Juvenile Idiopathic Arthritis

Incidence ~1 in 10,000
Prevalence ~1 in 1,000

Juvenile Idiopathic Arthritis

- Systemic arthritis
- Oligoarthritis
- Polyarthritis-RF negative
- Polyarthritis-RF positive
- Psoriatic arthritis
- Enthesitis-related arthritis

Frequency of major pediatric connective tissue diseases

<table>
<thead>
<tr>
<th>DISEASE</th>
<th>NUMBER PT's</th>
<th>%</th>
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</thead>
<tbody>
<tr>
<td>Juvenile arthritis</td>
<td>7368</td>
<td>65.2</td>
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<tr>
<td>SLE</td>
<td>1214</td>
<td>10.7</td>
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<tr>
<td>Juvenile dermatomyositis</td>
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<td>5.8</td>
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<tr>
<td>Systemic sclerosis</td>
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<td>Localized sclerosis</td>
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<td>Polyarteritis nodosa</td>
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<td>0.4</td>
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<td>Kawasaki's disease</td>
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<td>2.3</td>
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<td>Henoch-Schonlein purpura</td>
<td>838</td>
<td>7.4</td>
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<tr>
<td>Other vasculitides</td>
<td>491</td>
<td>4.3</td>
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</table>

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Juvenile Idiopathic Arthritis

Systemic arthritis - arthritis in one or more joints, with or preceded by fever of 1 weeks duration which is documented to be daily for at least 3 days and accompanied by one or more of the following:
- Evanescent rash
- Generalized adenopathy
- Hepatosplenalgia
- Serositis
Juvenile Idiopathic Arthritis

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Juvenile Idiopathic Arthritis

- Oligoarthritis - arthritis affecting 1-4 joints in the first 6 months of the disease. Two subcategories are recognized:
  - Persistent oligoarthritis - affecting 4 or fewer joints throughout the course
  - Extended oligoarthritis - affecting more than 4 joints after the first 6 months of disease

Juvenile Idiopathic Arthritis

- Polyarthritis-RF negative - arthritis affecting 5 or more joints during the first 6 months of the disease; test for RF is negative

Juvenile Idiopathic Arthritis

- Polyarthritis-RF positive - arthritis affecting 5 or more joints during the first 6 months of disease; at least 2 tests for RF are positive during the first 6 months of disease
### Juvenile Idiopathic Arthritis

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### Psoriatic arthritis

- Psoriasis or arthritis and two of the following:
  - Dactyliitis
  - Nail pitting and onycholysis
  - Psoriasis in a first degree relative

### Enthesitis-related arthritis

- Psoriatic arthritis - arthritis and enthesitis or arthritis or enthesitis with at least two of the following:
  - Presence of or history of SI joint tenderness or inflammatory lumbosacral pain
  - HLA B27 positivity
  - Onset of arthritis in male over 6 years of age
  - Acute anterior uveitis

### Signs and symptoms of disease

- Peak age of onset: 2-4 years
- 10% of all JIA cases
- Male to female 1:1 ratio
- Arthritis pattern: polyarticular, often knees, wrists and ankles; also fingers, neck and hips
- Extra articular features: daily fever, evanescent rash, pericarditis, pleuritis, hepatosplenomegaly
Systemic arthritis

- Laboratory findings: anemia, elevated WBC, elevated sed rate, elevated CRP, elevated ferritin, elevated platelets
- Therapy: less responsive to standard therapy of methotrexate and TNF alpha agents; IL-1 antagonist helpful [Kineret]

Parvovirus B19 Infection

Systemic JIA with Tenosynovitis and Cyst Formation

Oligoarthritis

- Peak age of onset: less than 6 years
- 50-60% of all JIA cases
- Male to female ratio 1:4
- Arthritis pattern: knees++; ankles, fingers+
- Extra articular features: uveitis 30%
Oligoarthritis

- Laboratory findings: ANA positive in 60%, mildly elevated ESR and CRP
- Therapy: NSAIDS, intra-articular steroids; methotrexate may be required
Juvenile rheumatoid arthritis: asymmetric growth

Growth Retardation

Polyarthritis-RF Negative

- Peak age of onset: 6-7 years
- 30% of all JIA cases
- Male to female ratio 1:3
- Arthritis pattern: symmetric or asymmetric; small and large joints; cervical spine; TMJ
- Extra articular features: uveitis in 10%

Laboratory findings: ANA positive in 40%; RF negative; ESR elevated; CRP mildly elevated or normal; mild anemia

Therapy: initial therapy with methotrexate and NSAIDS; if unresponsive add anti-TNF agents or other biologics

Polyarticular JIA
Polyarthritis-RF Positive

- Peak age of onset: 9-12 years
- Less than 10% of all JIA cases
- Male to female ratio 1:9
- Arthritis pattern: aggressive symmetric polyarthritis
- Extra articular features: rheumatoid nodules in 10%, low grade fever

Symmetric Polyarticular Arthritis

Rheumatoid Nodules

Psoriatic Arthritis

- Peak age of onset: 7-10 years
- Less than 10% of JIA cases
- Male to female ratio 1:2
- Arthritis pattern: asymmetric arthritis of small of medium sized joints
- Extra articular features: uveitis in 10%, psoriasis in 50%
Psoriatic Arthritis

- Laboratory findings: ANA positive in 50%, ESR mildly increased, mild anemia
- Therapy: NSAIDS and intra-articular injections; second line agents are used in polyarticular disease if synovitis persists (at times the synovitis can be particularly destructive).

Psoriatic Arthritis with Dactylitis

Psoriatic Onycholysis

Psoriatic Onycholysis with Dactylitis

Enthesitis-related arthritis

- Peak age of onset: 9-12 years
- 10% of all JIA cases
- Male to female ratio 7:1
- Arthritis pattern: predominately lower limb joints affected; sometime axial skeletal joints
- Extra-articular features: acute anterior uveitis; association with reactive arthritis and IBD

Enthesitis-related arthritis

- Laboratory findings: HLA B27 positive in 80%
- Therapy: NSAIDS and intra-articular steroids; methotrexate or sulfasalazine; anti-TNF agents needed for axial skeletal disease

HLA B27+ Spondyloarthritis
Patient Evaluation

- History
  - Pain: character, location, frequency, time of day, mitigating/exacerbating factors
  - Fevers
  - Rashes
  - Weight Loss
  - Fatigue

- Physical Exam
  - Joints: warmth, swelling, tenderness, range of motion (± hypermobility or restriction)
  - Complete exam from head to toe

Patient Evaluation

- Laboratory Evaluation
  - CBC, ESR, CRP, CMP, ANA, RF, CCP, HLA B27

- X-Rays
  - Usually normal at presentation, but may reveal pathology other than arthritis as etiology of pain

- Ophthalmology Evaluation – once diagnosis of JIA is made

False Positive ANA Tests

- Asymptomatic positive ANAs are common
  - up to 32% of titers of 1:40
  - up to 13% of titers of 1:80
  - up to 3% of titers of 1:320

- First degree relatives of patients with lupus

- Infectious diseases
  - Viral: EBV, CMV
  - SBE, TB

- Drugs – Dilantin, Hydralazine, TNF-blocking agents

- Lymphoproliferative Disorders

False Positive ANA Tests

- A positive ANA is very non-specific. In isolation it does NOT make a diagnosis of any specific illness.

- In the setting of specific historical AND physical findings, along with the full laboratory evaluation, a positive ANA can HELP confirm a diagnosis of autoimmune illness.

THERAPY

- Non-steroidal anti-inflammatory drugs (NSAIDs)
- Joint Injections
- Disease Modifying Anti-rheumatic Drugs (DMARDs)
  - Methotrexate, Biologics
  - Hydroxychloroquine, Sulfasalazine, Leflunomide
- Corticosteroids
- Physical Therapy
- Orthopedic Surgery

NSAID’s

- Provide mild analgesia and have modest anti-inflammatory effect when taken regularly for 10-14 days

- Used as a first line drug in mild juvenile arthritis cases

- Do NOT act as disease modifying drugs

- Ineffective when used as monotherapy in most patients
**NSAID’s  
Major Side Effects**
- Gastrointestinal toxicity with risk of ulceration and bleeding
- Allergic reactions can occur but desensitization is possible
- Other major side effects can include renal insufficiency and hypertension, but these are rare in children unless there is underlying renal disease

**METHOTREXATE**
- Drug of first choice
- Has been in use for JIA since the early 1980's, and widely used since the early 1990's
- Advantages:
  - Effective in the majority of patients
  - Inexpensive
  - Very safe with appropriate monitoring
  - Now able to monitor MTX polyglutamate levels to assess adequacy of dose as well as compliance

**METHOTREXATE**
- Disadvantages:
  - Requires monthly (or q. o. monthly) laboratory monitoring for side effects
  - GI intolerance in some patients
  - Risk of birth defects
  - Onset of benefit is delayed; initially seen 4-6 weeks after initial dose is given; the starting dose is not usually the effective dose

**METHOTREXATE**
- Side Effects:
  - Hepatotoxicity
  - Oral ulcers
  - Bone marrow suppression
  - Nausea, vomiting, abdominal pain, diarrhea
  - Fatigue
  - Increased risk of infection—especially respiratory

**METHOTREXATE**
- Side effects are mitigated by use of folic acid 1- mg daily
- Methotrexate is NOT chemotherapy
- In doses used in rheumatology it acts as an anti-inflammatory medication
- Mechanism of action: Methotrexate is a folate analogue and binds to dihydrofolate reductase with high affinity and inhibits purine biosynthesis.

**TNF-α Inhibitors**
- Enbrel (etanercept)
- Humira (adalimumab)
- Remicade (infliximab)
- Cimzia (certolizumab pegol)
- Simponi (golimumab)
Other Biologics

- Orencia (abatacept)
- Kineret (anakinra)
- Rituxan (rituximab)

Childhood Malignancy and Bone Pain

- Leukemia
- Lymphoma
- Neuroblastoma
- Histiocytosis
- Osteogenic sarcoma
- Ewing’s sarcoma

Signs of Malignancy

- Child appears miserable
- Low-grade fevers
- Night pain
- Pain out of proportion to physical findings
- Pain in both bones and joints
- Pallor, petechiae
- Hepatosplenomegaly
- Lymphadenopathy

Acute Rheumatic Fever – Modified Jones Criteria (1992)

- Major Criteria:
  - Carditis
  - Polyarthritis
  - Sydenham’s Chorea
  - Erythema Marginatum
  - Subcutaneous Nodules

- Minor Criteria:
  - Clinical - fever, arthralgias
  - Laboratory – elevated ESR and CRP; prolonged PR interval

High Probability of diagnosis with 2 major OR 1 major and 2 minor criteria PLUS evidence for a preceding group A strep infection

Acute Rheumatic Fever – Subcutaneous Nodules
### Juvenile Dermatomyositis

#### Clinical Manifestations
- Muscle weakness 100%
- Proximal pelvic girdle 95%
- Proximal shoulder girdle 75%
- Neck flexors 60%
- Pharyngeal muscles 45%
- Distal extremity muscles 30%
- Facial and extraocular muscles 5%
- Arthritis 25%
- Skin 85-100%
- Gottron's papules 80%
- Heliotrope rash 15%
- Malar rash 40%
- Photosensitivity 40%
- Ulcerations 25%
- Calcinosis 40%
- Raynaud's 15%
- GI involvement 10-60%
- Pharyngitis 40%
- Dysphagia 10%
- Hemorrhage 5%
- Lung involvement 15-80%
- Fibrosis <1%

#### Treatment
- Glucocorticoids 2 mg/kg per day initially
- Methotrexate
- Hydroxychloroquine
- Azathioprine
- Cyclosporine
- Cellcept
- Cellcept
- IVIG
- Anti TNF agents
JDM – Rash of Face/Hands

JDM – Heliotrope/ Facial Rash
I would like to thank my son and wife for providing me with technical assistance.