ture, $+4^{\circ}\text{C.}$, activity persisted for three days. An attempt was also made to determine the size of the agent responsible. The washings could contain substances of quite different sizes. It could not be said that the lower limit of size was fixed; the upper limit was fixed, but not the lower. The most common incubation period was two to three days, but a few colds developed after five or six days, which was the limit of the period of observation; therefore the present observation period was not ideal, though the majority of colds would probably exhibit themselves within that time. It did not appear to signify whether the subject had had a cold during the previous month or had had no cold for six months. "The only thing we are certain about is that we have got some agent in the common cold filtrates which will induce colds in a percentage of the people; all the other results are tentative."

Questions

Dr. PARRISH said they were not yet at "the end of the beginning" of this investigation. The suggestion that women were much more susceptible to colds than men might be followed up; also an investigation might be undertaken into the determining factors in colds—an infection plus, probably, some depression of resistance due to climate, under-nourishment, or some other factor.

Asked whether any complement-fixation tests had been tried, Dr. ANDREWES said that this had been kept in mind, but it was suspected that they would have to get the virus present and growing in greater concentration before that could be successful.

Did the particle size exclude the possibility of a filter-passing bacterium? Dr. FULTON replied that the filtrates had been cultivated under conditions which would be likely to grow these agents, and no growth had been observed at all.

Dr. ANDREWES, in reply to a further question, said that no intensive studies had been made on secondary infection because most of the laboratory work had been done at the National Institute for Medical Research, Hampstead, and the clinical work at Salisbury, but now that there was a bacteriologist on the spot it would be possible to do more along that line. No attempt had been made to induce secondary infections.

A questioner wished to know whether the filtrates had been stained and smeared and small bodies seen. There was a possibility of the use of fluorescent dyes in this connexion. Dr. FULTON said that that had not been tried. The electron microscope or ultra-microscope, said Dr. ANDREWES, had not been applied to the filtrates because the use of these instruments required considerable concentration of the material.

Dr. CHALMERS, in reply to a question as to whether one of the pair of volunteers who had a cold could pass it on to his partner in the flat, said that if a volunteer resisted the artificial cold given to him, and his partner took it, the former would resist also cross-infection. On the other hand, people who developed colds during the period of quarantine frequently conveyed such colds to their partners. He explained that each pair was given the same material.

In reply to Dr. J. A. H. Brincker, Dr. CHALMERS said that it was always recorded whether the volunteer had undergone tonsil or adenoid operations, but no correlation had yet been worked out. In further answer Dr. Chalmers said that only in two cases had a volunteer developed tonsillitis, and in one case bronchitis, which lasted for about a week. As for precautions against infection conveyed by those who handled food for the volunteers, he said that any member of the small domestic staff who developed a cold reported it at once. The handling of food was very carefully supervised.

Dr. SUTHERLAND said that he understood that during these experiments only one person had had to go to bed with the cold, and he only for a short time, which rather suggested that the type of cold was not comparable with that experienced by the ordinary patient. Dr. CHALMERS replied that the people were always asked the date of their previous cold, and how many colds they customarily had in a year, and whether they had had to stop work and go to bed, and the answer to the last question was invariably "No."

Dr. ANDREWES said that it was possible that the cold encountered in the outside world was a mixture of a virus and a bacterial infection, while in the unit a pure virus infection was given. The people had less chance of picking up secondary

organisms from one companion in the unit than from mixing with a number of people. The volunteers were given a post-card and asked to describe what happened after their return to ordinary life. Frequently those who while in the unit had developed a cold, which had cleared up, developed a worse cold a day or two after resuming contact with the outside world.

Dr. ASHWORTH UNDERWOOD asked whether consideration had been given to the extension of the time of observation to seventeen days or three weeks, especially in view of the small number of samples. Dr. ANDREWES said that the time would have to be a number of weeks for convenience of administration. If one or two odd colds were found turning up when they should not, he did not think it would upset the experiment. They would have to tighten up their regulations and extend the period of observation.

Dr. CHALMERS, in reply to a question as to whether particulars of menstruation were taken in the case of the women volunteers in view of the frequency with which the nasal mucosa became congested just before or during the menstrual period, said that such particulars were recorded, but so far there had been no opportunity to work them out.

Dr. ANDREWES, who was asked whether it would be possible during the incubation period to get some information as to the flora of the nose, said that this was possible but hardly worth while, because there was such an enormous literature on bacteriology in relation to the nose and very little had come out of it.

Asked about work in America, Dr. ANDREWES said that two teams were working there on lines similar to their own; one of them was using as volunteers prisoners in a reformatory.

Dr. W. BUTLER asked whether those concerned were satisfied that the whole clinical field of the common cold was embraced. If the experiment were reversed, and the virus excluded, would there not be a certain number who would get a common cold, though perhaps distinguishable in some respects from the colds which were virus-produced? Dr. ANDREWES replied that he was constantly talking to people who spoke of pneumococcal and bacterial colds. Some colds might be caused by such organisms, but he would like to have an opportunity of studying such colds in order to learn whether it was possible to reproduce them with cultures. It would be interesting to take one of these pneumococcal colds and use a filter and see whether the cold could be reproduced with the filtrate.

Correspondence

Endocrines in Gynaecology

SIR,—I shall be glad of an opportunity of replying to the interesting and instructive letters from your correspondents during the past few weeks. The emphasis has been laid chiefly on the principle of receptor substances, or the specific sensitivity of the various tissues to the action of individual hormones, having been recognized for many years. This is well illustrated by the letters of Dr. G. I. M. Swyer, Dr. S. L. Simpson, Dr. Raymond Greene, and others. I did not wish to suggest that the receptor mechanism was a new concept. It is the basis of much of the maintenance of physiological processes of the body, including the intricacies of immunology.

In my address published in the *Journal* of Jan. 18 (p. 79) I said, "I have *seldom* seen it [the idea of receptors] mentioned, and *never* considered, in therapeutics." The italics should have been used in the original publication. While agreeing with your correspondents that the conception of receptors is not new, yet I still feel that, compared with the enormous amount of therapeutic energy devoted to the activating hormones, relatively little or no consideration has been given to laboratory or clinical research on the responsiveness of the organs we wish to treat. The important point is not so much the recognition of the principle of tissue receptivity but how far the idea has provided a basis for research into its tangible reality. So far very little.

I confess that I cannot understand Dr. Swyer's appeal (Feb. 1, p. 98) not to "complicate" the issue by adding the notion of receptor substances. All biological processes are complicated, but this should be, and has already been, a stimulus

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