one clinical feature of the four required by the present American Rheumatism Association criteria for classification as SLE and no convincing
rheumatoid arthritis.

On the second admission she was confused, febrile, and weak after pneumonia (and possibly due to the high binding value of 60%). Complement levels at this time were not reduced, so that there was no serological evidence of active SLE renal involvement. Thus on this occasion there was no clinical evidence of active SLE, though the DNA binding value was now high. Was she taking a pyrazole anti-inflammation agent? Grayson et al. have reported a high DNA binding of 54%, in a patient with ankylosing spondylitis given phenylbutazone and oxyphenbutazone, who develop a selective neuropenia and in whom both DNA binding values and neutrophil counts reverted to normal after phenylbutazone was stopped.

Although DNA binding activity can be a valuable confirmatory investigation in SLE, being both more specific and more sensitive than search for LE cells in a peripheral blood film, a raised value is not in itself diagnostic and adequate clinical correlation are also necessary. We suggest that such a patient merely had rheumatoid arthritis and developed Sjögren's syndrome and pericarditis, and that the DNA binding activity rose after possible discontinuing the procedure as a result of one of the drugs given concurrently.

Care should certainly be taken with antibiotics in patients with Sjögren's syndrome because of their tendency to develop drug allergies. The term "Sjögren's syndrome" is best used to describe certain associated features which may develop in patients with rheumatoid arthritis, SLE, and other "connective tissue" diseases, and the term "Sjögren's disease" is best avoided, since it implies a separate disease entity in the category of rheumatoid disease and SLE.

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1 Hughes, G R V, and Whaley, H. British Medical Journal, 1972, 2, 533.

Acanthamoeba meningoen cephalitis in Britain

Sir,—Owing to an unusual combination of circumstances, including clinical work1 and cultures2 done in separate institutions, a unique fatal case of Acanthamoeba meningoen cephalitis in Britain in 1969 was originally diagnosed by Apley et al. as due to Naegleria sp. I wish to correct this identification so that this report will no longer be used to support a particular conclusion for Naegleria and also to permit its inclusion, as the most virulent yet recognised, in the limited but diverse number of human infections apparently caused by Acanthamoeba.3 The reclassification is necessary because Naegleria, by phase contrast, does not look like the amoeba from the CSF illustrated by Apley et al, while Acanthamoeba does. Also, the description, "they had three or four spiky pseudopodia and moved very slowly," describes Acanthamoeba in CSF, but not N fowleri or N gruberi, which are monopodial in locomotion.4

Naegleria sp was isolated from the CSF of the child who died and the surviving plasmatocytes. However, site isolate proved to be N gruberi rather than the pathogen, N fowleri, and was not the primary pathogen because: (1) it cannot form pseudopods like the amoeba seen in the CSF; (2) careful experiments proved it to be non-pathogenic in mice; and (3) as do other N gruberi, it dies at febrile temperatures.5 Saygi et al. showed that the isolate could act as a secondary invader in mice. In the human infection Naegleria could have been a secondary invader or a synergist with Acanthamoeba.

In Naegleria meningoen cephalitis death usually follows hospital admission by 2-3 days,1 but the aged spread cyanin B, which kills N fowleri in mice,4 prolonged the survival of the patient on a respirator.1 This drug was started after amoebae were isolated in the CSF in 1969 when the child went into coma. However, sulphadiazine active against Acanthamoeba in mouse brain,6 was started on admission (and was given to the survivors) and is a more likely antiamoebic agent.

No Acanthamoeba grew from CSF, although one was isolated from where the children had played.7 Sulphadiazine was given for two days before the first spinal tap and probably prevented Acanthamoeba growth in culture. Acanthamoeba-like amoebae were seen in the CSF sample, but the part sent for culture was three days in transit, probably with sulphadiazine present.

For future reference, it seems likely that repeated culture of nasopharyngal samples, as well as immediate culture of the CSF samples, would have been useful. Cultures can be simply made on non-nutrient agar with living Escherichia coli. Also by hindsight, circulating antibodies could have been sought.

The opinions or assertions contained herein are the private views of the author and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense.

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A "Corrected" calcium concept

Sir,—Dr R A Pain and his colleagues in Adelaide (13 December, p 617) conclude that it is not valid to "correct" measured serum total calcium concentration for varia tions in serum albumin concentration using an average regression coefficient. This is because they found a wide variation in the regression of calcium on albumin between individuals—as wide as from 0.007 to 0.053 mmol calcium/g albumin.

There are two reasons for considering this range of values to be highly improbable. Firstly, if individual regression coefficients were really as different as they suggest it is most unlikely that two patients with the same correlation coefficient of 0.867 between calcium and albumin concentrations in specimens from 200 patients with albumin values ranging from 20 to 48 g/l. Secondly, using these regression coefficients, normal persons with calcium values of, say, 2.40 mmol/l (9.6 mg/100 ml) and albumin values of 44 g/l would have an absurd range of calculated non-protein-bound calcium concentrations—from 0.07 to 2.37 mmol/l (0.28 to 9.5 mg/100 ml). When we used the average regression coefficient of 0.0247 mmol/g in our 200 patients the range of calculated non-protein-bound calcium concentrations was even narrower—1.25-1.60 mmol/l (5.0-6.4 mg/g)—very similar to reported ranges for ultrafiltrate calcium.1,4 We believe that the reason for the wide range of regression coefficients found by Dr Pain and his colleagues is that they have put insufficient attention to the effect of analytical variation. We have been unable to correct our routine patient data as these were not presented, but examination of the data of Pedersen2 and of Berry et al.,3,4 which Dr Pain and his colleagues incorporated in their calculations, shows that individual regression coefficients vary most widely when the changes in albumin concentration induced by postural changes or tourniquet are smallest (see fig). As the changes in albumin concentration become greater, so the regression coefficients approach their overall median value of 0.025 mmol/g. It is not surprising that the effect of analytical variation is greatest when the measured differences are smallest. (A simple way to minimise the effect of analytical variation would be to make numerous analyses on each sample.)

Because the effects of analytical error on individual regression coefficients will tend to cancel each other out we have some confidence in the overall median value for the total of 62 regression coefficients derived from the data of Pedersen,2 Berry et al.,3,4 and the Adelaide group. It is 0.025 mmol/g. This is virtually identical with the average regression coefficient that we reported in 1973 of 0.0247 mmol/g (0.989 mg/g) between

Relation between individual regression coefficients and changes in serum albumin induced by posture (Pedersen2,4) and tourniquet (Berry et al.4). The triangle at the top of the figure is the average regression coefficient ± 2 SE for 200 patients with albumin values varying from 20 to 48 g/l (Payne et al.).