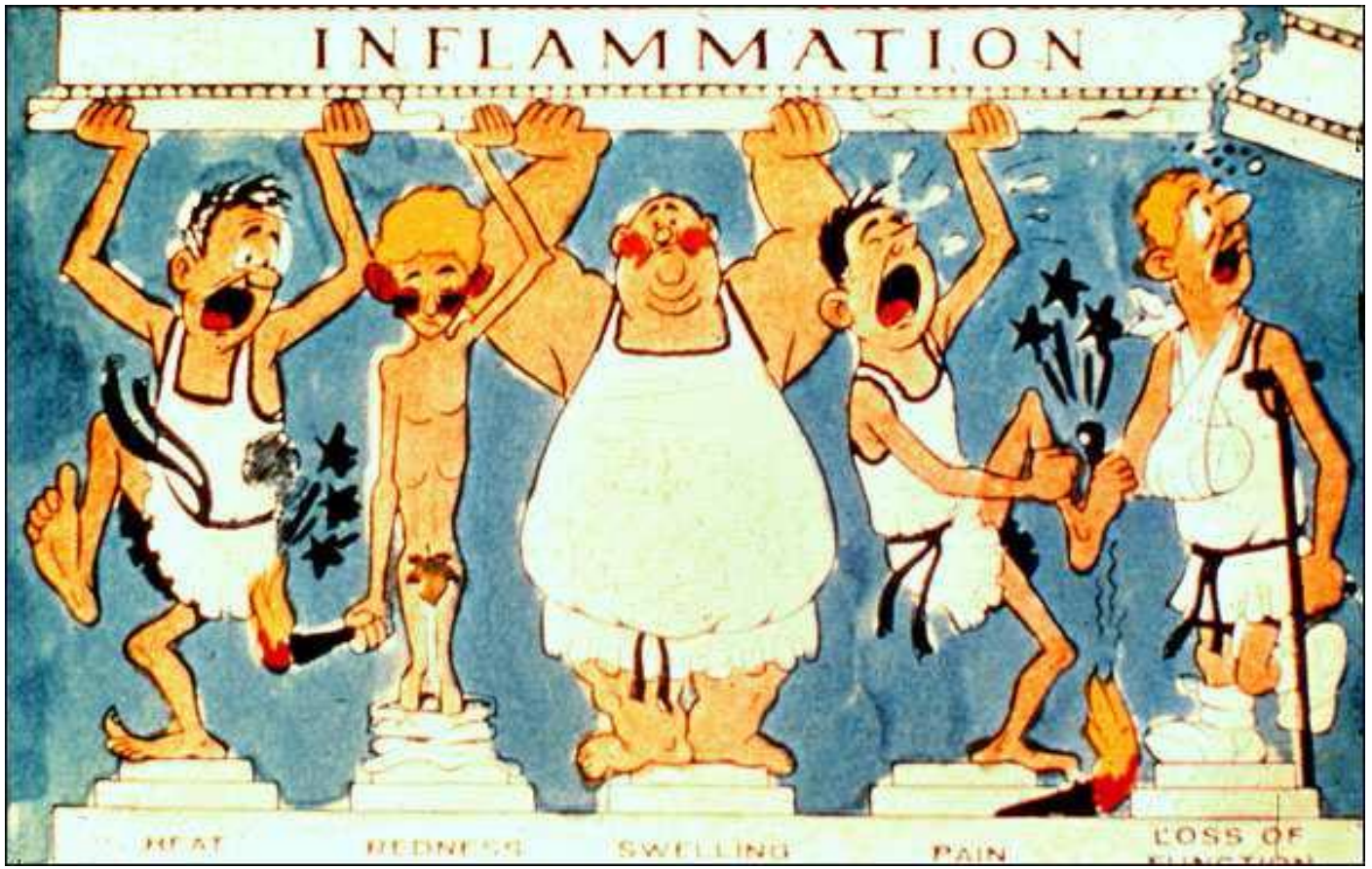
Pediatric autoimmune diseases

Bernadett Mosdósi

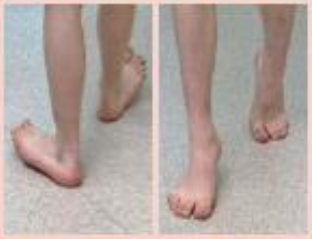
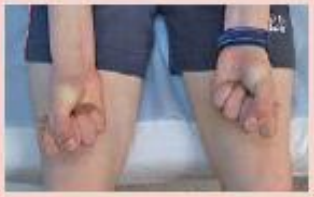
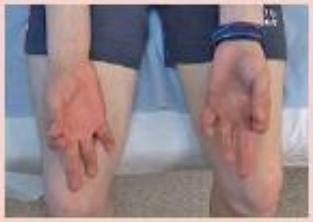
Arthralgia ----- Arthritis



calor rubor tumor dolor functio laesa

www.arthritisresearchuk.org

FIGURE	SCREENING MANOEUVRES	WHAT IS BEING ASSESSED?
	'Touch the tips of your fingers'	• Manual dexterity • Coordination of small joints of fingers and thumbs
	Squeeze the metacarpo-phalangeal joints for tenderness	• Metacarpophalangeal joints
	**'Put your hands together palm to palm' and 'Put your hands together back to back'**	• Extension of small joints of fingers • Wrist extension • Elbow flexion
	**'Reach up, "touch the sky"' and 'Look at the ceiling'**	• Elbow extension • Wrist extension • Shoulder abduction • Neck extension
	'Put your hands behind your neck'	• Shoulder abduction • External rotation of shoulders • Elbow flexion

FIGURE	SCREENING MANOEUVRES (Note the manoeuvres in bold are additional to those in adult GALS[2])	WHAT IS BEING ASSESSED?
	Observe the child standing (from front, back and sides)	• Posture and habitus • Skin rashes – e.g. psoriasis • Deformity – e.g. leg length inequality, leg alignment (valgus, varus at the knee or ankle), scoliosis, joint swelling, muscle wasting, flat feet
	Observe the child walking and **'Walk on your heels' and 'Walk on your tiptoes'**	• Ankles, subtalar, midtarsal and small joints of feet and toes • Foot posture (note if presence of normal longitudinal arches of feet when on tiptoes)
	'Hold your hands out straight in front of you'	• Forward flexion of shoulders • Elbow extension • Wrist extension • Extension of small joints of fingers
	'Turn your hands over and make a fist'	• Wrist supination • Elbow supination • Flexion of small joints of fingers
	'Pinch your index finger and thumb together'	• Manual dexterity • Coordination of small joints of index finger and thumb and functional key grip

CHRONIC ARTHRITIS in CHILDREN

- Juvenile idiopathic arthritis: 80 %
- SLE:10 %
- DM: 5 %
- Scleroderma: 2 %
- Vasculitis: 2 %
- Febris rheumatica: 1 %

- ***http://www.arthritisresearchuk.org*** ***pGALS***

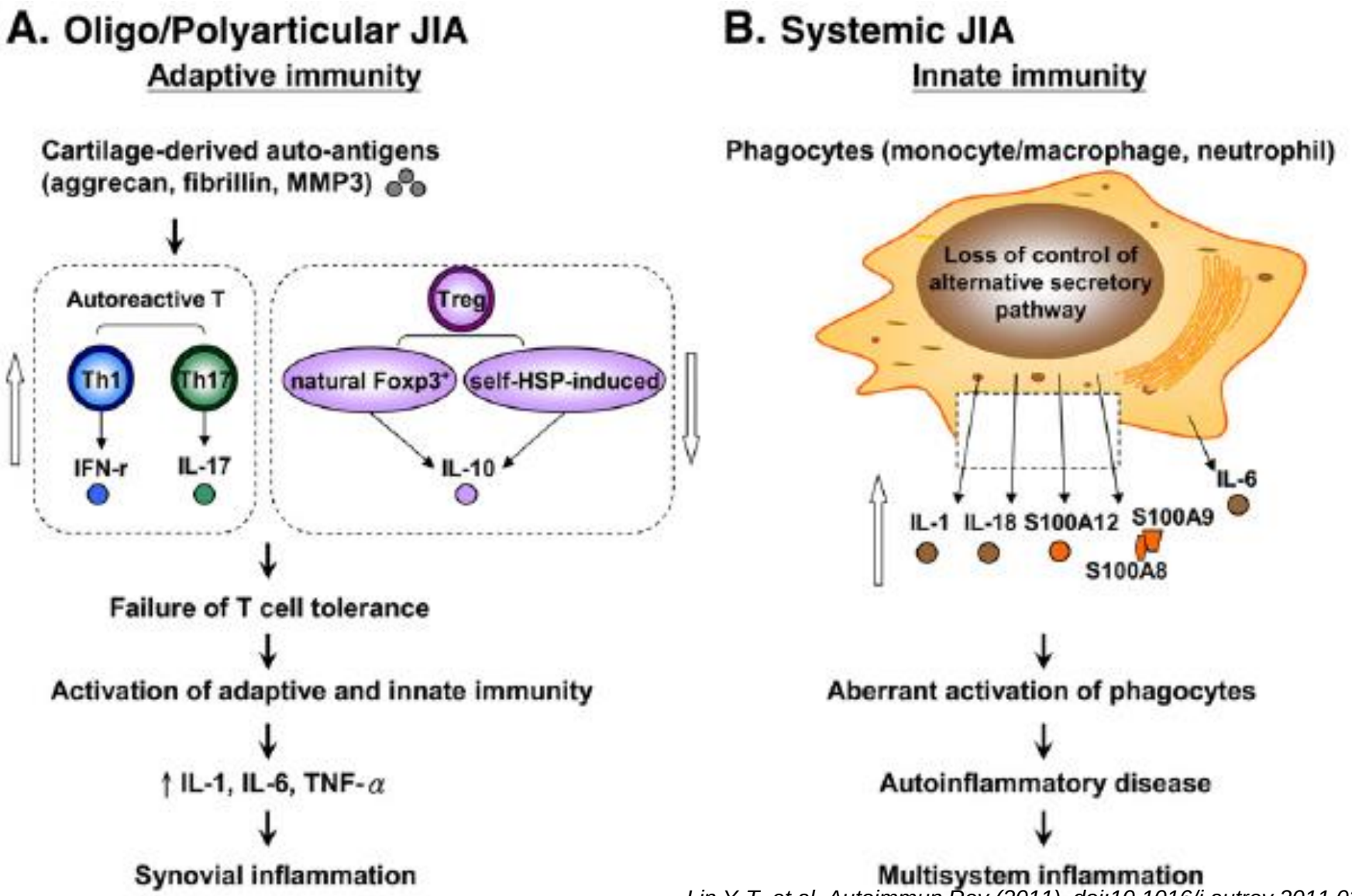
JUVENILE IDIOPATHIC ARTHRITIS (JIA)

- Definition:
  - < 16 y
  - arthritis > 6 weeks (chronic)
  - Other etiology (SLE, dermatomyositis, scleroderma, vasculitis, rheumatoid fever) are excluded.

Juvenile idiopathic arthritis (JIA)

ILAR classification	Rate (%)	Age of onset (y)	Gender
Systemic onset JIA (SoJIA)	4-17	1-18 (1-6)	F=M
Polyarticular JIA RF+	2-7	9-14	F>>M
Polyarticular JIA RF-	11-28	2-4; 6-12	F>>M
Oligoarticular JIA	27-56	2-4	F>>>M
Arthritis psoriatica (PsA)	2-11	2-4; 9-11	F>M
Enthesitis related JIA (ERA)	3-11	9-14	M>>F
Not differentiated	11-21		

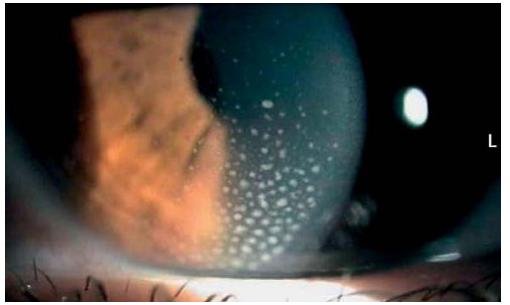
Pathogenesis of JIA



Lin Y-T, et al. Autoimmun Rev (2011), doi:10.1016/j.autrev.2011.02.001

I. OLIGOARTICULAR JIA

- **≤ 4 joints** during the first 6 months and:
  - Psoriasis excluded, not male older than 6 y, RF neg., HLA-B27 neg.
- young girls
- **asymmetric** *inflammation* of the knee, ankle
- *ANA* pozitive in 70-80% – chronic anterior **uveitis** in 30% !!!
- 2 *subgroups*:
  - Persistent
  - Extended: > 4 joints during the first 6 months



II. POLYARTICULAR JIA

- **≥ 5 joints** during the first 6 months
- **2 subgroups**:
  - RF positive (2 occasions): adolescent girls
  - RF negative: heterogenous group
- Clinical signs:
  - Symmetric involvement of the **small joints** of the hand and feet; **temporomandibular,** sacroiliacal joint
  - rarely large joints
  - Morning stiffness, rheumatoid nodules
  - Low-grade fever, lymphadenomegaly, hepatosplenomegaly

III. SYSTEMIC JIA (SOJIA)

- Symptomes:
  - **Fever** (> 2 weeks), intermittent, 1-2 peaks/day,

  + at least one of the followings
  - **Rash** (90%), during fever episodes
  - **Lympadenopathy, hepato(spleno)megaly** (80%)
  - **Serositis** (pleuritis, pericarditis, peritonitis) (60%)
  - **Arthritis** (often not present at onset):oligo-polyarthritis, myalgia

Systemic JIA (SoJIA)

- **Differential diagnosis**
  - Infection: bacterial endocarditis, sepsis, Brucellosis, Typhus, viral infections
  - Leukaemia, lymphoma, neuroblastoma
  - Autoimmune diseases: SLE, Kawasaki, polyarteritis, IBD,
  - Rheumatic fever
  - Autoinflammatory syndromes (periodic fever syndromes)
- **Therapy**
  - NSAID (indomethacin, ibuprofen)
  - Steroid, DMARDS: methotrexate
  - Biologic therapy (anti IL-1R, IL-6R)
  - BMT

IV. ENTHESITIS RELATED JIA /ERA/

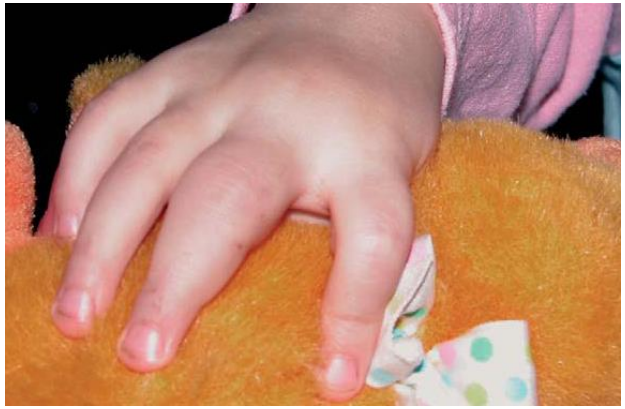
- Corresponds the juvenile onset spondylarthropathy of adults
  - **Enthesitis**: Achilles tendon insertion, tarsal area, plantar fascia
  - **Arthritis**: Large joints of the lower extremities, often **hip**s !

    Axial joints are involved later

    Asymmetric fashion
- **HLA-B27** positivity
- Acut anterior uveitis, sacroileitis associated IBD, Reiter syndrome

V. PSORIATIC ARTHRITIS

- **Criteria**:
  - Arthritis + psoriatic plaque or
  - Arthritis + 2 of the followings: positive family history of psoriasis, **dactylitis**, **nail-pitting**
- Arthritis can prescend the skin/nail lesions !



DIAGNOSIS OF JIA

- Comprehensive history and physical examination
- ***There is no specific diagnostic test for JIA !!!!***
  - RF → small percentage of patients with polyarticular JIA
  - ANA → strong association with oligoarticular JIA and chronic uveitis, iridocyclitis
  - HLA-B27 → spondylarthropathy
- X-ray, US, MR
- **Ophthalmology**

DIFFERENTIAL DIAGNOSIS of ARTHRITIS

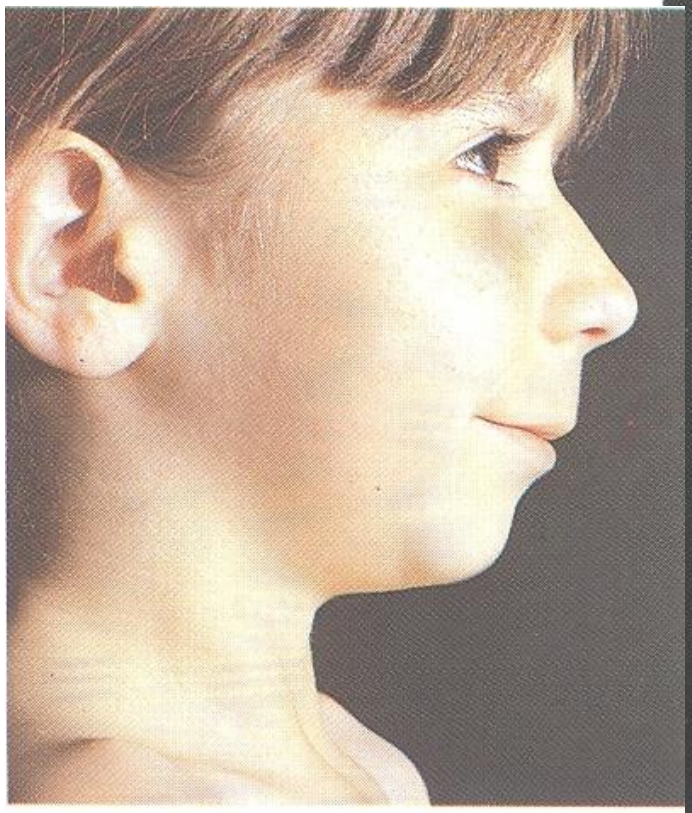
- Trauma
- Septic arthritis (Staphylococcus, Streptococcus)
- Lyme arthritis
- Other infection-related arthritis:
  - Virus: Parvo B19, HBV, herpes, adeno, Mycoplasma pn.: non-destruktive
  - Reactive arthritis:
    - Salmonella/Yersinia/Campylobacter infection
    - Reiter sy.: HLA B27+ arthritis, conjunctivitis, urethritis
  - Reumatic fever
  - Lyme disease
- Malignancy, periodic fever sy., toxic synovitis
- Autoimmun diseases: JIA, SLE, DM, scleroderma, Sjögren sy., systemic vasculitides

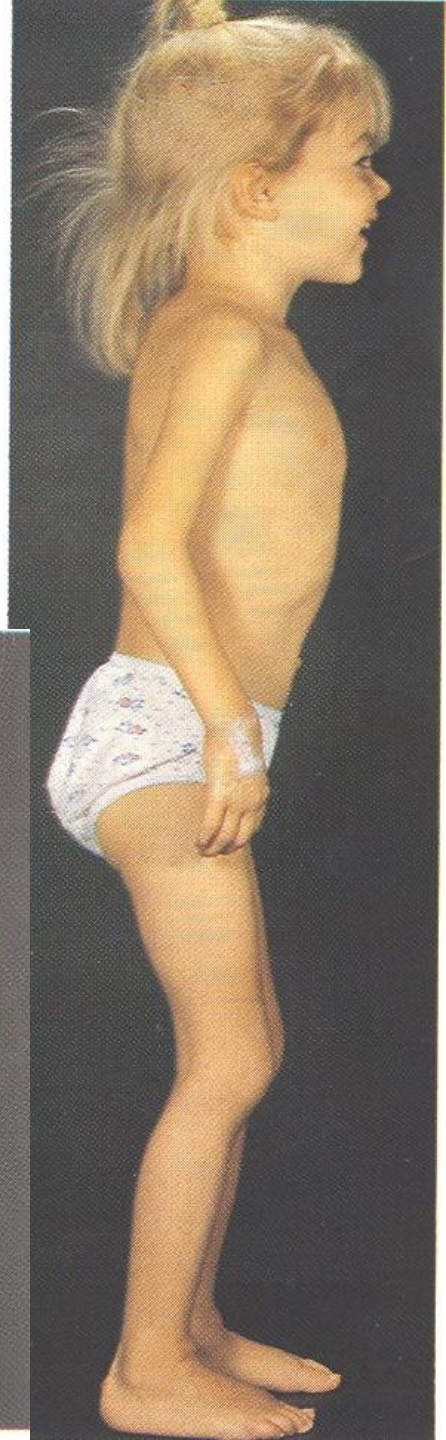
MANAGEMENT OF JIA

- **Drugs:**
  - NSAID: naproxen, indometacin, diclofenac, salicylates
  - Corticosteroids:
    - Severe SoJIA, bridging therapy in other form of JIA bridging, uveitis
    - Intraarticular (oligoarticular JIA): triamcinolon hex.
  - DMARD (disease modifying anti-rheumatic drug):
    - MTX, salazopyrin
  - Biologic agents (anti –TNF alfa, -IL-1,6): etanercept,adalimumab, tocilizumab
- **Physiotherapy!**
- **Psychological support**

Probably consequences of JIA

- Length difference
- Contracture
- Growth retardation
- Osteoporosis
- Caries
- Early atherosclerosis





CONNECTIVE TISSUE DISEASE

Girls predominant

Typical clinical sign

More organs is affected

Immunological laboratory abnormalities

Genetical determined + enviroment

Corticosteroid and DMARD therapy

JUVENILE SLE

- Chronic multisystemic autoimmune disease with flares and remissions
- Autoantibodies against cell nucleus
- Etiology:
  - Genetic susceptibility
    - HLA B8, DR2, DR3
    - Immuncomplex scavanger mechanisms
    - Apoptosis genes, peripheral tolerance genes
  - Hormones, environmental factores
- Female predominance
- Rare: Inciden.: 0,4-0,6/100 000

  Prevalen.: 10/100 000

Juvenile SLE

- **General symptomes:**
  - Fever
  - Fatigue
  - Loss of weight
- **Seeking for:**
  - Arthritis
  - Photosensitivity, Oral ulcers – painless!
  - Haematuria, proteinuria ! – kidney biopsy
  - Alopecia
- **Acut exacerbations**
  - Convulsion, psychosis, anemia, uremia, pulmonary bleeding

SLE: ARA criteria

- Malar rash („buttefly” rash)
- Discoid lesions
- Photosensitivity
- Oral ulcers
- Non-erosive arthritis
- Pleuritis and/or pericarditis
- Renal involvement (proteinuria)
- Central nervous system manifestations (convulsion/psychosis)
- Hematologic abnormalities
- Immunologic abnormalities (a-dsDNS/a-Sm/aPL)
- Positive ANA
- **Dg: At least 4 out of above listed (during any interval of observation !!!!)**

Juvenile SLE

- **Kidney** involvement (66%)

  Mild GN – nephrosis sy. – renal insufficiency. Renal biopsy!

- **CNS** (20-30%)

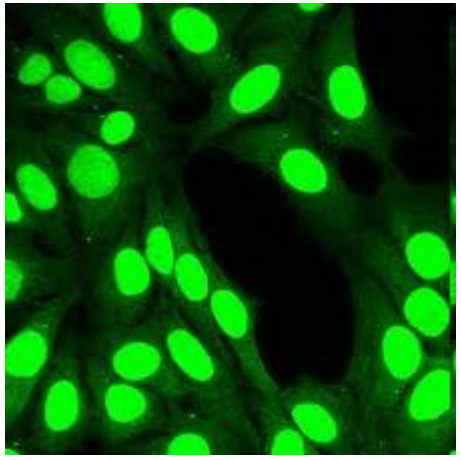
  lupus headache!, pszicho-organic sy., disturbancies of cognitive functions, psychosis, epilepsy, cranial és peripheral neuropathies

- **Lung**

  Recurrent pleuritis, alveolitis occuring as acut, life threatening exacerbation or chronicly, resulting in fibrosis, restrictive ventillation dysorder, pulmonary hypertension.

Juvenile SLE

- **Laboratory:**
  - Elevated ESR, acute phase reactants
  - Anaemia, leucopenia, tctpenia
  - Immunserology:ANA, dsDNA, ENA, antiphospholipide,C1Q antibodies
  - Decreased complements

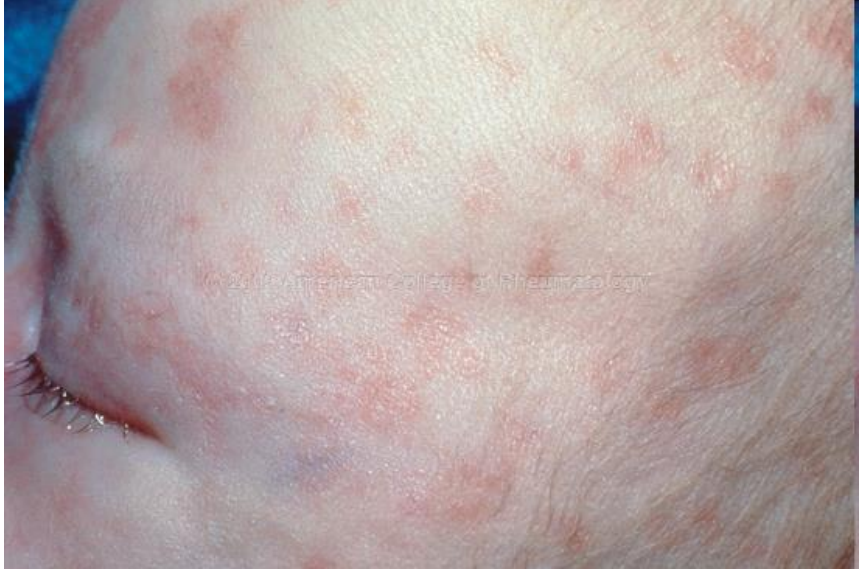


Juvenile SLE

- **Therapy:**
  - Corticosteroids
  - NSAID (musculosceletal symptomes)
  - Hydroxychloroquine (rash, arthritis)
  - Azathioprine, MTX, cyclosporin, mycofenolate mofetil
  - Cyclophosphamide (renal, CNS symptomes)
  - Plasmapheresis

- **Agressive treatment: renal, CNS manifestations !**
- The 10 yr survival 80 %

Neonatal lupus



- Clinical manifestation:
  - Skin: general maculo-papular rash
  - Hepatosplenomegaly
  - AIHA, thrombocytopenia, leucopenia
  - ***Congenital heart block*** *(mater: a-SSA+)*
- *Therapy:*
  - *Corticosteroid, immunglobulin, pheresis*

JUVENILE DERMATOMYOSITIS

- Rare inflammatory disease that predominantly affects the muscles and skin
- Female:male = 2:1.
- Incidence 0,3-0,4/100 000 children

- Two peaks: 5-9 y; 10-14y

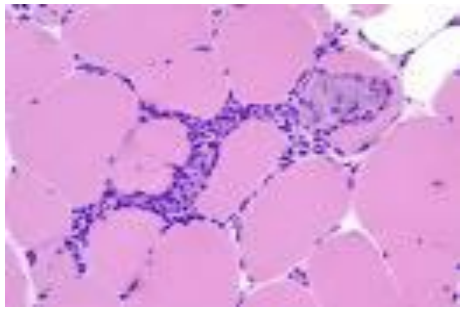
- Etiology is unknown, autoimmune etiology is supposed

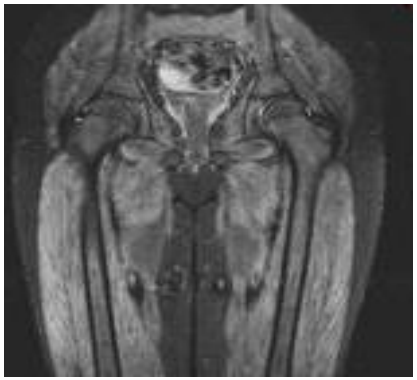
Clinical manifestations

- **Muscle**: neck flexor !, proximal muscle, symmetrical weakness,
- Muscle pain, tender, brawny, indurated
- **Skin** lesion:
  - Gottron sign, papula
  - Heliotrope eyelids, periorbital edema
- **GI:** *dysphagia,* ulceration !
- **Pulm**.: respiratory difficulty, *aspiration,hypoventillation !*
- Cardiac: *myocarditis,* electrocardiographic changes
- Artralgia, arthritis

Juvenile dermatomyositis

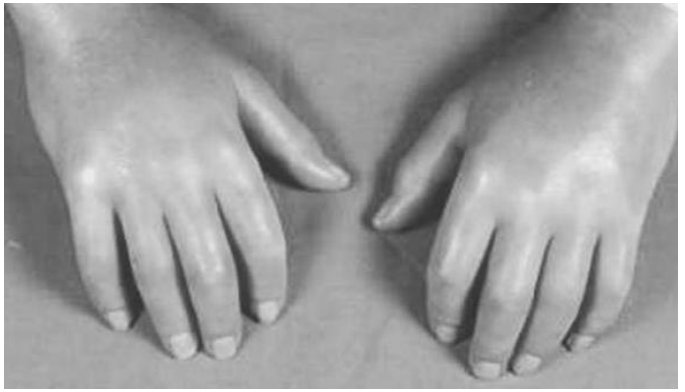
- **Diagnosis**
  - **Laboratory**: CK (MM isoenzyme), LDH, aldolase, AST, ESR
  - EMG (in 70-90% pos.),Muscle biopsy (in 60-70% pos.)
  - Muscle strength assessment
  - **MR**
- **Therapy**
  - Early, agressive therapy !
  - Corticosteroid, tapered slowly --- DMARD
  - Immunglobulin: 2 g/kg !
  - Cyclophosphamid





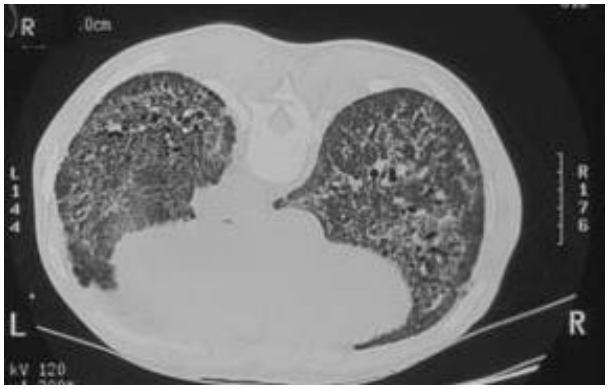
JUVENILE SYSTEMIC SCLEROSIS

- Rare, potentially life-threatening autoimmune disease, currently uncurable
- JSSC is characterized by cutaneous and visceral fibrosis
- Hallmarks: **Raynaud phenomenon and vascular changes**
- Overall incidence: 0,2-1/100 000, 10% of that begins in childhood
- Female predominance



Juvenile systemic sclerosis

- Clinical manifestations
  - Skin: edematous
  - Joints: arthritis, arthralgia
  - Raynaud phenomenon
  - **Cardiopulmonary involvement**: fibrosis, pulm. hypertension, myocardial dysfunction
  - GIT signs: disturbed motility of the esophagus, intestines, malabsorption



VASCULITIDES

- **I. Small and Medium Vessel Vasculitis**
  - A. Immune Complex Mediated
    - 1. Henoch-Schonlein Purpura
    - 2. Hypersensitivity vasculitis
    - 3. Polyarteritis nodosa (PAN)
    - 4. Urticarial vasculitis
    - 5. Cryoglobulinemia
    - 6. Connective tissue diseases (SLE, JRA, dermatomyositis, scleroderma, Behcet disease)
  - B. Antineutrophil Cytoplasmic Antibody (ANCA) Associated
    - 1. Wegener's granulomatosis
    - 2. Microscopic polyarteritis
    - 3. Churg-Strauss syndrome
    - 4. Drug-induced vasculitis

HENOCH-SCHÖNLEIN PURPURA (HSP)

- Most common systemic vasculitis in childhood
- Small-vessel vasculitis
- Epidemiology:
  - 3-10 y
  - winter, following upper airway infection
- Pathomechanism: IgA-immuncomplex deposition

Henoch-Schönlein purpura

- **Skin:** Symmetric purpura on the lower extremities, gluteal area, occasionally on upper extremity
- **Arthritis, arthralgia**: 65-85%, ankle, wrist
- **GIT:**
  - Abdominal pain, bloody stool
  - In 3-5% intestinal infarction, intussusception, acut abdomen
- **Kidney** (~ IgA nephropathy)
  - Hematuria: 50-75%
  - Nephritis, nephrosis, RPGN
- Other: CNS, heart, lung, testis

Henoch-Schönlein purpura

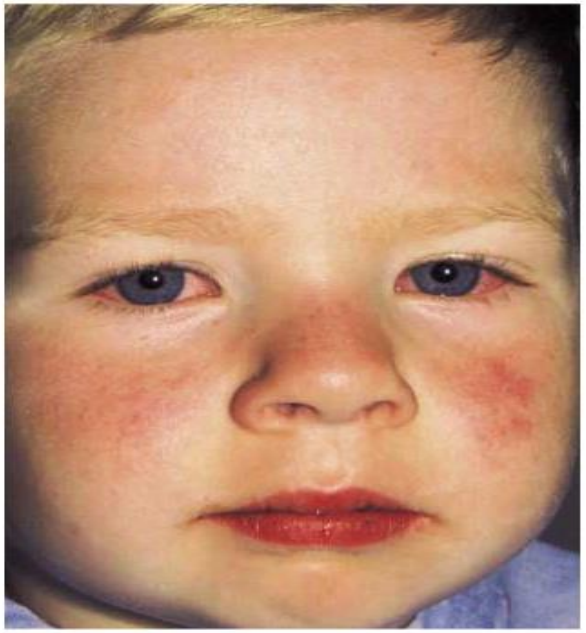
- **Diagnosis**
  - Clinical signs
  - Laboratory – stool examination, urine !
- **DDg**
  - ITP, SLE, HUS
- **Therapy**: symptomatic
  - Joints: NSAID
  - GIT, kidney (after biopsy): steroid, immunsuppressive th.

KAWASAKI DISEASE (KD)

- Acute febrile systemic vasculitis
- affecting the **small and medium-size vessels**
- Etiology: infection?
- Superantigenes?
- Epidemiology: <5 y
- **Dg: fever + 4 other signs**

Diagnosis

- **<u>Clinical signs:</u>**
  - Fever > 5 days
  - Cheilitis, conjunctivitis, strawberry tongue, pharyngitis
  - Palmar, plantar erythem, swelling of the hand, foot, periungual desquamation
  - Polymorph exanthems
  - Cervical lymphadenopathia
- **Dg: fever + 4 other signs**
- Ddg: scarlet fever, toxic shock sy., Stevens - Johnson sy., SoJIA



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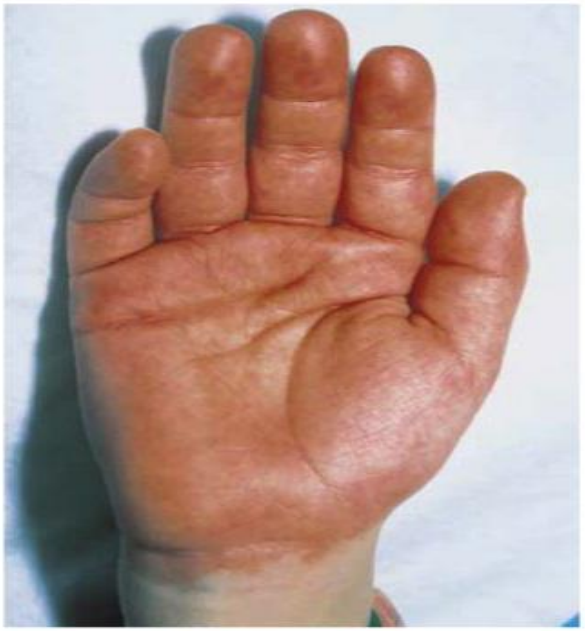

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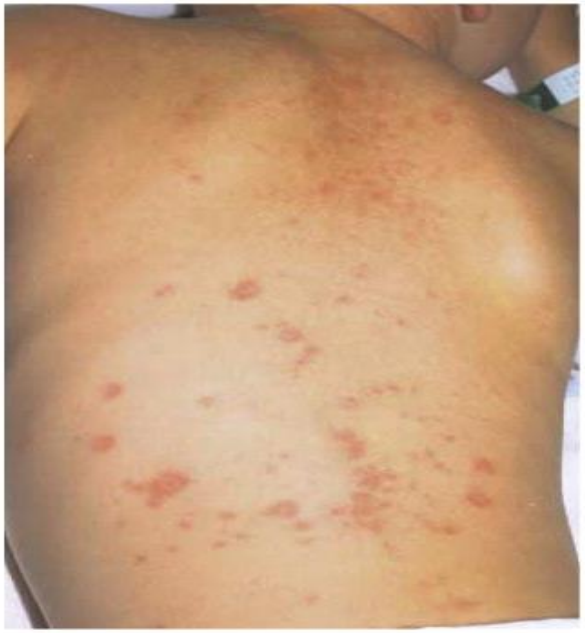

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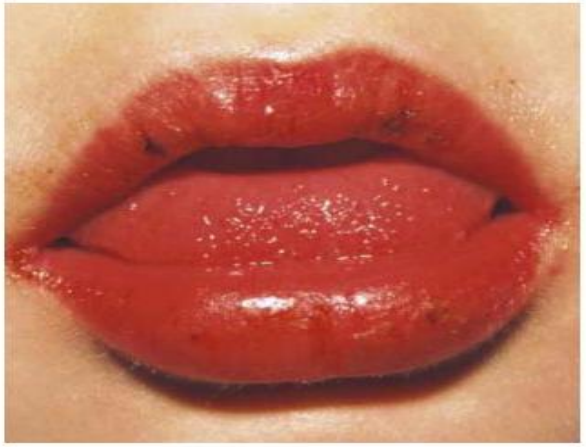

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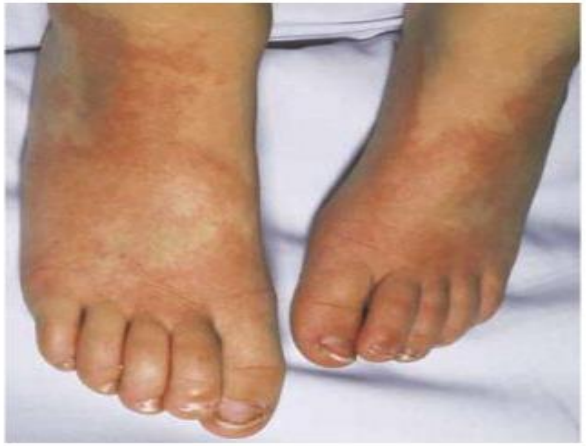

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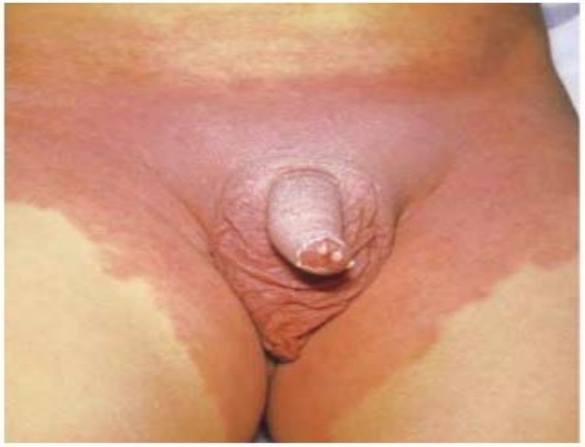

F

Kawasaki disease (KD)

- Complication: **coronary aneurysma**, ischemic heart disease
- Laboratory:
  - Elevated acute phase reactants, transaminases, LDH
  - **Thrombocytosis** can be of diagnostic value (on 2. week)
- ECG, Echo (at diagnosis, then on 10., 30. days)
- Therapy:
  - **Immunglobulin**: 2 g/kg/day. During the first 10 days!
  - Salicylic acid (80-100mg/kg/day) during thrombocytosis
  - +/- corticosteroid

BÁTOR TÁBOR

a Hole in the Wall Camp sm

Thanks for your attention!