it has alone the theoretical advantage of inducing immune tolerance,[1] has a suppressive effect on experimental autoimmune disease,[2] and is more effective than other alkylating agents in suppressing antibody production.[3]

Accepting the fact that patients may be too few for a controlled trial, I feel that patients given treatment of this type should have frequent scientific assessment of the activity of their disease. In the case of S.L.E. one might expect a record of frequent estimations of α_2-globulins, complement components, cryoglobulins, serum DNA, and RNA antibodies, as well as L.E. cells and antinuclear factor.—I am, etc.,

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1 Dukor, P., and Dietrich, F. M., *International Archives of Allergy*, 1968, **34**, 32.
2 Gerebtzoff, A., Lambert, P. H., and Miescher, P. A., *Annual Review of Pharmacology*, 1972, **12**, 287.
3 Lemmell, E., Hurd, E. R., and Ziff, M., *Clinical and Experimental Immunology*, 1971, **8**, 355.

Treatment of Systemic Lupus Erythematosus

SIR,—With reference to the report by Dr. M. L. Snaith and his colleagues (28 April, p. 197) concerning the choice of immunosuppressive drugs in systemic lupus erythematosus, our experience has been that the marrow-depressant effect of azathioprine when used in the treatment of rheumatoid arthritis in a dose of 2·5 mg/kg/day or cyclophosphamide in a dose of 1·5 mg/kg/day has been relatively easily controlled with adequate monitoring of the blood, including platelet counts.

An important difference, however, has been the effect of cyclophosphamide on fertility in the male. We found that six male patients on azathioprine had entirely normal sperm counts. In contrast, of six males on cyclophosphamide, five were found to be azoospermic and one had a count of only 5 million/ml. If chlorambucil produced amenorrhoea in four of six patients in Dr. Snaith's series, it seems likely that its effect on fertility is similar to that of cyclophosphamide.

We would suggest, therefore, that there are strong grounds for first considering azathioprine when an immunosuppressive agent is indicated in young patients with connective tissue disorders.—We are, etc.,

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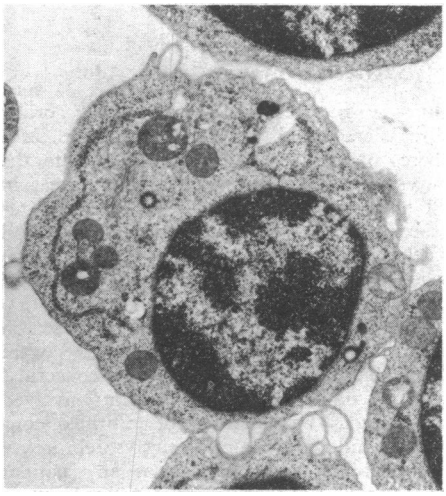
Surface Particles on Leukaemic Lymphocytes

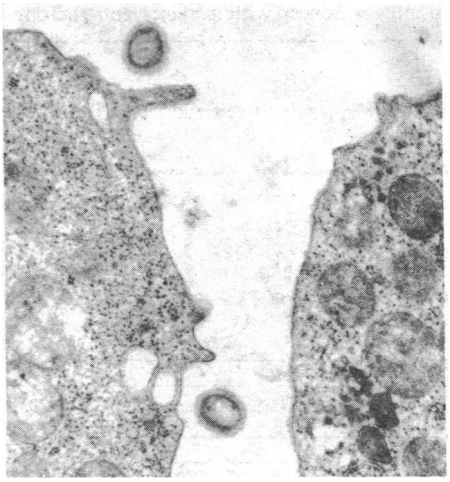
SIR,—In a previous letter (20 January, p. 172) I reported the presence of surface particles on leukaemic lymphocytes from five cases of chronic lymphatic leukaemia and one of acute leukaemia.

After this report had been published a patient aged 41 who was 26 weeks pregnant was diagnosed as having chronic lymphatic leukaemia—a very rare coincidence. Blood was taken from the patient a day after leukaemia was diagnosed. Lymphocytes were separated as described by Hughes and Caspary,[1] the procedure taking about 2½ hours. The patient was admitted again for obstetric reasons at 38 weeks and the baby was born four days later. Blood was taken immediately from the umbilical cord and an hour later from the mother. A third specimen of blood was taken from the mother three weeks later. From all samples of blood lymphocytes were separated and embedded with the same procedure as described in detail elsewhere.[2]

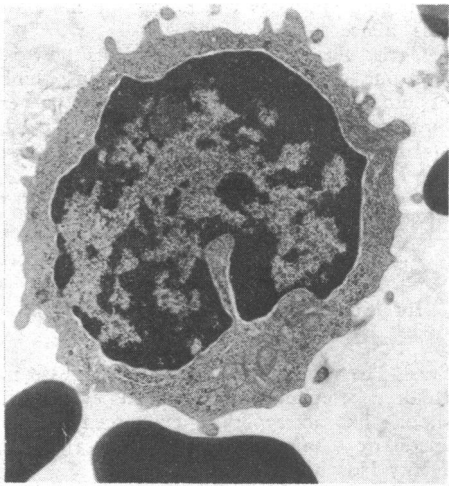
Membrane blebs on the surface of the lymphocytes were a striking feature of the first sample of maternal blood (fig. 1).



Though these blebs were present on the surface of lymphocytes in the second and third samples they did not appear to be as common as in the first. Most of the lymphocytes from the second sample contained granular dense structures similar to those of polymorphs. In all three samples from the mother, besides the blebs, particles were seen budding from the surface of the lymphocytes and a few were free, as described in my previous letter (figs. 1 and 2).



Lymphocytes from the umbilical cord blood appeared quite normal, though they showed pseudopodia; they did not have blebs or particles similar to those in the lymphocytes of the mother (fig. 3).



It has been thought that surface blebs might be artefacts due to the fixation and embedding technique, but the present study clearly indicates the presence of surface blebs and particles in the lymphocytes of the mother with chronic lymphatic leukaemia, as in the other six leukaemic patients studied, while their absence from the lymphocytes from the cord blood and from those of normal subjects does indicate their relationship to the disease. It must be borne in mind that the random sampling variations in the electron microscope may easily give a misleading assessment of the frequency with which a particular structure is encountered, and that this difficulty is increased by the possibility of artefacts even in seemingly "well fixed" material. Although 10 times more lymphocyte blocks were cut from the cord blood sample than from the samples from the mother, there was no evidence that maternal lymphocytes are to be found in the blood of the child.

I would like to thank Dr. F. Clark for his courtesy in allowing access to his patients.
—I am, etc.,

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1 Hughes, D., and Caspary, E. A., *International Archives of Allergy*, 1970, **37**, 506.
2 Narang, H. K. *Journal of Hygiene*, 1973. In press.

FIG. 1—Lymphocytes from 41-year-old leukaemic patient 26 weeks pregnant. Note the surface blebs and particles. x 11,240.
FIG. 2—Lymphocytes from the same patient showing two free virus-like particles. x 19,355.
FIG. 3—Lymphocytes from umbilical cord blood of baby of the same patient. Note normal lymphocyte. x 8,765.

Mute of Malady

SIR,—With reference to your leading article (31 March, p. 755), elucidation of the underlying cause of mutism may be helped by demonstration of thought content. This may confirm a diagnosis of schizophrenic or depressive stupor and can be helpful in the management of elective mutism and some conversion symptoms.

A time-honoured method of achieving this in adults is by amylobarbitone sodium abreaction.[1] Investigators of mute patients, however, are understandably reluctant to administer a powerful central nervous system depressant to patients who may have grave organic brain damage or be suffering from drug effects. Intravenous diazepam has been