm in chronic osteomyelitis



THANK YOU

