rather than a deterrent to research. Some failure in physiological advance fifty and more years ago was due to the passion for simplifying processes which we know now to be of the most amazing complexity. Renal excretion and carbohydrate metabolism are two of innumerable examples. And now the clinical failure of endocrine treatment implies that until the problem becomes more "complicated" for the physiologist we shall make no further progress from our present static position. "Static" is the word. For some years we have achieved no real advance in this branch of endocrinology.

Prof. E. A. Doisy, of St. Louis University, has written personally to point out that it was the late Dr. Edgar Allen who concluded that cornification of the vagina is due to a hormone found in the Graafian follicle of the ovary. The important work of Stockard and Papanicolaou undoubtedly influenced the pioneer work on the ovarian hormones which was done by Dr. Allen and Prof. Doisy.

While discussing the general difficulties of hormone therapy I dwell upon the paramount importance of the nervous factor in the control of the hormone system in man, and thus I agree strongly with Mr. Everard Williams when he draws attention (Feb. 8, p. 234) to the overriding influence of emotional disturbances acting through the nervous system in producing symptomatic effects in the various end-organs. It is almost certain that emotion such as the fear and fright of the air raids acted both through the pituitary and directly on the end-organs through their nervous supply. In addition to Mr. Williams's examples of menstrual troubles I remember the remarkable effect of the near-by bursting bomb in starting the immediate onset of premature labour.

Some correspondents have discussed details of treatment. Dr. Donald Fraser (p. 234) makes a plea for progesterone in metropathia. I quoted the work of Dr. Scowen in support of this treatment and also success following the use of testosterone. It is nevertheless true that many cases suffer relapses, which will compel us ultimately to treat these patients by x rays or hysterectomy. Dr. Raymond Greene's remarkable case of cure of eunuchism (March 8, p. 311), as proved by a subsequent pregnancy, is of great interest, and an encouragement to treat similar and less well established cases on the lines he describes.

But perhaps the best summing-up of the difficulties of endocrine therapy is given by Dr. A. P. Cawadias (March 22, p. 390) when he describes the disorder not as a separate disease of one or more of the six chief glands but as a pathological "complex" based upon irregular function of the whole psychosomatic system, including the endocrine glands, and all in relation to environmental factors. Through all your correspondents' letters can be traced agreement, with varying emphasis, on some fundamental points. The idea of cell receptors in the end-organs is by no means new, but it has not yet been exploited by researches which might enable us to expand our resources in treatment.

Finally, the patient apparently suffering from an endocrine disorder such as metropathia, amenorrhoea, and many others must be regarded not as one suffering from a terminal symptom but as a victim of genetic liability and environmental stress. The second of these will include such varied factors as nutrition, human relationships, conditions of work and play—indeed, all the manifold impacts inherent in our modern and troubled civilization.—I am, etc.,

London, W.1.

ALECK BOURNE.

d-Tubocurarine in Electric Convulsion Therapy

SIR,—I have read with interest the articles on the use of d-tubocurarine in electric convulsion therapy, and in view of the fact that Drs. J. A. Hobson and Frederick Prescott (April 5, p. 448) state that they intend to adopt this method "as a routine" I should like to make some comment on this. Whereas one cannot fail to be impressed by the use of this method in a few of the cases mentioned, I consider that it is high time that some of the nonsense written about the dangers of E.C.T. should be contradicted by those of us who use this form of therapy on a large scale. In this hospital alone an average of 400 convulsions are administered each week, and in a period of six years well over 100,000 treatments have been carried out without major accident. It should be noted that some of the patients treated were over 75 years of age.

The occurrence of fractures and dislocations is, in my opinion, to be attributed to faulty technique rather than to the method itself, and I consider that the use of restraint by nurses is to be strongly deprecated, as it most definitely introduces a factor which may be fraught with danger. Figure 1 in Dr. Hobson's article (p. 447) illustrates this point. It should be quite unnecessary for anyone to actively restrain a patient during an electrically induced convulsion unless, of course, in the very rare instance where a patient may be in danger of falling out of bed.

The first case described by Drs. A. Gillis and D. D. Webster (p. 451) is of great interest, but it is unfortunate that the authors do not state the exact time which had elapsed between the receipt of injury and the commencement of E.C.T. I can see no reason why E.C.T. should have been contraindicated in the second case in the absence of vertebral injury, as severe back pain is not a very uncommon symptom but one which usually disappears during the course of treatment.

In making these criticisms I do not wish to detract in any way from the value of d-tubocurarine in a few cases, but, as the authors admit, it calls for skilled technique, and as the method itself is not without danger it should surely be used with the greatest discrimination.—I am, etc.,

St. James Hospital, Portsmouth.

W. LIDDELL MILLIGAN.

Phaeochromocytoma

SIR,—Are not the symptoms of phaeochromocytoma of the adrenal medulla, described in two interesting articles in the *Journal* of April 26 (pp. 563 and 564), suggestive of those of the so-called "anxiety crisis" writ large? As a victim of these crises, the full nature of which can be understood only by those who undergo them, I have the most profound sympathy with the young woman who "was 'nervous' and anxious to demonstrate that her disease was not functional."

No reasonable person would be anxious to demonstrate that his symptoms had their origin in so grave a condition as a suprarenal tumour, but neither does a reasonable person find it satisfying to be told that his prostrating attacks are purely functional, due to some underlying worry of which he has never been conscious. His own rational brain gives him all sorts of reasoned assurances as his bout develops, but his instinctive feelings are filled with the most positive certainty of his imminent exitus and are suffused with fear, not the fear which he may have felt when exposed to real and obvious danger such as heavy air-raids, but the horrible paralysing fear which arises in the worst type of nightmare and which strips from him the last vestige of his self-respect.

My own attacks have beset me for more than a dozen years. During the intervals between them it is easy to tell myself that if their origin was serious I should not have continued to survive, yet each bad one finds me as vulnerable as any of its forerunners.

As I grow older in practice I find myself more and more convinced that much illness which we now glibly dub "nervous" and hand over to the psychiatrists will be found to have a purely physical basis, which may well have a quite trivial importance when compared with its effect on the psyche. If the day ever comes when necropsy by a skilled pathologist is obligatory for everyone, it will probably bring an enormous acceleration in medical learning, and it is at least possible that our present unsatisfactory fumbling with the human mind will be diverted into more useful channels.

In view of the personal nature of this letter may I have your leave to sign myself

X.

The Adrenal Medulla and Hyperpiesis

SIR,—In regard to the annotation on the adrenal medulla and hyperpiesis (April 26, p. 572), we have repeatedly tried to discover whether the adrenaline content in the blood is raised in hypertony, but without success. But the following experiments which O. Weiss and I performed many years ago are significant.

Adrenaline was injected into a cat and arterial pressure taken by kymograph. There was a very pronounced rise of pressure but lasting only a moment. After the arterial pressure in this cat had returned to normal, blood was taken from it and injected in another cat. The latter animal produced the same

adrenaline reaction as the first. Thus it has been established that, although the adrenaline content of the blood in the first cat was still abnormally high, after an initial rise of pressure it did not further affect the blood pressure level. But after severing the nerves from the blood vessels of the ear, the adrenaline effect lasted for hours. It is quite clear that the vasoconstrictors and vasodilators counteract any factor which tends to produce abnormal pressure. The level of pressure is conditioned by the requirements of the body and not by abnormal substances in the blood such as adrenaline or renin, which tend to raise the pressure. This is the reason why it is so very difficult either to raise or to lower arterial pressure for any length of time.—I am, etc.,

Liverpool.

I. HARRIS.

The Revolution in Anaesthesia

SIR,—Dr. John Halton (April 19, p. 543) has painted a fanciful picture of the benefits conferred by curare on the inefficient anaesthetist. No one will gainsay that curare is, in certain circumstances, of great help to surgeons and anaesthetists, but the patient is the most important person in the operating theatre and the benefits conferred on the patient are more questionable. When anaesthetized by ordinary methods he has at least a reasonable expectation of recovering consciousness and of a convalescence free from complications. In a series of over 50 gastrectomies relaxed with curare which have come under my observation the incidence of collapse of the lung base, confirmed by x-ray, is 20%, and this high figure has been confirmed by other observers. Bleeding with curare is often considerable, and I have been asked by a surgical colleague to refrain from using it for this reason alone. Several deaths have been reported from regurgitation of stomach contents into the lungs. Relaxation *can* be carried a little too far.

The introduction of a new drug is always accompanied by a pendulum-like swing of enthusiasm followed by a swing in the reverse direction, after which the true position of the drug in medicine is determined. I suggest that the time has come to cry halt and reflect on the lethal possibilities of this very potent drug. Dr. Halton has spoken of a revolution in anaesthesia, but history contains many examples of revolutions which have not proved beneficial.—I am, etc.,

London, W.1.

MASSEY DAWKINS.

SIR,—Dr. John Halton's masterly exposition on the use and abuse of modern anaesthetic technique (April 19, p. 543) will be greeted with acclamation by every anaesthetist who understands the physiology of respiration and is thoroughly conversant with the action of the drugs and agents which he uses. My only comment is that he made some omissions in his true and vivid picture; he made no mention of the final "shot" of "tubarine" to enable the peritoneum to be closed and to guarantee the production of "the twilight of that half-world known as 'recovering from the anaesthetic,'" which justifies matrons of nursing homes pressing for the abolition of curare (*Journal*, Jan. 18, p. 111; Feb. 8, p. 234).

He rightly stresses, but no one could overstress, the need for maintaining adequate tidal exchange and the avoidance of anoxia; he omits to mention the danger of an insidious build-up of carbon dioxide responsible for the production of so-called "cyclo shock" (*Anesthesiology*, 1947, 8, 15). Surely when the respiratory centre is depressed by opiates, barbiturates, and what you will in the way of anaesthetic agents and has its peripheral response stultified by intercostal paralysis, possibly combined with diaphragmatic paralysis or paresis, the final physiological insult is to expose it to excess of carbon dioxide by cutting down the absorber or adding from a cylinder.

No absorber is too efficient; the danger of losing the "Bohr effect" and producing the "acardia" spoken of by Yandell Henderson is a relic of the past and could only be produced now by the most energetic hyperventilators, who could, no doubt, also squash your alveolar capillaries flat and kill you with a chest full of oxygen. Equally nefarious is the practice of relying primarily in times of crisis on alleged antidotes such as "prostigmin," picrotoxin, "coramine," etc., rather than maintaining normal or near normal oxygen-carbon-dioxide balance.

As one of the first to suggest that the advent of curare cast doubts on the theories of Crile (*Proc. roy. Soc. Med.*, 1946, 39,

410) may I join with Dr. Halton in his hope that the rational use of curare will make it a milestone in anaesthesia rather than that by abuse it should become a tombstone.—I am, etc.,

Aylesbury.

H. W. LOFTUS DALE.

B.C.G. Vaccination by International Exchange

SIR,—The Scandinavian countries, with their many years' wealth of B.C.G. experience, are now exporting not only advice but also personnel. Dr. Konrad Birkhaug, who was in charge of the B.C.G. laboratory in Bergen before and during the war, has gone to the U.S.A., where the State Health Department has borrowed his services. In Denmark the Danish Red Cross has a scheme for B.C.G. teams, each consisting of a doctor, two nurses, and a secretary, to go to Warsaw, Budapest, and Rendsburg to vaccinate their populations, children first. What about a loan of Scandinavian experts to England? Assuming that B.C.G. vaccination is not an all-British watertight compartment, I would suggest that the Ministry of Health or the National Association for the Prevention of Tuberculosis sends a "come-over-and-help-us" call to their opposite numbers in one of the Scandinavian countries, say Sweden.—I am, etc.,

Sunnfjord, Norway.

CLAUDE LILLINGSTON.

Acid Drinks and Sulphonamide Therapy

SIR,—The danger of renal complications during sulphonamide therapy and the importance of giving extra fluids to patients receiving these drugs are universally recognized, but the necessity for avoiding acid fluids and maintaining alkalinity of the urine have not been given the same prominence in the literature.

The M.R.C. War Memo. No. 10 (Medical Use of Sulphonamides) states that 30–80% of the total dosage can be recovered from the urine either as the sulphonamide itself or as its acetyl derivative. The following table, also taken from the Memorandum, shows the solubilities of some of the sulphonamides and of their acetyl derivatives in both acid and alkaline urine, and from this I have worked out the daily output of urine necessary to hold 3 g. of each of the sulphonamides in solution—that is, 50% of an average daily dose.

	Solubility in Urine (mg./100 ml.)		Volume of Urine Needed to Dissolve 3 g.	
	Acid	Alkaline	Acid,	Alkaline
Sulphathiazole ..	102	859	3,000 ml.	350 ml.
Acetyl sulphathiazole ..	10	265	30,000 "	1,200 "
Sulphadiazine ..	17	187	17,500 "	1,500 "
Acetyl sulphadiazine ..	50	229	6,000 "	1,300 "
Sulphamezathine ..	130	335	2,300 "	900 "
Acetyl sulphamezathine ..	86	216	3,500 "	1,400 "
Sulphamerazine ..	38	209	8,000 "	1,400 "
Acetyl sulphamerazine ..	78	227	3,800 "	1,300 "

This table shows that with an average daily output of 1,500 ml. the urine *must* be alkaline, otherwise part of the sulphonamide excreted will be thrown out of solution.

In most hospitals extra fluids are supplied in the form of imperial drink, lemonade, or orangeade. These substances are highly acid, as the following rough experiment shows. Samples were taken from the patients' jugs in the wards and neutralized with sodium bicarbonate. The quantity of bicarbonate required to neutralize 1 oz. (28 ml.) of each fluid was as follows:

Orangeade ..	15 gr. (1 g.) of bicarbonate
Lemonade ..	15 gr. "
Imperial drink ..	11 gr. (0.72 g.) "

Thus with a daily intake of only 3 pints (1.7 l.) of the fluids in question the amount of bicarbonate required to neutralize it works out at 900 gr. (60 g.) for lemonade and orangeade and 660 gr. (44 g.) for imperial drink—this before alkalization of the patient can begin. The usual routine practice of giving a dose of alkali with the tablets can only serve to neutralize a small part of the fluid with which they are washed down, and the forcing of fruit drinks increases the acidity of the urine.

It is therefore apparent that if renal complications are to be avoided when giving sulphonamides, all fruit drinks must be strictly forbidden, and the extra fluids required must be given as water, milk, tea, etc.—I am, etc.,

London, E.7.

PETRONELLA POTTER.