Animal Experiments

SIR,—I was very surprised to see in your leading article on animal experiments (25 December 1971, p. 762) the statement that animal experiments can and do cause "severe suffering." I was under the impression, apparently mistakenly, that the Home Office regulations prevented this happening. Surely there can be no justification for the suffering of laboratory animals.

Through the ages homo sapiens—the animals, could they speak, would term our species "homo rapiens"—has had all manner of specious excuses for inflicting torture on both animals and humans, often in the name of some transcendental virtue. That it is necessary in our society for these defenceless creatures to be used at all in the sad conditions of laboratory processes is regrettable. It should be done only after very careful consideration and in a manner to avoid misery and suffering. Not to do so is to negative the spirit which is held to be the basis of all our ethics and is a reflexion on us all.—I am, etc.,

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Blood Viscosity and Blood Flow

SIR,—There is just one snag in Mr. J. A. Dormandy's interesting study on alteration in blood viscosity following the infusion of dextran 40 (low-molecular-weight dextran) or Hartmann's solution (18 December 1971, p. 716). Assuming a mean blood volume of 5 litres in his experimental subjects, the rapid addition of 500 ml of intravenous fluid would lead to a temporary expansion of the blood volume of approximately 10%. I would expect this to result in a similar increase in cardiac output, and therefore also of peripheral perfusion. Though this in no way detracts from the principles demonstrated by Mr. Dormandy that peripheral arterial blood flow is intimately related to viscosity, and that dextran 40 has no special advantages over Hartmann's solution, it suggests that perhaps only half of the improved perfusion is due to reduced viscosity, increased cardiac output being responsible for the remainder.—I am, etc.,

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Amenorrhoea after the Pill

SIR,—The *B.M.J.* takes some weeks to reach Malta, so allow me to refer to your interesting leading article on amenorrhoea after the pill (27 November 1971, p. 510). I think that, apart from amenorrhoea, there is an important related risk which is not adequately realized by medical practitioners. It is the hazard of prolonged anovulation following long-term use of the pill in adolescence. I read a communication on this subject at the Nineteenth British Congress of Obstetrics and Gynaecology held in Dublin in May 1971.

In my series of 37 women treated for anovulatory infertility it was found that the group who had received no pill in adolescence, or else did so for less than six months, were much more readily responsive to treatment than the group who had been given the pill in adolescence for six months

or more. In the former group of 19 women 15 responded to clomiphene and the remaining four to Pergonal (human follicle-stimulating hormone). In the other group of 18 women only seven responded to clomiphene, then three to Pergonal, but eight were still anovulatory.

The pill is widely prescribed to adolescent girls either as a contraceptive or else to provide a facile remedy for dysmenorrhoea or irregular menstruation. It should be prescribed with great caution at this age, because it may seriously impair the subsequent resumption of regular ovulation with a consequent liability to infertility. In fact, it is probably contraindicated when there is a history of oligomenorrhoea or of irregularity in the menstrual cycle.—I am, etc.,

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Vaccination against Rubella

SIR,—The increasing use of oral contraception provides an excellent opportunity for immunizing large numbers of young women against rubella at a time when they are strongly motivated to think about the future of their potential offspring. At the second visit for prescription for the pill there is the additional advantage of the certain knowledge that no pregnancy is present. This surely is the ideal occasion on which to administer rubella vaccine.

It is clear from Dr. Constance A. C. Ross's letter (8 January, p. 109) that serological screening for rubella is impracticable, and one wonders whether it is even necessary—any more than attempts to screen for polio would be considered before administering polio prophylaxis. Rubella vaccination should be offered to all who are at risk. As pregnancy is the only known contraindication to its administration it should be given to all who may shortly become pregnant and not confined to the age 11-14, as is the present policy.

In recent years I have offered rubella vaccine to all patients who seek contraceptive advice. I explain to them that they will have to pay 20p for their prescription, as free vaccine is not provided outside the officially designated ages. They have all agreed that this is the best 20p-worth that they are ever likely to spend. Is there any reason why this inoculation should not be offered at family planning and local authority contraception clinics?—I am, etc.,

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Tropical Splenomegaly, Sickle-cell Trait, and *P. falciparum* Infection

SIR,—The tropical splenomegaly syndrome¹ is thought to be due to chronic infection with malaria, though malaria parasites are rarely demonstrated in these patients. Haemoglobin AS is thought to protect from severe *P. falciparum* infection² and tropical splenomegaly is uncommon in the presence of haemoglobin AS.³ We would like to present details of a patient with tropical splenomegaly syndrome and haemoglobin AS in whom a very scanty number of *P. falciparum* gametocytes were found only after injection of adrenaline.

The patient, a negro male aged 8 years, was born in Nigeria, and was in Biafra during the war there. He arrived in England in May 1971 and complained of abdominal pain. He had no diarrhoea, vomiting, or other symptoms, and no pyrexia. He was reported to have had worms in 1966. On admission to hospital in October 1971 he was quite well, with a normal temperature. The spleen was enlarged and firm, but not tender, and palpable three in (7.5 cm) below the costal margin. The liver edge was just palpable. A few small lymph nodes were felt in the neck, axillae, and groins. Mucous membranes were of good colour. The chest was clear.

Investigations: Haemoglobin 10.4 g/100 ml; W.B.C. 12,300 mm³ (polymorphs 35%, lymphocytes 48%, eosinophils 14%, monocytes 3%). No malaria parasites were seen in thick or thin blood films, but one hour after a subcutaneous injection of adrenaline scanty *P. falciparum* gametocytes were recognized in thick films. The sickling test was positive, and haemoglobin electrophoresis showed haemoglobin AS. The stools showed ova of hookworm, roundworm, and whipworm. Immunoglobulins: IgG 2244 mg/100 ml, IgA 87 mg/100 ml, IgM 156 mg/100 ml. Red-cell glucose-6-phosphate dehydrogenase 5.6 IU/g haemoglobin.

Other investigations revealed no important abnormalities.

The worm infestations were treated with bephenium and piperazine. The malarial infection was treated with chloroquine and primaquine. After six weeks antimalarial therapy the spleen had become much smaller and was palpable 1 in (2.5 cm) below the left costal margin.

One brother, aged 9 years, has sickle-cell trait but no malaria parasites in thick blood films. Another brother, aged 7 years, has a negative sickling test and no malaria parasites. Neither of these children has a palpable spleen.

This case has all the features of tropical splenomegaly syndrome. A specific finding in some varieties of tropical splenomegaly syndrome has been infiltration of the liver with lymphocytes, but liver biopsy was not considered justified in our patient. Reduction in the size of the spleen with antimalarial therapy is usual.^{4,7} Hyperglobulinaemia is present, but IgM is not so often raised as IgG.^{4,5,7} It is unusual for patients with tropical splenomegaly syndrome to have sickle-cell trait. Hamilton *et al.*³ failed to find any patient with sickle-cell trait in 143 patients studied for tropical splenomegaly syndrome in Uganda, but calculated that according to the prevalence rate, they should have found at least 10 patients to have haemoglobin AS. Since their report in 1969 a total of 3 of 48 patients in two series^{4,6} have been shown to have haemoglobin AS. Their assumption that tropical splenomegaly syndrome does not occur in patients with sickle-cell trait is now disproved; and their proposition that severe malaria (which is uncommon in sickle-cell trait²) may be a necessary factor in the pathogenesis of tropical splenomegaly syndrome is no longer tenable on this evidence. Although scanty malaria parasites are sometimes present in these cases, studies of the aetiology of this syndrome would be rendered easier by the more frequent demonstration of malaria parasites, and we would suggest that future studies should include examination of blood films after injection of adrenaline before