Indeed, in his 1961 Report the Minister states²: "Returns for the previous years were scrutinized during the year and in selected cases, where 'acceptance rates' for vaccination in infancy were apparently deteriorating, inquiries were made. A factor influencing this fall appeared to be postponement of smallpox vaccination until 1 year of age or later."

I am in favour of vaccination in the second 6 months of the child's life, but if this policy is to be abandoned I would rather accept Professor Dick's plea for epidemiological control than rely on an indifferent acceptance rate in the second year of life, with but very shaky evidence that the post-vaccinal mortality rate would be any lower.—I am, etc.,

County Hall,
Truro, Cornwall.

E. R. HARGREAVES.

REFERENCES

- ¹ Ministry of Health, *Memorandum on Vaccination Against Smallpox* (memo 312/Med 1946—revised 1956 and 1962). H.M.S.O., London.
- ² *Report of the Ministry of Health for the Year 1961. Part II: On the State of the Public Health, 1962*, p. 56, Cmd. 1856. H.M.S.O., London.

Insulin Ineffectiveness

SIR,—On reading your report (November 10, p. 1250) of the Cambridge meeting of the Medical and Scientific Section of the British Diabetic Association (September 28–29) I recalled some work which may bear upon the views of Dr. C. N. Hales given at that meeting.

In the *Biochemical Journal* of 1924 or 1925 I published some simple observations on normal human subjects who had been kept without any food or drink for some 36–40 hours, at which time it had been found that a considerable ketosis was established, and, I suggest now, almost certainly a high blood non-esterified fatty acid level was present. In these conditions the blood sugar was usually a low normal, the respiratory quotient (uncorrected for urinary nitrogen) was normal, and the urine contained all the usual acetone bodies with the ratio of β -hydroxybutyric acid to aceto-acetic acid about 1.5 to 2.5 or so. On administering 50 g. of glucose in these conditions it was easy to show (control data having been obtained in normal conditions) (a) an abnormal blood-sugar curve with glycosuria; (b) much diminished rise in R.Q. (normal rise to 1.0 after 12 or so hours' starvation); (c) disappearance of ketone bodies in about an hour.

In those days it seemed reasonable to speak of some lag in insulin secretion and, certainly, delay in the anti-ketogenic action of the sugar and respiratory metabolic response. But it may be more reasonable to suppose now that the ketone body production and excretion were rather the expression of anti-insulin action.

In later work it could be shown that these effects could all be accentuated by ingestion of 100 g. molten butter in similar conditions. Further, the disappearance of the ketone bodies from the urine was accompanied by a fall of blood sugar well below the initial value, which seemed to be attributable to an abnormally high stimulation of the islet cells.

In other experiments (with Dr. (now Professor) R. W. B. Ellis) at a later date in similar conditions of starvation it was possible to negative the apparent inactivity of endogenous insulin by the ingestion of 300 ml. of 5% ethanol, hypoglycaemic levels of blood sugar being rapidly reached as well as fall of R.Q. to the theoretical level for ethanol, and a large rise in blood lactic acid (all experiments at complete rest). This

latter was almost certainly due to the secretion of adrenaline secondary to the hypoglycaemia.

It may be of some interest to repeat these experiments with the more erudite methods now available, and especially the apparent anti-glucagon effect of alcohol.—I am, etc.,

Istituti Clinici di Perfezionamento, M. W. GOLDBLATT.
University of Milan.

REFERENCE

- ¹ Goldblatt, M. W., *Biochem. J.*, 1925, 19, 948.

Aetiology of Schizophrenia

SIR,—Dr. Clifford Allen (December 1, p. 1475) rather overlooks the point of my letter (November 10, p. 1259), which is that we must look beyond individual glands and their hormones to the gland responsible for hormonal balance. All that he says of the adrenal is true, but the balance between it and other glands of internal secretion is the function of the pineal. The neurological aspects associated with metabolic disorders clamour for co-ordination, and this means co-ordination with disorders in other systems.

When Sir Macfarlane Burnet speaks of the dependence of immunity on the thymus (September 29, p. 807) he also points to something deeper: "the development of the immunological competence of the body is part of the process of morphological and functional differentiation in the embryo."

Richter¹ says that "the brain develops first because it is required early as a controlling centre for the neuro-endocrine functions of the body. The medulla and hypothalamus are the first regions to mature in the embryo." This is hardly exact enough for our purpose—what part of the medulla and hypothalamus appear first? This is likely to be the channel through which genetically stored information is translated into specific protein structure.

No one suggests that either the adrenal or the thymus controls hormonal balance, but this function is claimed for the pineal.²

Are we sure that the pulsating point which appears in the chick within 24 hours of fertilization is the origin of the vascular system only or does it represent nerve as well?—I am, etc.,

London W.14.

GRIFFITH EVANS.

REFERENCES

- ¹ Richter, D., *Schizophrenia*, 1957. Pergamon Press, London.
- ² Hubble, D., *Brit. med. J.*, 1961, 1, 523.

Anticoagulant Treatment

SIR,—Dr. L. Poller's answer (November 24, p. 1402) to Professor J. McMichael's comment (October 13, p. 992) would appear to contain contradictory statements, some of which I think need serious consideration.

Prothrombin Time.—Dr. Poller criticizes the omission of the number of days patients were below the 10% in Hilden's trial.¹ Yet he admits he keeps his patients "a little higher" than 10%. How much above 10% and how regularly this is attained he does not mention. We are all only too familiar with the sudden changes in the prothrombin times in patients receiving coumarin drugs, hence the necessity for frequent laboratory control.

Haemostasis and Thrombosis.—Dr. Poller states: "The aim, in fact, is to give adequate protection against further thrombosis without interfering with the normal process of haemostasis." This simple sentence has wide implications. Surely thrombosis is not caused by abnormal coagulability only. Factors other than blood