

Infection-related arthritis in children

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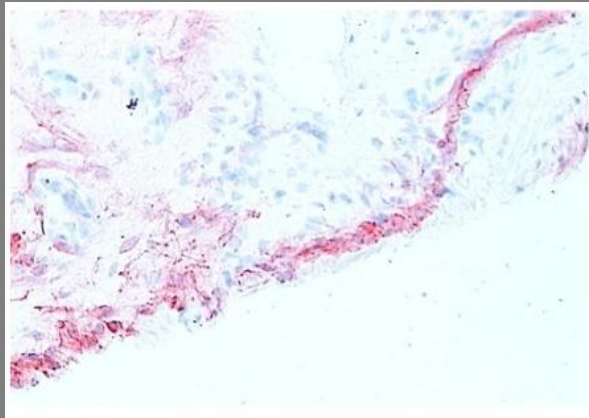
Reactive arthritis at the turn of the century

The Billings-Rosenow era (1880-1930)

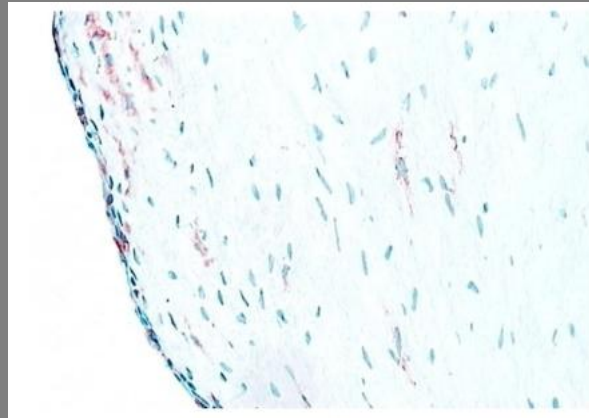
- **In 1930 50% of inpts. with RA in a Hospital in Boston were edentulous.**
- **Purges and bladder lavages were very common. ASA was developed by Hofman (Bayer) in 1893.**
- **Surgery: tonsillectomy, vas deferens resection etc..**



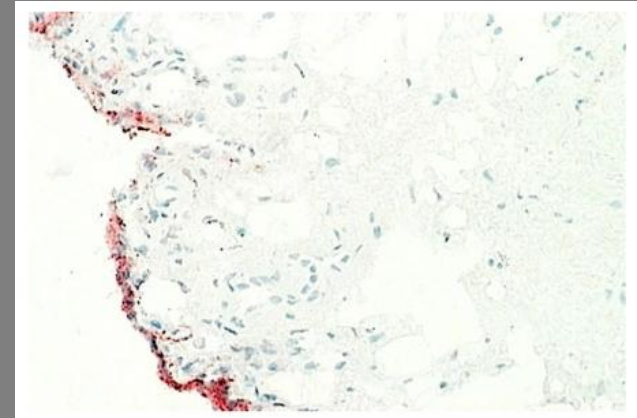
Normal synovial membrane: subpopulations



CD 55 (Fibroblasts)



CD 68 (Macrophages)

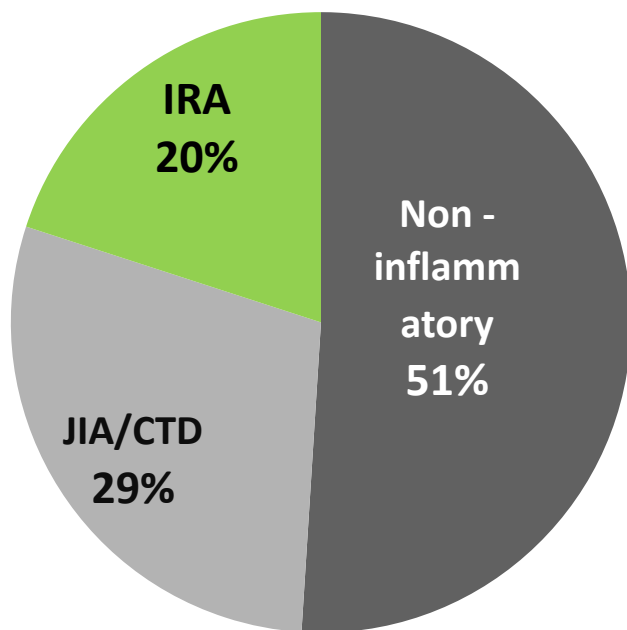


ICAM-1

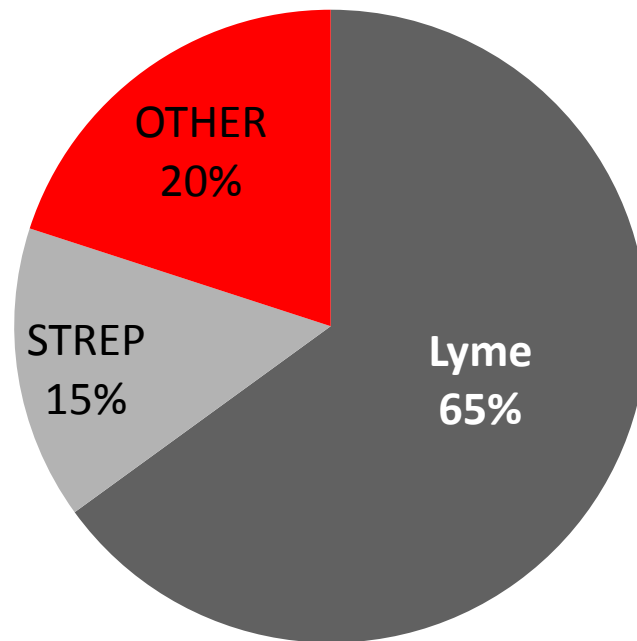
duPont Children's Hospital

2009-2012: new patients

ALL NEW



INFECTION-RELATED ARTHRITIS



Infectious arthritis: what's in your neighborhood?

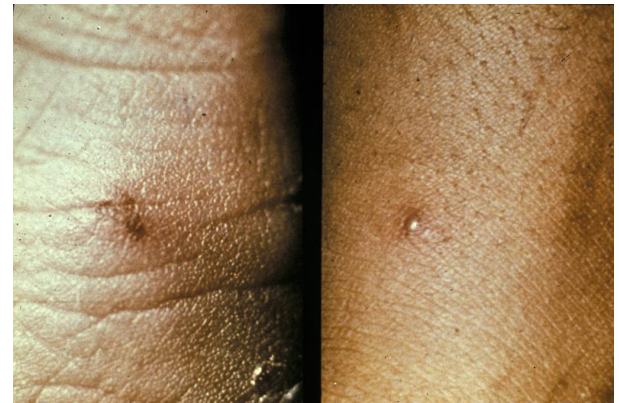
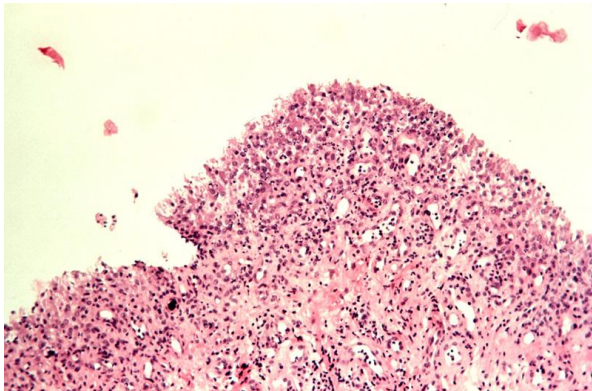
- What is in you environment: HIV, TB, Q fever, Brucella, Lyme, Chikungunya, Ross river, Valley fever, HB, HC?
- Mid Atlantic states
 - *Borrelia burgdorferi*
 - GAS
 - HPV-B19
 - EBV
 - Reactive intestinal (salmonella, yersinia) and venereal (Chlamidia)

Infection-related arthritis: multiple mechanisms

| Type of arthritis | Main Microorganisms | Main mechanism |
|-------------------|---|---|
| Septic | Staph. aureus, Strep. Group A, Streptobacillus moniliformes, Kingella, Mycobacteriae tuberculosis and leprae. | Joint space invasion by viable bacteria or other microorganisms |
| Viral | Rubella, Ross River Valley, Chikungunya?? Varicella, mumps | Synoviopathic infection by replicating virus. In general more severe than post viral |
| Post infectious | Parvovirus B19, Hepatitis B, EBV, GAS, Mycoplasma, Giardia lamblia, Coccideoides | Immunologic mechanism after viral clearance |
| Reactive | Yersinia, Chlamydia, Salmonella, Shigella, C diff | Remote infection with non viable bacterial particle in synovial membrane |
| Mixed | Borrelia burgdorferi | Infectious stage followed by sterile isotopic chronic inflammation |

A few reminders on septic joints

- **Overdiagnosed: carefully search for effusions in other joints**
- **Osteomyelitis with intracapsular metaphyseal disease, transphyseal blood vessels in babies**
- **Dislocation in neonatal septic hip and polyarticular in neonates with GBS**
- **FOR GC CULTURE BLOOD, JOINT AND CERVIX: chronic subacute gonococemia, with low grade intermittent fever, oligoarticular, fastidious growth**



1-MIGRATORY ARTHRITIS

- LARGE INTERMEDIATE JOINTS
- MIGRATION IS FAST (24-36 hr), sometimes neatly clock or counter clock wise
- A MIGRATING “MONOARTHRITIS” WITH RESOLUTION (OR ALMOST) OF PREVIOUS JOINTS (“THE JOINT OF THE DAY”)
- POLYARTICULAR: average 5 joints
- SPECIFIC FOR POST-INFECTIOUS **but** NOT 100% SENSITIVE FOR ARF
- PERIARTICULAR COMPONENT WITH REDNESS
- VERY PAINFUL

The Jones criteria

EVIDENCE OF GROUP A STREPTOCOCCAL INFECTION

MAJOR

- CARDITIS
- **POLYARTHRITIS (*)**
- CHOREA
- ERYTHEMA MARGINATUM
- SUBCUTANEOUS NODULES

(*) Almost always migratory

MINOR

CLINICAL

- PREVIOUS RF OR RHEUMATIC HEART DISEASE
- ARTHRALGIA
- FEVER

LABORATORY

- ACUTE PHASE REACTION: ESR, CRP, LEUKOCYTOSIS
- INCREASED PR INTERVAL

2 MAJOR OR 1 MAJOR + 2 MINOR

D. Jones 1948 (JAMA 1944; 126: 481-484)

Committee AHA Circulation 1965 Vol. XXXII-aha 1992, 1997, 2000, 2002



ARF PEARLS

- ESR>50 mm/hr
- Fever ~ 38.5 daily, may not be there if CHF
- TACHYCARDIA, GALLOP, LOOKING ILL, MURMURS
- ECHO IN 1ST WEEK
- ARTHRITIS RESOLUTION IN WEEKS OR SOONER WITH ASA
- **ASO** HAS TO BE HIGH (oops, not always)
- PSRA (“Scarlatinal arthritis”. Pediatrics 1959): to be or not to be.
 - 7-15 days from GAS
 - Hips and small joints
 - Lasts more than 6 weeks

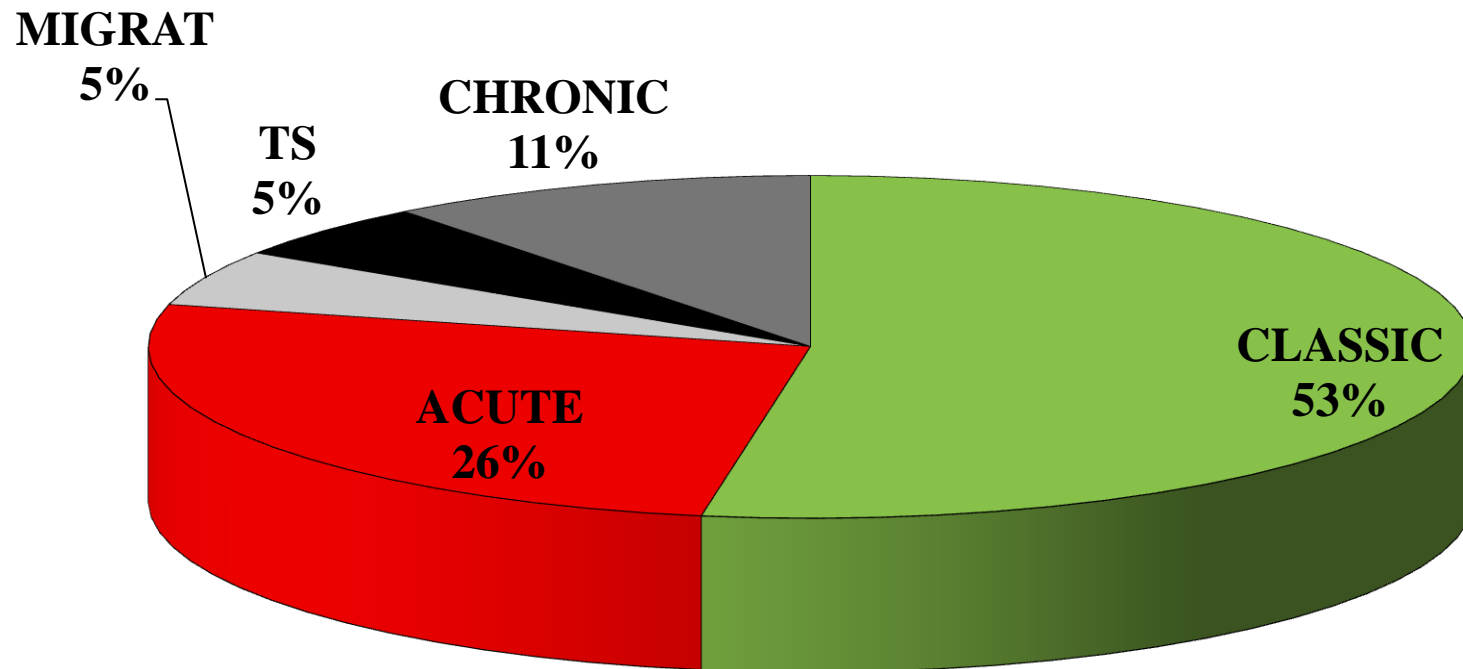
2-INTERMITTENT MONOARTHRITIS







LYME ARTHRITIS PRE-RX



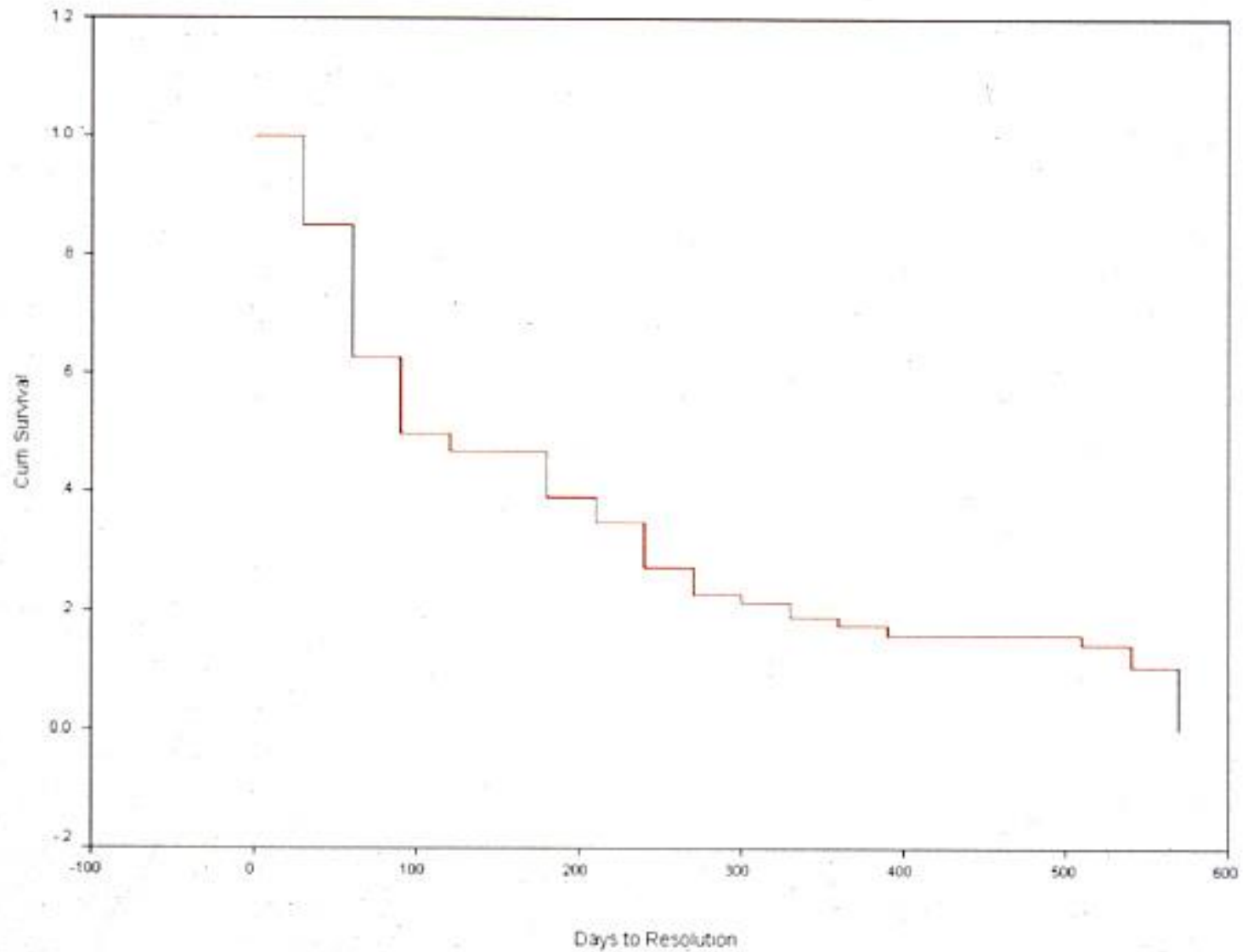


Lyme Arthritis

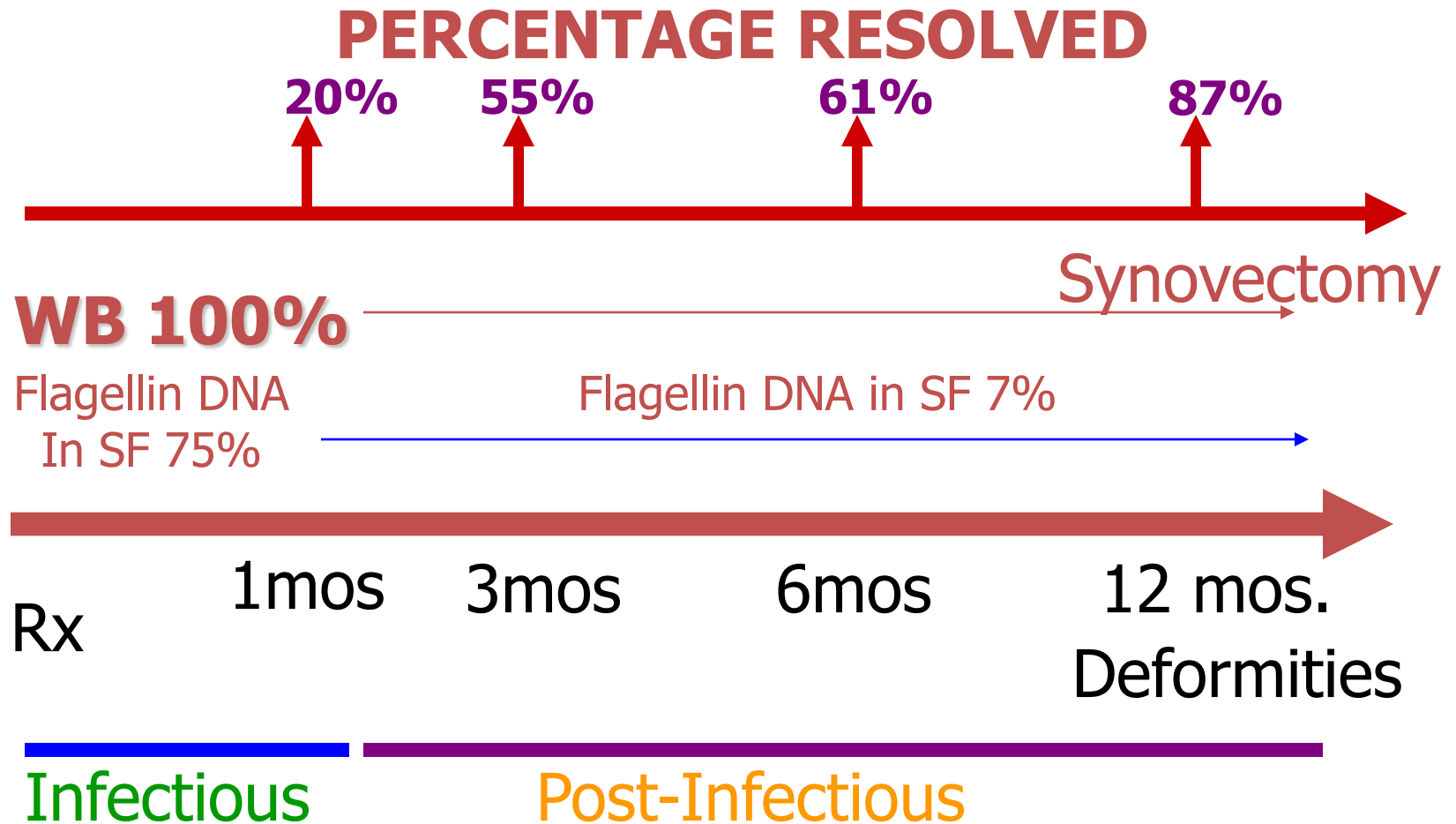
- **60% of untreated patients with EM develop LA**
- **<1% of treated patients with EM develop LA**
- **10% of LA patients have Hx of EM**



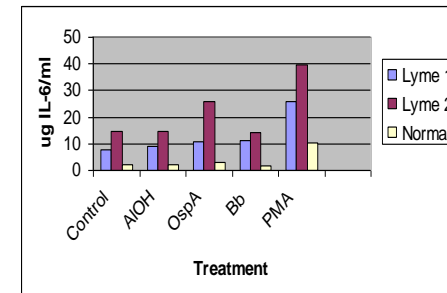
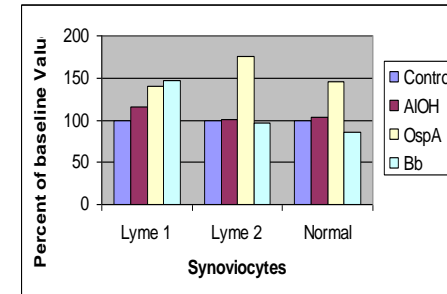
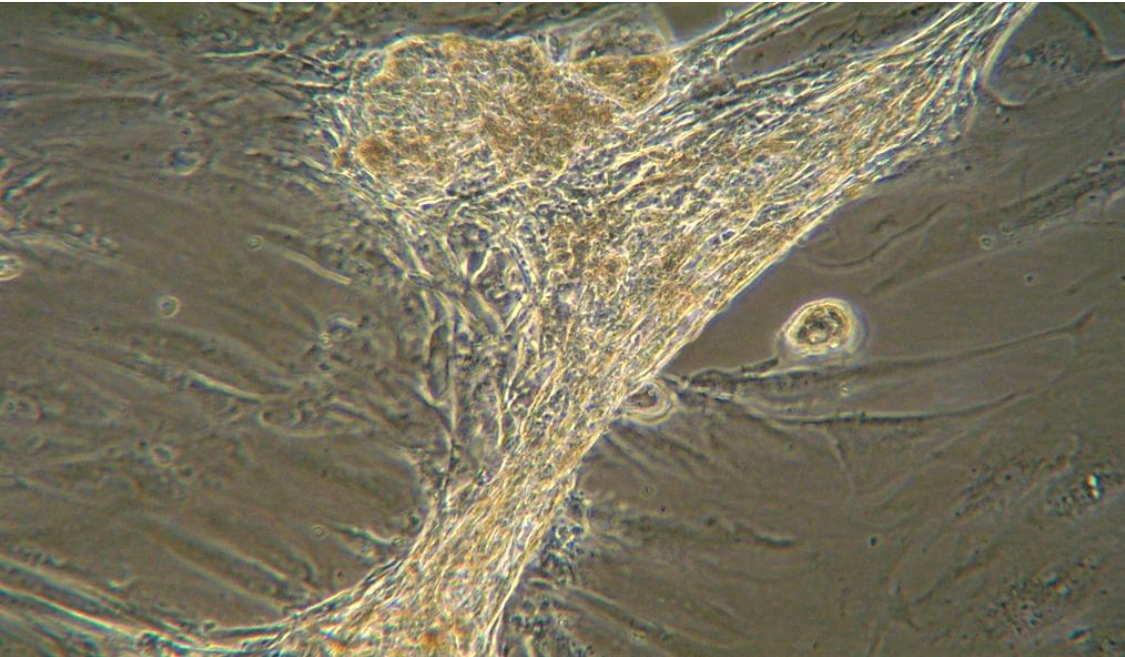
Resolution of Synovitis



LA AND ARLA



Lyme FLS IL-6 Release upon stimulation



Lyme Results:

- Compared cultured FLS from controls with ARLA and LA.
- 170 genes were differentially expressed: Pair-wise comparisons of groups using t-test
 - 158 genes were differentially expressed between controls and LA
 - 119 genes between controls and ARLA
 - 13 genes differentially expressed between LA and ARLA

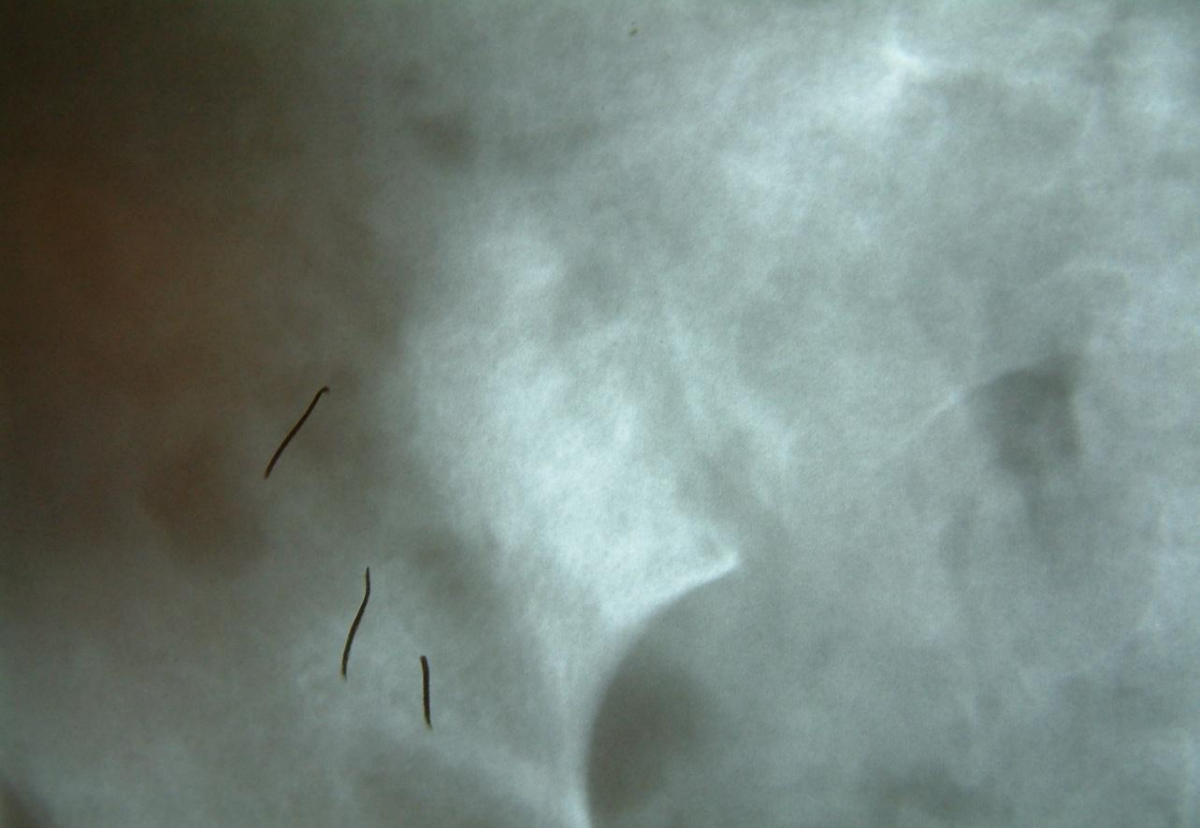


3-ACUTE OLIGOARTHRITIS with ENTHESITIS: *Reactive arthritis*

- Children (dysenteric)
 - Salmonella
 - Campylobacter
 - Yersinia
 - Shigella
 - **C. Diff**
- Young men (STD)
 - Chlamydia (1/3 OF TRANSIENT Knee MONOARTHRITIS)
- ASK ABOUT DIARRHEA 4-6 weeks PRIOR.

Reactive arthritis: some facts

- ESR IN THE 60-80 mm/hr
- Any acute arthritis: ask about urethral or proctocolitic symptoms 3-6 weeks prior
- **SYSTEMIC FORMS:** conjunctivitis, sterile urethritis, balanitis circinata, keratoderma blennorrhagica
- **HLA B27**



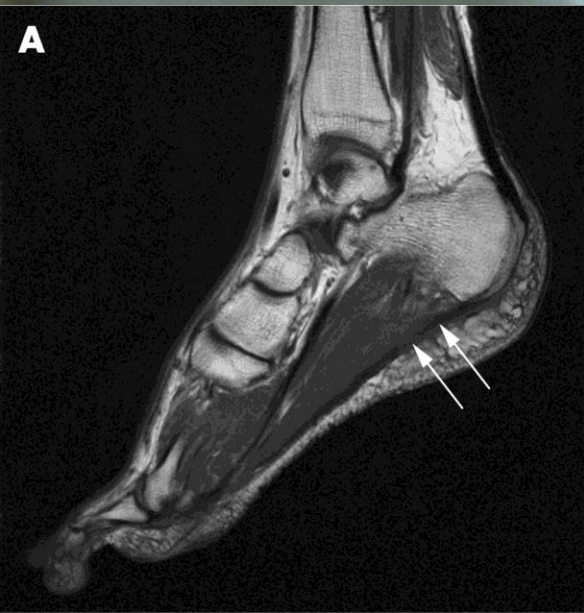
Enthesopathy



Reactive arthritis as an acute Spondyloarthropathy

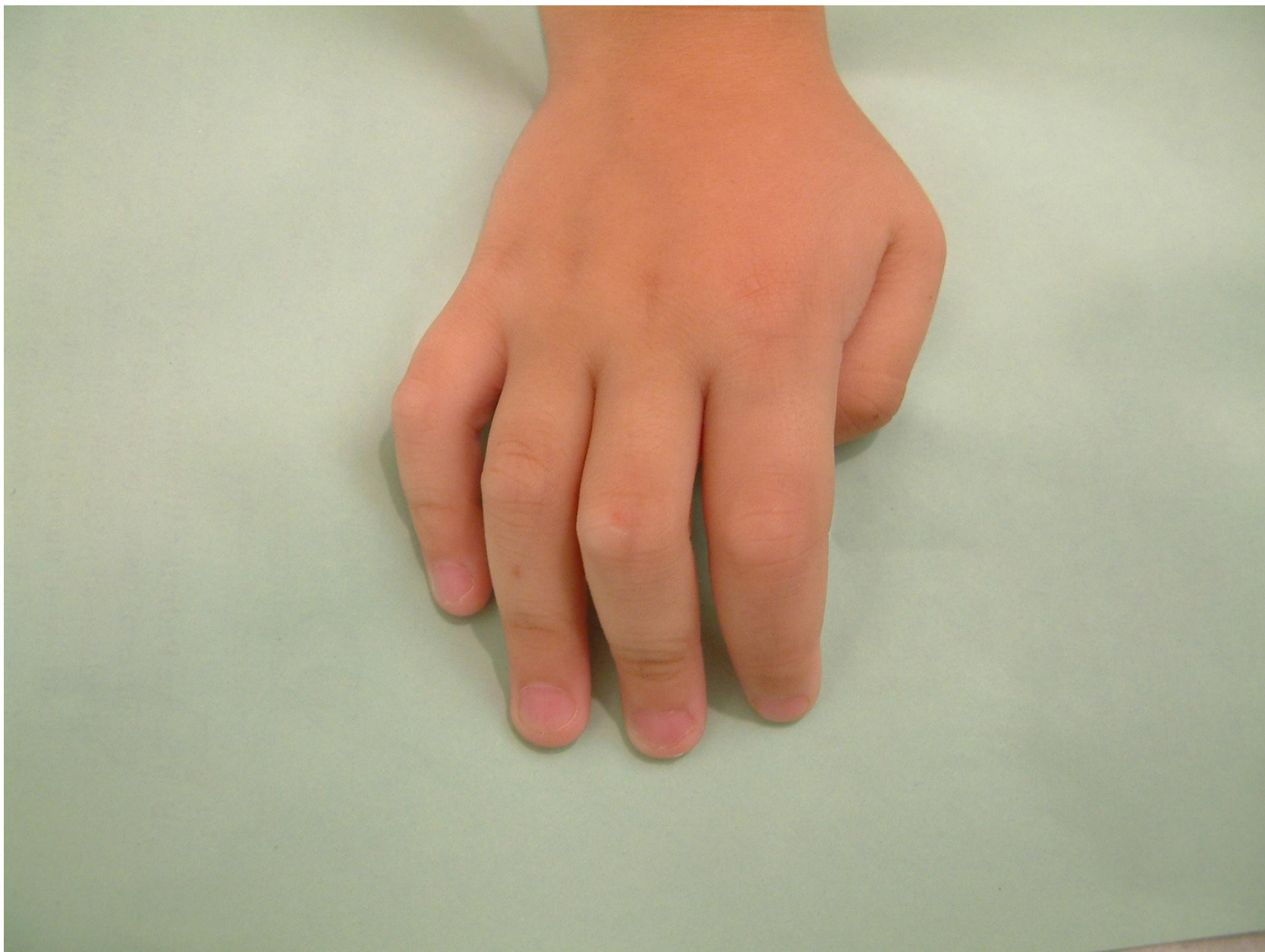
B27 +

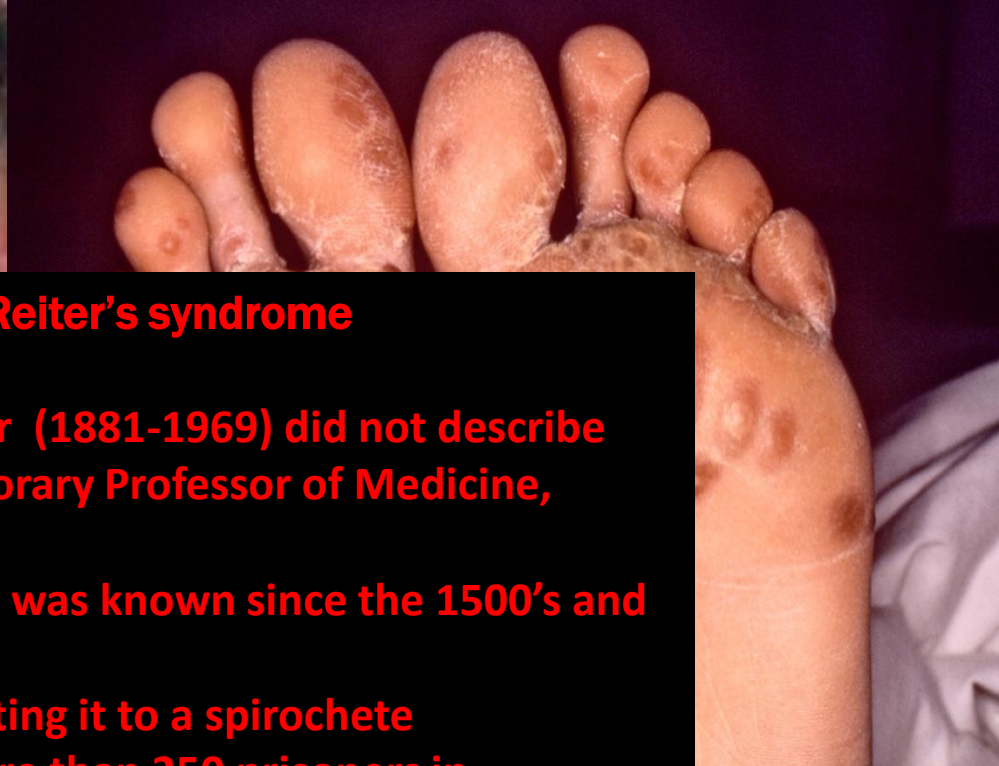
Can become chronic ERA-like (*)



* Cuticca R et al, Clin Exp rheum 1992, 10: 288







The non-Reiter's syndrome

- Hans Conrad Julius Reiter (1881-1969) did not describe "his" syndrome, Herr honorary Professor of Medicine, Berlin 1936
- Dyad urethritis + arthritis was known since the 1500's and Collins described the triad
- Reiter was wrong attributing it to a spirochete
- He injected typhus to more than 250 prisoners in Buchenwald
- He was an SS officer, participated in the T7 program and was found guilty in Nuremberg



C Diff study: 2014

- 13 patients (111 + for C Diff)
- Age: 13.2 years
- Migratory (85%) and polyarticular (54%)
- Median joint count : 6: (1-Knees; 2-ankles, 3-wrists and 4-elbow)
- Very painful and with concurrent fever in 60%
- Median time GI-joints 30 days , median time to resolution 16 days
- Massively under-recognized

4-Acute polyarticular: “Viral arthritis”

- ACUTE ONSET
- SOMETIMES HELPFUL EXTRA-ARTICULAR FINDINGS
- PATTERN AGE DEPENDENT
- SELF-LIMITING







PCR POSITIVE
SEROPOSITIVE

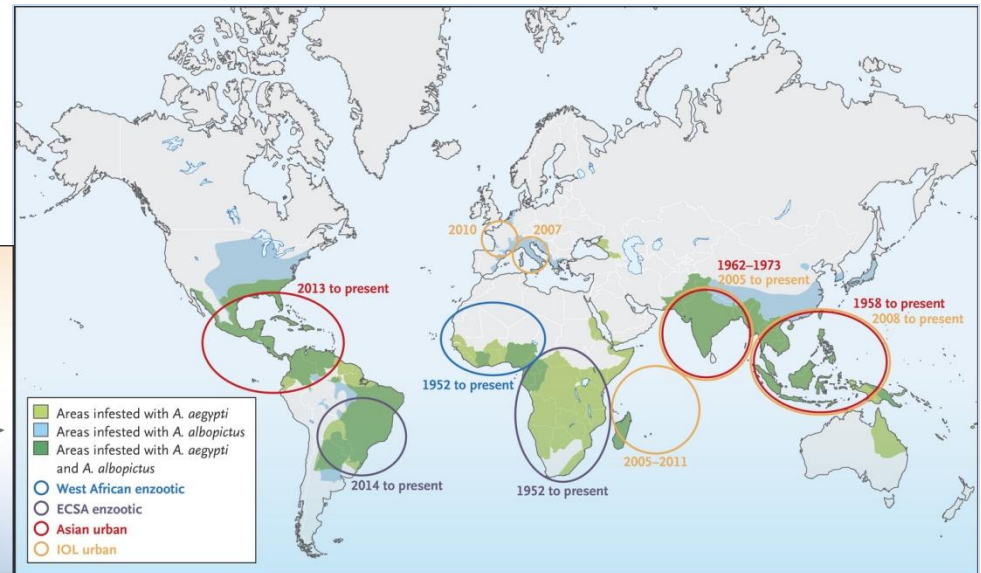
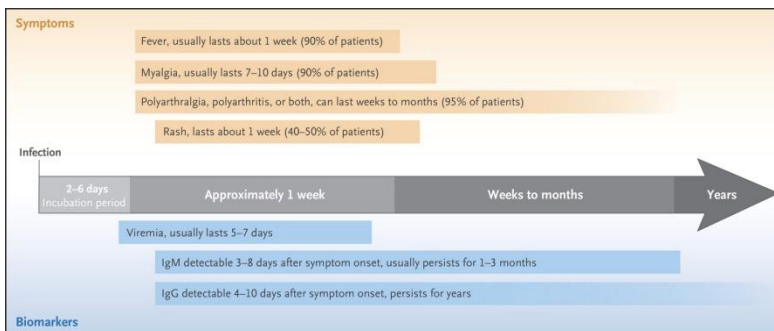
HUMAN PARVOVIRUS B19

PARVOVIRUS ARTHRITIS

- FIRST CAUSE OF VIRAL ARTHRITIS in the US
- SPRING, SMALL EPIDEMICS
- RASH 1/3
- HIP 1/3
- > 3 MONTHS 1/3
- OLYGOARTICULAR IN YOUNG CHILDREN POLYARTICULAR IN YOUNG WOMEN
- LOW GRADE FEVER
- IgM gone in 3 months, IgG present forever in 60% of Americans

Viral arthritis

- Rubivirus: wild rubella and vaccine
- Togavirus
 - Rubivirus: Rubella virus and vaccine
 - Alphavirus: Ross River, **Chikungunya** and others
- Parvovirus B19
- Hepadnavirus: Hep B and C
- Adenovirus
- Herpesvirus: EBV, CMV
- Paramyxovirus: Mumps



HIV

- Spondyloarthropathy or psoriatic
- Persistent oligoarthritis
- Polyarthralgia during viremia

Chikungunya

- Incubation 5-10 days
- Fever and rash (intense with desquamation) lasting 3 days
- Typical adult symmetrical large and small joint “viral” arthritis pattern lasting at least 8 weeks
- RF CCP, ESR tend to be normal. ANA~ 30%
- NSAIDs (not steroids)

• *Miner JJ et al, A&R 2015 67: 1214*

• *Weaver SC et al. NEJM 2015; 372: 1231*

Valley fever (S Joaquin)

- *Coccidioides immitis*
- Usually a pneumonia
- Arthritis
- E. Nodosum

Non-pyogenic bacterial arthritis

- **Brucella (Malta fever):** typical large joint disease with peri-articular involvement undulant fever (*)
- **Bartonella:** concurrent with EN
- **Kingella *kingae*:** toddlers, preceding URI with stomatitis, 7 days for culture, associated with osteomyelitis
- **Mycobacteria:** mono or oligo. Septic (granulomatous) or reactive (non-granulomatous)

* Gomez-Reino FJ. *Et al Ann Rheum Dis* 1986; 45: 256





THANK YOU!!



Vit.D 25OH total: 17 ng/ml (30-100)
Diagnosis?