One emergency case was admitted to Mayday Hospital with the baby's head already delivered by forceps but with the shoulders impacted. The baby was dead on admission.

Among the seventy-eight stillbirths which occurred in the two hospitals there were twenty-six premature fetuses, taking the weight of 5 lb. 8 oz. or less as the standard of prematurity. In every case except one abnormalities, foetal or maternal, or both, were found. The table of individual weights and maternal and/or foetal abnormalities (Table III) makes interesting reading.

The infant deaths which occurred among the 3,086 live births numbered forty-three: Mayday Hospital, twenty-seven; St. Mary's Hospital, eleven; domiciliary, five. The infant death rate for the Service is therefore 13.9 per 1,000 live births.

Among the thirty-eight neo-natal deaths which occurred in the two hospitals there were twenty-six premature infants. As in the case of the stillbirths, maternal and/or foetal abnormalities were present in many instances. The birth weights and associated conditions are set out in Table IV.

Summary and Comments

A series is recorded of 3,144 consecutive deliveries without a maternal death due to pregnancy. The stillbirth rate for the series is 28.9 per 1,000 total births. The infant death rate for the series is 13.9 per 1,000 live births.

A description of the Croydon County Borough Obstetric Service is given, with reference to personnel, hospital accommodation, clinics, and routine ante-natal supervision.

Tables are given showing the major abnormalities treated, and the maternal and/or foetal abnormalities associated with the stillbirths and infant deaths.

It will be seen from the tables that the lower segment operation has been the operation of choice for Caesarean section (66 per cent.). Reference is also made to the use of spinal anaesthesia in fifty-nine out of the seventy-four Caesarean sections (80 per cent.), and to its particular suitability for the lower segment operation.

The number of booked patients admitted to hospital with toxæmia, including all cases of hypertension and/or albuminuria, was 363—that is, 12 per cent. of the total of 3,015 booked patients. No cases of eclampsia occurred among these patients. In the four emergency cases of eclampsia three babies were stillborn and one died.

Reference has been made to the care taken to ensure the fullest co-operation between the Service and the practitioners, which must be one of the greatest essentials in bringing the maternal mortality figures to the irreducible minimum. It must be agreed that such co-operation has been attained to a very gratifying degree in the period covered by the series reported, the successful outcome of which is due in no small measure to the foresight of the practitioners who sent their cases to us in time to institute proper treatment. This is true, not only of the greater proportion of emergencies but also of many of the booked patients, who were sent to the clinics on account of abnormalities which their doctors thought should be treated in hospital, and whose supervision we gladly undertook.

In view of the great interest which the scientific world has shown in the plight of the refugees from Germany and Central Europe, so many of whom are the wives or children of scientific workers, attention may be drawn to a pamphlet published by the Welfare Department of the Central Office for Refugees, Bloomsbury House, Bloomsbury Street, London, W.C.1. The pamphlet is entitled "Entertaining our Refugee Guests," and reveals a great need for personal help for many of the victims of persecution.

ON SOME SEASONAL CHANGES IN THE PITUITARY GLAND OF THE EEL

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In January, 1937, the Zoological Society of London published in its *Proceedings* a note on some seasonal changes in the pituitary gland of the eel (*Anguilla vulgaris*); these observations were put on record because they appeared to be of some biological significance in relation to the sexual changes that take place in the period just previous to the migration of the eel. This communication records the results of monthly observations of the pituitary body of the eel over a period of three years, and includes the findings of three series of specimens taken from fish caught between May and October: during the later two months more than one specimen was examined. The conclusions reached from these prolonged observations confirmed the results of the first series—namely, that there was a great increase in size of both anterior and posterior lobes in the last two months before the migration commenced, and that there was a remarkable activity of the cells of the posterior lobe and a pronounced change in the type of cell in the anterior lobe. Through the kindness of the late Professor Woollard, and latterly of Dr. Amoroso, I was allowed to avail myself of the services of his expert technician, Mr. Hancock, and at Lowestoft I was also helped (through the courtesy of the Ministry of Agriculture and Fisheries) in the preparation of material for study by Mr. Clarke, the chief laboratory assistant.

For descriptive purposes I propose to use the terms employed in Sharpey-Schafer's *Histology* (1920), and to speak of the pars anterior, and the pars posterior, which in fish consists of pars intermedia and pars nervosa. In that textbook there is a good illustration of a sagittal section of the base of the brain and pituitary body of the cat. If we omit the pars tuberalis, this section is very similar to a section of the eel's pituitary: the pars intermedia is less vascular than the pars anterior, but more so than the pars nervosa, around which it extends in the cat; this is still more so in the eel, in which the pars nervosa dips down into pockets of a large glandular pars intermedia. This consists of a number of acini the peripheral part of which is composed of four layers, more or less, of cubical cells; and, separated from them by a homogeneous substance, there is a central layer of ependyma cells surrounding the neuroglia of the pars nervosa. In the active state a very different picture is seen. The peripheral cells are almost entirely replaced by a yellow-staining granular secretion. Many empty ovoid cells are present, and frequently the granular secretion is replaced by masses of refractile brown colloid. Surrounding each alveolus is a meshwork of fine capillaries, and within them are small masses of brown colloid together with a few blood corpuscles. The blood vessels supplying this meshwork come from small peripheral arteries which can be traced inwards to form an anastomosis into which the capillaries enter. The blood from the acini is collected by small veins that group themselves into three areas from which a large vessel proceeds. These three vessels unite to form a single trunk opposite the infundibulum, and this passes caudally to enter the lobus infundibuli.

The evidence as to the direction of the circulation in this system is as follows. We have observed in the course of the branching nerve fibres entering the pockets of the pars intermedia small globules of colloid that are homogeneous and refractile, and we have also noted vessels running parallel to them from which these globules have presumably escaped. Pöpa and Fielding (1933) have described similar colloid globules in the hypophysis-portal vessels of the mammalian pituitary, and they state that "the direction in which the blood flows may be gauged by their colloid accompaniment. As colloid (whatever it

may be) is formed in the pituitary and not in the brain, its association with vessels may be taken as indicating that the direction of the flow is certainly hypophysio-hypothalamic. Sometimes the colloid globules occur in the lumen of the vessels and sometimes in the intervascular tissue of the neural portion of the stalk." It is therefore important to note that in our sections the globules occur within the perivascular sheath at the point of junction of the capillaries described above and in the lumen of the large central vessel which runs backwards to the base of the lobus infundibuli. Our very definite observation, in a large number of sections, of the colloid material within the enclosing capillaries of the acini seems of some importance, as De Beer speaks of the probability that products of the pituitary other than those of the anterior lobe may be blood-borne.

The Anterior Lobe

Compared with the posterior lobe the anterior is very vascular. It consists of groups and columns of epithelial cells with dilated sinusoids. The cells are either chromophil or chromophobe: the former are either acidophil or basophil. The acidophil cells are granular and spherical, and stain pink with eosin, while the basophil cells stain with haematoxylin and are larger than the eosin-staining cells, though their granules are smaller. The sinusoids vary very much in size, and in that part of the anterior lobe which faces the infundibulum there is a wide depression occupied by what appears to be stringy secretion, and deep sinusoidal pits dip down into the epithelial portion of the gland. Anterior to the infundibulum the neural stalk descends from the anterior margin of its wall. In the midst of the secretion above mentioned there are numerous refractile globules similar to those described above, and in two consecutive sections we counted twenty of varying sizes, while between the hilus of the gland and the entrance to the infundibular cavity we have been fortunate enough to cut in a longitudinal direction a small vessel containing a row of globules like a string of beads, and around it were many scattered globules lying free. This vessel communicates with those of the pia mater clothing the ventral margin of the lobus infundibuli, and from these vessels ascending branches supply the tissues of the neural stalk. Refractile globules are found in the stalk, free in the infundibulum and in the surrounding tissues. Having attempted to give a short account of the anatomy of the pituitary gland in the eel, it will be necessary to review some established facts relating to the general physiology of the organ. Professor Hogben (1927) refers to the part played by the secretion of the pituitary gland in determining the normal rhythm of colour change in amphibia. He points out that the pituitary is a specifically vertebrate structure from which no active substance has as yet been isolated in a pure form. Extracts of the pituitary of mammals, birds, reptiles, and fishes (teleostean and elasmobranch) have a powerful excitatory effect on the mammalian uterus. Extracts of the pituitary of all classes of Amniota, Amphibia, and Teleostei exert a pressure-diuretic action on the mammal. In fact, the posterior lobe of the mammal, while a storehouse of probably several substances of very great activity, has not yet been conclusively proved to have any functional significance. There is, on the other hand, the clearest evidence for regarding pituitary secretion as the main factor in co-ordinating the pigmentary responses of amphibia to the changing conditions of their environment.

In writing on the anterior pituitary in the last edition of Evans's *Recent Advances in Physiology*, Newton (1936) states:

"In spite of only three types of cell being present in the anterior pituitary gland—basophil, eosinophil, and chromophobe—there seems no escape from the evidence which pointed to it as the birthplace of a phenomenal number of hormones. These act on the general bodily growth, carbohydrate metabolism, the gonads, the thyroid, etc." In con-

nexion with our present subject it is obvious that its effect on the mammary gland need not be considered. "The hormones are known so far only by their effects, but in the case of many of them extracts have been obtained which exhibit one type of activity to the exclusion of the others and which nullify the corresponding effect of hypophysectomy."

The growth hormone and the gonadotrophic hormone interest us most in our discussion of the appearances of the anterior pituitary of the eel in the spring, summer, and autumn months; but the effect of the thyroid may also be discussed. It may be stated now, in reference to the seasonal changes, that in the early months—May, June, July, and August—the gland is much smaller than in September and October, when there is a great increase in size. There is a slight variation in different years as to the time at which migration starts, and there is a corresponding variation in the histological picture. In one year migration continued until November, and in another only till September. We have found that, as above described, the posterior lobe becomes distended with secretion, and that brown colloid masses are found in the alveoli and also in the capillaries. The changes in the anterior lobe are equally striking. It becomes more vascular, the sinusoids are distended, and there is a very striking increase in the eosinophil cells. Before reviewing the bearing of the above facts on the seasonal changes I will give a short account of the changes in external characteristics of the eel during the months preceding the journey to its Atlantic breeding-place.

Changes in the Eel

We are all familiar with the life history of the eel and the epoch-making researches of J. Schmidt, but it may be wise to recall the changes that occur in the make-up of the eel from the time it ceases to be an elver until the time it disappears into the depths of the Atlantic.

In the first year of its freshwater existence, as it gradually assumes the characteristics of the "yellow eel," there is a diminution in size, just as there is when the leptocephalus becomes an elver. After a number of years spent in fresh water—rivers, estuaries, or lagoons—the dorsal surface changes its colour from greenish yellow to nearly black, the sides come to look like a freshly coined penny with metallic reflections, while the belly becomes silver-white and the eyes appear to increase greatly in size. It is now known as the "silver eel," and, having put on its wedding garment, it is ready for migration; the sexual organs begin to develop, but they do not attain full development until the fish has entered the sea. Other changes are noted. To quote Tate Regan (1911): "The snout is less flattened, the body is more rounded, plumper, and firmer to the touch; the pectoral fins are longer, more pointed, and blackish in colour." Internally, the digestive tract is shrunken, as they cease to feed; the fish loses its muddy flavour, and its firm white flesh makes it more fit for the table.

From the physiologist's point of view three changes have taken place: (i) colour changes due to expansion and contraction of melanophores and xanthophores; (ii) eye changes, which may perhaps be regarded as an exophthalmic condition due to a thyrotrophic stimulation; and (iii) development of the sexual organs due to a gonadotrophic stimulation. No doubt there are other profound metabolic changes, which I shall refer to later.

The Problem of Migration

The significance of the above observations and their bearing on the more recent views on the problem of migration can now be discussed. Professor F. H. A. Marshall, in his preface to Walter Heape's *Migration, Emigration, and Nomadism* (1931), mentions that Heape suggested that the immediate stimulus for a breeding migration came from a periodic increase of the internal secretion elaborated by the gonads. Mr. John Hammond in 1925 explained his own observations on growth and reproduction by assuming that the anterior pituitary

hormone is responsible at different times for stimulating both these processes, its physiological effect being transferred from one function to the other, in the process of individual life. Heape was very definite in his view that the impulse to migrate is induced by changes in the functional activity of certain organs included in the reproductive system, "the details of which must be left in the hands of the student of the physiology of the reproductive system." Reading Heape's work carefully, however, leaves us with the impression that he recognized the switching off of the endocrines from a growth-producing function to a gonadotrophic function; but the work of Parkes and others, which has thrown so much light on the gonadotrophic function of the anterior lobe of the pituitary, had not then been published. Referring to the eel Heape says: "Comparison with a great variety of other animals, and especially fishes, induces me to hold a strong opinion that the development of the reproductive glands is due to a switching off of energy which was previously engaged in the metabolic processes which result in growth."

Our earliest knowledge of the functions of the pituitary gland were connected with growth in certain pathological conditions; and it is now known that in mammals the anterior lobe secretes a growth hormone, which produces, if in excess, gigantism in children, and in adults acromegaly. Extracts of the pars distalis cause growth to take place, when it has ceased as the result of the removal of the pituitary. It is interesting to note the condition somewhat analogous to gigantism in those eels that have been prevented from making the gametic migration. To quote Roule (1933):

"Not all eels set out on this hazardous journey. Some at the period of puberty cannot, from the nature of the locality, leave the lake or pool in which they are too closely imprisoned. Like the sterile trout of the deep lakes, and for the same reason, their ovaries—for these eels are usually females—change and atrophy; rendered sterile, the eels grow fat and larger. Eunuch eels of this sort have been kept in captivity for twenty or thirty years."

We are continuing our monthly observations on the eel during the present season, and hope to have the opportunity of obtaining a "eunuch eel" in order to note the differences, if any, in the histology of the anterior lobe. We have already noted the colour changes, and suggested that they may be the result of the activity of the posterior lobe; we submit that the eye changes may be due to the action of an anterior pituitary hormone on the thyroid gland. Tate Regan has described how, during thunder, eels become restless and active. It is only on certain dark nights that eels run. In Norfolk it is the custom for eel-catchers to keep a few silver eels in a perforated trunk in the water; and they do not put down their eel-sets unless these eels become restless, which is a signal that the other eels are running and that the night is favourable for a good catch. We have described elsewhere the presence of two lateral ganglia which pass to the pituitary in fish from the ventrolateral margins of the lobus infundibuli; these are connected, by descending fibres from the nucleus rotundus, with the co-ordinating centre of sensory impressions in the dorsal part of the lobi inferiores. We can thus visualize a means by which the pituitary gland may be controlled by external conditions.

The above observations must be looked upon as a preliminary note on a biological experiment which can be conducted under perfectly natural conditions and could be very widely extended. The significance of the refractile globules described requires further research, and there seems to be every possibility that we shall be able to confirm the presence of a hypophysis-portal circulation in fish, such as has been described by Popa and Fielding in higher vertebrates.

Conclusions

In an attempt to gauge the biological significance of this investigation we must briefly refer to the present state of our knowledge of the function of the pituitary. Since

Pierre Marie noted in the 'eighties that acromegaly was associated with tumours of this gland much clinical evidence has accumulated. In man and the higher vertebrates abnormalities of the pituitary may be the cause of unusual growth and sexual development. Extracts of the posterior lobe of the pituitary are well known and are in constant clinical use, but we are not certain as to the exact functional significance of the posterior pituitary in the normal body. Professor Hogben and others have proved that colour changes in amphibia are under the control of the posterior lobe, which contains a "specific stimulant which will induce contracted melanophores to undergo maximum expansion." In fact, there is clear evidence that the pituitary may regulate colour changes in vertebrates. It is probable, therefore, that the pigimentary changes in the eel that occur previous to the onset of migration are produced by the secretion of the posterior lobe, which, as we have seen, is increased and modified at this period. It is known that a growth hormone is present in the anterior pituitary, because pituitary-less tadpoles, when reared, show arrested development of the thyroid and fail to undergo metamorphosis: pituitary grafting accelerates growth and metamorphosis in normal tadpoles. These and other facts point to the conclusion that the anterior lobe controls the activity of the thyroid, and we can infer that it is also associated with growth control. The enlargement of the eel's anterior pituitary and the other changes that occur at approaching puberty may produce excessive thyroid activity, and this hyperthyroidism may be the cause of the prominence of the eyes and apparent enlargement noted in the silver eel.

Before the gonads develop in the eel, or at any rate in the very early stages of their development, there is a great increase in size of the anterior lobe and also in the number of acidophil cells. The gonadotrophic hormone of the anterior pituitary is well known, because hypophysectomy causes gonads to lose weight and the accessory organs to atrophy. Implantation of anterior pituitary substance and injection of suitable extracts before puberty, cause precocious sexual maturity, and since both ovary and testis responded to pituitary hormones before puberty it is assumed that the hypophysis has not yet begun to secrete a sufficient amount to produce its effect. The anterior pituitary is increased in size in nearly all species during pregnancy; so that we feel there is enough evidence to associate the above-mentioned conditions with the beginning of gonad development in the eel. If for any physical conditions an eel that is ready to migrate is restrained from going on its journey, it may grow and become of an immense size, and live in captivity for many years; this suggests the analogous gigantism of a eunuch, and it may be that the gonadotrophic hormone is replaced by the growth hormone, which, we have seen, is also present in the anterior lobe in these conditions.

In conclusion I may add that it is shown that in the teleostean thalamus a lateral ganglion on each side of the infundibulum is connected with the pituitary gland and also with the centre for co-ordinating the impulses from the organs of special sense; it is therefore quite easy to explain how the effect of dark nights and thundery weather can be the final urge that starts the migration.

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