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PITUITARY EXTRACT

WITH SPECIAL REFERENCE TO

ITS ACTION AND THERAPEUTIC USE IN MIDWIFERY.

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Thesis submitted for the M.D. Glasgow

by

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Introduction.

The great advances which have been made in Organo-therapy in recent years lead one to hope that the field for the activities of animal extracts will be largely extended.

The thyroid gland substance and the suprarenal extract are now in every day use, and their value is unquestioned. The former is the specific treatment for Myxoedema and Cretinism, and is of use in some forms of Goitre. The latter is one of the most powerful styptic drugs we possess. It acts by causing local vaso-constriction. After absorption it raises the blood pressure most powerfully. This action has been taken advantage of in the treatment of Shock, and in the circulatory weakness of the acute fevers.

The active principle of the suprarenal extract has been isolated, its chemical constitution determined, and a synthetic preparation produced which answers to the tests of the natural extract.

In the year following their discovery of the suprarenal extract, Oliver and Schafer described the physiological effects produced by extracts of the pituitary body, but it was not till some years later that the attention of the profession was drawn to this substance as a therapeutic agent. This was probably due to the fact that the action of the two extracts (suprarenal and pituitary) seemed similar, and that in the case of the

former the action was much more marked.

In a paper published by Blair Bell[2] in 1909, the drug was brought prominently into notice, and its action in cases of shock, uterine atony, and intestinal paresis was described. Other observers have obtained similar results, and the whole evidence goes to show that we have in pituitary extract a most valuable drug for the treatment of shock and uterine atony, and one which is much superior to suprarenal extract in these conditions. The active principle has not yet been isolated, but much recent work on this subject has been done by many observers.

Lewis, Miller, and Matthews[3] made extracts of the various anatomical component parts of the pituitary body, and found that the chief pressor substance was contained in the pars intermedia. They also describe a depressor substance soluble in alcohol which is present in the anterior part, the pars intermedia, and the pars nervosa. The separation of this depressor substance from the extract will make the drug more valuable and the action more certain.

Dale,[4] experimenting with the extract on cats, found the urine excreted after injection of the extract capable of producing a rise of blood pressure when injected into another cat, thus proving that the pressor principle is excreted in the urine.

In the following pages I propose to give a general account of the recent work on the therapeutics of the extract, with special reference to its value in midwifery practice, and to illustrate it by reports on cases where

I have tested the drug.

Prior to using the extract I made a series of observations on blood pressure in pregnancy and during the puerperium, using for the purpose a Riva Rocci Sphygmomanometer, and, in forming an opinion on the value of the drug, I took records before and after injection, the rise in blood pressure being an index of the action of the drug, and the duration of the increased pressure an important factor in determining its power to maintain contraction of the uterus.

I found in the normal parous woman a gradual rise in blood pressure up to the onset of labour, and a gradual fall after labour. This rise in blood pressure is probably due to the internal secretion of some pressor substance.

Dixon and Taylor[5] thought that the placenta produced such a pressor substance, and produced an extract from placental tissue which had a pressor effect when injected into the blood stream, but Rosenheim[6] showed that the pressor substance was due to incipient putrefaction in the placenta, and had the same chemical composition as the pressor substance (~~animal~~ amine) obtained from putrid meat.

It is now known that extract of fresh pituitary substance acts powerfully on unstriped muscle and raises blood pressure, so it might not be unreasonable to suggest that the pituitary body may have a controlling influence on the advent of labour.

The value to the obstetrician of a drug which will produce powerful and sustained contractions of the uterus goes without saying, and in extract of the pituitary body (infundibular portion), I believe we have such a drug.

Historical.

There are records in ancient medicine of animal substances being used in the treatment of disease, but it is only in recent years that the subject has been placed on a scientific basis.

The pituitary body, so-called because of the belief of the old anatomists that it discharged pituita or mucus into the nose, was regarded by most of the scientists of last century as a mere vestigial relic of prehistoric usefulness, and was called by Van Gehuchten "l'organe enigmatique." (Harvey Cushing[2])

With the growth of scientific methods and the development of the modern spirit of enquiry, this organ, among others equally obscure, was submitted to experimental researches with results which so far are excellent, and which hold out hopes of still more valuable ones in the near future.

Of these obscure organs the thyroid has yielded the most notable triumphs in treatment. It was found that complete removal of the thyroid produced symptoms akin to Myxoedema, and that administration of the fresh gland or extracts from it checked the condition, and if the treatment were kept up the condition disappeared. In cases where the gland is atrophied the continued administration has given remarkable results.

The suprarenals come next in the category of useful-

ness.

Oliver and Schafer's[6] researches on these bodies were the starting point of a line of enquiry which has brought within its purview many of the organs of the human body. They made extracts of the suprarenals, and injected them into the blood stream of animals, and found that a considerable rise in blood pressure resulted. This, they discovered, was chiefly due to vaso-constriction of the peripheral vessels. The value of a drug which so rapidly raised blood pressure was soon recognised, and it was tried in cases of shock and other forms of circulatory weakness with good results.

Working on similar lines they experimented with the pituitary body and found that extracts of it also produced a rise in blood pressure.

There the matter was allowed to rest for a time, the suprarenals overshadowing the pituitary. Researches into the character of the suprarenals continued and eventually their active principle was isolated. Herring[5] in 1904 compared the action of the suprarenal and pituitary extracts on the arteries, and came to the conclusion that the vaso-constriction was of the same kind, and was produced by stimulation of the same structures. Later Bell and Hick[9] described their action on the uterine muscle and came to the same conclusion. Dale[4] after a long series of experiments proved that the pituitary extract acts directly on unstriped muscle, whereas the suprarenal

acts through the sympathetic nerves (Langley[10], Brodie and Dixon[11], Elliott[12]).

The earliest recorded experiments on human beings were performed by Mairet and Bosc[13] in 1896, who injected the extract from two pituitary glands of the ox into a healthy individual. There was a slight elevation of temperature, increase of frequency of the pulse, urine increased in quantity, and was richer in urea and phosphates. This state lasted twenty-four hours.

In the following year Schiff administered the gland to a healthy person without noticing the slightest change in the urinary secretion.

In 1907 Parisot[14] injected 3 c.c. doses of the extract into normal individuals. A rise of blood pressure and slowing of the pulse were the invariable results, diuresis was always marked but there was no qualitative change in the urinary secretion. The persons became more sleepy.

Delille[15], 1906-7, performed similar experiments using extracts of the posterior lobe, anterior lobe, and the whole gland. The extract of the anterior lobe produced no effect, that from the whole gland increased the blood pressure, slowed the pulse and produced diuresis, that from the posterior lobe produced the same symptoms in a more marked degree.

Blair Bell[2] in 1909 used the extract in cases of shock, uterine atony, and intestinal paresis with marked effect. C. L. Frazer[16] reported a case of inversion of

the uterus with great loss of blood and shock where, after replacing the uterus, he gave the extract in a rectal saline injection with "marvellous effect."

The investigation of the extract is still going on, and, with the increase in clinical experience of the action of the drug, its place in pharmacy as a tried and trustworthy preparation will soon be acknowledged.

Anatomy and Development.

The pituitary body is situated in a depression of the sphenoid bone, the pituitary fossa or sella turcica, where it is retained by a fold of dura mater named the diaphragma sellae, which roofs in the fossa leaving a small opening for the infundibulum, which connects the pituitary body with the base of the brain. It is a small reddish grey mass, oval in shape, measuring one third of an inch from before backwards and half an inch from side to side and consists of three parts, which show marked differences in structure, development, and function.

The anterior part, the largest, is oblong in shape and somewhat concave behind. This part together with the next part (the pars intermedia) is developed from a tubular prolongation of the primitive buccal cavity or stomatodæum.

About the fourth week of intrauterine life there appears a pouch like diverticulum of the ectodermal lining of the roof of the stomatodæum. This, the pituitary involution or pouch of Rathke is the rudiment of the anterior lobe of the pituitary body and extends upwards in front of the cephalic end of the notochord and the remnant of the pharyngeal septum, and comes into contact with the under surface of the forebrain.

It is then constricted off to form a closed vesicle, but remains for a time connected to the ectoderm of the stomatodoeum by a solid cord of cells. This vesicle

sends out hollow processes into the surrounding mesoderm, and is gradually converted into a mass of small tortuous tubules lined with columnar or cubical cells. When fully developed the anterior part consists of a number of isolated vesicles and slightly convoluted tubules lined with columnar epithelium, ~~and~~ united together by a very vascular connective tissue. A colloid substance is present in the vesicles which suggests a resemblance to the thyroid body, but unlike that of the thyroid it contains no iodine (Halliburton)[17].

The Pars intermedia lies between the anterior and posterior lobes, and is developed in connection with the anterior lobe. It consists of finely granular epithelial cells in layers closely applied to the posterior lobe and adjacent brain (Halliburton)[17].

Handelsmann and Horsley[18] differentiate these cells into those lining the cleft between the anterior and posterior lobes (pars intermedia fissurae), and those forming a circle round the infundibulum (pars intermedia infundibuli). Colloid material is present between the cells.

The posterior lobe is developed as a down-growth from the floor of the embryonic brain, and during foetal life contains a cavity continuous with that of the third ventricle of the brain. This cavity becomes obliterated in man and the higher vertebrates, but persists in some animals (e.g. the cat), in others (e.g. the dog) the neck only is hollow. This down-growth expands at its

lower end forming the posterior lobe; the upper narrow portion or neck which connects it with the brain is called the infundibulum. In man the posterior lobe contains no nerve cells, but consists mainly of neuroglia with islets of epithelial cells, and colloid material from the parsintermedia is found.

In certain of the lower vertebrates (e.g. fishes) nervous structures are plentiful and the lobe is of large size (Gray's Anatomy)[19].

Physiology.

The question as to whether the pituitary body or one of its parts if necessary to life has been investigated by many observers. The whole organ has been successfully removed by Marinesco[20] in cats and by Vassale and Sacchi[21] in dogs, and more recently by Paulesco[22] and Harvey Cushing.[23] In all cases death resulted within fourteen days of the operation. The symptoms observed were fairly constant, viz. lowering of body temperature, anorexia and lassitude, muscular twitchings and tremors which tended to develop later into spasm, and finally dyspnoea. Many of these symptoms improved after the injection of an extract of the organ. Paulesco and Cushing removed the posterior lobe only without producing fatal effects, but they found that removal of the anterior lobe always resulted in death. Handelsmann and Horsley[18] in a recent communication give the results of a series of experiments on fifty-four animals. In fifteen cases they removed the whole gland completely as was proved post mortem by microscopic examination. Eight of the fifteen died within 48 hours from shock, haemorrhage, or infection, and not in their opinion from loss of the gland. Three died within four days, but did not exhibit any of the symptoms characteristic of loss of the gland. The cause of death in their opinion was oedema cerebri where not due to one of the above named causes. Three of the four remaining cases (all monkeys) died naturally on the

13th, 14th, and 39th days showing no characteristic symptoms, but dying from asthenia as monkeys do in captivity. The last one was killed while in good health on the 115th day. They observed a parallel death rate in animals where the gland had not been completely removed. In three animals they removed the anterior part of the gland without fatal result, so disproving Cushing's conclusions. They suggest that if the gland is absolutely essential to life the survival in these cases could only be attributed to the preservation of the acini of the parsintermedia infundibuli, but they consider that their experiments are too few to clear up the point. They also found no evidence of changes in other internal secretion-glands which could be attributed to lesions of the pituitary.

Most observers agree that the gland produces an internal secretion which is necessary to life and Handelsmann and Horsley's experiments do not disprove this theory. In order to further test the functions of the organ an elaborate series of experiments have been made with extracts of the gland.

Oliver and Schäfer[1] were the pioneers in this line of investigation. They injected an extract of the whole gland into animals, and described a rise in blood pressure as the result, but concluded that the effect was similar to that produced by suprarenal extract.

Then Howell[24] made extracts from the anterior, and from

the posterior lobes, and found the latter contained the pressor principle. This was confirmed by Schafer and Vincent[25], and more recently Lewis, Miller, and Matthews[3] made extracts of the various parts of the gland. Their results may be briefly enumerated. Extracts of the pars-intermedia intravenously injected gave a decided rise in blood pressure, extracts of the posterior lobe not so marked a rise, extracts of the anterior lobe a fall followed by a rise slightly above the level existing at the beginning of the experiment. The contents of a cyst of the parsintermedia gave a marked pressor effect. They conclude that the pressor substance is elaborated in the parsintermedia, and passes into the posterior part (pars nervosa), since it is unlikely that the two parts, which are histologically so different, would secrete a substance having the same pressor effect.

Schäfer and Magnus[26] discovered that the extract had a diuretic effect due, they supposed, to a selective action (vasodilator) on the vessels of the kidneys. Dale[27] was the first to record its effect on the uterus. He found that it produced uterine contractions. This he discovered during an enquiry into the action of ergot. To Blair Bell[2] is due the honour of putting this fact to practical use. After a series of experiments in conjunction with Hick[9], in which they discovered that the pituitary extract had, besides its action in raising blood pressure and in causing contraction of the uterus, a

definite action on intestinal muscle, he began to test it clinically. He mentions a case of shock following an operation for removal of a large fibromyomatous uterus with dense adhesions and coexisting suppurative appendicitis. The patient was pulseless at the end of the operation, and he administered an injection of pituitary (infundibular) extract with good results, saline infusion was also kept up, and he says that the saline is necessary in these cases to keep up the effect of the pituitary extract.

Its effect on the uterus, he says, is immediate and convincing. He gave injections in two cases of Caesarean section, and almost immediately the uterus contracted into a blanched ball, and relaxed subsequently to only a moderate degree. Thus showing that the danger of subinvolution after Caesarean section, with the risk of sepsis from retained clots and discharges, can be prevented. In post-partum haemorrhage he found it acted promptly and satisfactorily. He noted in his experiments on pithed rabbits that, after injection of the extract, marked peristalsis was set up, and, acting on this, he tried the drug in cases of intestinal paresis with good results.

As to the mode of action off the extract it was generally held that it was similar to suprarenal extract so far at least as regards vasoconstriction. The points of similarity of the two extracts may be briefly mentioned, both raise the blood pressure, peripheral vasoconstric-

tion being a principle factor in the effect (Oliver and Schafer), in both the active principle is limited to a small, morphologically independent portion of the gland developmentally related in the case of the pituitary body to the central nervous system, and in the suprarenals to the sympathetic system. Langley[10.] showed that suprarenal extract produces symptons exactly similar to those which are produced by stimulating nerves of the true sympathetic system, and this was confirmed later by Brodie and Dixon,[11.] and by Elliott.[12.] The pituitary extract on the other hand does not do so but acts directly on unstriped muscle. Dale[4] in an exhaustive series of experiments proved this conclusively. He experimented on various organs and systems containing unstriped muscle and gland cells, using Ringer's solution to which he added pituitary extract or suprarenal extract as required. With the pulmonary arteries whose muscular coats are not under the control of the sympathetic (Brodie and Dixon) he found that the pituitary extract produced constriction, and the suprarenal a slight dilatation. This has been confirmed by De Bonis and Susanna.[28.] The action on the renal arteries was not so marked but was still present. This Dale puts down to a relative insensitiveness of the renal arteries to the extract. It was found by Schafer and Magnus[26.] that the kidney expanded when pituitary extract was injected, and diuresis resulted. The various drugs of the digitalis group cause a similar action when

injected, but when perfused through the renal arteries they cause vasoconstriction, and there is no evidence that they act on nervous structures.

The uterus of the cat, in which animal the uterine tone and contractions are inhibited in the non-pregnant and stimulated in the pregnant animal by sympathetic nerves or suprarenal preparations (Cushny[29], Kehrer[30], Dale[31]) he found contracted powerfully on injection of pituitary extract both in the non-pregnant and pregnant state. He found that the muscular coats of the intestine and bladder contract in response to the pituitary extract, and not to suprarenal extract. He confirmed Schäfer's and Herring's[32] observations as to its action on glandular secretions. It does not cause secretion of the saliva nor of the pancreatic juice, whereas the suprarenal extract does.

He found that ergotoxine (the specific alkaloid of ergot) does not inhibit the action of pituitary extract injected after administration of ergotoxine. He had previously found that this substance inhibited sympathetic nerves, and that suprarenal extract injected after its exhibition produced a fall in blood pressure and a relaxation of the pregnant uterus in the cat.

Peptic digestion according to Schäfer and Herring[32] reduces the pressor effect of pituitary extract, but does not affect its diuretic action, but Dale found that it had no effect on either the pressor or diuretic action. On the other hand he found that trypsin destroyed both

actions. He further discovered that the urine of a cat treated with the extract contained the active pressor principle as I mentioned before.

His conclusions from these experiments are that pituitary extract acts directly on unstriped muscle, and not through the sympathetic system. Second doses are relatively ineffective suggesting that the active principle is not readily destroyed or rendered inactive in the body. A second dose, although not increasing the blood pressure, produces diuresis just as the first dose does, and also causes contraction of the uterus. This seems to imply that the same active principle produces both the rise inblood pressure and the diuresis.

Pathology.

The pituitary body has been the seat of new growths cysts, sarcoma, and adenoma, but the symptoms were those of intracranial tumour. Pathological conditions of the gland have been associated mainly with acromegaly, a disease which was first differentiated by Mairet[13] in 1896, although Cunningham in 1879 described a typical case in which a tumour of the pituitary body was found after death. Mairet was of opinion that the disease was closely associated with disease of the pituitary body, and that the overgrowth of the tissues and bones which are characteristic of acromegaly was due to excessive secretion. In support of this theory Cushing[7] found reduction in size of some enlarged bones on removal of the gland. On the other hand undoubted cases of acromegaly have been described where there was no evidence of disease of the gland. Deficiency of secretion is said to cause a form of arrested development known as Infantilism.

Pharmacology.

The active principle of the pituitary body is contained chiefly in the pars intermedia, and consists of a pressor substance soluble in salt solution but insoluble in alcohol and ether, and of a depressor substance soluble in all three. Neither of these substances is destroyed by boiling. Peptic digestion has no effect on the pressor substance, but tryptic digestion destroys it. When the extract is injected into a healthy person there is a rapid rise in blood pressure with slowing and augmentation of the heart beat, followed later by marked diuresis. The rise in blood pressure is very rapid. Within three minutes after an intramuscular injection I have found the blood pressure rise from 30 to 40 millimetres of mercury. If the injection is made into a mucous membrane the vasoconstriction is evident, the part becomes pale and remains so for some time. This vasoconstriction is due, as has been shown by many observers, to direct action of the extract on the unstriped muscular coat of the arteries. The diuretic action is attributed by some observers (Schäfer and Herring) to a separate active principle. They found that a second injection of the extract produced diuresis without any material rise in the blood pressure thus showing that the diuresis was not secondary to the rise in blood pressure. They further found that peptic digestion reduced the pressor, but did not impair the diuretic effect.

Dale on the other hand found no alteration from peptic digestion. He points out that the second injection acts strongly on the uterus although there is little rise in blood pressure, but does not consider that the principle which acts on the uterine muscle is different. from that which acts on the muscular coats of the arteries. He concludes from his experiments that the renal arteries are relatively insensitive to the vasoconstrictor effect of the extract, thus accounting for the swelling of the kidney and the diuresis, and is of opinion that there is no evidence of a separate diuretic principle.

The active principle diffuses slowly through animal membranes and, as it is destroyed by pancreatic digestion, is best given by intramuscular or intravenous injection.

The preparations I have used in my trials have been those prepared by Burroughs, Wellcome and Co. and Parke Davis and Co. The dose used was 1 c.c. equal to 0·2 gramme of the fresh gland but in Parke Davis' newer preparation the dose was 0·5 c.c. which was equal to 0·2 gramme of the fresh gland.

Clinical Work.

Before proceeding to use the drug in Midwifery, I made a series of observations on the blood pressure in labour and during the puerperium by means of the Riva Rocci Sphygmomanometer. I found that as a rule the blood pressure was high during the labour, and fell gradually afterwards, the pulse rate dropping pari passu.

Owing to the relatively high blood pressure I was rather anxious as to the result of injecting so powerful a pressor substance as pituitary extract.

I append reports of the cases on which I tried the drug, and will sum up the results afterwards.

Case. 1. A primipara, aet. 22. She had been in labour 24 hours. The os was fully dilated, and the waters gone. Presentation Occiput to the left posterior. I failed to alter the presentation. The pains were very weak and infrequent. The blood pressure was 150 Hg. and the pulse 100. I gave an intramuscular injection of 1 c.c. pituitary extract (B.W. & CO.) into the gluteal region. The blood pressure just afterwards was 170 Hg. pulse 90. Pains came on much stronger and more frequently but the head would not advance so I applied Forceps and delivered with some difficulty. The blood pressure after the birth of the child was 180 Hg. and pulse 85. Within a quarter of an hour after the birth of the child the placenta was extruded and the uterus contracted firmly. There was very little haemorrhage.

In twelve hours the blood pressure had dropped to 150 Hg. and the uterus was still well contracted. On the next day the blood pressure had fallen to 140 Hg. and there was a bright red raised rash on the buttocks with a rise in temperature to 101°F. The temperature remained up for a week, but I think this was due to sepsis as the woman was not properly nursed and her surroundings were of an unsatisfactory character. She made a good recovery. Diuresis was marked.

Case II. A multipara, aet. 36. She had been in labour some hours. The os dilated and waters gone. No pains. Presentation 1st cranial. I gave a drachm of the liquid extract of ergot by the mouth and came back in an hour with my sphygmomanometer. Her blood pressure then was 160 Hg. and pulse 115. There were still no pains. I waited six hours and then applied forceps and delivered. The blood pressure just before the application of forceps was 135 Hg. and pulse 100. After the birth of the placenta the blood pressure dropped to 110 Hg. Three hours later I was called as she was bleeding. I found her collapsed and a considerable loss of blood had taken place. I had no pituitary extract then so I administered 1/100 gr. of ergotinine intramuscularly combined with 1/100 gr. of strychnine. The uterus contracted well and the haemorrhage stopped. Next day her blood pressure was 115 Hg. pulse 110. On the fifth day her blood pressure was

97 Hg. and pulse 108 so I administered 1 c.c. of pituitary extract (B. W. & Co.). In three minutes the blood pressure was 120 Hg. and the pulse 100; in ten minutes the blood pressure rose to 140 Hg. pulse 98. Six hours after the blood pressure was 118 Hg. and remained about that level during the rest of the attendance. She made a good recovery and had no rise in temperature and no rash; diuresis was also noted in this case.

Case III. A primipara, aet. 26. I found the os fully dilated and head well advanced in the 1st cranial position. The abdomen large, a twin pregnancy. The second child was a footling presentation, both born without difficulty. Ten minutes after the birth of the second child I gave an intramuscular injection of 1 c.c. pituitary extract (B.W. & Co.). The blood pressure before the birth of the children, 125 Hg. and pulse 80. In two minutes after the injection there was a violent contraction of the uterus and the large placenta with the cord was shot out. The uterus contracted to a small ball, and there was no loss of blood. The blood pressure afterwards was 150 Hg. pulse 75. The blood pressure remained high for the next 24 hours. There was marked diuresis. No rash appeared. She had a rigor on the night of the third day but no evidence of any sepsis. This rise in temperature continued for a week with no bad symptoms. She made a good recovery.

Case IV. A primipara, aet. 20. I found labour well advanced. Presentation 1st Cranial. Blood pressure

125 Hg. pulse 90. The pains were very feeble and infrequent. After waiting an hour there was no improvement in the pains. I gave intramuscularly 1 c.c. Pituitrin (P.D. & Co.). Three minutes after the injection the blood pressure was 170 Hg. pulse 70. The pains came on very strongly and the birth occurred in half an hour after the injection. Two hours after the injection the blood pressure was 160 Hg. pulse 80. On the second day the blood pressure dropped to 145 and on the third day to 140 Hg. On the fourth day it was down to 125 Hg. There was no elevation of temperature and no rash but marked diuresis. The uterus after expulsion of the placenta remained firmly contracted.

Case V. A primipara, aet. 26. This case progressed satisfactorily till the head reached the outlet of the pelvis where there was some narrowing. I applied forceps and got the head through the narrow part and then removed the forceps and the labour terminated naturally. After the birth of the placenta haemorrhage came on and the uterus remained flabby so I gave an injection of 0·5 c.c. Pituitrin (P.D. & Co.).

(This preparation being double the strength of the original extract I used half the dose.) The effect was marked, the uterus contracted promptly and the bleeding stopped. The blood pressure which before the birth of the placenta had dropped from 126 Hg. to 120 Hg. rose within ten minutes to 150 Hg. This pressure was main-

tained for the next 24 hours. The pulse also became slower from 100 before the birth of the placenta to 80 after the cessation of the haemorrhage. Diuresis was also present. The uterus remained well contracted. No rash supervened and no rise in temperature took place. The patient made a good recovery.

Case VI. A primipara, aet. 22. This was a case of precipitate labour. The blood pressure before the birth of the placenta was 120 Hg. and pulse 98. As a precaution I administered 0·5 pituitrin (P.D. & Co.) before the placenta was born. In three minutes the uterus contracted and expelled the placenta. There was no haemorrhage. The blood pressure afterwards was 145 Hg. and pulse 78. Twelve hours later the blood pressure was 140 Hg. and the pulse 80. There was a slight rash on the buttocks, no rise in temperature, but marked diuresis. The case progressed satisfactorily.

Case VII. Multipara, aet. 36. This case had been in labour six hours when first seen. I found the os full, the membranes intact, and the presentation, 1st cranial. The blood pressure was 140 Hg. and the pulse 95. Labour proceeded normally. The blood pressure before and after the birth of the placenta remained 140 Hg. I administered 0·5 c.c. of Pituitrin (P.D. & Co.) after the birth of the placenta, and in four minutes the blood pressure was 170 Hg. and the pulse 78. The uterus became considerably smaller after the injection. The

blood pressure remained high for the next twenty four hours but on the third day it dropped to 125 Hg. There was no rash, no rise in temperature, but diuresis was present. The patient showed no ill effects from the drug.

Case VIII; Multipara, aet. 38. In this case the os was fully dilated the membranes intact and pains absent. I ruptured the membranes. The presentation was lst Cranial. After waiting an hour, as the pains were few and weak, I decided to try Pituitrin and gave 0·5 c.c. intramuscularly. The blood pressure before injection was 135 Hg. and the pulse 97. Ten minutes after the injection the pains came on sharply and the blood pressure rose to 150 Hg. the pulse then being 80. Birth took place in twenty minutes from the time of the injection and the third stage was completed ten minutes later. Four hours later the blood pressure was still 150 Hg. and the pulse 78. On the second day the blood pressure was 140 Hg. but it dropped on the third day to 123 Hg. In this case diuresis was not a marked feature and there was no rash and no rise in temperature. The patient made an uninterrupted recovery.

Case IX. A primipara, aet. 25. A case of protracted labour. The patient became very exhausted and as a precautionary measure ten minutes after the birth of the child I administered 1 c.c. Pituitary Extract (B.W. & Co.). The uterus promptly responded and shot out the placenta. The patient's condition was much improved after the in-

jection. Her blood pressure before the injection was 130 Hg. and afterwards 160 Hg. The pulse fell from 100 to 84. At the end of twenty-four hours the pressure was 140 Hg. and the patient's condition very good. There was no rise in temperature, no rash but marked diuresis. The patient made a good recovery.

Case X. A multipara, aet. 37. She had been in labour ten hours. The os was fully dilated and the waters gone, presentation first cranial. The blood pressure was 140 Hg. and the pulse 98. I gave 0·5 Pituitrin (P.D. & Co.) and the pains improved. The blood pressure rose to 170 Hg. and the pulse dropped to 80. About a quarter of an hour after the injection the baby was born and the placenta followed rapidly. The uterus contracted well and there was no haemorrhage. The blood pressure six hours afterwards was 165 Hg. and next day had fallen to 150 Hg. On the third day it was 125 Hg.

There was no rash and no rise in temperature but marked diuresis.

Case XI. I had an opportunity of trying the drug in an early case of Grave's disease. The chief symptoms were palpitation and tremors, and the thyroid gland was distinctly enlarged. The exophthalmos was very slight. I gave in all three injections of the extract. The blood pressure before treatment was 120 Hg. and the pulse 100. After the first injection the blood pressure

rose to 140 mg. and the pulse fell to 86. The pressure remained up for twenty-four hours, and then came back to original level, the pulse did not rise but remained between 86 and 90. I gave the second injection on the third day and got a rise in blood pressure to 128mg. the pulse falling to 84. The pressure came back to the original level in ten hours but the pulse remained steady. The third injection was on the sixth day and the rise in pressure was only to 124 mg. the pulse remaining steady. There was a slight improvement in the tremors, but otherwise the treatment did not seem of much avail. Diuresis occurred after each injection. The patient was a girl of 20 years old. She has since gone into hospital with a view to operation.

Summary and Conclusions.

	Blood pressure.		Pulse.		Result.
	Before injection.	After.	Before.	After.	
.	150 Hg.	170 Hg.	100.	90.	Increased Uterine Contractions.
.	97 Hg.	140 Hg.	108.	98.	Conteracted Shock.
.	125 Hg.	150 Hg.	80.	75.	Violent Uterine Contraction.
.	125 Hg.	170 Hg.	90.	70.	Increased Uterine Contractions.
.	120 Hg.	150 Hg.	100.	80.	Stopped post-partum Haemorrhage.
.	120 Hg.	145 Hg.	98.	78.	Prevented post-partum Haemorrhage.
.	140 Hg.	170 Hg.	95.	78.	Uterus contracted well.
I.	135 Hg.	150 Hg.	97.	80.	Increased Uterine Contractions.
.	130 Hg.	160 Hg.	100.	84.	Uterus contracted well.
.	140 Hg.	170 Hg.	98.	80.	Increased Uterine action.

In all my cases I found that the extract had a definite action on the uterus causing increased contraction; that it caused a rapid rise in blood pressure which was maintained for from twelve to twenty-four hours; that there was a marked slowing of the pulse rate; and that diuresis was produced. Of the two cases in which I got a rise in temperature, Case I. had undoubtedly some septic mischief. She was not kept clean and there was a

perineal tear which did not heal well. In Case III. I could find no evidence of sepsis but as I had no increase in temperature in any other case I feel inclined to place the cause of the rise in temperature here to sepsis. In Case II. it is interesting to note the blood pressure after ergot by the mouth. I unfortunately did not have my sphygmomanometer with me before the administration but an hour afterwards the pressure was 160 Hg. and dropped in six hours to 110 Hg. Later on when I administered the ergotinine and strychnine the pressure must have been very low as the patient was almost pulseless and in twelve hours it was 115Hg. But the high pressure did not last and on the fifth day had fallen to 97 Hg. This was an opportunity for trying pituitary extract for shock and it proved admirable, the pressure rose rapidly to 140 Hg. and although six hours after it had dropped to 118 Hg. that level was maintained, and the patient's recovery was undoubtedly facilitated by the use of the drug.

In two cases a rash was noted, but only in case I. did it give any trouble.

In Case V. the value of the extract in post-partum haemorrhage was distinctly evident. It promptly stopped the haemorrhage, and the uterus remained well contracted afterwards. In Case VI. I think I am justified in saying that had it not been for the extract post-partum haemorrhage would have supervened. The other cases

show that the drug has a decided action on the uterus and that it is free from danger. Had there have been an adherent placenta in any of the cases in which the drug was given before the completion of the third stage of labour, I quite anticipate I would have had considerable trouble in emptying the uterus. I think there is a certain amount of risk in giving the extract before the end of the third stage. In post-partum haemorrhage I think it will supersede ergot or any of its preparations. In shock its power of rapidly raising the blood pressure, and maintaining it at a high level for some hours makes it a most valuable drug.

As I said in the introduction "the value to the obstetrician of a drug which will produce powerful and sustained contractions of the uterus goes without saying, and in extract of the pituitary body (infundibular portion) I believe we have such a drug."

My cases are few but I think I am justified in saying that they support my belief.

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