LETTERS TO THE EDITOR

IgG rheumatoid factor synthesis in synovial fluid

Sir: Winchester *et al* two decades ago proposed that IgG rheumatoid factor (RF) could be locally produced in plasma cells that line the synovium.¹ We conducted a short study looking at paired samples of synovial fluid (from the knee joint) and serum from patients with definite rheumatoid arthritis to determine if the production of IgG RF is localised in the synovial fluid. Thirty six serum samples and synovial fluids were obtained from patients diagnosed with rheumatoid arthritis, all collected within one day of each other. The synovial fluids were treated with hyaluronidase enzyme² (Sigma, USA) before testing. Serum samples and synovial fluids were also tested for the presence of IgG antibody to adenovirus. Adenovirus antibody levels have been used to establish local production of antibody in cerebrospinal fluid in syphilis³ and HIV⁴; this antibody is common and can be used to determine if non-specific 'leaking' of immunoglobulins from serum has occurred. This should be more accurate than comparing total levels of IgG, which are difficult to measure in low concentrations.

An enzyme immunoassay (EIA) was developed for the detection of IgG RF using rabbit IgG on the solid phase and anti-Fab₂ to identify bound IgG RF. We measured levels of IgG RF in these serum samples and synovial fluids and determined a ratio of synovial fluid to serum on each patient. A cut off value for the assay was determined from 144 control serum samples from blood donors, and a stringent method of standardisation was used to account for the day to day variation that occurs in EIA tests. These values were compared with ratios of synovial fluid to serum of adenovirus IgG antibody. Patients with rheumatoid arthritis positive for IgG RF and normal controls were significantly different ($p < 0.05$). The table shows the results of the ratios for the two antibodies IgG RF and adenovirus IgG in the synovial fluids and serum samples of these rheumatoid patients. A significant difference ($p < 0.05$) was shown between the IgG RF ratios and the adenovirus antibody ratios for the patients with rheumatoid arthritis. This finding strongly suggests that IgG RF had been produced locally. Further work is required to determine if selective accumulation of IgG RF in synovial fluid of other joints correlates with disease activity in rheumatoid arthritis and whether there is selective accumulation in the absence of this disease.

Ratio of IgG rheumatoid factor (RF) optical density to adenovirus IgG optical density in synovial fluid and serum of patients with rheumatoid arthritis

	Ratio IgG RF	Ratio adenovirus IgG
Mean	1.31	0.426
Range	0.411-2.24	0.156-0.741

$p < 0.05$.

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- Winchester R J, Agnello V, Kunkel H G. Gammaglobulin complexes in synovial fluids of patients with rheumatoid arthritis: partial characterization and relationship to lowered complement levels. *Clin Exp Immunol* 1970; 6: 689-70.
- Hellsing K. Immune reactions in polysaccharide media. *Biochem J* 1962; 112: 475.
- Cerny H F, Hambie E A, Lee F, Farshy C, Larsen S A. Adenovirus ELISA for the evaluation of cerebrospinal fluid in patients with suspected neurosyphilis. *Am J Clin Pathol* 1985; 84: 505-8.
- Lloyd A, Wakefield D, Robertson P, Dwyer J M. Antibodies to HIV are produced within the central nervous system of all subjects with all categories of HIV infection. *Aust NZ J Med* 1988; 18: 854-60.

Postpartum autologous plasma transfusion: effect on RA

Sir: A 32 year old white woman with rheumatoid arthritis (RA) for six years affecting many joints had been treated with various drugs, including auranofin, aurothioglucose, and D-penicillamine, without appreciable benefit. The patient discontinued her drugs and became pregnant, and her disease was moderately well controlled with prednisone 5-7.5 mg/day. By the seventh month of pregnancy the patient was in clinical remission and was taking no drugs. During the third trimester the rheumatoid factor had fallen from 1/320 to 1/80, but the patient had a Westergren erythrocyte sedimentation rate of 39 mm/h and C reactive protein of 8.7 mg/l. She had an uncomplicated delivery and five days postpartum donated a unit of blood from which 300 ml fresh frozen plasma was obtained and stored at -70°C. The patient noted gradual relapse of disease activity 10 days postpartum. On the 18th postpartum day the patient

demonstrated mild to moderate polysynovitis and consented to autologous plasma transfusion of 250 ml. Within 48 hours after transfusion the patient noted dramatic improvement in her condition, which unfortunately lasted only one to two days (see table). There were no adverse reactions to the autologous transfusion.

The ameliorating effect of pregnancy in patients with RA has been well described.³⁻⁵ This patient's case suggests that certain plasma component(s) produced during pregnancy had immunosuppressive properties that also suppressed the rheumatoid factor but did not significantly affect the C reactive protein. As the benefit of autotransfusion on disease activity occurred after storing fresh frozen plasma at -70°C and lasted for only one to two days, the plasma factor(s) which suppresses disease preserves well at -70°C and has a short half life. A control pregnant patient with no RA had blood drawn during the third trimester showing negative rheumatoid factor, negative C reactive protein, and erythrocyte sedimentation rate 14 mm/h, indicating that pregnancy alone does not affect these disease markers.

Although this is the first known report of a postpartum autologous transfusion in a patient with RA, there are several reports of heterologous postpartum transfusions in rheumatoid patients.⁶⁻⁸ Two reports^{6,7} showed benefit and one report⁸ did not. The differences in these studies may reflect the wide ranges in concentration of the pregnancy associated plasma factor(s) responsible for suppressing disease activity in pregnant patients. This study avoided this problem by using autologous postpartum plasma during disease remission. Several reports have been published suggesting that the pregnancy associated α_2 glycoprotein has disease suppressive properties,⁹⁻¹³ but another report refuted this claim.¹⁴ More recent work suggests that some yet unidentified pregnancy associated glycoprotein(s) has immunosuppressive properties.¹⁵

In conclusion, this case further supports the possibility that a pregnancy associated plasma factor(s) has immunosuppressive properties in treating RA, and further work in identifying this factor(s) should be eagerly pursued.

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Effects of autologous postpartum transfusion on rheumatoid arthritis.* Percentage change is shown in parentheses

	Results of examination:		
	Before transfusion	Day 3	Day 6
Number of swollen joints	22	6 (-73)	22
Number of tender joints	24	3 (-88)	27
Joint swelling index†	24	6 (-75)	24
Joint tenderness index‡	25	3 (-88)	29
Average grip-strength (R/L hands)§	128/144	236/180	174/154
Mean grip strength (both hands)	136	208 (+72)	164 (+28)
Duration of morning stiffness (h)	3	2	4
Rheumatoid factor	1/640	1/160	
Erythrocyte sedimentation rate (mm/h)	22	24	-
C reactive protein (mg/l)	3.01	3.94	-

*Sixty eight joints were evaluated.^{1,2}

†The index assigns a numerical value to the degree of swelling (0=no swelling; 1=mild swelling; 2=moderate swelling; 3=severe swelling) and represents summation of these values.

‡The index assigns a numerical value to the degree of tenderness (0=no tenderness; 1=mild tenderness; 2=moderate tenderness; 3=severe tenderness) and represents summation of these values.

§Average of three grip trials per hand.

||Two months postpartum rheumatoid factor 1/320.