Fruhling and his co-workers¹ put forward the thesis of viral origin for morphological, virological, and epidemiological reasons. These authors studied 81 necropsies of children mostly under the age of 1 year with endocardial fibroelastosis. Virologic studies in the last 28 cases disclosed in 13 cases the presence of Coxsackie B (chiefly B3) in the myocardium. In a few cases the virus also was isolated from other viscera. In additional animal experiments and clinical observations the authors demonstrated evidence for placental transmission of Coxsackie B virus. They assume that sometimes immune tolerance acquired by the mother and/or the foetus against Coxsackie virus is responsible for the presence of the virus much later. Fruhling *et al.* conclude that endocardial fibroelastosis is a malformation caused by prenatal virus pancarditis in early pregnancy. They interpret the hypoplastic left-heart syndrome as involution by retractile sclerosis secondary to the same inflammatory process. There was an increase in the number of cases of fibroelastosis per year in Strasbourg corresponding to three epidemics of Coxsackie B infections in Eastern France between 1952 and 1961.

More recently Szanto and his colleagues² found myocarditis at necropsy in two-thirds of 60 cases of endocardial fibroelastosis. Whether or not this proves the aetiology of endocardial fibroelastosis remains an open question. But the viral theory certainly demands serious consideration.—I am, etc.,

The Children's Hospital,
Cincinnati, Ohio, U.S.A.

E. PASSARGE.

REFERENCES

- ¹ Fruhling, L., Korn, R., Lavillaureix, J., Surjus, A., and Fousseureau, S., *Ann. Anat. Path.*, 1962, 7, 227.
- ² Szanto, P. B., Lacera, D., and Novak, G., *ibid.* (in press).

Drug and Viral Jaundice

SIR,—Your leading article (11 July, p. 69) on the epidemiology of infectious hepatitis is of interest to psychiatrists who may be faced with the problem of patients on monoamine oxidase inhibitor (M.A.O.I.) drugs who develop jaundice. Present virological and biochemical tests cannot distinguish between drug jaundice and infectious hepatitis in an individual case.

Epidemiological methods may be helpful. If a psychiatric patient who is on an M.A.O.I., chlorpromazine, or any other drug develops jaundice whilst in a hospital ward, serial S.G.O.T. and S.G.P.T. levels should be estimated in the rest of the patients and in the staff of that ward. If the jaundice is infectious on average 8 to 10 non-icteric cases will develop in about 10–50 days and will show rising transaminase levels, but this will not occur with purely drug jaundice.

In general practice and in out-patients the problem is more difficult. There is a good case for making infectious hepatitis a nationally notifiable disease. In the U.S.A., where the disease is notifiable, 7-year peak incidences are seen. If these peaks also occur in the U.K., and if a peak incidence coincides with the introduction of a new M.A.O.I. drug, the drug may appear to cause the jaundice. The

periodic variation in the incidence of infectious hepatitis may be one explanation why psychiatric drugs seem to have caused more jaundice in some years than in others.

Information from 56 general practitioners whose patients were treated for depressive illness in the out-patient department at St. Thomas's revealed that in the period 1958–63 there were three cases of jaundice in patients on antidepressant drugs, 17 cases on chlorpromazine, and 33 cases not on these drugs who were diagnosed as infectious hepatitis. These figures are not very informative unless we know the total patients on these drugs and the attack rate of infectious hepatitis in the practice populations in a 5-year period.

We can make some guesses. Fifty-six practices, averaging 2,500 patients each, showed 33 cases of infectious hepatitis in five years. For every icteric case there would be about 10 non-icteric cases who have subsequent immunity, and a substantial majority of adults who remain uninfected, or are not susceptible. We may guess that only one-tenth are at risk for developing clinically icteric infectious hepatitis. Rough estimates from personal inquiries suggest that on average about 60 patients in one practice may be on M.A.O.I. drugs at some time in a 5-year period and about 200 on chlorpromazine. This gives an incidence rate of jaundice from the above figures of 1 in 425 for infectious hepatitis with jaundice, 1 in 1,120 for antidepressant drugs, and 1 in 660 for chlorpromazine, for the populations at risk and during a 5-year period.

We hope that the Committee on Safety of Drugs will soon have something more positive to offer than warnings on the use of M.A.O.I. drugs, as they are collecting national figures; but these will not mean much unless the incidence of jaundice indistinguishable from drug jaundice is known on a national scale. Perhaps the Royal College of Psychiatrists will be able to collaborate with the College of General Practitioners on this subject.

We must remember salvarsan jaundice. This disappeared when needles were autoclaved in V.D. clinics.—I am, etc.,

ERIC D. WEST.

Department of Psychological Medicine,
St. Thomas's Hospital,
London S.E.1.

Chlormethiazole

SIR,—Your "To-day's Drugs" section (18 July, p. 171) reviews the above-named drug (Heminevrin), recommended for acute alcoholic and manic states, stating that as yet no trials have been carried out in this country or the U.S.A., and that there was still in-

sufficient evidence to assess the value of the drug when given orally.

A controlled, double-blind trial comparing this drug with a placebo has just been completed at St. Bernard's Hospital. The patients concerned included approximately 100 male and female alcoholics admitted in states of varying degrees of alcoholic intoxication; they were given the drug in the form of tablets for six days. Patients were observed by doctors and the nursing staff during this period in regard to their general condition, to certain symptoms, and to possible side-effects. There was a statistically significant difference between the effects of the active drug and the placebo, as can be seen in the Table below.

Your review states that the drug should not be given in the presence of depression. No evidence could be found in our trial to support this statement. Thus, of 24 alcoholics who were *not* depressed at the time of admission, and received the placebo, 10 developed depression subsequently during the trial period, whereas the corresponding figures in the patients receiving the active tablets were two out of 21 patients; this difference is statistically probably significant ($0.05 > P > 0.01$). Out of a total of 49 alcoholics in the Heminevrin group one was still depressed on the sixth day of the trial, as against 10 out of 48 patients in the placebo group. This difference is statistically significant at the 1% level. So many alcoholics are in a state of (reactive) depression when presenting themselves for treatment (in our present series over 50%) that it seems important to us to stress the point that in our experience depression in itself does not contraindicate the administration of Heminevrin, which we found to be a valuable drug in the management of the withdrawal period in alcoholics.

We hope to be able to publish a more detailed report of the trial in the near future.—We are, etc.,

St. Bernard's Hospital,
Southall, Middlesex.

M. M. GLATT.
H. R. GEORGE.

T.A.B. Reactions

SIR,—Reference the letter from Dr. A. J. Zuckerman (11 July, p. 119), intradermal T.A.B. was introduced into the Army at the time of the Suez crisis to enable vaccinated men to proceed without delay, and not to be incapacitated by systemic reactions. It was never suggested that there would be no local reaction.

Although a day's rest is ideal after intradermal T.A.B., it is not essential. Anyone who has experienced both types of vaccination will have no hesitation in choosing intra-

Day of Treatment	Preparation	No. of Patients	Assessment of Therapy by Doctor		Comparison between Preparations χ^2 -value and Level of Significance
			Greatly Improved and Improved	Unchanged and Impaired	
1	Heminevrin	48*	24	24	7.599 0.01 > P > 0.001
	Placebo	48	11	37	
2	Heminevrin	49	33	16	15.765 P < 0.001
	Placebo	48	13	35	
3	Heminevrin	49	35	24	8.748 0.01 > P > 0.001
	Placebo	48	20	28	

* 1 form incomplete.