

Influence of Internal Secretions on Sex Characters.

AT the Edinburgh meeting of the British Medical Association Dr. F. A. E. Crew opened an interesting discussion in the Section of Physiology and Bio-chemistry on the "Influence of Internal Secretions on Sex Characters." The importance of the organs of the endocrine system in regulating and controlling sex characteristics has been recognised for the past thirty years or so, but it is only recently that we have come to have a clear understanding of the rôle of the component members of this glandular system and the balanced action which exists between them.

Crew classified the sex dimorphic characters as (1) primary genotypic, (2) secondary genotypic (including the primary gonadic), and (3) secondary gonadic. There is no difficulty in demonstrating the dependence of the secondary gonadic characters on the physiological activity of the gonad. It is now established that the gonad influences the growth of the long bones, the development of the muscular and nervous systems, and plays an important part in general metabolism. The gonad also exerts a powerful influence over the structure and functions which form the secondary sex-dimorphic characters.

The function of the gonads in regulating growth and development may be studied by the usual experimental procedure, namely, (1) removal of the gonad, (2) implantation of the gonad, and (3) administration of preparations of the gland.

The effect and results of removal of the gonad will vary according to the development of the body and the physiological condition at the time that the operation is carried out. These conditions may be summarised as (1) pre-pubertal, and (2) post-pubertal. The first result of castration before the age of puberty is the hinderance to further development of the reproductive system. Castration on one side produced no effect, the retention of a single testis being sufficient to maintain normal function. In the human, castration at the same stage is known to prevent the growth of hair on the face, the development of the thorax, pelvis, and to preserve the voice of childhood. Further, metabolism is disturbed, the deposition of fat is marked, accumulating under the breasts and in gluteal regions.

The effect of castration on the development of the long bones has been well studied, and the evidence is now clear that the absence of the active gonad leads to an abnormal growth of bony tissues. Poucet in 1897 found that the bones and skeleton of the castrated rabbit were larger than those of the control. Geddes has also shown that the process of ossification is prolonged, and that the long bones are unduly long. These findings do not necessarily imply that the processes of nutrition and growth are opposed to reproduction. After castration, there is not only absence of the internal secretion from the gland, but there is further a loss of balance in the endocrine system during a period of rapid development of the body structure.

Castration after onset of puberty is followed by disappearance of the beard and redistribution of the body fat and hair. It is clear that castration never induces any condition resembling the female type; the condition is infantile and not female. Extirpation of both ovaries in the human after puberty is followed by cessation of menstruation. Atrophy of the genitalia is also well marked. The operation may also lead to emotional disturbances, headache, fainting, and intestinal disturbances.

Probably the most interesting results which have been obtained are those on gonad implantation. There is no difficulty in demonstrating that an animal which has been castrated at an early age will develop normally if a testis is successfully implanted. It is also possible to restore the female characters by implanting ovarian tissue after ovariectomy. The degree of restoration possible will depend on (1) the age of the animal at the time of castration or ovariectomy, (2) the condition of the tissues at the time of implantation, and (3) the interval between the two operations. It will be seen that restoration is not possible if pathological changes have taken place in the tissues after removal of the gonad. Further, secondary sex characters can be re-established, as has been shown by Nussbaum. Castration of the male frog inhibits the development of the sexual pad on the first digit of each fore-limb, but after introduction of pieces of testis into the dorsal lymph sac, the swelling on the thumb and hypertrophy of the muscles of the fore-limb took place as in the normal animal.

It is possible to feminise a male by castration and subsequent implantation of ovarian tissue; the mammary glands are stimulated into activity while the male sex organs diminish in size. The converse is also possible, namely, to masculinise a female by ovariectomy and subsequent implantation of testes. These experiments certainly suggest that the sex hormones are specific.

Much attention has recently been devoted to implantation of testicular grafts from anthropoids into the human host. The success of these operations will depend not only on the technique of the operation but also on the ability of the host to provide the nutrition necessary for the continued life of the implant. The effect of the graft on the body will depend on the condition of the tissues at the time of operation. It is possible to supply and supplement the gonadic hormone and to re-establish the balance between the components of the endocrine system. It is not possible, however, by increase of sex hormone to re-establish a physiological condition if pathological changes have taken place.

In Crew's study of about one hundred and fifty hermaphrodite pigs, he has found only testicular tissue present, though usually intra-abdominally. The sex characters, however, fell into a graded series from a normal male up to an almost female type of animal. A certain minimum threshold of secretion exists which is essential before

differentiation of the sex characters can occur. A condition of ovo-testes is frequently found amongst pigs either on one or both sides. The ovary is always cephalic and on the left side, showing that differentiation must take place from right to left and from cephalic to caudal poles. If the ovary was able to initiate the development, the animal would tend to develop female characters during its early days, the degree of maleness appearing later in life depending upon the extent to which the secretion of the slower differentiating testes was able to counteract the ovarian secretion. This would explain the tendency to maleness exhibited in the human by girls as they grow older. Macmillan's recent discovery of a chemical test for sex should prove useful in the solution of these problems.

Evidence that the ovarian extract as at present used is responsible for the slow ante-pubertal growth of the female sex-organs is not conclusive. The supposed hypertrophy is sudden, occurring within forty-eight hours, and it only produces the changes associated with œstrus. Injection into the new-born rat is without effect, while injection into the animal three weeks old produces œstral changes. Further, ovarian extract does not produce the psychical changes normally associated with the œstrus cycle. Parkes, from his investigations, concluded that the ovarian extract at present in use probably contains the responsible factor for the production of œstral changes, and that another substance is responsible for the pubertal and psychical changes.

Evidence was put forward by Glynn in the discussion for the supposed relationship of the suprarenal cortex to secondary sex characters. This evidence is summarised under the four headings :

- (1) Embryological—Cortex of the suprarenal gland and the ovary and testis are derived from the same source.
- (2) Physiological—Enlargement of the suprarenal glands during pregnancy.
- (3) Pathological—In hermaphroditism there is bilateral enlargement of the suprarenals in the female.
- (4) Clinical—Hypernephroma or tumour of the suprarenal associated with pseudo-hermaphroditism.

In females suffering from adrenal hypernephroma, there is often atrophy of the mammary glands, ovary, and uterus, with cessation of menstruation, alteration in metabolism, mainly fat metabolism, and a general tendency to increase the male primary and secondary sexual characters at the expense of the female.

Tumour formation in the adrenals leads to a profound disturbance of normal metabolic conditions, and it is possible that while the endocrine glands may exert no direct influence upon the secondary sex characters, yet they may have a pronounced indirect effect by bringing about abnormal conditions of metabolism. Crew has demonstrated that cockerels, fed on thyroid from the time of hatching, developed female colour and type of feathering. Further, gonadectomy and gonad implantation do not lead to any apparent change in the metabolism of the animal, and, after operation, the endocrine glands appeared to be normal. It appears probable, then, that the secondary sex characters are under control of the gonad secretion, but with abnormal conditions of metabolism, a new threshold for the differentiation of the tissues is established.

The British Association at Leeds.

THE general opinion on all hands seems to be that the meeting of the British Association in Leeds has been a great success; certainly from the point of view of the citizens of Leeds, they will be remembered as a fitting celebration of the arrival of summer. After the most dismal August in the recorded meteorology of the area, the meetings have heralded a change to sunny weather and blue skies, with that bracing keenness in the air that prevents lassitude. Whilst the excursions have thus been made doubly enjoyable, the weather has also been appropriate for the strenuous follower of sectional activities.

Comparatively few seats were empty when the president's address was delivered in the Majestic Picture Theatre. This meeting was noteworthy for the announcement by the president of the Council's support of a movement to purchase Charles Darwin's home and estate at Downe, so that it may be retained in perpetuity for the nation. The enthusiastic applause of the vast audience showed their cordial sympathy with the proposal. Sir Oliver Lodge, who, in the absence of the retiring president, H.R.H. The Prince of Wales, was in the chair and introduced Sir Arthur Keith, alluded in felicitous terms, as also later did the president him-

self, to the generous anonymous gift of £100,000 to the appeal fund of the University of Leeds—a sum to be devoted to the erection of the new library. The announcement of this gift in the press on the same day as the inaugural meeting naturally added to the general enthusiasm with which the proceedings were initiated, and gave added force to the vice-chancellor's hope, expressed in his opening remarks of welcome at the inaugural meeting, that on a future occasion the University may be then able to accommodate all the activities of the Association within its walls. It has since been announced that the University owes this gift to Sir Edward Brotherton, a well-known chemical manufacturer with works at Leeds and Liverpool, to whom the University was already indebted for a gift of £20,000 for bacteriological research. Sir Arthur Keith's reference to the possibility of acquiring Darwin's house at Downe has borne fruit, for an amount sufficient to purchase and maintain the house has been offered by Mr. G. Buckston Browne, whose name will be associated with this gift to the nation.

Both the University and the civic authorities have thrown themselves whole-heartedly into the work of entertaining their guests; the dinners