UNIVERSITÀ DEGLI STUDI DI MESSINA
DIPARTIMENTO DI SCIENZE PEDIATRICHE MEDICHE E CHIRURGICHE
U.O.C. di Genetica e Immunologia Pediatrica
Direttore: Prof. Carmelo Salpietro
Sezione di Immunolnfettivologia e Reumatologia Pediatrica
Responsabile: Prof.ssa Romina Gallizzi

ARTRITE IDIOPATICA GIOVANILE

L' Artrite Idiopatica Giovanile non è una singola malattia, ma comprende tutte le forme di artrite che:

Insorgono prima dei 16 anni di età

Persistono per un tempo maggiore di sei settimane

Hanno cause sconosciute

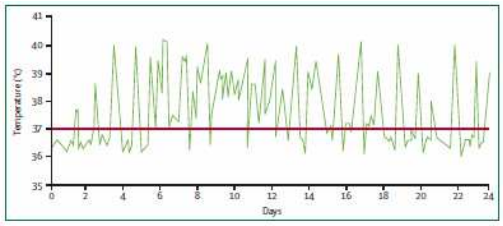
Prevalenza: 16 - 150 per 100 000

AIG
ILAR CLASSIFICATION
(Durban 1997-Edmonton 2001)

1. **Artrite sistemica**
2. **Oligoartrite**
3. **Artrite Poliarticolare FR negativa**
4. **Artrite Poliarticolare FR positiva**
6. **Artrite- Entesite**
7. **Artrite Psoriasica**
8. **Artrite non classificata**

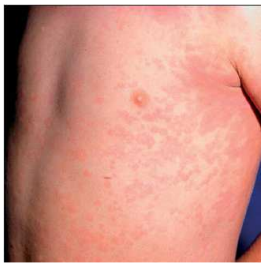
Artrite Sistemica

Requisiti per la diagnosi: **Artrite + Febbre** → **durata > a 2 settimane**



Lancet 2007; 369: 767–78

E uno o più dei seguenti:

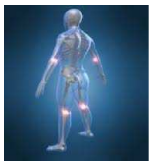


1) Rash eritematoso tipico,evanescente, non fisso (che di solito coincide con il picco febbrile)

2) Epatomegalia o splenomegalia

3) Linfoadenopatia generalizzata

4) Sierosite



Lancet 2007; 369: 767–78

Artrite

a)Simmetrica

b) Poliarticolare

c) Spesso assente all'insorgenza

Indagini di Laboratorio

a)Leucocitosi

b) VES e PCR molto elevati

c)Trombocitosi

d) Anemia microcitica

Complicanza
(5-8% AIGs)

MAS — ***M**acrophage **A**ctivation **S**yndrome*

Febbre

Pancitopenia

Epatosplenomegalia

Coagulopatia

MOF

***Pand*: Most common differential diagnoses of systemic juvenile idiopathic arthritis**

- Infection
  - Septicaemia
  - Bacterial endocarditis
  - Brucellosis
  - Typhoid fever
  - Leishmaniasis
  - Viral infections
- Malignancy
  - Leukaemia
  - Lymphoma
  - Neuroblastoma
- Rheumatic fever
- Connective tissue diseases
  - Systemic lupus erythematosus
  - Kawasaki syndrome
  - Polyarteritis
- Inflammatory bowel disease
- Castleman's disease
- Autoinflammatory syndromes

Oligoartrite

Meno di quattro articolazioni nei primi sei mesi di malattia

Escluse

- **Artrite Psoriasica**
- **Anamnesi familiare positivs per psoriasi**
- **HLA-B27**
- **FR positivo**
- **maschio di età superiore a 6 anni**

Oligoartrite

Femmina

Insorge prima dei sei anni di età

Artrite Asimmetrica

- **Ginocchio**
- **Caviglia**

ANA Positivi (70-80%)

Alto rischio di Iridociclite(30%)

Persistente: ***meno di 4 articolazioni***

Estese: ***più di quattro articolazioni dopo sei mesi di malattia***

	Definition	Examination frequency
High risk	Oligoarticular or polyarticular onset, <7 years at onset of arthritis, and ANA test positive	Every 3-4 months
Medium risk	Oligoarticular or polyarticular onset, <7 years at onset of arthritis, and ANA test negative Oligoarticular or polyarticular onset, >7 years at onset of arthritis, and ANA test positive or negative	Every 6 months
Low risk	Systemic onset of disease	Every 12 months

Adapted from: Section on Rheumatology and Section on Ophthalmology. Guidelines for ophthalmologic examinations in children with juvenile rheumatoid arthritis. Pediatrics 1993; 92: 295-96 with permission from American Academy of Pediatrics.

Artrite Poliarticolare Fattore-Reumatoide positiva

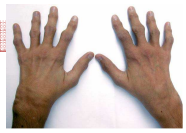
- **5 o più** articolazioni nei primi sei mesi di malattia
- FR positivo

Femmine adolescenti

Poliartrite Simmetrica/Piccole articolazioni delle mani e dei piedi

Manifestazioni extrarticolare: insufficienza aortica di grado severo

Precoci lesioni erosive



Artrite Poliarticolare fattore reumatoide negativa

- **5 o più** articolazioni nei primi 6 mesi di malattia
- FR negativo

3 sottogruppi

- Simile oligoarticolare eccetto che per il numero di articolazioni
- Sinovite simmetrica delle grandi e piccole articolazioni
- Sinovite, non essudato, contratture alla flessione rigidità

Artrite-Entesite

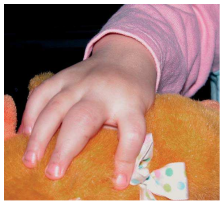
Maschi

Età superiore a 6 anni

Positività HLA-B27

Entesite tendine di Achille, fascia plantare, area tarsale

Artrite di solito colpisce le piccole articolazioni delle estremità degli arti inferiori



Artritie Psoriasica

Rash psoriasico tipico o, se assente il rash, presenza di artrite e di una delle seguenti condizioni:

- anamnesi familiare positiva per psoriasi
- dattilite
- pitting ungueale

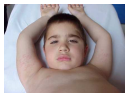
Artrite Indifferenziata

Pazienti con artrite che non soddisfa i criteri d'inclusione delle varie forme

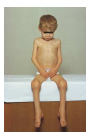
AIG

Tipo di esordio

Diagnosi
a) clinica
b) biologica
c) eziopatogenetica

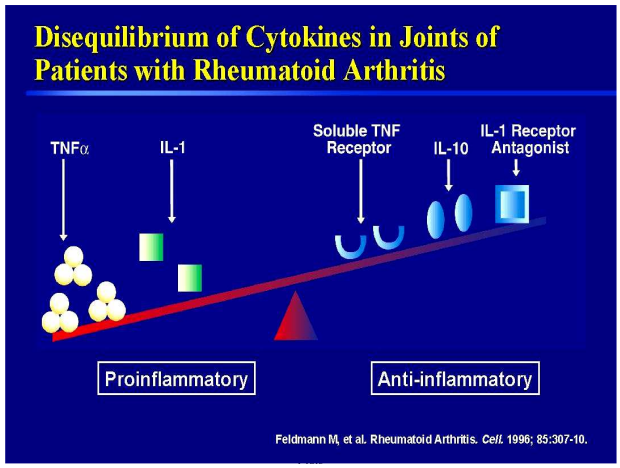


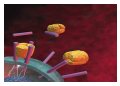
sistemico 10%



poliarticolare 30%

oligoarticolare 60%





Ruolo del TNFα nell'AIG

Quasi sempre aumentato nel liquido sinoviale e nella membrana sinoviale

Lepore L, Clin Exp Rheumatol 1994;12:561-5
Eberhard BA, Clin Exp Immunol 1994;96:260-6
Kutukculer N. Clin Rheumatol 1998;17:288-92

FANS/NSAIDs

Nella forma oligoarticolare i FANS possono essere utilizzati in monoterapia

Table 4 NSAIDs Approved for Use in Children

Drug	Ages	Dose/Max Dose
Naproxen*	2 yrs	7.5 to 10 mg/kg BID to 500mg/dose
Ibuprofen*	6 mos	30 to 40 mg/kg/day ÷ TID/QID to 2400 mg
Meloxicam*	2 yrs	0.25 mg/kg daily to 15 mg
Indomethacin	No caute/15y	1.5 to 3 mg/kg day ÷ TID to 200 mg
Celecoxib†	2 yrs	6 to 12 mg/kg/day ÷ BID to 400 mg
Tolmetin	2 yrs	20-30 mg/kg/day ÷ TID
Oxaprozin	6 yrs	20-30 mg/kg/day once daily to 1800 mg
Etodolac	6 yrs	20 mg/kg once daily to 1200 mg

Table 3 Core Set Criteria for Improvement in Juvenile Idiopathic Arthritis

1. Number of Active Joints
2. Number of Joints with Loss of Motion
3. Physician's Global Assessment
4. Parent's Global Assessment
5. Childhood Health Assessment Questionnaire
6. ESR

Patient must have at least a 30% improvement in 3/6 items and a worsening of 30% in no more than one item to achieve an ACR Pedi 30. ACR Pedi 50 and 70 require a 50 or 70% improvement in 3/6 items with worsening of 30% in no more than 1 item.

- **efficace nel 50-60% di pazienti**
- **Più del 10% presenta dolore addominale**

Guidelines for diagnosis and treatment in oligoarticular and poliarticular juvenile idiopathic arthritis

B. Bader-Meuniera*, C. Woutersa, C. Job-Deslandrec, R. Cimaz, M. Hoferf, P. Pilletg, P. Quartiera

AINS		
Indométacine	2–3 mg/kg par jour en 2–3 prises p.o (dose maximale : 150 mg/j)	Hors AMM avant 15 ans
Naproxène	20–30 mg/kg par jour en 2 prises (dose maximale : 2400 mg/j)	Hors AMM pour les doses préconisées
Ibuprofène	30–40 mg/kg par jour en 3–4 prises dose maximale : 2400 mg/j)	Hors AMM pour les doses préconisées
Diclofénac	3 mg/kg par jour en 2 prises (dose maximale : 225 mg/j) taux de salicylémie max 150–200 µg/ml 2 h après la prise	AMM
Corticoïdes systémiques (prednisone)	Doses variable selon la présentation clinique	
Méthotrexate	Une fois par semaine : 10–15 mg/m² (sans dépasser 25 mg/semaine)	AMM. Per os le matin à jeûne ou voie sous-cutanée
Léflunomide	10 mg/L, 73 m² max 20 mg/j	Hors AMM
Sulfasalazine	10 à 15 mg/kg par jour en traitement d'attaque[a]	AMM pour la polyarthrite rhumatoïde uniquement
	30 à 50 mg/kg par jour en traitement d'entretien	
Etanercept	0,4 mg/kg sc × 2/semaine (sans dépasser 25 mg × 2/semaine) Ou 0,8 mg/kg sc × 1/semaine (sans dépasser 50 mg/semaine)	AMM pour l'enfant âgé de plus de 4 ans pour les formes polyarticulaires
Adalimumab	40 mg/14 j sc	AMM à partir de 13 ans pour les formes polyarticulaires
Tocilizumab	8 à 12 mg/kg par 14 j iv	Hors AMM (étude en cours)
Abatacept	10 mg/kg IV j1, j15 puis toutes les 4 semaines	Hors AMM (demande en cours)

Archives de Pediatrie 2010;17:1085-1089

Intra-articular Triamcinolone in Juvenile Idiopathic Arthritis

JIA subtype		
Oligoarticular	17	(46%)
Entesitis related	10	(27%)
Polyarticular	4	(11%)
Psoriatic	4	(11%)
Systemic	2	(5%)
Type of joint injected		
Knee	48	(%)
Ankle	13	(%)
Wrist	8	(%)
PIP	8	(%)
Hip	6	(%)
Elbow	6	(%)
Subtalar	4	(%)
MCP	2	(%)
Current systemic treatment		
NSAIDs	17	(46%)
NSAIDs + DMARD[s]	15	(40%)
NSAIDs + Low dose corticosteroid + DMARD[s]	5	(14%)

WHAT THIS STUDY ADDS?

Infiltrazione Intra-articolare di triamcinolone esacetonide rappresenta un importante strumento terapeutico soprattutto nella forma oligoarticolare.

Comparison of the efficacy on intraarticular CS therapy administrered alone or in combination with MTX in children with JIA. Multicentric study. 2009. PRINTO

Indian pediatrics Volume 45 december 17, 2008

Methotrexate Withdrawal at 6 vs 12 Months in Juvenile Idiopathic Arthritis in Remission. A Randomized Clinical Trial Paediatric Rheumatology International Trials Organization (PRINTO). Ravelli A et al

364 pts

Characteristics	Group 1 (n = 183)	Group 2 (n = 181)	P Value
Female sex, No. (%)	119 (65)	123 (68)	.55
Age at inclusion, y	11.2 (2-18)	10.7 (2-18)	.81
Age at disease onset, y	5.4 (1-16)	6.1 (1-15)	.43
Disease duration, y	3.2 (0-13)	3.0 (0-16)	.62
Juvenile idiopathic arthritis subtypes, No. (%)			
Persistent oligoarthritis	54 (30)	42 (23)	.17
Extended oligoarthritis	34 (19)		
Polyarthritis, negative rheumatoid factor	54 (30)		
Polyarthritis, positive rheumatoid factor	9 (5)		
Systemic-onset juvenile idiopathic arthritis	14 (8)		
Enthesitis-related arthritis	7 (4)		
Psoriatic arthritis	11 (6)		
Treatment and laboratory values at inclusion			
Methotrexate dose, mg/m^2 per wk	10.0 (1-17)		
Time taking methotrexate, y	1.3 (0-12)		
Taking nonsteroidal anti-inflammatory drugs, No. (%)	76 (42)	60 (33)	.12
Erythrocyte sedimentation rate, mm/h	9 (0-20)	8 (0-19)	.48
C-reactive protein, mg/L	1.0 (0-2.5)	0.9 (0-2.2)	.62
Laboratory values at withdrawal			
Erythrocyte sedimentation rate, mm/h	9 (5-17)	8 (4-19)	.78
C-reactive protein, mg/L	0.3 (0-1.4)	0.2 (0-2.0)	.70
MRP8/14, ng/mL	510 (60-2640)	480 (110-3310)	.94

Abbreviation: MRP8/14, myeloid-related proteins 8 and 14 heterocomplex.
SI conversion factor: To convert C-reactive protein values to nmol/L, multiply by 9.524.
[a]Group 1 comprised patients discontinuing methotrexate after 6 months in remission; group 2, those discontinuing methotrexate after 12 months in remission.

Nei pazienti con AIG in remissione la sospensione del MTX dopo 6 mesi vs 12 mesi dalla remissione di malattia non aumenta il rischio di ricadute.

JAMA, April 7, 2010
Vol 303, No. 13

Anti-TNF	Etanercept Infliximab Adalimumab (Golimumab)
Anti-IL1	Anakinra (Canakinumab) (Rilonacept)
Anti-IL6	Tocilizumab
CTLA4-Ig	Abatacept
AntiCD20	(Rituximab)

Preliminary evidence that etanercept may reduce radiographic progression in juvenile idiopathic arthritis

Nielsen S, Ruperto N, Gerloni V, Simonini G, Cortis E, Lepore L, Alpigiani MG, Zulian F, Corona F, Alessio M, Barcellona R, Gallizzi R, Rossi F, Magni-Manzoni S, Lombardini G, Filocamo G, Raschetti R, Martini A, Ravelli A; Italian Pediatric Rheumatology Study Group.

METHODS: Patients included in the Italian ETN registry who had a standard radiograph of both hands and wrists in the posteroanterior view made at start of treatment and after 1 year were included in the study. The clinical response was assessed by means of the ACR Pediatric definition of improvement. Radiographic progression was determined by calculating the change in the Poznanski score between the baseline and the 1-year radiographs.

RESULTS: A total of 40 patients were studied. The frequency of ACR pediatric 30, 50, and 70 response at 1 year was 77%, 72%, and 50%, respectively. The median change in the Poznanski score between baseline and 1 year was + 0.3 units, meaning that, on average, patients experienced improvement in radiographic progression.

CONCLUSION: Our pilot study provides evidence that ETN is potentially capable of reducing the progression of radiographic joint damage in JIA. This finding deserves confirmation in a controlled trial.

Clin Exp Rheumatol

Grazie per l'attenzione