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## Teratogenesis and Lymphocyte Stimulation

SIR,—We should like to point out an apparent correlation between the teratogenic effect and the lymphocyte-inhibiting effect of a series of agents (see Table). The lymphocyte inhibition is manifested as a blocking of antigen or phytohaemagglutinin-induced transformation in vitro.

### Agents Which Inhibit Lymphocyte Transformation and Cause Foetal Malformation

Agent	Reference to Inhibition of in vitro Lymphocyte Transformation	Reference to Role as Teratogenic Agent
Thalidomide	Coulson, Summers, Lindahl-Kiessling, Tucker, and Hellmann (unpubl)	Leck and Millar <sup>3</sup>
Steroids	Roath and Cuppari <sup>4</sup>	Walker and Fraser <sup>5</sup>
Chloroquine	Hurvitz and Hirschhorn <sup>6</sup>	Hart and Naunton <sup>7</sup>
Rubella virus	Olson, South, and Good <sup>8</sup>	Rhodes <sup>9</sup>
Measles virus	Smithwick and Berkovitch <sup>10</sup>	Hagströmer <sup>11</sup>

Two explanations may be considered to account for this correlation. The first is based on the theory that there is a mechanism of immunological abortion of deformed foetuses. The agents listed are known to inhibit lymphocytes in vitro and might reasonably be expected to act similarly in vivo; thus they could be visualized as inhibiting the maternal lymphoid system and so preventing an immunological attack on a deformed foetus. This concept was first put forward by Hellmann, Duke, and Tucker<sup>1</sup> specifically to explain the mechanism of action of thalidomide. However, if this explanation were true one would expect a general increase in a variety of foetal deformities rather than specific effects.

The second possible explanation is that these agents inhibit enzymatic or other biochemical mechanisms common to both stimulated lymphocytes and the induced cells

of certain developing limb or organ buds of the foetus. An intracellular pathway has been proposed between the antigen recognition site and the nucleus in lymphocytes, and it has been suggested that the various lymphocyte-inhibiting agents listed in the Table act by blocking different stages of the proposed biochemical sequence.<sup>2</sup>

It is not unreasonable to suggest the existence of an intracellular biochemical pathway leading from a receptor site for the inducer substance to the nucleus of a foetal cell. Certain similar enzymatic or other biochemical mechanisms may feature in the intracellular pathways of both of these two cell types which have in common the capability for rapid proliferation in response to the appropriate trigger. It is possible that the blocking phenomena postulated for the lymphocyte pathway may also occur in the pathways of susceptible foetal cells and so blight the further development of the particular anlage.

Inhibition of lymphocyte transformation in vitro may provide a useful empirical screening test to detect possible teratogenic effects of drugs.

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—We are, etc.,

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## Outbreak of Liver Fluke Infestation

SIR,—Thirty-seven cases of liver fluke (*Fasciola hepatica*) infestation have been diagnosed in the rural area of Tidenham, near Chepstow. This appears to be the largest outbreak on record in Britain. The classical picture of malaise, night sweats, urticaria, weight loss, and pain under the right costal margin was present in most cases, but several were only diagnosed following routine checking of the symptom-free relatives of those affected. There was no evidence of clinical jaundice in any of the cases to date.

The diagnosis was established by finding an eosinophilia with a raised E.S.R., abnormal liver function tests, fasciola ova in the stools, and a positive complement fixation test. Occasionally ova were found in patients with a normal blood picture.

Treatment given to the adults has been emetine hydrochloride by injection, 30 mg./day i.m. for 18 days, and oral chloroquine for children in doses of 5 mg./kg./day for three weeks. This has been well tolerated and there has been a good clinical response in most cases. The blood picture is being checked and repeated stool specimens examined at regular intervals following treatment.

Sporadic cases are still presenting at the present time and we feel this may continue