

Disease activity in polyarteritis nodosa. Serum creatinine and erythrocyte sedimentation rate (ESR) declined following immunosuppressive treatment (open arrow), but there were further acute neurological events (small arrows). Day 0 = day of admission with first stroke.

renal and visceral disease, late deaths (within two years) are largely attributable to cerebrovascular, and to a lesser extent cardiac, events.²

The addition of cytotoxic agents to corticosteroids may be more efficacious than steroids alone in treatment of PAN³; this approach, or the use of higher dose immunosuppressive treatment, should be considered for patients with PAN who have evidence of cerebrovascular disease. The early recognition and appropriate treatment of PAN significantly improves prognosis;⁵ our case, and the frequent deaths from cerebrovascular disease in PAN, suggests that cerebral involvement in this condition requires further attention and may merit more aggressive treatment.

Improved renal function indicates a good renovascular response to immunosuppressive treatment. In contrast, there were repeated further neurological events recorded as cerebral infarcts. As far as we know this variable response between the cerebral and renal circulations has not been described previously.

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Synovial fluid T cells in HTLV-I positive RA

Sir: Human T lymphotropic virus type I (HTLV-I) is closely associated with the aetiology of adult T cell leukaemia/lymphoma and HTLV-I associated myelopathy/tropical spastic paraparesis.¹ Molecular features of the virus, which involve the relative tropism for CD4 positive T cells and a unique ability to immortalise the infected cells,¹ suggest that HTLV-I may have a role in modifying the inflammatory process.

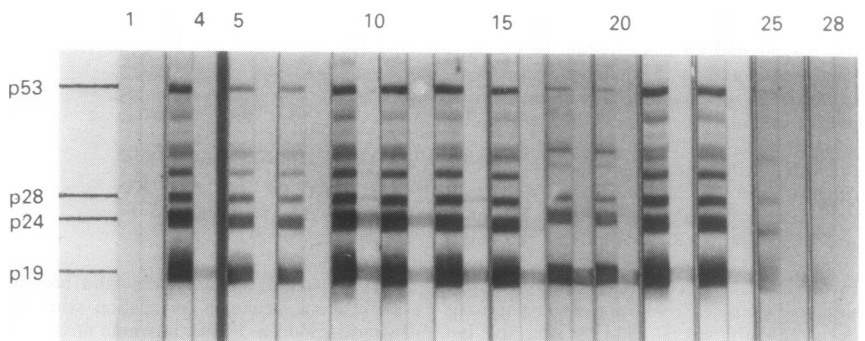
Recently, HTLV-I has been implicated in chronic arthritis as a manifestation of carrier state infection.²⁻⁵ Similarly, a study of transgenic mice demonstrated the arthritogenic capacity of HTLV-I.⁶ It remains to be determined, however, whether HTLV-I has a role in triggering rheumatoid arthritis (RA), modifying inflammation in the synovial compartment, or inducing a new clinical manifestation. In this study we estimated the

influence of HTLV-I on cellular immune responses in the affected synovial compartment in a random sample of 12 patients with RA, six positive for HTLV-I antibody (particle agglutination method) (group A) and six negative for the antibody (group B); T cell subsets in the synovial fluid were also analysed.

All 12 patients had RA, according to the American Rheumatism Association criteria, with affected knee joints from which the synovial fluid was collected. The paired peripheral blood samples were obtained concurrently. Western blot analysis confirmed the presence of IgG and IgM antibodies to HTLV-I antigens in the serum samples and synovial fluids of group B patients (figure). Atypical lymphocytes with nuclear convolutions were detected in synovial fluids obtained from five patients in group B. Peripheral blood and synovial fluid mononuclear cells were isolated and cryopreserved in liquid nitrogen until tested. Dual immunofluorescence staining was used to determine the distribution of T cell subsets as previously described.⁷ Student's two tailed *t* test was used to compare differences between groups A and B, and *p* values less than 0.05 were considered significant. Paired samples from peripheral blood and synovial fluid were evaluated by two tailed paired Student's *t* test, and *p* values less than 0.01 were considered significant.

The table summarises the distribution of T cell subsets in the patients' peripheral blood and synovial fluid samples. No significant differences in the percentages of each T cell subset in synovial fluid were noted. Changes in synovial fluid T cell subsets as compared with those in peripheral blood, including increases in the percentage of CD8+, HLA-DR bearing CD4+ and CD8+, and CD11b negative CD8+ lymphocytes and a decrease in the percentage of CD45RA bearing CD4+ lymphocytes, were determined as previously described.⁸ No significant differences in these changes were found between groups A and B.

These results showed that the patients with RA who were HTLV-I infected had the same pattern of distribution of T cell subsets in synovial fluid and peripheral blood as patients with RA negative for the HTLV-I antibody, showing that HTLV-I infection does not affect phenotypic cell populations in the affected synovial compartments. In addition, to evaluate the relation between HTLV-I and arthritis it will be necessary to carry out further studies on arthritic patients, including both patients with RA and patients with



Western blot analysis in the serum and synovial fluid samples from the patients with rheumatoid arthritis positive for antibody to HTLV-I by particle agglutination method. Odd numbered lanes show the results for HTLV-I IgG antibodies, and even numbered lanes show that for HTLV-I IgM antibodies. Lanes 1 and 2 are negative controls, lanes 3 and 4 positive controls. The samples of lanes 5, 6, 9, 10, 13, 14, 17, 18, 21, 22, 25, and 26 are the serum samples, and those of lanes 7, 8, 11, 12, 15, 16, 19, 20, 23, 24, 27, and 28 are the synovial fluids of the patients.

Comparison of the distribution of T cell subsets in the peripheral blood (PB) and synovial fluid (SF). Values are given as means (SD)

T cell subsets (% or ratio)	(A) HTLV-I seropositive RA		(B) HTLV-I seronegative RA	
	PB	SF	PB	SF
CD4+	39.7 (6.8)	36.0 (6.4)	25.9 (11.4)	34.5 (4.4)
CD8+	26.9 (11.3)	47.9 (9.7)*	24.6 (4.0)	54.0 (4.2)*
CD4+/CD8+	1.68 (0.71)	0.79 (0.26)	1.09 (0.45)	0.65 (0.12)
CD4+ HLA-DR+	3.0 (0.8)	24.8 (8.3)*	2.7 (2.9)	20.2 (7.9)*
CD8+ HLA-DR+	4.4 (2.6)	37.9 (7.7)*	3.6 (1.7)	35.2 (11.2)*
CD4+ HLA-DR+/CD8+ HLA-DR+	0.91 (0.52)	0.68 (0.27)	0.71 (0.46)	0.57 (0.11)
CD4+CD29+	22.4 (4.3)	32.3 (6.8)	16.1 (10.2)	33.2 (5.4)
CD4+CD45RA+	18.7 (4.9)	2.5 (2.2)*	10.7 (4.5)	1.4 (1.2)*
CD4+CD29+/CD4+CD45RA+	1.24 (0.27)	19.42 (9.83)*	1.62 (0.80)	48.39 (40.16)
CD8+CD11b+	11.8 (5.3)	5.8 (4.5)	12.6 (3.3)	7.1 (3.6)
CD8+CD11b-	15.0 (10.1)	42.1 (12.8)*	12.0 (4.8)	46.2 (7.0)*
CD8+CD11b+/CD8+CD11b-	1.12 (0.82)	0.18 (0.17)	1.26 (0.76)	0.17 (0.11)

Differences were statistically significant between peripheral blood and synovial fluid. *p<0.01. No significant differences were observed between groups A and B.

arthritis which does not fulfil the RA criteria. If some subtle changes are present in HTLV-I infected arthritic patients, further analysis using functional assays of lymphocytes may be useful for detecting these changes.

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False negative results of anticardiolipin antibody test

Sir: It has been reported that certain anticardiolipin antibodies (ACAs) react against the cardiolipin-β₂ glycoprotein I (β₂-GPI)

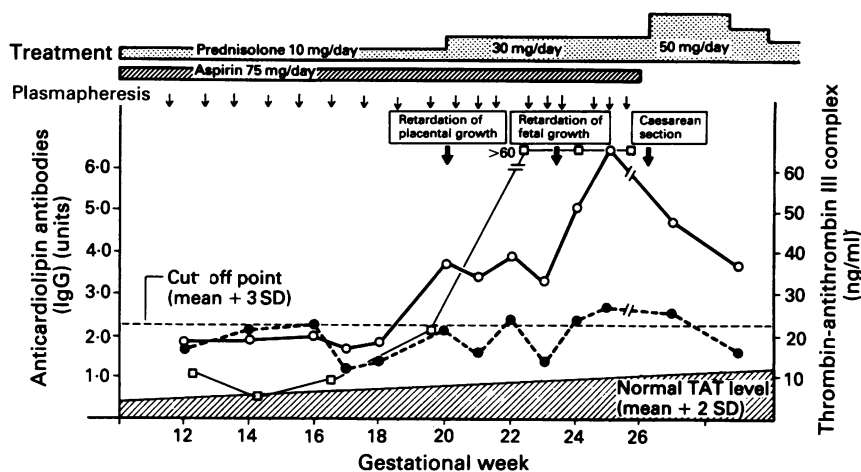
complex^{1,2} and that the binding of ACA is enhanced by adding β₂-GPI to the conventional enzyme linked immunosorbent assay (ELISA) system.^{3,4} Possibly, therefore, false negative results of ACA are determined and recorded unless β₂-GPI is added to the ELISA system in some patients with antiphospholipid syndrome.

We present the case of a 30 year old woman who was diagnosed for systemic lupus erythematosus in 1980. She had previously had two fetal losses. In 1985 her first pregnancy resulted in intrauterine fetal death during the 20th week of gestation. During her second pregnancy in 1988 retardation of fetal growth and oligohydramnios progressed during the 20th week of gestation and resulted in fetal death during the 22nd week of gestation. Small multiple infarctions in the placenta were recognised.

In 1989 she was admitted to our hospital during the fourth week of gestation. She had no special physical signs. Laboratory findings were white blood cell count 4.5×10⁹/l, haemoglobin 104 g/l, platelets 16.8×10⁹/l,

erythrocyte sedimentation rate, 4 mm/h and low concentrations of complements were recorded; C3 460 mg/l (normal 700-1300), C4 230 mg/l (normal 300-500), and CH50 21.4 U/ml (normal 32-36). The antinuclear antibody titre was 1/640 (homogeneous) and anti-DNA was 2.7 IU/ml (normal <7.0). The SS-A antibody titre was 1/32 and SS-B antibodies were absent. No antibodies to Sm or RNP were detected. Latex agglutination test for rheumatoid factor was 1/160. Cryoglobulin and circulating immune complexes (C1q binding assay) were not detected. Anticardiolipin antibodies of IgG and IgM were negative by the conventional ACA assay performed without β₂-GPI.⁵ The activated partial thromboplastin time was 31.4 s (control 32.0). Lupus anticoagulant⁶ and Venereal Disease Research Laboratory tests were negative. No abnormal findings of blood urea, creatinine, and urine analysis were noted. A raised concentration of the thrombin-antithrombin III complex (TAT), which has been reported as a marker for thrombosis,⁷ was recorded as 10.1 ng/ml. Prednisolone 10 mg/day and aspirin 75 mg/day were given. For prophylactic treatment double filtration plasmapheresis was carried out once a week from the 10th week of gestation.

Clinical status and laboratory findings of the patient stabilised by the 19th week of gestation. During the 20th week of gestation circulating immune complexes and TAT increased to 15.9 ng/ml (normal 10.0) and 21.8 ng/ml (normal <8.3) respectively (figure). Retardation of placental growth was recognised by echogram. Therefore, prednisolone was increased to 30 mg/day and plasmapheresis was carried out three times during the next two weeks. The TAT concentration, however, increased beyond 60 ng/ml and retardation of fetal growth was again detected during the 23rd week of gestation. Fetal distress was noted during the 26th week of gestation, and therefore caesarean section was performed; a



Lab data		
ANA (<1/20)	1/320	1/320
Anti-DNA (<7.0 IU/ml)	3.1	3.2
Anti-SSA	1:4	1:8
CIC (<10.0 μg/ml)	<10.0	15.9 <10.0
APTT (s/control: s)	31.4/32.0	31.6/32.0 30.8/31.6
TM (<3.7 ng/ml)		2.6 4.8 7.4

Concentration levels of anticardiolipin antibodies determined with (—○—) and without (—●—) the presence of β₂ glycoprotein I. The plasma thrombin-antithrombin III concentration is indicated as —□—. Normal range (mean+2SD) of the thrombin-antithrombin III concentration during the course of pregnancy is indicated by the shaded area, which was determined by testing 30 women with uncomplicated pregnancy. ANA=antinuclear antibody titre; CIC=circulating immune complexes; APTT=activated partial thromboplastin time; TM=thrombomodulin.