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### Elevation of D8/17-positive B lymphocytes in only a minority of Dutch patients with post-streptococcal reactive arthritis (PSRA): a pilot study

SIR, The last decennium has witnessed a resurgence of reactive arthritis secondary to infection with  $\beta$ -haemolytic group A streptococci (GAS) [1]. Nowadays, post-streptococcal reactive arthritis (PSRA) is recognized as a clinical syndrome distinct from the classic acute rheumatic fever (ARF) [2–5]. The major differences between ARF and PSRA are the predominant age of occurrence and the relative risk of developing carditis. Genetic studies reveal differences in the association of HLA DRB1\*01 and HLA DRB1\*16 with ARF vs PSRA.<sup>6</sup> These HLA alleles may represent an individual's genetic susceptibility factor for developing a humoral hyper-responsiveness secondary to GAS: the elevated D8/17 binding to B lymphocytes *in vitro* occurs

with a high frequency (63–100%) in ARF and has therefore been proposed as a susceptibility marker for ARF [7–10]. Here we report preliminary data on the binding of monoclonal antibody (mAb) D8/17 to B lymphocytes in a series of Dutch PSRA patients.

We performed a systematic prospective observational study of eight consecutive patients at a Dutch out-patient department of rheumatology who presented with arthritis after streptococcal pharyngitis in the Dutch region of Friesland between May 1998 and May 1999. In all patients, antistreptolysine-O (ASO) and antideoxyribonuclease B (antiDNase B) titres were measured simultaneously and monitored sequentially at presentation and 6 weeks and 3 and 6 months after the primary throat infection. A significant rise and fall of ASO and/or antiDNase B titres was required prior to inclusion, as described previously [5]. Patients were included only if PSRA was diagnosed according to accepted criteria [1–5].

All PSRA patients were assessed for B-cell expression of D8/17, except one whose blood sample was lost. Blood was collected in acid citrate dextran tubes (ACD solution B tubes; Terumo Europe, Leuven, Belgium) and the whole-blood staining procedure was done the same day. Fluorescence-activated cell sorting (FACS) was performed within 24 h. Staining was done by adding 30  $\mu$ l of immunoglobulin (Ig) M monoclonal antibody (tube A) or 30  $\mu$ l of the D8/17 antibody (a generous gift from Dr J. B. Zabriskie, The Rockefeller University, New York, USA) (tube B) to 100 30  $\mu$ l whole blood. After incubation for 1 h at 4°C, the suspension was washed with 2 ml phosphate-buffered saline (PBS) with 0.5% bovine serum albumin (Sigma Aldrich, Zwijndrecht, The Netherlands) and centrifuged at 2500 r.p.m. for 2 min. To both pellets, 5  $\mu$ l CD19-PE (IQP, Groningen, The Netherlands) and 5  $\mu$ l Gt-anti-Ms-IgM-FITC (Southern Biotechnology Associates, Birmingham, AL, USA) bovine serum albumin (Sigma Aldrich, Zwijndrecht, The Netherlands) were added for half an hour at room temperature. After incubation, the red cells were lysed with 2 ml FACS lysing solution (Becton Dickinson, Leiden, The Netherlands) for 10 min, centrifuged, and washed. The pellet was resuspended in 100  $\mu$ l PBS with 0.5% bovine serum albumin and stored at 4°C until measured on the FACStar (Woerden, The Netherlands). Measuring was done by placing a gate round the CD19-positive B cells; 2000 cells were counted. The results for D8/17-positive B cells obtained by FACS analysis were classified as negative when expression was <8.0% (<P95) and as positive when expression was >8.0% (>P95 D8/17 as determined in a control group).

Eight Dutch patients [female/male ratio 7/1; mean (S.D.) age 32 (12) yr] with arthritis were included (complete data sets for seven patients are shown in Table 1). A positive throat culture with GAS was obtained in only three patients. Arthritis was present in all patients; the mean (S.E.M.) number of affected joints was 7.9 (2.6). No manifestations of carditis, conduction block or erythema were observed. Transient

TABLE 1. Demographic and laboratory data of seven PSRA patients

	Patient							Group data: mean (s.d.)
	1	2	3	4	5	6	7	
Age (yr)	54	18	32	32	31	19	37	32 (12)
Sex	F	F	F	M	F	F	F	F/M = 6/1
Previous ARF	—	—	—	—	—	—	—	
Throat culture	GAS	GAS, <i>H. infl.</i>	Neg	Neg	Neg	GAS	Neg	3/7 GAS
No. of arthritic joints	19	6	1	2	3	10	14	8 (7)
Fever	+	—	—	+	+	+	—	+/- = 4/3
ESR (mm/h)	73	13	22	84	90	69	69	59 (30)
CRP (mg/l)	44	3	9	96	40	69	68	47 (34)
D8/17	2.1	3.2	4.1	4.4	6.9	8.0	9.6	5.5 (2.7%)
ASO (U/l)	1200	340	1200	1200	300	2400	300	990 (760)
AntiDNase B (U/l)	2500	240	1600	500	400	6400	2000	1950 (2150)
ASO/antiDNase B ratio	0.48	1.42	0.75	2.40	0.75	0.38	0.15	0.90 (0.77)
Recovery (months)	6	2	3	4	4	2	5	3.7 (1.5)
Extra-articular phenomena	*			**			***	

Extra-articular manifestations: \*cholestatic hepatitis; \*\*transient nodal escape, minor aorta valve insufficiency and uveitis; \*\*\*corticosteroid (topical)-responsive iritis and episcleritis.

M, male; F, female; Neg, negative; *H. infl.*, *Haemophilus influenzae*.

cholestatic hepatitis was found in one and uveitis in two patients. Prophylaxis by monthly treatment with penicillin was advised for all patients in whom a primary GAS infection was suspected. All patients showed full recovery within a 1-yr follow-up period, which was uneventful. The binding of mAb D8/17 to B lymphocytes was assessed. The percentage of D8/17-positive B lymphocytes in PSRA patients ranged from 2.1 to 9.6% with a mean (s.d.) 5.5 (2.7%). A control group of 22 unselected (eight females, 14 males) healthy volunteers was used to determine the normal expression of D8/17. The percentage of D8/17-positive B cells had a normal distribution, with range 1.0–8.0% and mean (s.d.) 4.0 (2.2)%. Two of seven PSRA patients (patients 6 and 7) had elevated expression of D8/17 (>8.0%).

We conclude that arthritis secondary to streptococcal infection in our region of The Netherlands is not accompanied by cardiac or neuropsychiatric involvement. Only 29% of PSRA patients had an elevated percentage of D8/17-positive B lymphocytes, which is in contrast with the 63–100% in the ARF literature. The fact that five of seven (71%) of our patients had a normal percentage of D8/17-positive B lymphocytes may suggest non-susceptibility to developing ARF in the majority of Dutch PSRA patients. Further prospective multicentre studies are warranted to confirm these findings in larger patient populations.

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### Familial articular hypermobility and scapho-trapezial/trapezoid osteoarthritis in two siblings

SIR, We report two siblings with familial articular hypermobility (FAH) and lone osteoarthritis (OA),