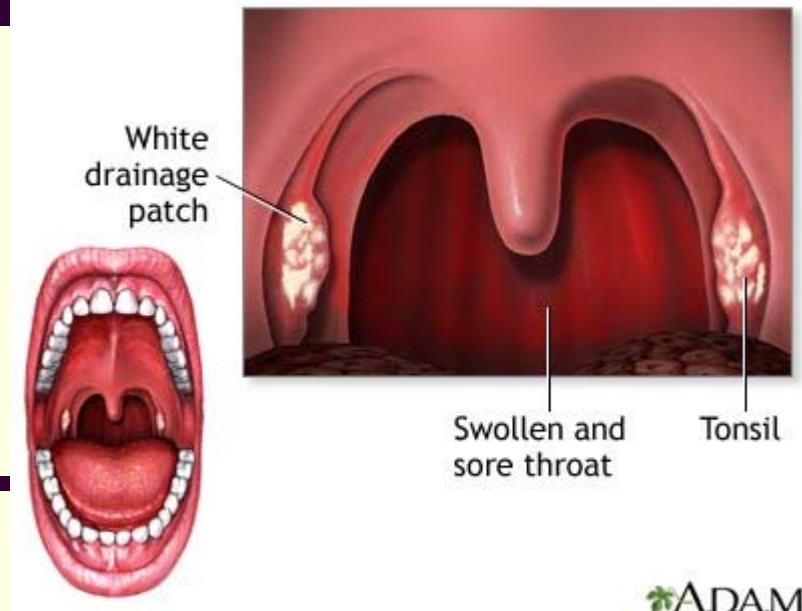


Rheumatic Fever

Vs. (?)

Post Strep Reactive Arthritis

ינואר 2009



Agenda

- **Introduction**

- **Articles**

- **Poststreptococcal reactive arthritis in children: is it really a different entity from rheumatic fever?**
- **Poststreptococcal reactive arthritis: what is it and how do we know?**
- **Differentiation of Post-Streptococcal Reactive Arthritis from Acute Rheumatic Fever**

- **Guidelines**

Post-streptococcal reactive arthritis (PSRA)

- **Definition:**
- **Arthritis of ≥ 1 joints**
- **Recent group A streptococcal infection**
- **Does not fulfill the Jones criteria for the diagnosis of Acute Rheumatic Fever (ARF)**

- **In 1982 - Goldsmith and Long –**
- **poststreptococcal syndrome in children**
- **symmetrical arthritis followed by intense arthralgia**
- **poorly responsive to aspirin therapy**

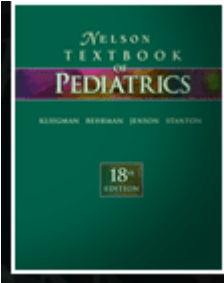
- **Some authors consider PSRA to be part of the spectrum of ARF**
- **Other authors consider it to be a different entity**

In 1993 Deighton:

	ARF	PSRA
Onset after GAS	2-3 weeks	10 days
Duration	Few days - 3 weeks	Prolonged/ Recurrent
Response to Aspirin	Usually dramatic	Slow and partial

In 1997 Ayoub and Ahmed:

- **PSRA:**
- **Arthritis of acute onset, symmetric or asymmetric, usually non-migratory, can affect any joint, persistent or recurrent**
- **Poorly responsive to salicylates/NSAIDs**
- **Antecedent GAS infection**
- **Failure to fulfill the modified Jones criteria for the diagnosis of ARF**



Jones Criteria - ARF

- 2 major
- 1 major + 2 minor

Major manifestations	Minor manifestations	Supporting evidence of antecedent GAS
Carditis	Arthralgia	Positive throat culture or rapid streptococcal antigen test
Polyarthritits	Fever	Elevated or increasing streptococcal antibody titer
Erythema marginatum	Elevated acute phase reactants	
Subcutaneous nodules	Prolonged PR interval	
Chorea		

Poststreptococcal reactive arthritis in children: is it really a different entity from rheumatic fever?

**Ercan Tutar · Semra Atalay · Erdal Yilmaz
Tayfun Ucar · Gulendam Kocak · Ayten Imamoglu**

2002Jun;22(2):80-3

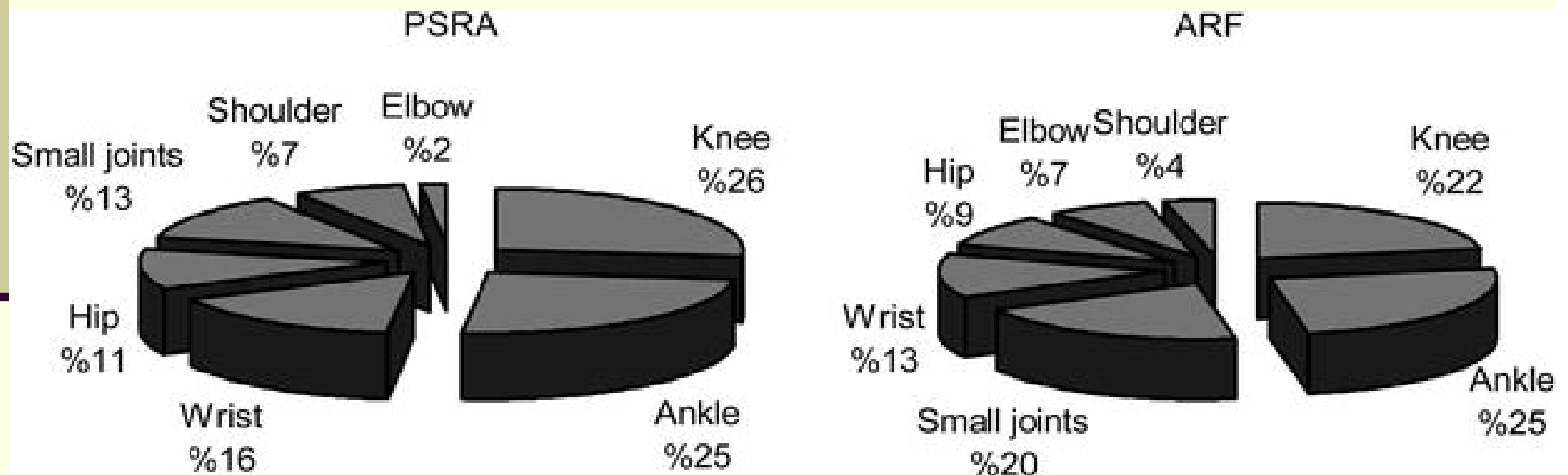


Results

- **PSRA - 24 patients**
- **ARF - 20 patients**
- **Latency period from upper respiratory tract infection - shorter in patients with PSRA ($P < 0.01$)**
- **However, 25% of the patients with ARF had also short (<10 days) latency periods**

Results

- No significant difference for the distribution of mono-, oligo-, and polyarticular disease between PSRA and ARF patients



Results

- **Unresponsiveness of articular symptoms to salicylate therapy within 72 h was more frequent in patients with PSRA ($P<0.001$)**
- **However, in a substantial part of the patients with ARF (nine patients, 45%), joint symptoms also had no response during the first 72 h**

Conclusion

- **Considerable overlap of symptoms, signs, and laboratory features of PSRA and ARF**
- **The authors conclude that these two conditions are actually different presentations of the same disease**

Poststreptococcal reactive arthritis: what is it and how do we know?

S. L. Mackie and A. Keat

**Systematic
Review**



2004 Aug;43(8):949-54

Main key points

- 188 cases - 1982 - 2002
- 47% children
- The clinical presentation – heterogeneous
- **Different** both from that of acute rheumatic fever (ARF) and from that of HLA B27-associated reactive arthritis.
- Carditis - rare

<i>Rheumatology</i>	Key messages
	<ul style="list-style-type: none">● PSRA is probably a heterogeneous group of disorders.● The assumed causal role of streptococcal infection remains unproven.● This subject requires clarification by prospective study of streptococcal infection or sore throat.

Differentiation of Post-Streptococcal Reactive Arthritis from Acute Rheumatic Fever

Barash J, Mashiach E, Navon-Elkan P, Berkun Y, Harel L, Tauber T, Padeh S, Hashkes PJ, Uziel Y; Pediatric Rheumatology study group of .Israel



Nov 2008;153(5):696-9

Study objectives

- **Search for differences in these 2 entities**
- **Well-defined, large cohort**
- **Discern whether these are 2 separate entities or varying clinical manifestations of the same disease**
- **Offer a simple clinical tool to differentiate between them**

Methods

- **<16 years old**
- **7 centers in Israel**
- **Israeli internet-based pediatric rheumatology registry**
- **1996 - 2005 (most after 2001)**
- **ARF with joint involvement - 68 patients**
- **PSRA - 159 patients**

Methods – cont.

- **ARF - diagnosed according to the revised Jones criteria**
- **PSRA - diagnosed in cases of arthritis involving ≥ 1 joints associated with proven group A streptococcal infection in a patient not fulfilling the Jones criteria**

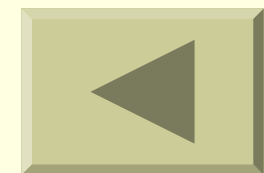
Results – Demographic Data

	ARF	PSRA
Age of onset	10.2 ± 3.0 years	9.3 ± 3.6 years
% Male	63%	54%
Number of persons in the household	5.9 ± 1.5	6.5 ± 2.1
Family history of ARF	7.2%	7.5%

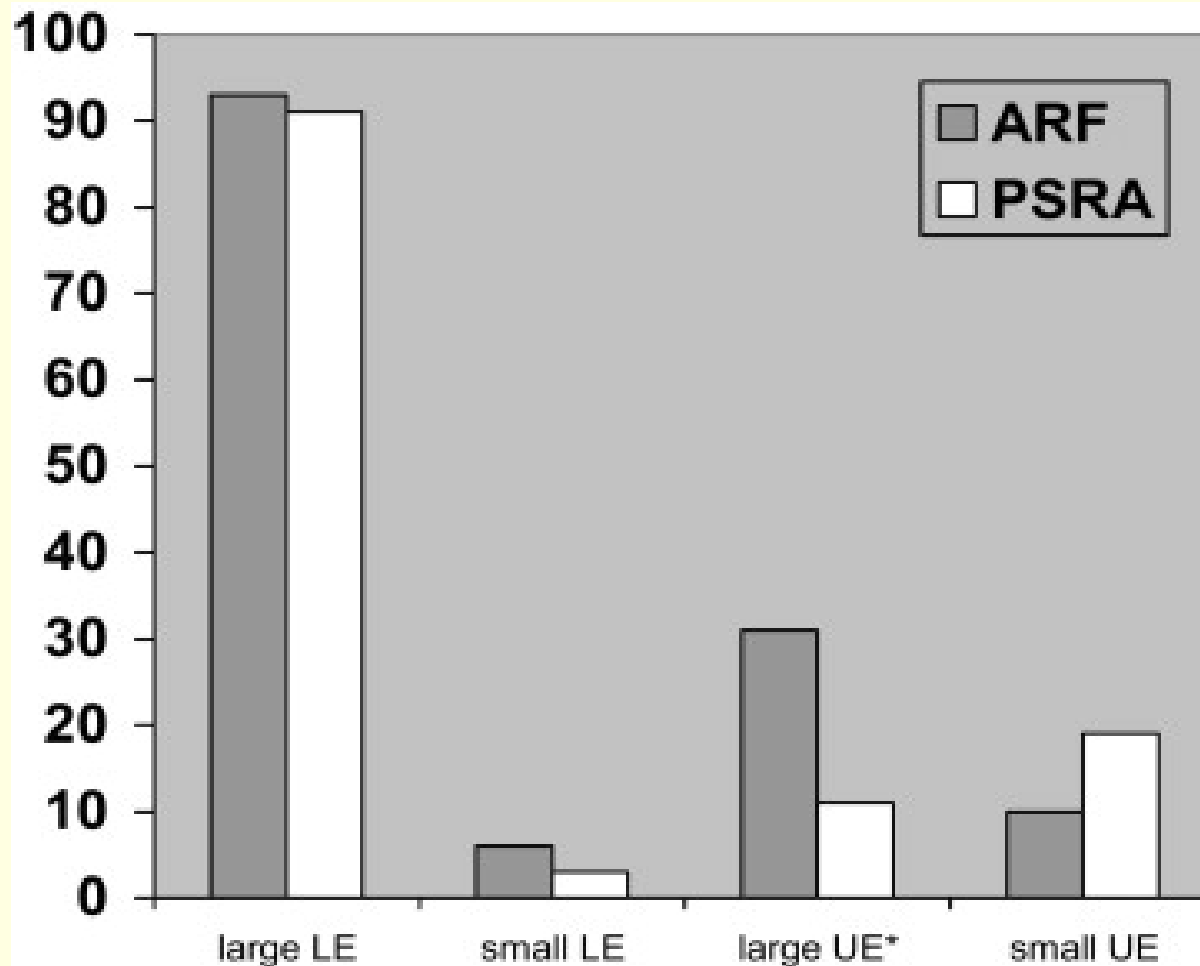
Table I. Clinical and laboratory data of patients with acute rheumatic fever and post-streptococcal reactive arthritis

	ARF (n = 68)	PSRA (n = 159)	P value
Fever °C (SD)	38.3 (0.4)	38.3 (0.5)	NS
% with <u>Fever >38</u>	66	16	.0004
Number of active joints (SD)	2.5 (1.2)	1.8 (1.3)	.0004
<u>Migratory arthritis %</u>	79	33	.004
Symmetrical arthritis %	40	22	.05
Carditis %	60	0	<.0001
<u>ESR (SD)</u>	92.2 (31.1)	57.1 (40.9)	<.0001
<u>CRP mg/L (SD)</u>	106.7 (83.5)	22.6 (44.1)	<.0001
<u>ASO IU (SD)</u>	1011 (1573)	889 (733)	NS
<u>Positive throat culture %</u>	77%	76%	NS
<u>Interval from pharyngitis to arthritis, days (SD)</u>	15 (9.2)	14.6 (10.1)	NS
<u>Response to treatment, days (SD)</u>	2.2 (1.7)	6.9 (5.9)	<.0001
<u>Relapse %</u>	7	21	0.013

ESR, Erythrocyte sedimentation rate; *CRP*, C-reactive protein; *ASO*, anti-streptolysin O; *response to treatment*, resolution of joint symptoms in response to anti-inflammatory treatment; *relapse*, relapse of joint symptoms after cessation of anti-inflammatory treatment; *NS*, not significant.



The distribution in percent with active joints in patients with ARF and PSRA



Large LE, Large joint lower extremity; *small LE*, small joint lower extremity; *large UE*, large joint upper extremity; *small UE*, small joint upper extremity. * $P = .0002$.

Results - Carditis

	ARF (n = 68)	PSRA (n = 159)	P value
Carditis %	60	0	<.0001

PRSA

- 2 patients - prolonged P-R intervals
- 3 patients - trace of mitral regurgitation

(was not considered pathologic)

Results – Treatment & Prophylaxis

	ARF	PSRA
Not treated with NSAIDS	1.4%	22%
Long-term prophylactic antibiotic treatment	87%	50%
Recurrence	12%	8%

Table II. Significant predictors of acute rheumatic fever by using stepwise logistic regression

Variable	Odds ratio	95% CI	Significance
ESR	1.015	1.000-1.031	0.043
CRP	1.016	1.004-1.028	0.007
Days to disappearance of joint symptoms	0.565	0.389-0.820	0.003
Relapse after cessation of treatment (yes/no)	0.026	0.002-0.390	0.008

Results – Prediction Equation

prediction equation: $-1.568 + 0.015 \times \text{sedimentation rate} + 0.02 \times \text{CRP} - 0.162 \times \text{days to resolution of joint symptoms} - 2.04 \times \text{return of joint symptom (yes = 1, no = 0)}$.

- If the value was >0 → ARF
- If the value was <0 → PSRA
- 79% sensitivity rate (correct classification as ARF)
- 87.5% specificity rate (correct classification as PSRA)

In contrary to other studies:

- **No axial involvement**
- **More patients with symmetrical arthritis in the ARF group**
- **Latency period between development of pharyngitis and joint symptoms did not differ between ARF and PSRA in this population**



Discussion

- **Several studies addressing the association of ARF and PSRA with class II HLA-DR antigens**
- **This association may suggest that the pathogenesis of PSRA, like that of ARF, may be related to the inheritance of certain class II HLA alleles**

Discussion

- The authors were able to differentiate between ARF and PSRA in >80% of the cases on the basis of 4 criteria:
 1. ESR at onset
 2. CRP at onset
 3. Number of days before resolution of joint symptoms after starting anti-inflammatory therapy
 4. Presence or absence of a recurrence of arthritis after discontinuation of anti-inflammatory therapy

Conclusions

- ARF and PSRA appear to be 2 **distinct entities**
- **ARF** –
- More acute presentation
 - Fever
 - Acute phase response
 - Greater number of joints
 - Cardiac involvement
- Response to treatment - much quicker
- Course of arthritis - shorter than in PSRA
- If PSRA was a milder form of the spectrum of ARF, we would not expect a slower response to treatment or a longer course of the arthritis



Conclusion

- **The authors suggest usage of the equation**
- **When there is doubt about the diagnosis, the authors suggest to favor the diagnosis of ARF and administer the usual antibiotic prophylactic treatment**
- **American Heart Association + the Red Book - antibiotic prophylaxis for 1 year, and if no carditis is observed, then prophylaxis should be discontinued**

Study Problems

- **Retrospective study**
- **Relatively small scale (n=227)**
- **Parental recall**
- **Physician diagnostic biases**

The Future

- **Large-scale prospective trials**
- **Acute treatment**
- **Penicillin prophylaxis**

- **Guidelines**

תודה רבה!

