Because the drug is almost insoluble in water, it was poorly absorbed from injections, and the most effective method of presentation was orally at 50 mg. per kg. per day for 14 days. There were no apparent side-effects of the drug in mice or rabbits, and the oral treatment resulted in complete destruction of all tetrathyridia, cysticerci, and hydatid cysts.
implies that repeated antigen absorption occurs. If this was not so, antibodies would disappear. Circulating antigen–antibody complexes can cause thrombosis, coagulation, damage to endothelium, increased arterial permeability, and imbibition, and immunological mechanisms which can cause arterial damage other than antigen–antibody complex formation have also been described. The likely implications to coronary heart-disease (C.H.D.) are apparent.

Our findings should not be studied in isolation. Much evidence supporting an immunological hypothesis has been reviewed. Other investigations have given no evidence to suggest that patients with C.H.D. have habitually consumed more liquid milk than control patients, but even if they had it would be consistent with the hypothesis.

Our studies suggest that about one-third of adult males have circulating antibodies to dried milk but only about 14% to egg-white. We have demonstrated a relationship between both egg and milk and infarction and subsequent death. At the same time no relationships were detected with the presence of antibodies to gluten. Furthermore, the relationships with milk and egg appeared to be independent, many patients having antibodies to milk alone, or egg-white alone. This variability in the immunological pattern, both with regard to the sensitivities within individual patents and with regard to the associations between C.H.D. and different antigens, is comparable to that found in conditions of known immunological aetiology, and argues against a secondary phenomenon.

Department of Pathology, West Wales Hospital, Carmarthen.

Medical Research Council Epidemiology Unit, 4 Richmond Road, Cardiff CF2 3AS.

P. C. ELWOOD

FIBRINOLYTIC ACTIVITY AND TREATMENT OF DIABETES

Sir,—Dr Bogie and Mrs Peers (May 18, p. 1000) have completely ignored compelling evidence indicating that diabetics treated with oral hypoglycaemic agents have increased morbidity and mortality due to cardiovascular disease compared with diabetic patients treated with diet or insulin. What needs to be determined is the mechanism(s) whereby cardiovascular disease is aggravated in such diabetic patients.

Although we have not detailed all of these in our letter, the following factors were examined and correlated with fibrinolytic activity: age, sex, weight, therapy, duration of diabetes, degree of control, presence and degree of cardiovascular disease, serum lipoproteins, fibrinogen, immunoglobulins, and complement. Renal function, results of retinal fluorescein angiography, and basement-membrane thickness. Our conclusions are based on these results and correlations. Despite the small number of patients studied, definite trends emerged with regard to fibrinolytic activity.

To try and prove that certain pharmaceutical agents can do no harm, your correspondents have unfortunately taken some of our results out of context. We have shown fibrinolytic activity to be comparable to control subjects in diabetics treated by insulin and that sulphonylureas and biguanides were detrimental to fibrinolysis, particularly in females. We have pointedly included in the study diabetics treated by diet alone and potential diabetics in order to be able to assess the effect of therapy on fibrinolysis. The results emphasise the fact that euglobulin-lysis time (E.L.T.) is reduced in untreated diabetics and the pre-diabetic state and further deteriorates with treatment with oral hypoglycaemics but is improved by insulin treatment.

We hold with other workers the view that oral hypoglycaemic agents should be used as sparingly as possible and that the patients’ need for such agents should regularly be reassessed.

Without experimental and epidemiological proof, I cannot accept the criticisms of Dr Bogie and Mrs Peers.

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N. R. FARID

FATE OF $^{125}$I-LABELLED FIBRINOGEN

Sir.—We have investigated the radioactivity of a leg-vein thrombus in a patient who had received human fibrinogen labelled with iodine-125. After total hip replacement he was given 100 μCi of radioactive fibrinogen. On the morning of the first postoperative day a high calf-count was noted, and its position was marked. 60 hours after the operation he died, and at necropsy the cause of death was found to be myocardial infarction. The thrombus was removed, and autoradiography of the specimen was carried out. Counts were made of the numbers of white blood-cells in representative areas of the specimen (fig. 1), and of radioactive grains, noting their relationship to the white cells. It was found that the majority of the radioactivity was in relation to the white blood-cells in the thrombus, with relatively little in the intervening matrix.

**Fig. 1.—The thrombus, showing areas in which counts were made.**

The distal end of the thrombus is on the left.

*See figure 1.*

**Table:**

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<th>Grains not in white cells</th>
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*See figure 1.*