MATTERS ARISING

Normal values of laboratory tests in elderly onset psoriatic arthritis

I read with interest the article recently published by Punzi *et al.*¹ The results shown in this study demonstrate higher levels of acute phase reaction markers such as ESR and CRP in elderly onset psoriatic arthritis patients (EOPsA) than those displayed by young onset psoriatic arthritis patients (YOPsA). The authors included 16 EOPsA (>60 years) and 50 YOPsA (<60 years).

I would like to comment that the information regarding normal values was restricted to the following words "CRP, normal values <0.6 mg/dl", no other information is given. It is not possible to know how and from whom these normal values were obtained. Even if a commercial test that includes their own controls was used, it is clear that you will need to test groups of normal subjects that cover the age spectrum of both groups of patients EOPsA and YOPsA. This strategy will allow you to estimate the influence of age in the higher levels of ESR and CRP exhibited by EOPsA. The inclusion of this control group of normal subjects is also recommended because YOPsA does not belong to the same age cohort that EOPsA does, and in fact, EOPsA represents a group of survivors from their original birth cohort more than YOPsA does.

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1 Punzi L, Pianon M, Rossini P, Schiavon F, Gambari PF. Clinical and laboratory manifestations of elderly onset psoriatic arthritis: a comparison with younger onset disease. *Ann Rheum Dis* 1999;58:226–9.

Authors' reply

In his comments on our paper,¹ Dr Nava regrets that little information was given on the normal values of laboratory markers of acute phase response (APR), in particular ESR and CRP, to support the observation that APR is higher in elderly onset psoriatic arthritis (EOPsA) than in younger onset PsA (YOPsA). This criticism probably derives from the possibility that the differences in ESR and CRP may simply be attributable to age rather than disease.

ESR and CRP are the most widely known and commonly used laboratory indices used to investigate APR and disease activity. ESR is a composite measurement depending on several factors, including in particular red cell and serum protein changes. Physiological changes able to influence one or more of these factors, such as sex and age, may in turn influence ESR. Since the first introduction of Westergren's technique, the most recommended method for ESR determination,² many studies have been performed to establish normal values in the elderly: irrespective

of sex, upper limits of 20 mm 1st h for subjects under 50 years and 40 mm 1st h for those older than 70 years are considered normal, acceptable values.³ Thus, the ESR mean values of 64.2 (35.3) mm 1st h found in our EOPsA patients must be viewed entirely above suspicion.

The differences between our EOPsA and YOPsA were even more evident for the CRP, a protein that best reflects the APR and that is only slightly influenced by age and sex. The normal values we reported (<0.6 mg/dl for any ages and sex) are accepted worldwide and, although some rare healthy subject may reach an upper limit of 1.0 mg/dl,⁴ these values mainly differ from the mean of 3.9 (2.0) mg/dl found in our patients with EOPsA.

In this context, however, another aspect might have seemed surprising: the low values of ESR and CRP found in YOPsA, 30.5 (30.0) mm 1st h and 1.33 (1.3) mg/dl respectively, reflecting difficulties in applying these indices to patients with seronegative spondyloarthritides and in assessing disease activity.^{5,6} Furthermore, in a recent, unpublished observation from the Italian Group of Psoriatic Arthritis Study, involving 1306 patients with PsA, CRP values of >1 mg/dl were found in only 52.9% of the patients. As the agents mainly responsible for CRP production are pro-inflammatory cytokines, mainly interleukin (IL) 6 but also IL1 and tumour necrosis factor, and as these cytokines are usually found at low levels in the synovial fluid of YOPsA,⁷ PsA may be considered a disease characterised by a frequent low synthesis of pro-inflammatory cytokines and usually mild APR. However, factors able to stimulate or deregulate the production of these cytokines, such as aging, trauma, infections or immunogenetic predisposition to severe polyarticular diseases,^{7–10} may be responsible for an increased APR and account for a wide spectrum of presentations typical of PsA.

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- Punzi L, Pianon M, Rossini P, Schiavon F, Gambari PF. Clinical and laboratory manifestations of elderly onset psoriatic arthritis: a comparison with younger onset disease. *Ann Rheum Dis* 1999;58:226–9.
- International Committee for Standardization in Haematology. Recommendation for measurement of erythrocyte rate of human blood. *Am J Clin Pathol* 1977;68:505–7.
- Sipe JD. The acute phase response in inflammation. In: Cohen AS, ed. *Laboratory diagnostic procedures in the rheumatic diseases*. Orlando: Grune and Stratton, 1985:77–94.
- Gabay C, Kushner I. Acute phase proteins and other systemic responses to inflammation. *N Engl J Med* 1999;340:448–54.
- Sheenan NJ, Slavin BM, Donovan MP, Mount JN, Mathews JA. Lack of correlation between clinical disease activity and erythrocyte sedimentation rate, acute phase proteins or protease inhibitors in ankylosing spondylitis. *Br J Rheumatol* 1986;25:171–4.
- Sitton NG, Dixon JS, Bird HA, Wright V. Serum biochemistry in rheumatoid arthritis, seronegative arthropathies, osteoarthritis, SLE and normal subjects. *Br J Rheumatol* 1987;26:131–5.
- Punzi L, Bertazzolo N, Pianon M, Rizzi E, Rossini P, Gambari PF. Value of synovial fluid interleukin-1 β determination in predicting the outcome of psoriatic arthritis. *Ann Rheum Dis* 1996;55:642–4.

- Torre-Alonso JC, Rodriguez Perez A, Arribas Castriello JM, Ballina Garcia J, Riestra Noriega JL, Lopez Larrea C. Psoriatic arthritis: a clinical, immunological and radiological study of 180 patients. *Br J Rheumatol* 1991;30:245–50.
- Gladman DD, Farewell VT. The role of HLA antigens as indicators of disease progression in psoriatic arthritis. *Arthritis Rheum* 1995;38:845–50.
- Punzi L, Pianon M, Bertazzolo N, Fagiolo U, Rizzi E, Rossini P, et al. Clinical, laboratory and immunogenetic aspects of post-traumatic psoriatic arthritis: a study of 25 patients. *Clin Exp Rheumatol* 1998;16:277–81.

RS3PE syndrome. The relation with HLA B7

We agree with Dudler *et al.*¹ that RS3PE is one way in which late onset polyarthritis can present. However, we believe it is more a clinical feature indicating a good prognosis rather than a specific syndrome. As they have admirably summarised its occurrence in a number of other conditions, in which the only linking feature is that the patients tend to be elderly, would support this view. The association with HLA B7 is as yet not proved, the incidence varying with the population screened (table 1).

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- Dudler J, Gerster J-C, So A. Polyarthritis and pitting oedema. *Ann Rheum Dis* 1999;58:142–7.
- Bhakta BB, Pease CT. Late-onset rheumatoid arthritis: is pitting oedema of the hands at onset a good prognostic indicator? *Br J Rheumatol* 1997;36:214–19.
- McCarty DJ, O'Duffy JD, Pearson L, Hunter JB. Remitting seronegative symmetrical synovitis with pitting edema. RS3PE syndrome. *JAMA* 1985;254:2763–7.
- Russell EB, Hunter JB, Pearson L, McCarty DJ. Remitting, seronegative, symmetrical synovitis with pitting edema - 13 additional cases. *J Rheumatol* 1990;17:633–9.
- D Chaoat, JY Perier, JM Le Parc, G Belange. Subacute oedematous polyarthritis of the elderly. *Presse Med* 1990;19:1705–8.
- Olivieri I, Padula A, Favaro L, Oranges GS, Ferri S. RS3PE syndrome with unilateral involvement. *J Rheumatol* 1994;21:372.
- Schaefferbeke T, Fatout E, Marce S, Vernhes JP, Halle O, Antonie JF, et al. Remitting seronegative symmetrical synovitis with pitting oedema: disease or syndrome? *Ann Rheum Dis* 1995;54:681–4.
- Cantini F, Salvarani C, Olivieri I, Barozzi L, Macchioni L, Niccoli L, et al. Remitting seronegative symmetrical synovitis with pitting oedema (RS3PE) syndrome: a prospective follow up and magnetic resonance imaging study. *Ann Rheum Dis* 1999;58:230–6.

Table 1 Frequency of HLA B antigens in patients with RS3PE

Reference	Number of patients	B7	%	B27	%
3	8	6	(75)	0	
4	13	6	(46)	0	
5	9	2	(22)	4	(44)
6	1	1		0	
7	9	2	(22)	2	(22)
2	19	2	(10)	2	(10)
8*	13	2	(15)		
8†	80	7	(9)		
8‡	12	2	(17)		
8§	126	14	(11)		

*RS3PE, †PMR no oedema, ‡PMR with oedema, §Controls.

Authors' reply

We are grateful to Drs Pease and Bhakta for their interesting comments on the relation of RS3PE and HLA B7. We agree with them that the association with HLA B7 is not yet proved, and that actually data from diverse groups tend to speak against it. We also found that their prospective study looking at pitting oedema in various subsets of late onset rheumatoid arthritis as a good and independent factor of good prognosis was very interesting.¹ Nevertheless, a syndrome is simply a group of signs and symptoms occurring together and characterising a particular abnormality. We believe that it is still useful to define RS3PE as a specific syndrome particularly regarding its excellent prognosis as compared with the other affections responsible for pitting oedema of the hands.² The fact that HLA B7 prevalence is perhaps not increased in RS3PE does not bother us. RS3PE could be related to another, yet unknown HLA type. Furthermore, specific overprevalence of an HLA type is not a requisite to define a specific syndrome or disease. Both rheumatoid arthritis and polymyalgia rheumatica have been related to HLA DR4, but nobody would argue that they represent different diseases.

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- 2 Dudler J, Gerster J-C, So A. Polyarthritis and pitting oedema. *Ann Rheum Dis* 1999;58:142–7.

Intra-articular corticosteroids in septic arthritis: beneficial or barmy?

We read with interest the paper by Wysenbeek *et al* about the treatment of staphylococcal septic arthritis in rabbits by intra-articular corticosteroids in addition to antibiotics¹ and would like to share our recent clinical experience that we feel pertinent to this scientific research.

Traditional teaching dictates that intra-articular corticosteroids are contraindicated in the management of septic arthritis, the appropriate treatment being antibiotics and lavage or surgical drainage. The following two cases of septic arthritis illustrate the apparent benefits of the unconventional use of intra-articular corticosteroids. Both patients presented with a septic arthritis of an osteoarthritic knee. The first patient, a 87 year old woman, had developed a staphylococcus aureus infection (sensitive to flucloxacillin) while the second, a 62 year old man, had a proteus infection (sensitive to cephalosporins). Surgical management was inappropriate because of frailty and warfarin treatment respectively. Despite treatment of both patients with appropriate intravenous antibiotics for two weeks and joint lavage, pain and synovitis persisted. At this stage, in both cases, knee aspirates and blood cultures on two separate occasions were negative. After a single intra-articular injection of 80 mg depomedrone and lignocaine (lidocaine) their symptoms resolved dramatically. Both were able to return to a full and independent life with no sequelae.

Our decision to use corticosteroids was based on the observation that bacterial antigens can promote cytokine proliferation² within the joint and activate chondrocyte proteases.³ We postulate that despite adequate treatment of infection, cytokine mediated inflammation persists and that intra-articular corticosteroid may limit damage and improve outcome. The use of intra-articular corticosteroids in addition to antibiotics in experimental staphylococcal septic arthritis in rabbits found no adverse effects of the corticosteroids and an improvement in joint histological-histochemical parameters.¹

We therefore propose that intra-articular corticosteroids may be useful in septic arthritis where: (a) synovitis persists despite adequate intravenous antibiotic treatment and lavage; and (b) repeat synovial fluid and blood cultures are found to be sterile.

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- 1 Wysenbeek AJ, Volchek J, Amit M, Robinson D, Boldur I, Nevo Z. Treatment of staphylococcal septic arthritis in rabbits by systemic antibiotics and intra-articular corticosteroids. *Ann Rheum Dis* 1998;57:687–90.
- 2 Saez-Llorens X, Mustafa M, Ramilo O, Fink C, Beulter B, Nelson JD. Tumor necrosis factor and interleukin 1 B in synovial fluid of infants and children with suppurative arthritis. *American Journal of Diseases of Children* 1990;144:353–6.
- 3 Williams RJ, Smith RL, Schurman DJ. Septic arthritis. *Arthritis Rheum* 1990;33:533–41.