The rapid disappearance of transfused allogeneic leucocytes^{9,10} from the circulations of adults, the possibility that leucocytes cross the placenta too slowly to allow of their ready detection in the peripheral blood, observations in the mouse indicating that transferred cells may be found in lymphoid organs normally,¹¹ and the avoidance of parturition led us to prefer a study of human fetal blood which, it was argued, might be receiving maternal leucocytes at the time of harvest. Five hundred and thirty-four cells were satisfactorily prepared from the cord blood, kindly provided by Dr. W. Barr, of five male infants delivered by Caesarian section (Table). Detailed analyses were consistent with an XY chromosome complement in all cells except one which was apparently 45, XO. Thus no evidence of a transplacental leucocyte traffic was obtained. Clearly negative findings such as this cannot entirely exclude the possibility of an exchange of cells, nor of course of subcellular antigen.

TABLE—Karyotypic Analysis of Leucocytes in Five Samples of Cord Blood from Male Newborns, Delivered by Caesarean Section

Sample Number	Cells counted	Number with 45 Chromosomes	Number with 46 Chromosomes	Number of XY Cells
1	15	0	0	15
2	100	14	86	100
3	277	14	263	277
4	116	15	101	115
5	26	1	25	26
Total	534	44	490	533

Hellström *et al.*¹² demonstrated inhibition of colony formation of embryonic cells by lymph nodal cells from female mice pregnant by mice of the same strain as the embryos, but not by those from females pregnant by males of another strain. The inhibition of colonies was abrogated by serum from females pregnant by males of the same strain as the embryos but not by that from females pregnant by males of another strain. The protectant in serum may be an immunoglobulin such as has already been demonstrated in cancer systems to which these findings are analogous. Thus it appears that a process of efferent immunological enhancement may act in both pregnancy and cancer, possibly explaining the occurrence of haemagglutinating and leuco-agglutinating antibodies and of specifically responsive leucocytes in pregnant animals and non-pregnant multiparae. The specificity of such a mechanism requires the same sort of exchange of information as the finding of immunological inertia necessitates.

Further investigation of the nature of the messages transmitted between mother and fetus seems necessary for comprehension of the immunological mechanisms involved by viviparous reproduction. Our studies agree with others that the transfer of whole leucocytes from the human mother to her fetus is not a frequent and easily detectable traffic.

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J. MAXWELL ANDERSON

Department of Surgery,
Royal Infirmary,
Glasgow C.4

M. A. FERGUSON-SMITH

Medical Genetics Unit,
The Royal Hospital for Sick Children,
Glasgow C.3

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Antibacterial Agents in Renal Failure

SIR,—Your leading article (20 March, p. 621) on antibacterial agents in renal failure is a useful review of the subject and is particularly valuable to those concerned with the management of infection in acute or chronic renal failure.

Very rightly you stress the difference between drugs which are potentially toxic even when renal function is normal and those which are not highly toxic such as the penicillins, the cephalosporins, lincomycin, isoniazid, and trimethoprim. It is somewhat surprising that you do not include in this group the macrolides, and especially the erythromycins. Parenteral erythromycin is probably the safest of all antibacterial drugs in terms of toxicity. Blood levels do not require to be monitored, and in the presence of Gram-positive infection superimposed upon uraemia the use of parenteral erythromycin should certainly be contemplated. So far as I am aware toxicity is no problem here, and in areas where facilities for monitoring blood levels, even of relatively "safe" antibacterial drugs, are not available the use of erythromycin should certainly be considered for the management of susceptible Gram-positive septicaemias.—I am, etc.,

J. MCC. MURDOCH

Department of Infectious Diseases,
City Hospital, Edinburgh 10

Drugs in Schizophrenia

SIR,—I was interested in your leading article (23 January, p. 189) on long-acting neuroleptics for the treatment of schizophrenia. Schizophrenia afflicts about 1% of the world population. High relapse rates form the crucial problem of classical treatment methods of schizophrenia. More patients are discharged from the mental hospitals after shorter terms of admission, but re-admissions have been increasing considerably. Prevention of drug evasion and hence of relapses is indeed the major concern in the management of schizophrenia.

I would, however, like to draw your attention to a chemical confusion in the article. Fluspirilene, which is indeed on trial on the Continent, is a diphenylbutylpiperidine derivative. It is chemically unrelated to the phenothiazines. Other long-acting non-phenothiazine drugs, such as pimozide and penfluridol, are effective neuroleptics which lower the relapse rate of schizophrenics. It seems unfortunate therefore that the article is entitled "Long-acting Phenothiazines in Schizophrenia." I would have preferred "Long-acting Neuroleptics in Schizophrenia."—I am, etc.,

PAUL A. J. JANSSEN

Janssen Pharmaceutica,
Research Laboratoria,
Beerse, Belgium

Methotrexate, Alcohol, and Liver Damage

SIR,—We were interested to read the article about liver damage due to methotrexate in patients with psoriasis (20 March, p. 625). Our findings differ from those of Dr. M. S. C. Dahl and his colleagues in one major regard. We have not found cirrhosis in any patient treated with methotrexate who did not regularly consume excessive quantities of alcohol.

Out of 39 methotrexate treated patients, 24 had abnormal liver biopsies. Twelve of these had mild to moderate hepatic fibrosis and three had cirrhosis. All of the latter were heavy drinkers but none of those with fibrosis had consumed much alcohol. The cumulative dose of methotrexate was greater in those patients with fibrosis or cirrhosis. Daily oral dosage was more often associated with these abnormalities than was intermittent parenteral therapy.

Little has hitherto been known about the liver in psoriasis and it is essential to control these observations. We have studied 20 patients with comparable severe psoriasis who had liver biopsies before methotrexate therapy was started. Seven had abnormal biopsies, three of which showed hepatic fibrosis. Though the difference between the proportions of patients with fibrosis in the treated and untreated groups is not statistically significant, we have observed five patients who developed fibrosis while taking methotrexate, having previously had normal liver biopsies. We are continuing this prospective study.

These data were presented at the winter meeting of the British Association of Dermatology in Birmingham on 6 March, 1971 and will be published shortly.

—We are, etc.,

J. ALMEYDA
H. BAKER
G. M. LEVENE
D. BARNARDO
J. W. LANDELLS

London Hospital, London E.1
and
St. John's Hospital for Diseases of the Skin,
London W.C.2

Genetic Cripples

SIR,—It is important that this topic by Dr. George Discombe (27 March, p. 723) should be ventilated every few years. While responsibility for any decisions arising out of the discussion must rest with those outside the profession as well as within it, it is our duty as "experts" to provide information for the basis of discussion which is as close to the truth as we know. And Dr. Discombe's calculations are so fallacious that no sound conclusion could possibly be reached if they were not challenged.

In defects of sex-linked dominant genes, such as haemophilia, about two-thirds of the defective genes are carried by females, as they carry two-thirds of the X chromosomes in the population at large. If we accept Dr. Discombe's figure of 20% for the reproduction rate of affected males, the rate of loss of haemophilia genes from the population at present is 80% of one-third, or about 26% per generation. This loss is presumably balanced by a mutation rate corresponding to about 26% of the present number of defective genes if the frequency of this gene is constant. Total elimination of the present