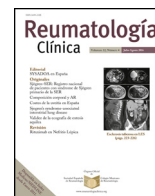




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## Brief report

### Evolution over thirty years of the profile of inpatients with reactive arthritis in a tertiary rheumatology unit

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#### ABSTRACT

Reactive arthritis (ReA) is sterile arthritis occurring after extra articular bacterial infection. The aim of this study was to analyze, over 30 years, clinical, biological and imaging characteristics as well as therapeutic management of new cases of ReA, comparing two periods.

*Methods:* retrospective monocentric study, data of all the patients followed in our unit between January 1st 1984 and April 2014 with the diagnosis of ReA were analyzed (clinical and biological features, management and outcome), and compared between two periods: from January 1984 to December 1993, and from January 2004 to December 2013.

*Results:* Sixty two patients fulfilling international diagnosis criteria were analyzed. There was no significant difference between the two periods in number of new cases, clinical presentation, biological data or outcome. Changes in therapeutic management were obvious with occurrence of anti TNF in the recent period.

*Conclusion:* Reactive arthritis is still a current rheumatologic problem in a developed country, with a need of early and tailored rheumatologic management.

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### Evolución durante 30 años del perfil de pacientes hospitalizados con artritis reactiva en una unidad de reumatología de tercer nivel

#### RESUMEN

Las artritis reactivas (ARe) son artritis estériles que se manifiestan después de una infección bacteriana extraarticular. El objetivo de este estudio es analizar, durante 30 años, las características clínicas, biológicas e imagenológicas, así como la gestión del tratamiento de la ARe, mediante la comparación de 2 periodos.

*Métodos:* Estudio retrospectivo monocéntrico. Se analizaron los datos de todos los pacientes diagnosticados con ARe en nuestra unidad entre el 1 de enero de 1984 y abril de 2014 (rasgos clínicos y biológicos, gestión y resultados) y se compararon con 2 periodos: de enero de 1984 a diciembre de 1993, y de enero de 2004 a diciembre de 2013.

*Resultados:* Se analizaron los datos de 62 pacientes que cumplieron los criterios de diagnóstico internacionales. No existió una diferencia significativa entre los 2 periodos en la cantidad de casos, presentación clínica, datos biológicos o resultados. Los cambios de la gestión del tratamiento fueron evidentes, con la aparición de anti-TNF en el periodo reciente.

*Conclusión:* La artritis reactiva continúa siendo un problema reumatológico actual en los países desarrollados, con una necesidad de tratamiento reumatológico temprano y personalizado.

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Reactive arthritis (ReA) is defined as arthritis developing 2–4 weeks after extra articular infection, without evidence of microorganism in the joint using classical culture tools.<sup>1,2</sup> The triggering infection is mainly located in gut or genito urinary mucosa. The classical clinical presentation is an acute oligo arthritis, mainly located at the lower limbs, with possibility of axial (sacro iliac and spine) involvement and enthesitis, as well as extra articular features (ophthalmologic or dermatologic symptoms). ReA is considered part of spondyloarthritis spectrum, sharing with this entity common clinical and imaging features, as well as frequent association with HLA-B27 haplotype.<sup>3,4</sup> Outcome is variable, with possibility of resolution after several months, or relapses or chronic evolution, leading sometimes, after years, to ankylosing spondylitis.

The aim of this study was to analyze, over 30 years, in new cases of ReA the clinical, biological and imaging characteristics, as well as management modalities, comparing two periods.

## Patients and methods

This is a descriptive, monocentric retrospective study of patients hospitalized in the Rheumatology department of the Centre Hospitalier Régional et Universitaire in Besançon, France, between January 1st 1984 and april 2014 with ReA as principal diagnosis, according to ICD codes M02 and M03. The charts were reviewed by experienced rheumatologists (AB, CP, DW) and patients were included if they fulfilled international classification criteria.<sup>2</sup> The following data were recorded: demographic characteristics, HLA-B27 status, initial infection (location and bacteriological species) and its diagnosis method, as well as the potential antimicrobial treatment. Clinical features of ReA were noted: delay between infection and rheumatologic symptoms onset, general symptoms (fever), tender and swollen joint counts, presence of enthesitis or dactylitis, axial symptoms, and extra articular symptoms (conjunctivitis, uveitis, balanitis). The rheumatic treatments and their introduction delay were collected, as well as the outcome. For this purpose, we studied and compared charts of patients with ReA over two periods, from January 1984 to December 1993, and from January 2004 to December 2013.

Results were expressed as numbers for the microbiological findings, and means or percentage for clinic-biological data.  $\chi^2$  test were used for comparisons of percentages, with Yates and Fisher corrections if needed, and Mann–Whitney if t test were not applicable. Significance threshold was *p* less than 0.05.

## Results

One hundred and twenty charts were analyzed, and 62 were finally included, the causes of exclusion were wrong diagnosis and absence of classification criteria fulfilment. They were 52 men (83.9%) and 10 women (16.1%) with a mean age of 34 years (12–69). Six patients (10%) had a familial history of inflammatory rheumatic disease, four of them had a familial background of spondyloarthritis. At admission, 20% of the patients were febrile, and 82% had elevated biologic markers of inflammation (mean CRP 94 mg/l, leukocytes (WBC) 10.2 G/l). A complete urethro-ocul-synovial syndrome was noted in 19.4%. The mean number of painful joints was 3, and of swollen joints 2.1; two patients had no synovitis, but in one case we noticed axial symptoms with buttock pain and a dactylitis. The most frequently involved joints were the knee, then ankle, wrist and tarsal joints; dactylitis was present in 19.4% of the cases. Inflammatory back pain was mentioned in 22.3% of the cases, and enthesopathy in 24.2%, mainly talalgia. Among extra rheumatic involvement, conjunctivitis was the most frequent (27.4%); three cases of palmar and/or plantar pustulosis and three cases of

**Table 1**  
Distribution of infectious agents.

Infectious agent	Number of patients positive	Serology	PCR	Culture
<i>Chlamydia trachomatis</i>	18	14	2	
<i>Ureaplasma urealyticum</i>	5	0	5	
<i>N. gonorrhoea</i>	4	3	1	
<i>Mycoplasma pneumoniae</i>	2	2	0	
<i>Chlamydia + Yersina</i>	1	1		
<i>Chlamydia + Strepto B</i>	1		1	
<i>Chlamydia + N. gonorrhoea</i>	1	X	X	
<i>Salmonella</i>	1			1
<i>Neisseria meningitidis</i>	1			1
<i>Anguillulosis</i>	1	1		
<i>Streptococcus B</i>	1		1	
<i>Yersina</i>	1	1		
<i>S. Aureus + Strepto B</i>	1		1	
Not found	22			

PCR: polymerase chain reaction.

balanitis were observed. HLA-B27 typing was positive in 36 out of 56 assessments (64.3%).

Urethritis was described in 43.6% and dysenteric syndrome in 21% of the cases. Eight cases exhibited no infectious symptoms, and in 7 of them, evidence of an infection was brought by systematic research. Rheumatologic symptoms appeared with a mean of 14.7 days after the supposed infection. Evidence of infection was found in 63.3%, with serological proof in 37%, PCR on urethral sampling in 14% and vaginal in 2%, blood and stool cultures in 2% of the 62 cases each. *Chlamydiae trachomatis* was the most frequent infectious agent (37% of the cases with evidence of infection), found in 83.3% by serology, 11% by PCR (urethral or vaginal), and 5.6% by both methods; in three cases it was associated with another infection (*streptococcus*, *Yersinia*, *gonococcus*). The following most frequent species were *Ureaplasma urealyticum* and *Neisseriae gonorrhoeae* (Table 1). In 35 cases, an antibiotic treatment for the inaugural infection was mentioned.

Non steroidal anti inflammatory drugs (NSAIDs) were used in 91.8% of cases. The absence of use was due to contra indications or intolerance. Disease modifying anti rheumatic drugs (DMARDs) were introduced in 51.8% of patients with a median delay of 60 days from the first rheumatic symptoms, with salazosulapyridin as the first choice. Use of TNF blockers was recorded in 15 patients (24.2%), mean age 35 years, with a median delay of 116 days.

The outcome was variable, and longstanding follow-up was available in 42 patients: with a mean follow-up duration of 34 months, 52% are in remission, under or without treatment, 44% developed spondyloarthritis, and 4% psoriatic arthritis.

The comparison of the two cohorts did not reveal any significant change in the frequency of ReA in hospitalized patients or in the profile of these patients (Tables 2 and 3) (age, sex, type of infection, rheumatologic presentation or outcome). In the most recent period, the use of Azithromycin for treatment of Chlamydia, and of anti TNF agents were more frequent.

## Discussion

Reactive arthritis may have two backgrounds: epidemic, with classical description during world war 1st,<sup>5</sup> and sporadic. It corresponds to arthritis related to a preceding infection outside the joint, mainly in the gut<sup>6</sup> or the genito urinary tract, with some classical species,<sup>7</sup> and other less frequent (e.g. *Clostridium*<sup>8</sup> or *N. gonorrhoea*).<sup>7</sup> The estimated annual incidence varies among studies and countries between 0.6 and 30/1,000,000 (4). Due to improvement in collective hygienic conditions, one may expect a reduction in incidence of ReA in developed countries. It has been recently shown a decline in ReA diagnoses despite an increase

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