is ample evidence from contemporary accounts that wheat has been consumed regularly in Ireland since early historic times,¹ although until the middle of the 19th century it was probably eaten regularly only by the more affluent. Specific finds of wheat are few; two that we have been helped to trace are those made by Hartnett³ in a bronze age grave in County Wicklow and by Walshe⁴ in a burial cairn in County Wicklow. Dr. Moynahan's remark that "bread wheats were not cultivated in the West of Ireland" is probably incorrect, but it does seem likely that wheat was not the staple cereal of the majority of the population.

With regard to dermatitis herpetiformis, we agree with Dr. Moynahan that this condition is rarely associated with coeliac disease in our experience, which amounts to one definite case among 40 adults and none among 190 children. However, the number of adult cases of coeliac disease studied is not large enough for our findings to be significant.

We agree with Drs. P. Asquith and W. T. Cooke (26 May, p. 484) that a study of HLA antigens in coeliac and normal populations would be worthwhile, and this is in progress. With regard to the suggestion that the combination of the foreign proteins of cow's milk and wheat may have a synergistic deleterious effect, we can only say that we have not yet encountered a child with coeliac disease in whom we could demonstrate milk protein allergy. Apart from the early weeks of treatment, when occasional mild lactose intolerance has occurred, all our patients have made satisfactory progress on cow's milk.

The suggestion of Drs. Asquith and Cooke that wheat cereals should be withheld until after 6 months of age from HLA8-antigen-positive siblings of coeliacs has merit. It would probably be justifiable to carry out a controlled trial of early and late feeding of wheat to such infants; however, apart from being dependent on the goodwill and co-operation of parents, it would need to extend over many years to have validity. We have been alarmed for many years by the early and heavy exposure of infants to wheat cereals and have endeavoured both privately and publicly to discourage this. An earlier onset of coeliac disease is certainly a result of early wheat feeding, and of 190 children with the disease, 11 presented before 6 months, 55 before 12 months, and 96 under 2 years. In addition to the encouragement of breast feeding, we believe that all infants should be maintained on milk alone for several months, if possible, that rice should be the principal cereal used when hunger demands it, and that wheat should not be introduced until about six months of age.

We wish to thank the following for providing information on cereals in Ireland: Professor M. Duignan, Dr. M. Mitchell, and Dr. E. Rynne, of University College, Galway, and Dr. J. Raftery of the National Museum of Ireland.

—We are, etc.,

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New Urinary Steroid in Hypertension

SIR,—We would like to report that during routine analysis of aldosterone in urine a new steroid was detected and thereafter isolated in patients with hypertension. Because this steroid occurs in measurable amounts only in patients with hypertension it has been given the name "hypersterone." The compound is obviously not identical with any steroid which has previously been suggested to be involved in hypertensive disease in man or animals.¹ The complete structure of hypersterone is not yet known, but we wish to present some characteristic data (see table).

A small amount of hypersterone was oxidized with periodic acid and submitted to combined gas chromatographic-mass spectrometric analysis and the oxidized compound was found to have a molecular weight of 360. This could correspond, for example, to an underivatized compound with a structure of aldosterone but with two additional hydroxyl groups. But there are also some other possible structures. The base peak was at m/e 345 and the fragments in the higher mass region were typical of a lactone derivative. However, in the lower mass region the spectrum was uncharacteristic, perhaps owing to the very small amount available for analysis or to thermal decomposition (very long retention time) or both. Because of the very labile nature of the compound a mass spectrum of the non-oxidized steroid has not yet been obtained. The infrared spectra of hypersterone and the oxidized derivative showed a stronger hydroxyl band than those which were obtained for 5 β -dihydroaldosterone- γ -etiollactone and 18-hydroxycorticosterone- γ -etiollactone. The steroid showed a strong absorption of ultraviolet light, suggesting a Δ^4 -3-oxo- configuration.

The oxidized form of hypersterone could be determined quantitatively by gas chromatography, the sensitivity of detection being 2.5 μ g per 24-hour urine specimen depending on the amount of interfering substances. With this method it could be demonstrated that hypersterone cannot be detected in normal urine, that it is not formed during the isolation procedure, and that it is not formed from aldosterone added to urine. The amounts of hypersterone excreted in patients with essential hypertension are in the same range as normal values for aldosterone in urine. In patients with hyperaldosteronism the excretion of hypersterone is normally somewhat increased, but usually the amount

of hypersterone in urine seems to be unrelated to that of aldosterone. Because of the very small amounts of hypersterone present in urine and the lability of the underivatized compound the characterization of the new steroid is extremely difficult, and we are therefore reporting our results at this early stage before its exact structure has been definitely established. Because the compound can now be at least semiquantitatively determined in urine it should be possible to obtain some information as to its role in hypertensive disease.—We are, etc.,

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- ¹ Melby, J. C., Dale, S. L., Grekin, R. J., Gaunt, R., and Wilson, T. E., *Recent Progress in Hormone Research*, 1972, 28, 287.

Glucagon and Growth Hormone

SIR,—In your leading article (27 January, p. 188) you conclude that stimulation with glucagon alone is an effective test for the ability to secrete growth hormone but, since it "takes longer to perform" and "is rather less reliable" than insulin-induced hypoglycaemia, glucagon stimulation should be regarded as a second-line test except in certain special situations. However, as you also note, with the insulin test serious hypoglycaemia may occur (we have seen this even in patients with a good growth hormone response) and medical supervision is required. These factors may induce a physician to perform glucagon stimulation first as a matter of safety and convenience. Perhaps more important, the reliability of glucagon stimulation can be improved when the patient is pretreated with propranolol two hours before the test is performed.¹ With this manoeuvre the physician on occasion may see a response of serum growth hormone when glucagon alone¹ or insulin hypoglycaemia² is ineffective.—We are, etc.,

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- ¹ Mitchell, M. L., Suvunrunsi, P., and Sawin, C., *T., Journal of Clinical Endocrinology and Metabolism*, 1971, 32, 470.
- ² Tiwary, C. M., Rosenbloom, A. L., and Julius, R. L., *New England Journal of Medicine* 1973, 288, 218.

Immunosuppression by Halothane

SIR,—Recently, increasing attention has been paid to the risk of anaesthetic contamination (leading article, 24 March, p. 693) and

Characteristic of Hypersterone

	Thin-layer Chromatography		Paper Chromatography: Benzene: Cyclohexane: Methanol: Water, 9:1:6:4 v/v (Rf values)	Gas Chromatography (1% OV-22) (Retention times relative to cholestane (= 1.0))
	CHCl ₃ : Dioxane 96:4 v/v (Rf values)	CHCl ₃ : Acetone, 1:1 v/v (Rf values)		
Hypersterone	0.16	0.41	0.28	
Aldosterone	0.16	0.57	0.45	
18-Hydroxydeoxycorticosterone	0.19	0.62		8.6
Aldosterone- γ -lactone ..	0.60			8.1
Oxidized hypersterone ..	0.47			

evidence has been presented that anaesthetics, especially halothane, may interfere with immune responses.¹⁻³ The evidence is based on studies of antibody formation in vivo¹ and mitogen-induced lymphocyte transformation in cultures with added halothane,² though normal responses have been reported with lymphocytes of anaesthetists exposed to chronic inhalation of various anaesthetics.⁴ Anaesthetists appear to have a higher death rate from malignancies of the lymphoid and reticuloendothelial tissues than many other doctors.⁵ There are also reports of an increased incidence of stillbirth, abortion, and fetal malformation among women anaesthetists.^{6,8} Anaesthetic-induced immunosuppression or cytotoxicity may have a role in all these phenomena.

We have studied the effect of halothane anaesthesia on the function of B and T lymphocytes in chickens. The parameters used include the humoral antibody formation in vivo and the mitogen-induced transformation of lymphocytes from birds after halothane anaesthesia. The mitogens used, phytohaemagglutinin (PHA) and concanavalin A (Con A) are known to activate T lymphocytes selectively in the chicken.^{9,10}

Twenty 4-week-old White Leghorn chickens were injected intraperitoneally with 2×10^8 sheep red blood cells (S.R.B.C.) and 2×10^7 killed *Brucella abortus* organisms on day 0. A second similar stimulation was given on day 7. Ten of these chickens were anaesthetized on days 4, 5, 6, 11, 12, and 13 for one hour on each day and the other 10 served as a control group. Halothane was given in a concentration of 1% v/v in a mixture of 30% oxygen and 70% nitrogen at a flow rate of 2.0 l/min. Bleedings for antibody titration¹¹ were carried out on days 7 and 14. For the studies on the mitogenic response, half of the chickens in both groups were killed by exsanguination from the heart on day 14. Spleen lymphocytes isolated separately from each chicken were cultured for 72 hours in humidified air and 5% CO₂ at a density of 10^6 cells/ml/tube in medium RPMI 1640 with the addition of penicillin 100 IU/ml and streptomycin 100 µg/ml. Special attention was paid to washing the cells free from the autologous plasma. Fresh normal chicken plasma (10%) was used to supplement the culture medium. PHA M (Difco) was used in a concentration of 50 µl/ml/culture and Con A in a concentration of 50 µg/ml/culture. All cultures were made in triplicate. To determine the mitogenic response 0.5 µCi of 5-iododeoxyuridine-¹²⁵I (specific activity 0.51-1 mCi/mg) was added to each culture for the final 18 hours incubation.¹² A stimulation index for each chicken was obtained by dividing the mean incorporation (counts/min) of 5-iododeoxyuridine-¹²⁵I in the experimental cultures with the mean incorporation in the control cultures.

The results, log₂ titres for antibody formation and stimulation indices for the mitogenic response, are given in the table as mean values $\pm$ S.E.M.

Halothane had no clear effect on humoral antibody response to a thymus-dependent antigen (S.R.B.C.) or a thymus-independent antigen (*Brucella*). A significant depression in the lymphocyte response to Con A was caused by halothane. PHA-induced uptake of iododeoxyuridine was also reduced, but the reduction was statistically less significant.

Our results indicate that halothane anaesthesia is able to suppress the function of T lymphocytes in the chicken. The effect was clearly detectable on the day following the final anaesthesia. Studies on human patients now in progress seem to support these results. The present findings do not reveal any effect on B cell function. However, it remains to be seen whether different timing of anaesthesia and antigenic stimulation will reveal an effect on the antibody response to thymus-dependent antigens.—We are, etc.,

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Psychiatric Nurse as Therapist

SIR,—I read the article by Dr. I. M. Marks and others (21 July, p. 156) with interest. The article does, I feel, open up some important matters.

There is little doubt that non-medically trained workers, be they nurses, clinical psychologists, physiotherapists, or Uncle Tom Cobbleigh, can be trained in treatment procedures and, given a modicum of intelligence, can carry these out effectively. Whether they should do so is another matter. The same argument has been applied to osteopaths, who no one will deny are often good at manipulating bones and joints, and in other countries people without full medical training have been employed as medical auxiliaries and taken over much of the family doctors' role—namely, that of treating the patients (as in Russia and China). Does the medical profession really want this—or indeed do we consider it ethical?

Surely the answer lies in pressing for adequate medical staff to deal with our proper role—namely, that of treating the patients under our care—rather than unloading treatment procedures on to people with relatively little background knowledge, paid at a lower rate of pay, and who have, as it were, sworn no Hippocratic oath.

This is the thin end of a very dangerous wedge from which the Government will be able to turn round and say, "You do not need more medical staff—this work can be done just as well without all your

expensive and long training." Just as well? Then why are we spending 10 years or so to qualify as experts in a field?—I am, etc.,

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Nerve Conduction Velocity and Hypertension

SIR,—Viskoper *et al.*¹ have claimed that a reduction in motor nerve fibre conduction velocity can be directly correlated with the level of the diastolic blood pressure in hypertensive patients. This association was particularly noticeable in patients with a diastolic pressure above 120 mm Hg. They suggested that nerve fibre conduction velocity studies would provide an objective measurable index of the severity of hypertension. In view of the importance of this suggestion we undertook further studies of a group of hypertensive patients and of a similar number of matched controls.

Fifty patients with hypertension and 50 normal controls were investigated in pairs which were matched for age, sex, weight, height, and occupation. There were 17 females and 33 males in each group. For the purpose of this study a patient was regarded as being hypertensive if the diastolic pressure was 100 mm Hg or greater. Thirty-five patients were being treated with methyldopa and the rest with guanethidine. Diabetes and impairment of renal function were excluded by blood urea and two-hour postprandial blood sugar estimations. Patients with absent pulses in the lower limbs and those with any neurological deficit were also excluded from further study. The fundoscopic findings were noted and the blood pressure was taken on three occasions in both the standing and lying positions, the mean reading then being calculated. To ensure against the effect of lowered temperature on slowing the nerve conduction the skin temperature of each limb was recorded with an Ellab thermocouple.

To study sensory conduction rates metal ring electrodes were placed around the fingers and the sensory potentials recorded at the wrist and elbow using metal disc electrodes 0.5 cm in diameter. Motor velocities were studied with similar recording electrodes placed over the appropriate muscle. The nerve trunks were supra-maximally stimulated at the wrist and elbow for the medial and ulnar nerves and at the ankle and knee for the lateral popliteal and posterior tibial nerves. The stimulus was provided by an American Electronics Laboratories stimulator using a fixed voltage of 250 V and a variable stimulus duration of between 0.01 and 0.03 msec.

The mean age of the patients studied was 54.35 (range 21 to 72) years, the mean diastolic pressure was 122.7 (range 100 to 180) mm Hg, and the mean systolic pressure was 183.3 (range 130 to 260) mm Hg. The conduction velocities for the corresponding nerves are given in the table and show no significant differences in the two groups studied. There was no correlation between either the systolic or diastolic pressure and the grade of hypertension. There was, however, a statistically significant negative correlation of nerve conduction velocities with the age of the patient; this feature was particularly well marked with respect to the

Antigen or Mitogen			Anaesthetized	Controls	P Value
S.R.B.C.	—1st stimulation		2.10 $\pm$ 0.75	1.78 $\pm$ 0.33	>0.10
	—2nd stimulation		3.30 $\pm$ 0.51	3.88 $\pm$ 0.71	>0.10
Brucella	—1st stimulation		7.50 $\pm$ 1.44	6.44 $\pm$ 1.09	>0.10
	—2nd stimulation		17.20 $\pm$ 2.27	14.33 $\pm$ 2.04	>0.10
PHA			7.45 $\pm$ 2.63	14.40 $\pm$ 2.63	<0.10
	Con A		2.71 $\pm$ 1.46	16.10 $\pm$ 3.47	<0.01