PITUITARY EXTRACT.

WITH SPECIAL REFERENCE TO ITS USE IN MIDWIFERY.

I.

INTRODUCTION.

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INTRODUCTION.

MARIE, in 1886, first drew attention to the condition known as Acromegaly, in which he showed that anomalies of growth were associated with pituitary tumour or hypertrophy. Before that time the Pituitary Body was thought to be a gland structure, which elaborated a secretion for the lubrication of the nasal cavities, or merely a vestigal relic certainly of very little importance to the higher animals. In the days when medicine was practised by the priests, the pituitary gland was supposed to be the envelope of the soul. Lying as it does in a most protected spot, encased in the bony sella tunica and anterior angle of the optic chiasma, research of the functions of the body was rendered difficult, but since that time considerable interest and speculation have been aroused with reference to this gland, and its effect on the metabolism of the individual.

It is only within recent years that, stimulated by the work of BROWN-SEQUARD on the internal secretion, and by the brilliant results obtained in experimental investigations

of the suprarenal and thyroid glands, scientific observers have given attention to the pituitary body; it is now looked upon as the growth centre, or the proportion regulator, of the individual. Many papers on the subject have been published; the bibliography is extensive. In the present thesis the writer proposes to give an account of the present state of our knowledge, and to give a resume of recent work on the Therapeutics of Pituitary Extract, with special reference to its value in Labour.

II.

HISTORICAL OUTLINE.

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The earliest writers believed the function of the pituitary gland was to discharge mucus-pituita into the nostrils. Later writers considered it the seat of the soul glands, thyroid, thymus, etc., but not till later years was it considered a gland of importance to life.

In 1778, SOEMMERING described the anatomy of the gland, when he showed its development from the epithelial pouch of the roof of the buccopharyngeal cavity, and in 1830, RATHE confirmed and elaborated these findings.

No work so far had been done on the histology of the gland till, 1885, FLEISH studied cell types of the anterior lobe, and described two varieties; chromophilic, acid or basic staining cells with abundant protoplasm, and chromophobic with no protoplasm or granules. SCHONEMANN, 1892, noted chromophils surrounding the central lumen, which contained colloid, which he considered similar to the colloid secreted by the thyroid and the active principle of the gland. OLIVER and SCHAFER first injected intravenously extract of the whole gland into an individual and found it produced a rise in blood pressure, which was of long

duration, due to the contraction of the peripheral arterioles also an increase of the force of the heart beat, which persisted after the destruction of the central nervous system. This was followed by the experiments of MARIE and BOX, who injected the extract of pituitary glands from an ox into a healthy individual and found the temperature was raised, the pulse more frequent and increased in force, the amount of urine increased and rich in urea and phosphates. These findings HOWELL confirmed two years later. In 1907, PARISOT experimented with similar results, but found no qualitative change in the urinary secretion, and DELILLE injected anterior lobe with no effect, but produced with the total extract a rise in blood pressure, slowing of the pulse, increased flow of urine, increased appetite, though he found that less effect was produced after several injections and the dose had to be augmented, and that results varied with the susceptibility of individuals and the same results were obtained with extract of the posterior lobe, but the effects were much more marked than with the total gland.

HALLION and CARRION, 1907, showed marked diuresis was due to stimulation of the renal epithelium, and the same year CYON exposed the gland, and, by stimulating it with electricity, showed a slowing and increase in force of the

heart with a rise in blood pressure, and concluded that the gland had a regulatory and protective function.

The extract of Pituitary Gland was introduced into therapeutics first by OLIVER and SCHAFER, who found that in cases of shock, surgical or otherwise, the extract produces basilar contraction of greater duration than that due to adrenin, which had until this time been used in these cases; and in Brit. Med. Journ. 191 x 08, an article points out that an intravenous injection of posterior lobe of the pituitary body raises the arterial pressure to a greater extent than in the normal state; a single injection influences the arterial tone for upwards of an hour without producing abnormally high arterial pressure.

Later FROHLICH, von FRANKL HOCHWARTS experimented on pregnant rabbits and showed that pituitary extract causes contraction of the uterus and raises the irritability of the organ, and on these findings, FOGES and HOFSTADTER were the first to use this product in cases of atonic post partum haemorrhage and HOFBAUER the first, for stimulating the pains in labour. JACQUER, 1912, experimented in the three stages of labour, and concluded that the administration of the drug was useful under certain conditions and with certain limits. SCHIFF found that administration of pituitary extract, though it had no

effect on the metabolism of a young man, caused in an old man, and a patient suffering from acromegaly, marked increase in the phosphorus secretion by the urine and the faeces, though there was no increase in the nitrogenous metabolism, and one man concluded that the pituitary influences chiefly the metabolism of tissues rich in phosphorus and poor in nitrogen.

In cases of acromegaly, MARINESCO found headaches were relieved, but there was no improvement in the state of the extremities, and BROADBENT reported great improvement in patients suffering from the disease.

III.

ANATOMY AND PHYSIOLOGY OF THE PITUITARY GLAND.

III.

ANATOMY.

The gland arises from the epithelial pouch, which buds off the roof of the buccopharyngeal cavity about the fourth week. This pouch meets and partly envelopes a corresponding prolongation (infundibular) from the adjoining base of the anterior cerebral vesicle, the tip of which becomes thickened into the infundibular body (pars neurosa). By the subsequent form of the spheroidal bone the lumen of practically all of Rathke's diverticulum except the tip becomes obliterated. This unobliterated tip comes to enfold the infundidular body, the hypophysis is connected with the tuber-cinerum by a stalk which varies in length and contains the infundibular recess of the third ventricle. This structure occupies the sella turcica and is enveloped in an adherent dural capsule, the upper diaphragm of which stretches from the four choroid processes and is perforated for the passage of the infundibular stalk. It is capable of distension upwards under the diaphragm and laterally toward the cavernous sinus but antero-posterior enlargement can take place only with deformation of the bony sella itself.

HISTOLOGY.

The anterior lobe, or pars anterior, consists of columns of cells surrounded by sinusoidal spaces into which numerous arterioles entering the gland break up.

The cells are of three types, chromophiles, acid staining and basic staining and chromophobes, with granules which are more abundant on the periphery of the blood sinuses. These cells vary greatly in their number and disposition, acidophiles are more abundant in the centre and basophils occupy the periphery. The question whether these cells with different staining affinities are actually different types or merely stages of the same type; BENDA is of the opinion that eosinophilcells are those charged with secretion and their number is increased in Acromegaly.

The posterior lobe, pars nervosa, or infundibular body is covered with a thin epithelial layer of neutrophilic elements, which thickens at the anterior part of the stalk into a mass of cells, and here fusion takes place between the pars intermedia and the pars anterior with cells of the transition type. Under certain conditions cells of the pars intermedia multiply and bend to form acini containing acid staining colloid substance which may be discharged into the posterior lobe. Should conditions of stasis occur this colloid substance accumu-

lates in the cystic acini and stains with basic stains regarded by BENDA as a product of cell degeneration. The pars nervosa consists of a meshwork of loosely woven neuroglia fibres radiating towards the infundibular body; between the fibres are spaces which contain acid staining hyaline bodies which arise from the cells of the pars intermedia.

The above description of the histology of the pars anterior suggests a typical gland of internal secretion discharging a stainable colloid substance (thaon) into the blood stream; but the posterior lobe, which is non-vascular, has in the neuroglia meshes a soluble colloid, or hyaline bodies which may be considered the products of secretory activity. The blood supply is liberal, anterior lobe being ramified with small arterioles which pass down the infundibular stalk; the posterior lobe is supplied by a single artery which enters below and behind, whereas the pars intermedia has a collateral circulation from both sources. The nerve supply is from the sympathetic fibres which pass along these vessels to the gland.

PHYSIOLOGY.

Formerly it was thought that this gland elaborated a secretion from the lubrication of the nasal cavities, by

the conception that it was merely a vestigal relic and of no great importance, and only after MARIE'S later papers in which anomalies of growth characterising acromegaly were shown to be associated with tumour of the pituitary, was there awakened an interest leading to many discoveries and it has now been proved to be a gland or organ of vital importance, owing to its well-protected position, its presence in all vertebrates, its persistence throughout life and its good and abundant blood supply. Injection of the extracts of the pituitary body have been of interest; first let us deal with the acute effects, as shown by other investigators.

OLIVER and SCHAFER injected intravenously extract of the whole gland and found a rise in blood pressure long continued due to peripheral vasoconstriction and augmentation of force of the heart-beat, later HOWELL found a slowing and strengthening of the pulse. Later a marked diuresis due to stimulation of the renal epithelium described by HALLION and CARRION, and DALE noted a stimulation of uterine, as well as intestinal, muscle to contraction.

Posterior lobe dilates the pupil, causes glycogenolysis, increases the flow of milk, hence we see the anterior lobe is relatively inactive, whereas the posterior lobe resembles adrenin, differing in the primary depressor and longer pressor response of the general circulation.

The chronic effects from repeated injection of the gland produced emaciation, although feeding rats with the extract had no effect. Gland transplantation experiments were futile, as the gland degenerates after implantation, but removal of the gland from puppies produced adiposity, dryness of the skin, lowering of the body temperature, increase of the carbohydrate tolerance, later stunted growth, reversive sex changes, and psychic disorders.

IV.

P A T H O L O G Y , S Y M P T O M A T O L O G Y .

CLINICAL MANIFESTATIONS OF DISORDERED PITUITARY FUNCTIONS - DISPITUITARISM.

(a) Hyperpituitarism.

(b) Hypopituitarism.

IV.

PATHOLOGY AND SYMPTOMATOLOGY OF DISORDERS OF THE PITUITARY GLAND.

In the study of the pituitary gland post-mortem, occasional gross lesions have been found, e.g. gumma, tuberculoma, or neoplasm; but more often studies failed to furnish satisfactory interpretation of the diverse histological changes which the pituitary body undergoes, owing greatly to its inaccessibility. We realise that the gland is altered by infection, trauma, diseases of the nervous system, by different ages, and during critical physiological periods, as adolescence, pregnancy and the climacteric. Also primary disease in other members of the ductless-gland series leads to secondary changes in the hypophysis itself and the obvious need of investigating the various accessory glandules still further complicates the matter.

There has been no uniformly established method of sectioning the gland, so that sections at random encourage misinterpretations. Many of the so-called tumours are in all probability mere hyperplasias and many neoplasms have become so compressed or flattened in the gland that it

easily escapes detection or identification.

In the anterior lobe, hyperplasia - that state of activity responsible for the skeletal over-growth and gigantism - the condition may exist without a great enlargement of the gland, just as Grave's Disease may exist without a great enlargement of the thyroid. ARNOLD and PONFICK* have reported cases of Acromegaly when the gland was normal, no tumour, with consequently no enlargement of the sella necessary. As will be shown later, in every case of increased intracranial tension from whatever source, there occur secondary changes in the hypophysis often with gross deformations and resultant functional disturbances which frequently elicit recognisable clinical manifestations.

Chemical.

The active principle of the posterior lobe is unaffected by boiling solution in water and salt solution. It has been shown that the depressor substance is soluble in alcohol and ether (SCHAFER and VINCENT)** as well as in watery

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* PONFICK: "Myxodem und Hypophysis. "Ztschr.f.klin.Med. 1899, XXXVIII.1.25

** ARNOLD: "Weitere Beitrage zur Akromegaliefrage". Virchows Arch. path. Anat.1894,CXXXVI-78.

Journ. Physiol. 1899-1900, XXV. 89.

solutions, whereas the pressor substance is soluble only in the latter. The active principle has a chemical kinship with Adrenalin; SCHAFER and HERRING showed it to be dialysable through parchment paper, and the gland does not yield a crystallisable body when subjected to processes similar to those used for obtaining the active principle of the adrenal medulla, also it is not destroyed in the gastric juice, therefore the substance is not a protein, as it withstands boiling, not adrealin, as it has different reactions, not thyroidin as it contains no iodine, so we conclude a definite substance secreted by the hypophysis alone. There is no established therapeutic dosage either for the fresh glands or their prepared extracts whether given by mouth, or subcutaneously, but different individuals vary exceedingly in their degree of tolerance and this has to be ascertained.

1. SYMPTOMS DUE TO PRESSURE ON NEIGHBOURING STRUCTURES.

The subjective discomforts deserve first consideration, these are more marked when the gland itself is the seat of hyperplasia or tumour, than when the growth is interpeduncular and intradural, as is the case with the majority of simple lesions causing primary hypopituitarism. Only in an advanced stage do the latter growths give rise to intra-

cranial discomforts of any severity.

Headaches are normally bitemporal, severe and persistent, when there is much glandular hypertrophy as presumably due to the distension of the glandular envelope. Pituitary headaches proper often subside with a stationary process or with a full distension of the capsule and widening of the sella tullica, though in some cases the fossa can become greatly enlarged by slow pressure, with but a minimum of discomfort.

Photophobia is another source of complaint, accompanied by visual disturbances. These are very common as the optic nerves suffer either from extension or the effect of the growth itself. Atrophy is a primary one, the disc shows no oedema and it is safe to say that amblyopia more often representa a physiological block to light impulses than an actual destruction of the nerves.

Some distortion of the visual fields is noticed, typical bitemporal hemianopsia may be rare, although homonycous defects are quite common. The primary defect usually first involves the colour boundaries alone in one upper temporal quadrant. This is followed by complete temporal hemiachromatopsia which gradually spreads downward till most of the temporal field is involved. In all cases the colour fields are involved first, the form fields later,

but rarely are the two eyes affected in an equal degree.

Other signs are epistaxis, discharge of mucus from the accessory sinuses or rhinorrhoea may occur.

DEFORMATION OF THE SELLA TURCICA.

X ray studies of the pituitary fossa first were done by OPPENHEIM, 1899, and have proved a most useful adjunct to the investigation of hypophyseal disease. They are merely of accessory value to the symptomatic manifestations, for often extreme hypopituitarism or hyperpituitarism may exist without much, if any, alteration in the shadow cast by the bony encasement of the gland.

There are three types of pathologically deformed and enlarged sellas, which may be distinguished:

(a) Those associated with thickening of the clinoid processes.

(b) Those associated with thinning from pressure,

(c) Those in which all outlines are destroyed.

(a) Here enlargement is accompanied by thickening of the walls and this type is confined to cases of acromegaly and gigantism uncomplicated by adenomatous struma formation, showing a tendency to osseous overgrowth.

(b) Here, as a result of primary glandular struma, absorption of bone from pressure atrophy is far the most

common.

(c) Here there occurs a complete absorption of the dorsum and a downward dislocation of the base. This change may be brought about either by a great enlargement of the gland or by a pressure downward of the growth which deforms and absorbs the bone by progressive enlargement.

2. GENERAL PRESSURE SYMPTOMS DUE TO INCREASED CRANIAL PRESSURE.

The condition is recognised when a choked disc is superimposed on a primary atrophy, but it may occur that a large intracranial tumour may envelop the optic nerves, but prevent the concentration of cerebrospinal fluid under tension into Schwalbe's sheath, hence the most reliable sign of tension may be wanting. Thus, headache may be the only symptom, for vomiting in these cases is unusual - and exceedingly rare.

3. THE SECRETORY AND GLANDULAR DERANGEMENTS PROPER.

Modifications of Skeletal Development.

(a) Overgrowth. (b) Undergrowth.

(a) The view that skeletal changes of Acromegaly and gigantism are due to a functional hyperplasia of the pars

anterior with the production of excessive or perverted type of secretion is not universally accepted. Arguments favouring the hyperpituitarism conception of Acromegaly are in the known conditions associated with skeletal over-growth, here one finds a hypertrophic enlargement of the gland, primary in acromegaly and gigantism and secondary in the case of eunuchism; also experimental extirpations of the hypophysis have been shown to retard skeletal growth, but, on the other hand, in the great number of cases as the malady progresses glandular insufficiency supervenes.

(b) Undergrowth. For skeletal development to be modified by glandular insufficiency, the process must start before full stature is attained; the more marked cases are those in which the glandular insufficiency occurs before adolescence.

Cutaneous and Subcutaneous Changes.

There is thickening of the epidermis, producing the coarse skin and coarse features, increase in size of the hair follicles, enlargement of the secretory glands, so that the skin becomes greasy and moist. Increase in the connective tissue giving the tissues a dense boggy feel, with apparent increase in the depth of the furrows of the face and hands, and causing enlargement of the hands and feet, with the appearance of oedema. In hypopituitarism

the cutaneous features are the reverse, skin smooth, transparent and dry, hair of scalp abundant, although the axillary and pubic hair may be sparse and thin.

Adiposity.

There is acquirement of an excessive subcutaneous deposit of fat with an increase in weight; it is thought that this fat accumulation is due to a posterior lobe insufficiency. These cases are able to assimilate large quantities of sugar, and it is possible that the Carbohydrates are transformed into fat.

Carbohydrate Tolerance.

Glycosuria is a frequent accompaniment of acromegaly, patients showing often an assimulation limit which averaged up to 400 gms of glucose. The sugar tolerance of these individuals has to be regarded as a measure of posterior lobe activity:- Polyuria, Polydipsia.

As we pointed out in an earlier section, extracts of the posterior lobe were shown by SCHAFER to possess diuretic properties, so any pathological lesion in the hypothysis will produce polyuria, in fact some cases of acromegaly, have been diagnosed and treated as cases of diabetes insipidus, on account of this symptom.

Usually patients complain of suffering from cold and

the subnormal temperature was merely one of the many evidences of the lowered metabolic activity characterising hypopituitarism. This is accompanied by a low arterial tension, a systolic pressure below 100^{mm} Hg., but in the stage at which they begin to complain of Asthenia the pressure may register as low as 70^{mm} Hg. A slowed pulse is a feature of most patients and blood films show eosinophilia. Drowsiness and torpidity are usual and chronic constipation, this latter symptom might be expected in view of the known effect of posterior lobe extracts in stimulating peristaltic activity.

4. POLYGLANDULAR MANIFESTATIONS.

Manifestations in other glands so often occur as an accompaniment of hypophyseal defect, but the symptoms and signs are so varied in type that it is often doubtful to which gland is attributable the various symptoms.

Interrelation between hypophysis and the testis or ovary appears to be more intimate than between any other members of the series. Where hypophyseal lesion comes on before puberty, we see a persistence of infantilism and no secondary sex characteristics. After adolescence, amenorrhoea or impotence occurs.

Changes in the thyroid are most commonly observed,

the gland found to have an excess of colloid, seldom, however, are there changes in the parathyroid.

Occasionally symptoms arise suggestive of functional insufficiency of the suprarenal bodies, pigmentation, asthenia, low blood pressure, hypoglycaemia.

Seldom is the thymus or pancreas affected, but our knowledge of the endocrines is still in its infancy, and until the relationship of the glands and their hormones to each other are more fully investigated, we cannot be sure of their manifestations.

V.

PHARMOCOLOGY OF PITUITARY EXTRACT.

(a) Action on Heart and Vessels.

(b) Action on Kidneys.

(c) Action on Uterus.

V.

PHARMACOLOCY OF PITUITARY EXTRACT.

HOWELL discovered, as we have already seen, that it is from the posterior lobe that the active extracts can be obtained. This observation is contrary to what we might have expected as, from the distinctly glandular nature of the anterior lobe, it would appear that it would be more likely to furnish the active physiological substances. An extract of the whole gland may be used therapeutically, but the posterior lobe is of greater importance, and value - composed partly of nerve fibres and cells - it exercises a powerful influence over the vasomotor nervous system; and the regulation of the blood pressure, especially in the brain; while the anterior or glandular part influences development of the form and size of the body and growth of the bones. The hormones supplied by the posterior lobe, including the pars intermedia, regulate the tone and contractability of plain muscular tissue, generally of the heart, stimulate the activity of the mammary gland, uterus and kidney.

Pituitary Extract can be administered as the dried gland or the liquid extract. The former is made in three

preparations respectively from the entire gland, the anterior lobe and the posterior lobe. In the liquid extract of the gland, either the entire, the anterior or posterior part is used, but the last is the most active. To obtain it, posterior lobes of the fresh glands are finely minced and extracted with acidulated water. The liquid is then heated to boiling for ten minutes in order to remove the coagulable protein, and then filtered and sterilised and sealed in ampoules.

The first observer to use Pituitary Extract clinically was Dr. GOLLA, who proved that the heart was slowed, due to the prolongation of the systole. He injected 3 mins. subcutaneously into the jaw and produced a definite local vaso-constriction lasting forty-five minutes. An interesting case of Addison's disease treated by subcutaneous injection showed a rise in blood-pressure from 120^{mm} Hg. to 150^{mm} Hg. and Pulse was slowed from 100 to 85 after half-an-hour. After three hours the pressure fell to 135^{mm} Hg. and the pulse rose to 95. OLIVER and SCHAFER found that this vaso-constriction produced by the extract of the posterior lobe, was of greater duration than that due to the injection of Adrenin.

We shall now consider in detail the action on the heart and vessels.

In a normal individual ½ cc of Pituitary Extract injected produced a rise in blood pressure, this rise was very pronounced and lasted a considerable time, and, as has been mentioned, the rise was due to a peripheral vaso-constriction of the arterioles. A second or subsequent dose, however, if given soon after the first, may produce a fall in pressure; this was noticed by SCHAFER and VINCENT and was supposed to be due to the presence of the depressor substance in the extract.

It also quietens and strengthens the heart-heat, and slows the pulse. This is brought about by a prolongation of the systole but, used as a routine, it produces arterial degeneration if used too long, therefore it is a drug for emergency, not routine use. In heart-failure from surgical or other causes, it is excellent, but care must be used in giving it in cases of heart-disease, arterio-sclerosis or kidney disease, especially of the aged, as the sudden increase in blood pressure might cause apoplexy. As a temporary cardiac stimulant in acute disease, such as pneumonia, pituitary extract has been found successful where strychnine and camphor have failed.

The volume and activity of the kidney are increased, consequently the amount of urine is augmented. This has been proved to occur whether the vagi are cut or not.

According to one writer, the output of urine in polyuria is reduced by the pituitary extract, increasing the capacity of the kidney to secrete a concentrated urine. It has been tried in Diabetes mellitus, but the effect is transient, only lasting for a few days.

Pituitary stimulates the uterine muscles and raises the irritability of the uterus; this has been observed by many investigators, although NEU*** says, these effects are observed only after the first injection. The uterine contractions caused by pituitary extract do not appear parallel with the increase of the blood pressure, and therefore cannot be considered to be the result. He advocates the use of adrenin as a much superior drug.

Given intramuscularly, after three to five minutes pains occur, if slight pains have been present, they become more violent, one pain follows another at about half-minute intervals. These pains are severe and continue so for ten minutes, then become more rhythmical and last for

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Clin. Journ. 8/23 364
Brit. Med. Journ. ii/16, 298.
P. J. CAMNIDGE. Pract. Oct. 1920, 244.

*** Munch. med. Wochenschr. 1924, iii.

about an hour.

It should not be injected during the first stage of labour in primipara, unless the os is dilated to the size of the palm of the hand, and in multiparae unless the os is the size of an orange and pains must have started, otherwise the energetic contractions may cause rupture of the uterus.

In the second stage, where pains have become weak and the head is well down, ½ cc injected intramuscularly acts like a charm. It avoids the necessity for the use of instruments in practice often when the delay in delivery is due to uterine inertia, but in cases of abortion it has little effect, especially in the early months.*

Where chloroform is given during labour, pains are likely to become less active, but if ½ cc of extract is injected deeply into the buttock every forty-five minutes, partial anaesthesia is maintained and, at the same time, the uterus is kept active.

Danger to the child has been held as a contraindication to the use of pituitary extract, but it must not be given too early, otherwise the foetus may be endangered. The foetal heart is usually slowed after an injection,

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* Lancet. ii/135, 44.

** Brit. Med. Journ. ii/22. 72.

therefore, it is necessary to keep a strict watch on the heart-beat. In cases where the child is born in a state of asphyxia pallida, some advocate the use of 3 cc of pituitrin intramuscularly with beneficial results.*

It is evident that when the action of Pituitary Extract ceases, the uterine muscle becomes relaxed, this occurs very quickly after the expulsion of the child. The uterus, which was well contracted at the beginning, always becomes soft later. On account of strong bleeding after the expulsion of the placenta, Ergot may be required, in fact some investigators prefer and advise Ergot, but we think 5 cc injected deeply into the buttock when the foetal head issues from the vulva shortens the third stage and prevents the post-partum haemorrhage, and reduces the loss of blood in this stage.

As a result of the shortening of the third stage, uterine manipulations and Crede are rendered unnecessary.

The involution of the uterus is aided; after-pains are diminished and retained placenta is a rare occurrence,** and the blood loss is minimised.***

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* Brit. Med. Journ. 1/24. 570.

** Seides: Surg. Gy. and Obs. 1/23. 108.

*** Borhangr A.O.G. iii/22.

VI.

CLINICAL WORK.

TRIALS OF PITUITARY EXTRACT IN A SERIES OF CASES OF NORMAL AND ABNORMAL LABOUR.

OBSERVATIONS OF ITS EFFECT ON THE UTERUS.

VI.

CLINICAL WORK.

In the following cases the Pituitary Extract used was one of the following preparations: Burroughs and Wellcome Extract, Infundin; Park Davis' Pituitrin, or Duncan Flockhart's. The two former the most frequently, but all were found of equal value clinically. In all cases, unless specially mentioned, the injection was given intramuscularly, either into the deltoid or gluteous muscle, as in two cases hypodermic injection produced sloughing, owing to the contraction of the peripheral arterioles, and was given up in favour of the intramuscular route.

(a) First, pituitary was given to healthy individuals, who had no signs of organic trouble.

Woman, aet 40, received ½ cc into the arm. She immediately complained of a numbness and coldness of the hand and forearm. The pulse before administration was 76, and the blood pressure 130^{mm} Hg. Immediately after injection the pulse rate slowed to 68, and the blood pressure rose to 140. After 30 minutes the pressure was 136, and the pulse 60. After one hour 132 and 64. After four hours pressure

132 and pulse 78. The patient complained of a headache and throbbing behind the eyes, but this feeling passed off, two hours after the dose.

The second case, a woman, aet 29, received ½ cc. Before injection the blood pressure registered 124^{mm} Hg. and the pulse 84; immediately after pulse slowed to 72 and the blood pressure rose to 140^{mm} Hg. After 30 minutes the readings were 68 and 142. After one hour, pulse 78, blood pressure 130, after 4 hours pulse 80, blood pressure 126. Neither discomfort nor headache was complained of, although the patient had an attack of acute colic, which lasted for five minutes and was relieved by a sudden call to stool.

(b) The following cases illustrate the benefit of Pituitary in shock:

A man, aet 54, was admitted to The Glasgow Royal Infirmary:- vomiting faecal matter and complaining of acute obstruction. The pulse was very weak and rapid 140, temperature 97°. His face was ashen grey and bathed in sweat and he was obviously seriously ill. The operation was immediate, laparotomy performed and the strangulated bowel relieved. The patient was so collapsed that it was feared he would not stand a resection, so a colostomy was fixed for the time and 1 cc of Pituitrin was injected into

the buttock and from an imperceptible pulse in 3 minutes it became stronger and slower 130, and after 30 minutes slowed to 118, and the blood pressure was 100^{mm} Hg. A second injection was repeated after two hours and the patient continued to do well.

Woman, aet 45, suffering from multiple fibromata, for which hysterectomy was performed. The patient was put back to bed after the operation with a pulse imperceptible at the wrist. Salines were administered and an injection of Pituitary given; with immediate good result, and the patient made an excellent recovery.

Woman, aet 37, suffering with a large multilocular cyst. The cyst was found to have a twisted pedicle and numerous adhesions to the bowel and omentum. The cyst was removed complete without rupture, but owing to the adhesions the operation was prolonged. At its completion the patient was profoundly shocked. Pulse thread-like and blood pressure 80^{mm} Hg. 1 cc of Pituitrin was given. Salines per rectum and in five minutes there was an improvement, pressure rose to 110 and pulse fuller. On the second day the abdomen was distended. As no flatus had been passed, ½ cc Pituitrin was given with the desired result and the discomfort was relieved.

(c) Used in the following cases of Cardiac Debility

and Low Pressure.

For its vaso-constriction action I tried it once only, in a case of Typhoid Fever. Knowing that the B.typhosus toxin is vaso-dilative in action, and as the symptoms of the illness drag on from week to week progressing in severity, instead of Digitalis or Strophantus I prescribed ½ cc Pituitrin 8 hourly, and gradually decreased the frequency of the dose till only given once in the twenty-four hours. The patient made an excellent recovery, and I may perhaps have given undue credit to the use of the drug, certainly the convalescence was shortened.

The post-influenzal cases with lowered blood pressure and debility seemed to me to be cases worthy of trial of Pituitary Extract. Accordingly in a series of ten cases I used the drug, giving it once daily in ½ cc doses; with most satisfactory results. In all cases the blood pressure registered between 80 and 110^{mm} Hg. and the pulse was rapid. After a week's treatment the patients benefitted and had gained in strength and well-being, having lost their langour and restlessness, and in many cases insomnia was improved.

One case of phthisis, a girl of 20, who had a definite lesion in the right apex, appeared to benefit, although the disease was in no way arrested. Her chief distressing symptoms were a quick pulse, restlessness and

and insomnia. The injection increased her appetite, the pulse was slowed, the restlessness diminished, sleep was promoted and the blood pressure raised, and in my opinion she benefitted from the treatment.

(d) Pituitary was given in a series of Normal Midwifery cases, thirty in number, of which eighteen were multiparae and twelve primiparae. All were examined on going into labour, and all had the vertex presenting. No case received the injection till the os was fully dilated and the head was on the vulva, then 1 cc was injected intramuscularly into the buttock: In none of these cases had there been any intense inertia, but after the injection it was noticed that, on an average of 3 minutes, the uterus became more tonic, the pains more severe, the uterus rose higher in the abdomen and, where the pains had occurred at intervals of five or more minutes, this period was in all cases diminished occurring in frequency of two to three minutes.

The child was born in all spontaneously, no case required forceps delivery. After the birth of the child the uterus remained quiet for an average time of three to five minutes, and then contractions again supervened and the placenta was expelled with the minimum number of pains, two to five usually expelled the after-birth, the period

from the injection to the birth of the placenta lasting 7 to 15 minutes, the blood loss being small and no case in the series had a post-partum haemorrhage.

Two cases, both primipara, suffered from torn perinaem. Herein there is danger, in my opinion, of giving the Pituitrin too early and in primipara,where the vulva and perinaeum are tense and tight, even after the injection, the head of the child must be well guided and the perinaeum moulded and stretched gradually to avoid undue laceration and tearing.

(e) The following cases illustrate the uses of Pituitary Extract in Midwifery Cases with Excessive Haemorrhage:

Woman, aet 24, primipara, delivered with forceps. The child was in the occipitoposterior position: after the birth, the pains were feeble, 45 minutes the pains became increasingly violent, the placenta was expelled, but I found the membranes were incomplete. Haemorrhage became severe, so I manually removed the membranes, gave 1 cc Pituitrin and within three minutes the bleeding had lessened and the uterus was firm and well contracted. No further bleeding occurred.

Woman, aet 27, II. para, was in hospital for her first pregnancy. Her child was still-born after a

prolonged labour. The head was in the right occipito posterior position, but could not be rotated and was delivered as a persistent occipito-posterior with forceps. The child weighed 10¼ lbs. After the placenta was delivered, she had a smart haemorrhage which was checked by an injection of Pituitrin and an intrauterine douche at 100° F.

During her second pregnancy she attended the Ante-Natal Clinic, and was advised to come into hospital for her confinement, as it was feared she would not be able to continue to full term, as the foetal head was large proportionately to the pelvis. At the 32nd week labour was induced. The position was again R.O.P., but was easily rotated and delivered. The placenta was expelled twenty minutes after delivery, but a severe post partum occurred; 1 cc was immediately injected and within three minutes the uterus had hardened up and there was only a slight oozing.

Woman, aet 29. IV para.

Her first pregnancy was normal, her second and third were normal deliveries, but the placenta, and membranes were adherent. Her fourth pregnancy she had haemorrhage at the eighth month. On February 23rd I was called to see her. She had lost a great amount of blood. Uterus

was flaccid and flabby and she was having no pains.

On examining, I found the os admitted three fingers and the placenta was felt overlapping the os. I ruptured the membranes, performed version and brought down a leg. Then gave 1 cc Pituitary and injected 2 pints of Saline intravenously. The patient was still very weak, but thirty minutes after the injection pains began, and there was no further haemorrhage.

One hour later a second dose of Pituitrin was given. Pulse 120, Blood pressure was 100^{mm} Hg., and her condition was improving. A dead child was born four hours after the first injection. No further haemorrhage occurred and contraction and retraction were good.

Woman, aet 38, II para.

Her first pregnancy was normal; with this pregnancy at the 4th month she had a "bleeding", described by the patient as "nothing alarming", and with rest and opiates no further trouble occurred.

At the fifth month she had another bleeding, and continued intermittently till five and a half months, when she had a smart haemorrhage, and I found her pale and collapsed. After she had sufficiently recovered to be examined, I did so and found the os admitted two fingers, but was dilatable to the extent of three. I ruptured the

membranes, performed version and brought down a leg; the foetus was expelled naturally three hours later. The placenta was adherent and had to be manually removed after which she had a profuse post partum haemorrhage. I immediately gave 1 cc Pituitrin, which had instant effect, and there was no further haemorrhage.

Woman, aet 30, II para was admitted late one evening to hospital, said to be three months pregnant and had had a severe haemorrhage. I examined and found the os dilated and the uterus contracting. A complete ovum was expelled but haemorrhage continued. I gave her 1 cc intramuscularly and an intra-uterine douche, with good results. On the following day, as there was a slight bleeding, and the uterus was flabby, I gave her another ½ cc with no further haemorrhage.

Two days later she complained of great discomfort, due to abdominal distension, so I administered a third ½ cc. Twenty minutes later flatus was passed and the distension was relieved. Convalescence was completed without any further complications.

(f) In the following two cases I used Pituitrin to lessen bleeding, although there was no amelioration of the existing condition.

Woman, aet 30, had three children, the youngest two

years old. Her health had been good till two months' previous to coming to see me, when she complained of frequent "floodings". On eliciting the history, I found she had metorrhagia and menorrhagia, and on examination I found the cervix hard and friable, bleeding on the slightest touch, a hard fixed mass in the anterior fornix adherent to the bladder wall; infiltration was extensive. Operation was refused.

One month later I was called to see her. She had had a severe haemorrhage, several large clots had been passed and she was bleeding profusely when I saw her. She was pallid, shocked, pulse was uncountable. I gave her immediately 1 cc Pituitary intravenously and salines. After fifteen minutes there was a great improvement, pulse 120, blood pressure 90 and no further haemorrhage. I returned to see her the same evening and found her condition satisfactory.

Five weeks later, I was again called to see her. The same symptoms were present, though not so severe. The same treatment was given, with immediate stopping of the bleeding. Unfortunately I was unable to follow up this case, as I removed from the district, but I mention it merely as an example of the use of Pituitrin on the uterus, when there is no pregnancy.

(g) The following Cases illustrate the use of the Pituitary Extract in Intestinal Atony and Paresis.

Woman, aet 37, suffering from a large tumour, diagnosed as ovarian cyst, was admitted to hospital for operation, the cyst was removed intact, weighed 8½ pounds. After the operation there was intestinal paresis and abdominal distension and retention of urine. I therefore gave her 1 cc Pituitrin for the two first complications and, knowing of the diuretic properties of the gland, hoped the third condition might be relieved, but, unfortunately, the patient had to be catheterised. After the one dosage, there was no return of the symptoms.

This case also came under my notice:-

Man, aet 46, suffering from intestinal obstruction. Ileosymoidostomy was performed. Calomel gr ¼ given two hourly with no effect. Glycerine enema gave no action of the bowels. At the second operation a right Lumbar Colostomy was performed and more calomel given with no result. Acute obstruction had now existed for five days, vomiting was present, and the patient in intense pain from distension and flatulence. 1 cc of Pituitrin was injected into the deltoid and within a few minutes much flatus was passed by the colotomy wound and relief obtained. This dose was repeated on two successive days, then was no

further necessary as no distension occurred again.

A young girl, aet 14, had always been very constipated. Even as a child daily cathartics failed to produce an evacuation of the bowels. Enemas also had been tried with no success. So was admitted to hospital suffering from scarlet fever, and it was during her illness that the sister-in-charge reported to me the condition of obstinate constipation. I gave her an injection into the deltoid, ½ cc Pituitrin, and two hours later she had a motion. The following day the bowels acted without any drugs, but on the third day there was no action. I repeated the dose with good results, but I foresaw that the injection would have to be continued to cure the constipation, as undoubtedly it was due to an insufficiency of Pituitary Hormone and, as the patient was leaving the hospital, I prescribed dried gland, posterior lobe only; gr.iv taken every other day.

She came to see me two months later, and had no trouble with the bowels since, although on discontinuing the drug she found the constipation again returned.

(h) Woman, aet 34, III para. Her first two pregnancies were normal. This patient had been in labour for eight hours. I examined her and found the os fully dilated, but the pains were becoming less forceful and were

decreasing in number, so I gave her 1 cc Pituitary into the buttock and immediately the pains became strong and occurred every two minutes. Within twenty minutes the child was born and the placenta followed after five minutes with no haemorrhage.

Woman, aet 44, VIII para. All per previous pregnancies had been easy, for her first she required chloroform and instruments, but usually never needed a doctor. I was called to see her, as she had been in labour off and on all day, but for the past two hours the pains had gone and she had begun to get alarmed. The vertex presented and the head was well down, the foetal heart 146 and strong, and a few strong pains would suffice, so she pleaded for chloroform, instead I gave her 1 cc Pituitary and, after two minutes, the uterus started contracting, and with three more pains the child was born. The placenta was not adherent and followed ten minutes later.

VII.

SUMMARY AND CONCLUSIONS.

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1. Primipara should not be given Pituitary until the os is fully dilated; it is fraught with danger to the mother and the child.

2. Multiparae benefit in the first stage if the pains are forceless, but Pituitary must not be given until the os is dilated to the size of an orange.

3. Pains in all cases must be present.

4. In the second stage it is excellent, often avoiding the use of forceps.

5. Given a few minutes before the birth of the child, the third stage is shortened.

6. The number of adherent placenta is diminished.

7. The blood loss is reduced to the minimum.

8. In cases of post-partum haemorrhage, it is good, acting more quickly and effectually in cases of emergency than Ergotin.

9. The best remedy for secondary uterine inertia, avoiding instrumental and manipulative interference.

10. As it occasionally produces asphyxia in the child, the foetal heart must be carefully watched.

11. For shock, due to lowered blood pressure operative or otherwise, it is the best remedy, superior to Strychnine, rectifying in the minimum time the results of collapse.

12. For intestinal paresis and atony, its good results are proved.

13. In labour it is a necessary adjunct to every armentarium but, like every drug, it has its definite uses and must not be used indiscriminately without first a thorough examination of the patient.

VIII.

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VIII.

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