fluid by phenol/chloroform extraction. DNA was obtained from synovial fluid cells by homogenisation in TRI reagent (Molecular Research Centre, Cincinnati, Ohio, USA). DNA extracts were stored at -80°C . DNA extracts were tested for B19 DNA by a nested PCR assay.⁸ DNA extracts from positive (viraemic) and negative control sera were included in each run.

The C reactive protein was above 10 mg litre⁻¹ in all but four rheumatoid arthritis patients, providing evidence of rheumatoid disease activity (table). In serum, 14 of 18 rheumatoid arthritis patients (77%) and eight of 11 non-RA patients (73%) were positive for anti-B19 IgG (table). In synovial fluid, nine of 18 rheumatoid arthritis patients (50%) and seven of 11 non-RA patients (64%) were positive for anti-B19 IgG (table). Serum and synovial fluid from all patients from both groups were anti-B19 IgM negative. Serum, synovial fluid, and synovial fluid cells from all patients tested negative for serum B19 DNA.

Nikkari *et al*⁹ found serological evidence of recent parvoviral infection in four of 135 rheumatoid arthritis patients and two of 62 controls. No evidence for the presence of B19 DNA was found in 18 synovial fluids, 21 samples of synovial fluid granulocytes, and 40 sera, all obtained from 65 patients with early rheumatoid arthritis. Results of the present study—in which B19 DNA was not detected in serum, synovial fluid, or synovial fluid cells of either rheumatoid arthritis or non-RA patients—are consistent with those of Nikkari. The PCR sensitivity of the present study was of the order of 10–100 genome copies per ml¹⁰ and is comparable to that of Nikkari.⁹ Although not part of the present study, B19 DNA has been found in rheumatoid synovia.^{6–10} However, results of these studies are conflicting^{6–10} and it may be that B19 viraemia frequently leads to persistence in synovial macrophages.¹⁰

In conclusion, from the data obtained in this study, a role for B19 in the pathogenesis of acute joint swelling in rheumatoid arthritis patients was not supported.

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- 1 Kerr JR. Parvovirus B19 infection. *Eur J Clin Microbiol Infect Dis* 1996;15:10–29.
- 2 White DG, Woolf AD, Mortimer PP, Cohen BJ, Blake DR, Bacon PA. Human parvovirus arthropathy. *Lancet* 1985;i:419–21.
- 3 Reid DM, Reid TMS, Brown T, Rennie JAN, Eastmond CJ. Human parvovirus-associated arthritis: a clinical and laboratory description. *Lancet* 1985;i:422–5.
- 4 Dijkmans BA, van Elsacker-Niele AM, Salimans MMM, van Albada-Kuipers GA, de Vries E, Weiland HT. Human parvovirus B19 DNA in synovial fluid. *Arthritis Rheum* 1988; 31:279–81.
- 5 Kandolf R, Kirschner P, Hofschneider PH, Vischer TL. Detection of parvovirus in a patient with 'reactive arthritis' by in situ hybridisation. *Clin Rheumatol* 1989;8:398–401.

- 6 Saal JG, Stendle M, Einsele H, Muller CA, Fritz P, Zacher J. Persistence of B19 parvovirus in synovial membranes of patients with rheumatoid arthritis. *Rheumatology* 1992;12:147–51.
- 7 Kerr JR, O'Neill HJ, Deleys R, Wright C, Coyle PV. Design and production of a target-specific monoclonal antibody to parvovirus B19 capsid proteins. *J Immunol Methods* 1995; 180:101–6.
- 8 Kerr JR, Curran MD, Moore JE, Erdman DD, Coyle PV, Nunoue T, *et al*. Genetic diversity in the non-structural gene of parvovirus B19 detected by singlestranded conformational polymorphism assay (SSCP) and partial nucleotide sequencing. *J Virol Methods* 1995; 53:213–22.
- 9 Nikkari S, Luukkainen R, Mottonen T, Meurman O, Hannonen P, Skurnik M, *et al*. Does parvovirus B19 have a role in rheumatoid arthritis? *Ann Rheum Dis* 1994;53:106–11.
- 10 Kerr JR, Cartron JP, Curran MD, Moore JE, Elliott JRM, Mollan RAB. A study of the role of parvovirus B19 in rheumatoid arthritis. *Br J Rheumatol* 1995;34:809–13.

Down syndrome with coexistent gout: report of six patients and possible reasons for the scarcity of descriptions of this association

Although the association between Down syndrome and hyperuricaemia is well known,^{1,2} gouty arthritis has rarely been encountered in Down syndrome regardless of persistent hyperuricaemia.³ To date, there have been only scattered reports on five Down syndrome patients with coexistent gout^{4–7}; in this report we describe six such patients.

The table summarises the data in our six patients. Important data not included in the table are as follows: the maternal grandfather of case 1 had suffered from severe gout; case 2 was extremely obese (body mass index 33.1); case 3 had a patent arterial duct and pulmonary hypertension and had severe polycythaemia, presumably resulting from the cardiovascular abnormality; although case 5 had a ventricular septal defect and

pulmonary stenosis, the laboratory test showed no polycythaemia.

The diagnosis of gouty arthritis was made by demonstrating crystals in the joint fluid in one patient (case 1), while that for the other five patients was performed according to the American Rheumatism Association preliminary criteria for the classification of acute gouty arthritis.⁸

The six patients in the present report had large joint arthritis as the first gouty symptoms, although in general approximately 70% of gouty patients are believed to have great toe arthritis as the first symptom. This tendency was also observed—though less markedly—in the previous reports on the five patients cited above. Thus only in the two cases reported by Ciompi *et al* were the first joints involved great toes.⁶ The tendency of gouty arthritis to occur in large joints in Down syndrome patients remains to be explained. In five of our patients, 24 hour uric acid excretion was relatively low (table). Whether this tendency is a characteristic of Down syndrome patients should be examined in later studies.

The pretreatment serum urate concentrations of our six Down syndrome patients were not only higher than the age matched male Down syndrome controls but also higher than age matched male gout patients and control male gouty patients (figure). These data may indicate that the occurrence of gouty arthritis is suppressed in Down syndrome patients. One explanation could be that leucocyte function, which is necessary to cause gouty arthritis, is reported to be impaired in Down syndrome patients.⁹

The mean age of onset of arthritis in our six Down syndrome patients (23.0 years, SD 6.4) was significantly lower ($P<0.001$) than the control male gouty patients (43.2 years, SD 11.8, $n=350$). In the five patients described in published reports,^{4–7} the age of onset of arthritis (21.6 years, SD 4.9) in the Down syndrome patients with coexistent gout was also younger than general gouty patients. The earlier onset of gouty arthritis

Pretreatment serum urate concentrations in Down syndrome patients coexistent with gout (Down + gout, age 23.0 years, SD 6.4), age matched male Down syndrome patients (Age matched Down, age 23.0 years, SD 5.3), age matched male gout patients (Age matched gout, age 23.2 years, SD 9.6), and male gouty patients (Gout, age 43.2 years, SD 11.8). Error bars are SD.

Cases with coexistent Down syndrome and gout

Patients	Sex	Onset age (year)	Serum urate (mg dL ⁻¹)	Hb (g dL ⁻¹)	LDH (IU litre ⁻¹)	Ccr (ml min ⁻¹)	Cua (ml min ⁻¹)	Cua/Ccr (%)	24 h ua (mg)
Case 1	M	18	12.4	16.3	255	69	2.4	3.48	320
Case 2	M	22	10.3	17.3	271	97	3.2	3.30	440
Case 3	M	15	11.7	21.5	304				310
Case 4	M	30	10.3	13.6	187	48	2.3	4.79	230
Case 5	M	31	11.5	14.8	232	51	1.9	3.73	360
Case 6	M	22	9.1	14.7	260				
Mean		23.0	10.88	16.4	251	71.3	2.63	3.86	325
(SD)		(6.4)	(1.20)	(2.8)	(39)	(24.6)	(0.49)	(0.81)	(87)

Ccr, creatinine clearance; Cua, urate clearance; Cua/Ccr, fractional urate clearance; 24 h ua, excretion of uric acid in 24 hours.

in the Down syndrome patients may be attributed to the shorter life span of Down patients compared to the general population. Thus individuals with Down syndrome who would have developed gouty arthritis at an older age may not have lived long enough to develop the disease, thereby reducing the average onset age of gouty arthritis in this group of individuals.

Formerly the average life span of patients with Down syndrome was very short. Recently, however, the life expectancy of Down patients has been dramatically improved.¹⁰ The fact that our institute alone has recently encountered six cases of Down syndrome with gout, despite there being only four previous reports on five such patients, may indicate an increase in the

frequency of gout in Down syndrome. If so, the numbers of such patients will increase in the near future in developed countries, where life expectancy of Down syndrome patients continues to improve.

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1 Fuller RW, Luce MW, Mertz ET. Serum uric acid in mongolism. *Science* 1962;137: 868-9.
2 Kaufman JM, O'Brien WM. Hyperuricemia in mongolism. *N Engl J Med* 1967;276:953-9.
3 Pant SS, Moser HW, Drane S M. Hyperuricemia in Down's syndrome. *J Clin Endocrinol Metab* 1968;28:472-8.
4 Cayla J, Rondier J, Auscher C, Perreau C, De Gery A. Goutte et mongolisme. A propos d'une observation. *Revue du Rhumatisme* 1974;41:203-7.
5 Nishida Y, Akaoka I, Nishizawa T, Maruki M, Aikawa T, Mitamura T, et al. A case of gouty arthritis associated with Down's syndrome. *J Ment Defic Res* 1976;20:277-83.
6 Ciompi ML, Bazzichi LM, Bertolucci D, Mazzoni MR, Barbieri P, Mencacci S, et al. Uric acid metabolism in two patients with coexistent Down's syndrome and gout. *Clin Rheumatol* 1984;3:229-33.
7 Dacre JE, Huskisson EC. Arthritis in Down's syndrome. *Ann Rheum Dis* 1988;47:254-5.
8 Wallace SL, Robinson H, Masi AT, Decker JL, McCarty DJ, Yu T-F. Preliminary criteria for the classification of the acute arthritis of primary gout. *Arthritis Rheum* 1977;20:895-900.
9 Gregory L, Williams R, Thompson E. Leukocyte function in Down's syndrome and acute leukaemia. *Lancet* 1972;i:1359.
10 Masaki M, Higurashi M, Iijima K, Ishikawa N, Tanaka F, Fujii T, et al. Mortality and survival for Down syndrome in Japan. *Am J Hum Genet* 1981;33:629-39.