1. Juvenile Idiopathic Arthritis (JIA)

Juvenile Idiopathic Arthritis (JIA)

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2. Arthritis - Definition.

Arthritis - Definition.

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- Swelling, warmth, redness and pain.
- Presence of two or more of the following:
  - pain on motion
  - pain on palpation
  - Increase warmth

3. Juvenile Idiopathic Arthritis Definition.

Juvenile Idiopathic Arthritis Definition.

- Constellation of clinical signs and symptoms during the **first six months** of illness.
- Onset before 16 years of age.
- Persistent arthritis for more than six weeks.
- **Exclusion of other conditions.**
- There are **no** laboratory studies to diagnose this disease (Exception may be late radiographics changes in the more severe forms).

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4. History

History

- Cornil in 1864, described a 29 year old woman who had chronic arthritis since the age of 12.
- Meryer Diaman-Berger in 1890, reviewed this subject, and published 38 cases (3 of his own).
- George Frederick Still in 1897 presented the classical description of chronic childhood arthritis on 23 children (12 of them with systemic features).
- Colver in 1937 published the first follow-up examinations of JRA.

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5. Epidemiology

Epidemiology

- The most frequent rheumatic disease of children, and one of the most common chronic illnesses of childhood.
- Major cause of functional disability and eye disease leading to blindness.
- Based on the ACR criteria, between 2 and 20 of every 100,000 children develop JIA each year, the overall prevalence is approximately 16 to 150 per 100,000.
- The course of the disease can be highly variable.

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6. Frequency of Rheumatologic Diseases

Frequency of Rheumatologic Diseases

Juvenile rheumatoid arthritis:	**5105 (67%)**
Systemic Lupus Erythematosus:	638 (8%)
Juvenile dermatomyositis:	456 (6%)
Systemic scleroderma:	60 (0.8%)
Localized scleroderma:	196 (2.6%)
Polyarteritis nodosa:	35 (0.5%)
Kawasaki's disease:	212 (2.8%)
Henoch-Schonlein purpura:	580(7.7%)
Other vasculitides:	434 (6%)
Total:	7578 (20%)

Data from 38,187 diagnoses from 33,000 consecutive patients entered into the Pediatric Rheumatic Disease Registry of the Pediatric Rheumatology Database Research Group, 1992 - 1998.

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7. Inflammation in JIA

Inflammation in JIA

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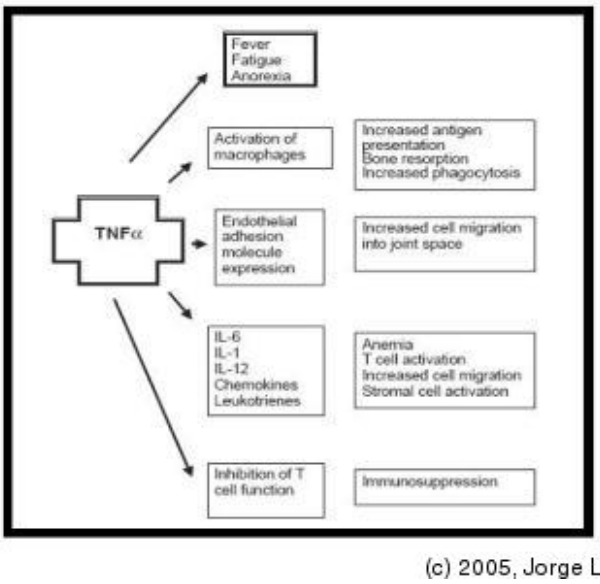
8. TNF role in JIA

TNF role in JIA



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9. Immunology

Immunology

- Autoimmune disease with a complex genetic trait (immunogenetically determined disorder or an antigen-driven immunologic response).
  - Disordered Th1/Th2 interaction.
  - Abnormal T-cell receptor polymorphism.
  - Immune complexes formation, complement activation and consumption, presence of autoantibodies and characteristics cytokines profiles.
- Cytokines profiles:
  - IL-6, IL-1, TNF-α: systemic onset JIA.
  - IL-1 α, IL-1 β, sIL-2R: poly-articular course.
  - sIL-2R, IL-1β, TNF-α: pauci-articular course.

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10. Juvenile Idiopathic Arthritis Sub-types

Juvenile Idiopathic Arthritis Sub-types

- **Systemic onset (Still's disease)**
  - Typical quotidian fever of at least 2 weeks duration and one or more: rash, lymphadenopathy, hepatosplenomegaly, serositis
- **Oligoarticular (< 4 joints or less)**
  - Persistent (never more than 4 joints)
  - Extended (after the first 6 months, more than 4 joints are involved)
- **Polyarticular (5 or more joints)**
  - Seropositive: Rheumatoid Factor (+)
  - Seronegative: Rheumatoid Factor (-)

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11. Juvenile Idiopathic Arthritis Sub-types

Juvenile Idiopathic Arthritis Sub-types

- **Psoriatic arthritis:** arthritis and psoriasis.
  - arthritis and two of the following: Dactylitis, nail abnormalities (pitting or onycholysis), family history of psoriasis (first degree relative).
- **Enthesitis-related arthritis:** arthritis and enthesitis
  - arthritis or enthesitis plus two of the following: sacroiliac tenderness, HLA-B27 (+), acute anterior uveitis, onset in a boy after the age of 8 years, family history of HLA-B27 associated disease (1st or 2nd degree).
- **Other arthritis:** conditions that does not meet any of the previous criteria or meet criteria for more that one category.

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12. Juvenile Idiopathic Arthritis Oligo-articular Sub-type

Juvenile Idiopathic Arthritis Oligo-articular Sub-type

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- Four or less joints involved
  - Mono-articular in 74 % (Only one knee in 50%)
- Is a moderate arthritis
- Represents 40 - 60% of the JIA
  - Persistent: < 4 joints through out the course of the illness.
  - Extended: after the first 6 months, involves > 5 joints.

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13. Juvenile Idiopathic Arthritis Oligo-articular Sub-type

Juvenile Idiopathic Arthritis
Oligo-articular Sub-type

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- Spares the hips and sacroiliac joints.
- ANA (+) in 60%
  - (75 - 85% in girls with uveitis),
- RF (-)
- HLA-A2 and DR5 (6,8).
- Iridocyclitis: 25 - 40% of cases (Sub-acute or Chronic).
- Age of onset: around 2 years
- F:M ratio - 5:1

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14. Oligo-articular JIA

Oligo-articular JIA

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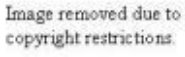
15. Juvenile Idiopathic Arthritis Iridocyclitis (Uveitis)

Juvenile Idiopathic Arthritis
Iridocyclitis (Uveitis)



- Sex (F:M): 6:1
- Frequency:
  - Pauciarticular
    - ANA (+): 40%
    - ANA (-): 25%
  - Polyarticular
    - RF (-): 5%
    - RF (+): <1%
  - Systemic: <1%

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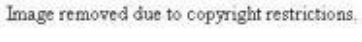
16. JIA - Iridocyclitis (Uveitis)

JIA - Iridocyclitis (Uveitis)



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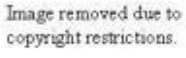
17. Juvenile Idiopathic Arthritis Polyarticular - Seronegative...

Juvenile Idiopathic Arthritis
Polyarticular - Seronegative



- Five or more joints involved.
- Rheumatoid factor (-) x 2, 3 months apart
- Symmetric polyarthritis of small and large joints.
- Represents 20 to 30% of all the JIA
- Is a severe arthritis in 10 to 15% of cases.

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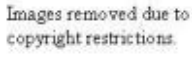
18. Juvenile Idiopathic Arthritis Polyarticular - Seronegative...

Juvenile Idiopathic Arthritis
Polyarticular - Seronegative



- Rheumatoid nodules do occur.
- ANA (+) in 25%
- HLA-DPw3.
- Iridocyclitis is rare (5%).
- Age of onset: 3 years.
- F:M ratio - 3:1.

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19. Juvenile Idiopathic Arthritis Polyarticular - Seropositive...

Juvenile Idiopathic Arthritis
Polyarticular - Seropositive

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- Corresponds to the Rheumatoid Arthritis (RA) seen in adults
- HLA- DR4 (DRB1*0401).
- Five or more joints involved.
- Rheumatoid Factor (+) x 2, 3 months apart.
- Symmetric polyarthritis of small and large joints.

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20. Juvenile Idiopathic Arthritis Polyarticular - Seropositive...

Juvenile Idiopathic Arthritis
Polyarticular - Seropositive

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- Represents 5 to 10% of all the JIA
- Is a severe arthritis in more than 50% of cases.
- Rheumatoid nodules are usually present.
- ANA (+) in ~75%.
- Iridocyclitis absent.
- Age of onset: 12 years.
- F:M ratio - 4:1.

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21. Juvenile Idiopathic Arthritis Systemic onset (Still's Diseas...

Juvenile Idiopathic Arthritis
Systemic onset (Still's Disease).

- Arthritis with or preceded by daily fever of at least 2 weeks duration, that is documented to be quotidian for at least 3 days and accompanied by one or more of the following:
  - Evanescent, non-fixed erythematous rash
  - Generalized lymph node enlargement
  - Hepatomegaly or splenomegaly
  - Serositis

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22. Fever in Still’s disease.

Fever in Still's disease.

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23. Rash in Still’s disease.

Rash in Still's disease.

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24. Lymphadenopathy in Still’s disease.

Lymphadenopathy in Still's disease.

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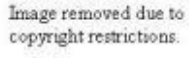
25. Juvenile Idiopathic Arthritis Systemic onset (Still’s ...

Juvenile Idiopathic Arthritis
Systemic onset (Still's Disease).



- Systemic or extra-articular manifestations.
- RF (-)
- ANA (-).
- Iridocyclitis is extremely rare.
- Age of onset: 5 years.
- F:M ratio - 1:1.

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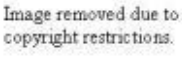
26. Juvenile Idiopathic Arthritis Systemic onset (Still’s ...

Juvenile Idiopathic Arthritis
Systemic onset (Still's Disease).



- Represents 10 - 20 % of all JIA
- Is a severe arthritis in 25% of cases:
  - Pauciarticular pattern.
  - Polyarticular pattern .

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27. Macrophage Activation Syndrome

Macrophage Activation Syndrome

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- "Cytokine storm": serious and sometimes fatal complication of Still's disease characterize by coagulation disorder, pancytopenia and decrease ESR.
- Might respond to high dose steroids and IV Cyclosporin

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28. Psoriatic Arthritis.

Psoriatic Arthritis.

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- Arthritis and psoriasis.
- Arthritis and two of the following:
  - Dactylitis
  - Nail abnormalities (pitting or onycholysis)
  - Family history of psoriasis (first degree relative).

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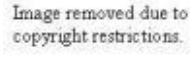
29. Enthesitis-related arthritis.

Enthesitis-related arthritis.



- Arthritis and enthesitis.
- Arthritis or enthesitis plus two of the following:
  - Sacroiliac tenderness
  - HLA-B27 (+)
  - Acute anterior uveitis
  - Onset in a boy after the age of 8 years
  - Family history of HLA-B27 associated disease (1st or 2nd degree).

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30. Juvenile Idiopathic Arthritis Treatment

Juvenile Idiopathic Arthritis Treatment

- Non Steroidal Anti-Inflammatory Drugs (NSAIDs)
- Disease Modifying Anti-Rheumatic Drugs (DMARDs)
- Cytotoxic Agents
- Biologic Agents
- Physical and Occupational Therapy

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31. Juvenile Idiopathic Arthritis Treatment objectives.

Juvenile Idiopathic Arthritis
Treatment objectives.

- Immediate:
  - Relieve discomfort.
  - Preserve function.
  - Prevent deformities.
  - Control inflammation.
- Long-term:
  - Minimize side effects of disease and treatment.
  - Promote normal growth and development.
  - Rehabilitate.
  - Educate.

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32. Juvenile Idiopathic Arthritis Poor Prognostic Indicators

Juvenile Idiopathic Arthritis
Poor Prognostic Indicators

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- Active systemic disease at 6 months.
- Polyarticular onset or disease course .
- Extended pauci-articular disease course.
- Female gender.
- Presence of rheumatoid factor and/or antinuclear antibodies.
- Persistent morning stiffness, tenosynovitis, subcutaneous nodules.
- Rapid appearance of erosions.
- Hip involvement or early involvement of small joints of hands and feet. .

From Gore and Fuster, Takei et al, and Casey and Petty.

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33. Juvenile Idiopathic ArthritisLong term outcome

Juvenile Idiopathic Arthritis
Long term outcome

- Historically, 70 to 90 percent of children with JIA have a satisfactory outcome without serious disability.
- A small percentage (about 5%) have a recurrence of arthritis as adults.
- Approximately 10 to 17 percent of children with JIA enter adulthood with moderate to severe functional disabilities.
- Delay in referral and initiation of an acceptable therapeutic program are associated with a poorer functional outcome.

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