

definitely stated that the therapeutic value of thyroidal, suprarenal and pituitary hormones is undoubted. In the case of other hormones, the evidence so far brought forward fails to carry conviction as to their value in the treatment of disease.

Professor E. H. STARLING, F.R.S.: Although I am unable to contribute anything to the discussion in relation to the actual therapeutic value of hormones, I may call the attention of the meeting to certain factors which must determine the action and limit the employment of these substances. By the term "hormone" I understand any substance normally produced in the cells of some part of the body, and carried by the blood-stream to distant parts, which it affects for the good of the organism as a whole. The hormones are thus the chemical means of correlation of the activities of different parts of the body. Their action may be either the increase or diminution of function, or the alteration of nutrition or rate of growth. In dealing with the therapeutic use of these substances, it is convenient to divide the hormonal actions of the body into two classes, which I may term the acute and the chronic.

A typical example of the first class is the well-known mechanism for secretion of pancreatic juice. The entry of acid chyme into the duodenum sets free in the cells of the mucous membrane a chemical substance, *secretin*, which is absorbed by the blood-vessels of the gut, and carried in the circulation to the pancreas, which it excites to secretory activity. As other examples of the same class I may cite the chemical regulation of the activity of the respiratory centre in accordance with the activity of the muscles, and the production of adrenalin under conditions of stress. Although carbonic acid, and probably adrenalin, are being constantly produced in the body, their amount may be largely increased under certain conditions. Thus the production of adrenalin may be regarded as a mechanism which is brought into play in times of stress, when the animal has to undertake active movements for offence or defence. Under these circumstances the increased muscular activity is accompanied by increased blood-pressure, increased blood-flow through the heart, and a maximal increase of the functional capacity of this organ. At the same time adrenalin, passing to the liver, causes a mobilization of the glycogen store of this organ, so that the blood is flooded with the food which can be most readily utilized by the muscles to supply the extra energy which they require. In all these cases it is essential that the reaction shall take place immediately, and

shall disappear as soon as the exciting cause is removed. The hormones of these reactions must, therefore, be capable of rapid disappearance from the body, either, as in the case of secretin or adrenalin, by oxidation and destruction, or, as in the case of carbonic acid, by elimination. The ready destructibility of secretin and adrenalin limits the employment of these substances in a substitution therapy. Administration of them by the mouth is practically useless. Though we can evoke with certainty the physiological action of these substances by introduction into the blood-stream, it is difficult to grade their action or to continue the injection at repeated intervals, as must be the case under normal circumstances. The only use of these substances is therefore as drugs. Adrenalin, for instance, is used for its local effects on the blood-vessels, and is practically useless to replace the functions of absent suprarenal medulla. It might be worth while, perhaps, to attempt to employ this substance in cases of failing heart. It is the most efficient cardiac stimulant that we know, and may increase the available energy of the heart contractions by two or three times. It would be necessary, however, to be very careful not to give too large a dose, since, although in the laboratory it is easy to dissociate the action on the heart from the action on the blood-vessels, when injected into the intact animal the stimulation of the heart's action and the increased tone of this organ would be accompanied by vascular constriction and increased resistance to the blood-stream. It is doubtful whether any good results can be expected to follow the use of secretin. Though it is an infallible excitant of pancreatic secretion, it is important to remember that this strongly alkaline juice normally enters the duodenum immediately after a certain amount of acid chyme, and the secretion of pancreatic juice only lasts while the contents of the intestine are still acid, and therefore giving rise to the secretin. Continued injection of secretin into a healthy animal causes after a time severe symptoms of collapse, which is apparently due to the changes in the intestinal mucous membrane produced by the entry and non-neutralization of the strongly alkaline pancreatic juice.

The second, or chronic, class of hormonal reactions offers the best chances for therapeutic interference, and includes the only definite instance we possess of successful substitution therapy. Examples of this class are the action of thyroid on metabolism, nutrition, and the functions of the central nervous system, the action of the anterior lobe of the pituitary body on the growth of bone and connective tissues, the action of the sexual organs on the development of the secondary

sexual characteristics, and the action of the growing foetus, or more probably the corpus luteum, on the growth of the mammary glands. Probably in this class, too, we should include the hypothetical action of the pancreas in regulating carbohydrate metabolism. In all these cases the chemical product of some organ passes into the blood-stream, and exercises a slow chronic effect on some distant organ or organs. There seems no reason in this case to predicate an excessive vulnerability of the hormone. It would certainly be advantageous if the hormone resisted the destructive actions of the body juices or of oxidation, since in this way the amount required would be economized. A priori, one would expect to obtain therapeutic results by administration of the hormone-producing organs in cases of their deficiency. This has, however, only been attained with certainty in one case—namely, the administration of the thyroid gland. When the hormone is administered by the mouth, if it is to have therapeutic results, two conditions must be met: (1) That there is a storage of the active substance in the gland or organ; (2) that the substance is not destroyed in the alimentary canal. These two conditions are satisfied in the case of the thyroid, perhaps because at one time in our evolution the thyroid was a gland opening into the anterior part of the alimentary canal. All our efforts, however, to reproduce the action of the ovaries, or testes, or of the corpora lutea, or of the anterior lobe of the pituitary, by administration through the alimentary canal or by the injection of extract subcutaneously, have so far resulted in failure or in results which are not definite.

I do not think, however, that there is any need for despondency on this account. We have by no means yet exhausted the various possibilities of extracting the active principles from these organs or of their administration. Experiment on man in these chronic conditions of insufficiency of organs may give us even more valuable information than experiments on animals, and although when working with man one is open to more fallacies, owing to the effects of suggestion or of spontaneous variations in the course of the disease, and to the fact that it is more difficult to control the effects which are actually produced by our treatment, I believe that we should continue to have faith in the future of the use of hormones as remedial agents, if only our faith is coupled with extreme scepticism as to the interpretation of results in any individual case.