PITUITARY EXTRACT

With notes on its action in Midwifery

recorded at

Queen Charlotte's Lying-in Hospital.

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by

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## Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introductory</td>
<td>1</td>
</tr>
<tr>
<td>Historical</td>
<td>6</td>
</tr>
<tr>
<td>Anatomy and Embryological Development</td>
<td>16</td>
</tr>
<tr>
<td>Physiology</td>
<td>21</td>
</tr>
<tr>
<td>Pharmacology</td>
<td>28</td>
</tr>
<tr>
<td>Clinical Work</td>
<td>30</td>
</tr>
<tr>
<td>Summary and Conclusions</td>
<td>51</td>
</tr>
<tr>
<td>Bibliography</td>
<td>54</td>
</tr>
</tbody>
</table>
Within recent years Organotherapy has made greater advances than perhaps any other branch of medicine.

Myxcedema and Cretinism have been definitely proved to be caused by a deficiency or total absence of thyroid gland secretion and an extract of this gland is now the specific treatment for these diseases. Experimental work on adrenalin, an extract of the suprarenal gland, soon proved it to be one of the most powerful styptic drugs we possess. Adrenalin acts by causing local vaso-constriction and powerfully raises the blood pressure, hence it is largely used in the treatment of shock. The active principle of adrenalin has been isolated and a synthetic preparation produced which answers to the tests of the natural extract.

A year after the discovery of suprarenal extract Oliver and Schäfer described the physiological effects produced by extract of the pituitary body.

For some time the extracts of pituitary and suprarenal gland appeared to have the same action, that of the latter being most marked, and in this way pituitary extract as a therapeutic agent fell into obscurity.

A little later Fröhlich and Frankel-Hochwart showed by their experiments that pituitary extract causes contraction of the uterus of pregnant rabbits. Foges/
Foges and Hofstadter used this extract in cases of atonic post partum haemorrhage and Hofbauer was the first in Germany to use pituitary extract for stimulating the pains of labour.

In this country a paper was published by Blair Bell in 1909, bringing pituitary extract prominently into notice and he described its action in cases of shock, uterine atony and intestinal paresis. Other observers soon confirmed these 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. This fact is all the more important since Malcolm Donaldson has just published a paper pointing out the fact that the use of adrenalin in the treatment of shock is in the majority of cases really harmful. He proved that whilst adrenalin increased the blood pressure, it also increased the pulse, thus putting more strain on the heart, pituitary extract, on the other hand, raises the blood pressure and slows the pulse.

That pituitary extract is of great value in the treatment of shock is proved by the fact that it is used as a matter of routine, in all Hospitals, for the treatment of surgical shock after severe operations. The active principle of pituitary extract has not yet been isolated, but much recent work on this subject has been done by many observers.

Lewis/
Lewis, Miller and Matthews made extracts of the various anatomical component parts of the pituitary body and found that the 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 anterior and the pars nervosa.

The separation of this depressor substance from the extract will make the drug more valuable and its action more certain.

Dale, experimenting with pituitary 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 substance is excreted in the urine.

The number of enthusiastic admirers of pituitary extract as a sovereign remedy for stimulating the pains of labour has grown larger and larger and it is in daily use for this purpose in all Maternity Hospitals.

During the eight months I was resident medical officer at Queen Charlotte's Hospital, I had a large experience in the use of pituitary extract and its prompt and certain action impressed me very markedly.

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 in which I have used the preparation.

Observations/
Observations on blood pressure in pregnancy and during the puerperium in a normal parous woman were first made, using for the purpose a Riva Rocci sphygmomanometer. Records of the blood pressure were taken before and after the injection of the pituitary extract, 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. The duration of the labour pains and the interval separating them was also estimated before and after injection of the extract. This was done by holding the hand easily and quietly on the uterus; this method is not without its drawbacks but it gives a clear idea of the intensity and strength of the pains.

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 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.

Rosenheim showed that the pressor substance was due to incipient putrefaction in the placenta and had the same chemical composition as the pressor substance (animal)/
(animal) obtained from putrid meat. It is now known that extract of fresh pituitary gland 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 preparation 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 preparation.

There is no doubt that in the case of weak pains in the second stage of labour pituitary extract is of the greatest use, because by means of this product, the application of forceps can certainly be avoided. In my opinion this one property is quite sufficient for pituitary extract to occupy a prominent place in obstetrics.
There are records in ancient medicine of animal substance 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".

With the growth of scientific methods and the development of the modern spirit of inquiry, 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 usefulness/
usefulness. In 1894 Oliver and Schäfer's researches on these bodies were the starting point of a line of inquiry 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 bloodstream 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 quickly 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 in 1895, the above two workers were the first to discover the fact that the extract of the pituitary body also produced a rise in blood pressure. They showed that this hypertension results partly from contraction of the vessels and partly from increased cardiac activity and that it is not affected by resection of the cord or destruction of the medulla. The peripheral effect of the hypertension was illustrated by the fact that if a fluid containing pituitary extract is circulated through the hinder extremities of the frog there is a reduction of the venous outflow. The increased cardiac activity was demonstrated by myographic tracings which they obtained with the heart after its removal from the living body. The effects of pituitary extract upon the circulation, though resembling those produced by adrenalin, differed in certain important particulars/
particulars. The vaso-constriction action was much slighter and the slowing of the pulse together with the inhibition of auricular contraction produced by adrenalin when the vagi are intact was absent in the case of pituitary extract. On the other hand, after resection of the vagi, pituitary extract produced not an acceleration but a retardation of the cardiac beats.

There the matter was allowed to rest for a time, the suprarenal overshadowing the pituitary.

Researches into the character of the suprarenals continued and eventually the active principle was isolated.

Howell, in 1898, discovered that it was extract of the posterior lobe and not that of the anterior lobe alone which produced peripheral vaso-constriction, slowing of the pulse and hypertension; he also found that a second injection given half an hour after the first had practically no effect on the circulation.

These findings were confirmed by Schäfer and Vincent, who discovered that the second injection is followed by a fall instead of a rise in blood pressure.

According to these authors, the fall in pressure is brought about by the action of a second substance with depressant properties which is obtainable by extraction with absolute alcohol, treatment of the alcoholic residue with ether and solution in sodium chloride.

The hypo-tension produced by injecting this substance is similar to that produced by the injection of cholin/
cholin but, unlike the latter, is unaffected by atropine.

Schäfer and Magnus found that the extract of the posterior lobe produced a well marked diuresis by reason of a selective vaso-dilator action on the vessels of the kidney and of a specific stimulation of the renal epithelium.

Livon confirmed the effects of pituitary extract in raising the blood pressure and slowing the pulse. The latter where the vagi were intact, however.

Silvestri obtained only a fall of blood pressure with extract of the posterior lobe even after the injection of a quantity equal to one fifth of the posterior lobe.

Garnier and Shava observed a rapid rise in pressure with slowing of the pulse, followed after ten to twelve seconds by a rapid transient fall in pressure which was again followed by a marked rise. The slowing of the pulse was not observed after resection of the vagi. Similar results were reported by Lockhart, Mummery and Legge.

Salvioli and Carraro considered that the peripheral muscular constriction which causes the hypertension depended more upon a direct action on the vessel walls than upon an excitation of the vaso-motor centres.

Ballion and Carrion, by means of plethysmographs of different organs, showed that the rise in blood pressure brought about by pituitary extract was associated with a vaso-constriction in various organs, more/
more especially in the nasal mucosa and thyroid gland. In the kidney there was, after an initial vaso-constriction, a prolonged vaso-dilation. They pointed out the antagonistic effects of pituitary extract and those of ovarian extracts. The latter produce a fall in blood pressure together with a vaso-dilation of the thyroid gland.

Falta and Ivocavi stated that they injected 2.5 c.c. of the extract of the glandular portion of the pituitary body into dogs and rabbits and obtained a marked fall in blood pressure, which in atropined animals lasted for a comparatively long time. The lowered pressure which at the end of forty seconds returned to the normal figure could be relieved by the injection of adrenalin or by the extract of the infundibular portion of the pituitary body.

Herring, in experiments with the living heart from frogs and mammals, showed that the slowing of the heart with pituitary extract was unaffected by resection of the vagi and considered that pituitary extract acted directly on the muscular fibres of the heart. He also 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.

Bell and Hick described the action of these extracts/
extracts on the uterine muscle and came to the same conclusion.

Dale, after a long series of experiments, proved that pituitary extract acts directly on unstriped muscle, whereas suprarenal extract acts through the sympathetic nerves.

(Langley, Brodie and Dixon, and Elliott.)

Schäfer (1909) studied the effect upon the pituitary body of mechanical injury or of partial destruction by means of a feeble thermo-cautery. Injury of the organ, when not extensive, causes no pronounced symptoms other than increased secretion of urine which is accompanied by increased production of colloid by the pars intermedia. This 'colloid' material contains active principles or hormones which act upon the heart, blood vessels and kidneys. Similar examples of the effect of injury were reported by Cushing and Goetach (1910).

The effect of another kind of injury is shown by the results of experiments carried on by Weed, Cushing and Jacobsen (1913). They attempted to produce a glycosuria in cats by puncture in the region of the pituitary body itself, with a resultant glycosuric response (provided there was available glycogen in the system) comparable to a picture of Bernard's centre itself.

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

Schiff a year later administered pituitary gland to a healthy person without noticing the slightest change in the ordinary secretion.

Violotz obtained a marked rise in blood pressure and contraction of the uterus in cases of atonic uterine bleeding and considers pituitrin superior to ergot for this condition.

Parisot in 1907 injected 3 c.c. doses of pituitary 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 quantitative change in the urinary secretion.

Delille (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.

Ott and Scott, and Schäfer and Mackenzie found that extracts of the posterior lobe of the pituitary body contain a powerful galactogogue substance more powerful than that produced by Corpus Luteum extract.

Blair/
Blair Bell in 1909 found that pituitrin caused powerful contractions in the pregnant, puerperal and menstruating uterus. It caused a prolonged rise of blood pressure, strengthened the heart and slowed the pulse. He found it of extreme value for causing efficient contraction of the uterus after delivery and checking post partum haemorrhage.

He also found it of good service in obviating or removing the distressing intestinal paresis and paralytic distension of the intestines which follow abdominal operations.

Hofbauer used pituitrin as a means of exciting and aiding labour pains. He records good results in cases of delayed labour pains and in placenta praevia.

Foges and Hofstädtler used pituitrin in cases of post partum haemorrhage and in delayed contraction of the uterus after Caesarean Section and received good results from its use. Hofstädtler further found that pituitrin permanently relieved 75% of cases of anuria or dysuria following labour or gynaecological operations.

Malinowsky used pituitary extract in cases of labour in the second stage and noted that the contractions of the uterus became stronger and more frequent. No cases of atony of the uterus occurred. He considered that pituitary extract is contraindicated where the mother is subject to cardiac or renal disease.

Stein, Bondy, Aarons, Jaeger, Hanch and Meyer, Eisenback and Adacter have used pituitary extract in cases/
cases of child-birth and uterine haemorrhage and atony, and all claim good results from its use as a powerful agent in producing uterine contractions without causing any ill effects to mother or child.

It has been long known that in the later stages of pregnancy there occurs regularly a definite hyperplasia of the pituitary body with hyperplasia of its cellular elements, a condition which must be considered physiological.

There is an actual increase in size and weight (Comte 1898) especially in the anterior lobe.

Erdheim and Stimme (1909) showed from their studies of a long series of glands from pregnant women, that the pituitary gland actually increased in size and weight, that there was a change in colour, particularly of the anterior lobe, from pinkish grey to white, a fact which they attributed to an increase in chromophil elements. Histologically there is seen a marked increase of large neutrophilic cells derived from the normal small chromophobe cells, the so-called "Hauptzellen" or chief cells. Within a few months post partum retrogressive changes occur and the pregnancy cells return to the type of chief cells and the gland once more assumes its normal appearance.

Herring (1906) believes that the colloid occurring in the posterior lobe of the pituitary body is a secretion of the epithelial lining the so called pars intermedia and that it passes through the meshes of/
of the posterior lobe to the ependymal lining of the third ventricle. It then passes between the ependymal cells and escapes into the cerebro-spinal fluid. This author showed that in rabbits after thyrodeectomy this colloid was increased in amount.

Cushing and Goetsch (1910) confirmed Herring's views and they showed by injection intravencously into rabbits that there is a substance in the cerebro-spinal fluid which gives the same reactions as extracts of the pars nervosa itself. "This would seem to establish the theory that the hyaline bodies of the pars nervosa regarded by Herring as products of secretion of the posterior lobe actually discharge into the third ventricle and represent the source of the active substance resembling pituitrin in the cerebro-spinal fluid."

The investigation of pituitary 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 EMBRYOLOGICAL DEVELOPMENT.

The pituitary body was regarded by the ancients as a glandular structure which discharged a mucous secretion (pituita-mucus) into the nostrils. The term Hypophysis cerebri was first applied by Soemmering in 1778.

The pituitary body consists of two genetically entirely different portions, a large anterior, glandular, epithelial portion called the anterior lobe or the "pars anterior" and a smaller posterior or nervous lobe, the "pars nervosa" or infundibular portion, composed of nervous tissue, the whole connected with the floor of the third ventricle of the brain by means of the stalk or infundibulum.

A further subdivision is made of the epithelial portion into the "pars intermedia" called also the intermediate lobe or the epithelial investment of the posterior lobe which also completely surrounds the pars nervosa and sends off epithelial cells into it.

The pituitary body is found in this form in mammals, birds and bony fishes. The pars intermedia is separated from the pars anterior by a cleft, the residual lumen of the extodermal invagination from the pharynx. The anterior lobe is developed - in man in the fourth week - from an ectodermal pouch which evaginates from the roof of the bucco-pharyngeal cavity in/
in the direction of the mid-brain and is called from
the name of the man who first described it,
Rathke's (1838) pouch. This process was later
described in greater detail by Mikalkowics (1875).
Rathke believed that the epithelial portion of the
pituitary body was derived from this pharyngeal invag-
ination but that it was of entodermal origin. Müller
(1871) also demonstrated that the anterior lobe is
derived from Rathke's pouch, but believed similarly
that it was of entodermal origin.

Later researches show that the pouch is derived
from the epithelium of the buccal cavity immediately
in front of the oral plate. By the subsequent growth
and formation of the sphenoid bone, the cavity of
Rathke's pouch becomes constricted off and obliterated
with the exception of the tip, which remains as the
cleft in the adult gland, a line of cleavage between
the thinner, less differentiated, posterior portion of
the hypophysial vesicle and the thicker, more highly
specialised and differentiated anterior lobe.

This posterior surface, which develops into the
pars intermedia, applies itself to a downgrowth of
nervous tissue from the mid-brain or third ventricle
called the infundibulum, which becomes the stalk of
the pituitary body. This process gives rise to the
posterior or nervous portion of the hypophysis.

The term "posterior lobe" in later investigations
has/
has come to mean the true nervous portion of the gland, together with its epithelial investment.

The original canal connecting the pituitary gland with the pharynx becomes constricted off and remains as a solid strand of cells connected with the pharyngeal epithelium, in which it is gradually lost. It was formerly the opinion of most observers that the embryonic remnants or "rests" of the original Rathke's pouch and its pharyngeal connection became entirely obliterated and were never to be considered again. The excellent work of Erdheim, Harujiro, Aroi and Haberfeld has demonstrated to us, however, that embryonic "rests" are frequently found in the adult along the path of ascent of the hypophysis from the pharynx to its final resting place in the sella turcica.

Erdheim (1904) was the first to emphasize the fact that it is not at all uncommon to find near the hypophysial cleft and applied to the infundibulum, inclusions of squamous, epithelial cells or even ciliated cells in groups, which represent presumably "rests" of the primitive ectoderm of Rathke's pouch and which undoubtedly give rise to certain epithelial growths and cysts which are frequently found in this region.

Erdheim drew attention also to the occurrence of hypophysial tissue in the pharyngeal vault in a number of foetuses and new born infants.

This/
This tissue was regarded as a remnant of the pharyngeal end of the canal connecting with Rathke's pouch and was called by him the "Rachendachypophyse". The latter was also described by Harujiro Aroi (1907) under the name of "Hypophysis Accessoria pharyngea". Occasionally a bony canal persists in the body of the sphenoid and connects the pharyngeal hypophysis with the floor of the sella turcica. The term "canalis craniopharyngeus" has been applied to it.

Here and there embryonic remnants are sometimes found in this canal in the body of the sphenoid bone. These findings stimulated Haberfeld (1909) to a very thorough study of the subject in a series of foetuses, newborn children, adults and in the aged. He showed that in a careful search of the pharyngeal vault, without regard to age or sex, there was to be found without exception a cell cord with a connective tissue envelope and consisting of cellular elements identical with those of the anterior lobe of the hypophysis. The length of this gland varied according to the age from 1 - 7 mm. and from 7/5 - 1 mm. in width and thickness. On account of the constancy of this tissue and its similarity in structure to the anterior lobe of the pituitary gland, he felt that it should be considered as an independent structure with a distinct function of its own and therefore suggested for it the name of "hypophysis pharyngea".

This/
This finding is important not only for pathology but also for physiology, for it becomes at once evident that in speaking of the effects of total removal of the pituitary gland one must always think of a possible compensating action of this glandular structure as well as of other embryonic "rests" mentioned.

One of the greatest difficulties which has stood in the way of investigators of the pituitary gland has been its inaccessibility. It lies in the most protected spot in the skull, encased in the bony sella turcica and in the anterior angle of the optic chiasm. A firm fibrous connective tissue layer, the diaphragma sellae, a part of the dura mater separates it from the cranial cavity and allows only of the passage of the pituitary stalk or infundibulum through a perforation in its middle.

The normal pituitary gland varies very much in size and weight. After birth it gradually increases in size and reaches its maximum between the thirtieth and fortieth year of life.

According to Schöinemann (1892) its average weight is 0.59 grm.
Physiology.

The question as to whether the pituitary body or one of its parts is necessary to life has been investigated by many observers. The whole organ has been successfully removed by Marinesco in cats and by Vassale and Sacchi in dogs, and more recently by Paulesco and Harvey Cushing.

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. Handelmen and Horsley, 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 microscopical examination. Eight of the fifteen died within forty-eight 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/
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 these 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 pars intermedia 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 were the pioneers in this line of investigation. They injected an extract of the whole gland into animals/
animals and described a rise in blood pressure as the
result, but concluded that the effect was similar to
that produced by suprarenal extract. Howell then made
extracts from the anterior and from the posterior lobes
and found the latter contained the pressor principle.
This was confirmed by Schäfer and Vincent and more
recently Lewis, Miller and Matthews made extracts of
the various parts of the gland. Their results may
be briefly enumerated. Extracts of the pars intermedia
intravenously injected gave a divided rise in blood
pressure, 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 pars intermedia gave a marked pressor effect.
They conclude that the pressor substance is elaborated
in the pars intermedia and passes into the posterior
part (the 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 discovered that the extract had a
diuretic effect due, they supposed, to a selective
action (vaso-dilator) on the vessels of the kidneys.
Dale was the first to record its effect on the
uterus. This he discovered during an inquiry into the
action of ergot. To Blair Bell is due the honour of
putting this fact to practical use. After a series of
experiments in conjunction with Hick, in which they
discovered that the pituitary extract had, besides
its/
its action in raising the 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 haemorrhages he found it acted promptly and satisfactorily. He noted in his experiments with 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 of the extract it was generally held that it was similar to suprarenal extract so far at least as regards vaso-constriction. The points of similarity of/
of the two extracts may be briefly mentioned - both raise the blood pressure, peripheral vaso-constriction being a principle factor in the effect (Schäfer and Oliver), 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 suprarenal to the sympathetic system. Langley showed that suprarenal extract produces symptoms exactly similar to those which are produced by stimulating nerves of the true sympathetic system, and this was confirmed by Brodie and Dixon and by Elliott. The pituitary extract, on the other hand, does not do so, but acts directly on unstriped muscle. Dale, 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 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. 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/
the extract. It was found by Schäfer and Magnus that the kidney expanded when pituitary extract was injected and diuresis resulted. The various drugs of the digitalis group cause similar action when injected, but when perfused through the renal arteries they cause vaso-constriction, 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 (Cushing, Kehrer, Dale), he found contracted powerfully on injection of pituitary extract both in the non-pregnant and in the 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 and Herring's observations as to its action on glandular secretions. It does not cause secretion of the saliva nor of the pancreatic juice, whereas the suprarenal 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 of a cat.
Peptic digestion, according to Schäfer and Herring, 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 in blood pressure and the diuresis.
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 and 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's beat, followed later by marked diuresis. The rise in blood pressure is very rapid. Within three minutes after intramuscular injection the blood pressure rises from ten to twenty millimetres of mercury. If the injection is made into a mucous membrane the vaso-constriction is evident, the part becomes pale and remains so for some time. The vaso-constriction 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 blood pressure, thus showing that the diuresis was not secondary/
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 does act 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 vaso-constriction 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 preparation I have used in my trials is pituitrin prepared by Parke Davis & Co.

The dose used was 0.5 c.c., which was equal to 0.2 gramme of the fresh gland.
CLINICAL WORK.

Pituitary extract has been used very extensively in the labour wards at Queen Charlotte's Lying-in Hospital during the last year with very striking results.

We found it especially useful in the treatment of two classes of case, (1) Accidental haemorrhage, where it is used now as a matter of routine, and (2) for weak pains in the second stage where for some reason, as in the case of an induction baby, we did not wish to apply forceps.

Unfortunately no records have been made of the use of pituitrin at this hospital, so I thought a few notes as to its action in these cases and its effect on the pulse, blood pressure and uterus would be extremely interesting.

It is certain that by the use of pituitrin in the case of weak pains in the second stage, the application of forceps can be avoided.

This fact will be fully appreciated by practitioners who will be saved the trouble of chloroform administration, and the attendant risks of sepsis from forceps delivery. I was unable to get many records of these cases, as in a large teaching school like Queen Charlotte's I needed them to demonstrate/
demonstrate the application of forceps to students.

Before making records on the above cases, I made a series of observations on the blood pressure in labour and during the puerperium, on a normal parous woman. The blood pressure was estimated by means of a Riva Rocci sphygmomanometer. I found that as a rule the blood pressure was high during labour, and fell gradually afterwards, the pulse rate dropping pari passu. In my experiments the duration of the pains was estimated by holding the hand easily and quietly on the uterus.

I know quite well this method is not without its drawbacks, but it gives a clear idea of the intensity and strength of the pains.

The pulse, blood pressure, the interval between and duration of the pains were noted before the pituitrin was given, and then ten minutes, half an hour, and every consecutive hour up to four hours after it was given. The preparation used was Parke Davis & Co.'s pituitrin, dose 0.5 c.c., equal to 0.2 gramme of the fresh gland. This was injected into the thigh in all cases.

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

Case 1. Accidental Haemorrhage - External and Concealed.

Mrs. H. Act. 42. 16th Gravida. 35 weeks pregnant.

Obstetric History. 12 children born alive. 3 miscarriages.

Pelvic/
Pelvic Measurements. Interspinous 9½"  
Intercristal 10½"  
External Congugale 7¾".

History. On 8th October one of her fellow workers in laundry fell down and this gave patient a great fright. She felt quite well on returning home and went to bed at her usual time. She had a severe haemorrhage at 5.45 a.m. and woke up with the bed clothes soaked in blood.

She called in Doctor in morning and he sent her into Queen Charlotte's where she was admitted at 11.40 a.m.


Per Vaginam. Os admitted two fingers. No placenta could be felt. Foetal head soft and boggy. Membranes unruptured.


0.5 c.c. Pituitrin given at 12.30 p.m. Os admitted two fingers.

12.40 p.m. Pulse 117. B.P. 120. Uterus contracting every 15 minutes; duration of contraction, 20 seconds.

1 p.m. Pulse 115. B.P. 127. Uterus contracting every 10 minutes; duration of contraction, 20 seconds.

2 p.m./
2 p.m. Pulse 110. B.P. 130. Uterus contracting strongly every 2 minutes: duration of contraction, 30 seconds.

Patient reached second stage at 2.15 p.m. and at 2.20 p.m. gave spontaneous birth to a macerated foetus weighing 5 lbs. 1 oz. and 18\(\frac{1}{2}\)" long.

The placenta was born six minutes after foetus and was accompanied by blood clot as big as itself. There was only 24 oz. of haemorrhage in third stage.

Mother made excellent recovery.

Case 2. Accidental Haemorrhage - Accidental and concealed.

Mrs. E. Aet. 35. 7th Gravida. 36 weeks pregnant.

Obstetric History. Six children born alive.

Pelvic Measurements. Interspinous 10". Intercristal 10\(\frac{3}{4}\)". External Conjugale 7\(\frac{3}{4}\)".

History. Patient admitted from district at 10.30 a.m. with history of severe haemorrhage at 2 a.m., about 2 pints blood having been lost.

Condition of patient when admitted gave rise to anxiety. She was very blanched, vomiting and having attacks of syncope. She was not losing and her pulse was only 98 and her temperature 98.6°F.

On Examination. Per abdomen. Uterus very tense, tender and distended, indicating concealed haemorrhage. Foetal parts very hard to palpate and position of child could not be made out. No foetal heart heard.

Per vaginam. Os admits two fingers, no placenta could be felt. Buttock of foetus presenting, legs extended/
extended. Membranes tense and unruptured.

Patient having very slight pains and not losing.

Treatment. Tight abdominal binder applied and membranes ruptured at 10.45 a.m.

11.30 a.m. Pulse 100. B.P. 95 mm. Hg. Uterus contracting weakly every 15 minutes. Duration of contraction, 20 seconds.

11.45 a.m. 0.5 c.c. Pituitrin injected. Os admits two fingers.

11.55 a.m. Pulse 98. B.P. 95 mm. Hg. Uterus contracting every 15 minutes. Duration of contraction, 20 seconds.

12.15 p.m. Pulse 98. B.P. 112 mm. Hg. Uterus contracting very strongly every minute. Duration of contraction, 30 seconds.

At 12.45 p.m., after having been in second stage five minutes, patient gave birth to a stillborn foetus which was followed immediately by the placenta accompanied by two large blood clots, indicating concealed haemorrhage. There was severe haemorrhage in third stage and another 0.5 c.c. Pituitrin was given. This had little effect on the uterus, so 20 mins. ermitin was given and a hot lysol douch, this completely controlled the haemorrhage.

Mother made excellent recovery.

Case 3. Placenta Praevia, - Marginal.

Mrs. C. Aet. 40. 13th Gravida. 40 weeks pregnant.

Obstetric History. Ten children born alive. Two miscarriages.

Pelvic Measurements. Interspinous 10\frac{1}{2}"
Intercrisal 11\frac{1}{4}"
External conjugale 8".
History. Patient admitted at 4.30 p.m. from district with history of having severe haemorrhage at 1.30 p.m. losing 1½ pints blood.


Per vaginam. Os admits two fingers. Edge of placenta can just be reached. Vertex presentation, left occiput anterior position. Patient not losing.

Treatment. As patient was very collapsed on admission and pulse 144, it was thought advisable to put on a tight binder, raise foot of bed and keep her quiet for a time. In two hours her condition had greatly improved, her pulse was down to 125 and she was having weak pains. The membranes were now artificially ruptured.

7.45 p.m. Pulse 125. B.P. 112 mm. Hg. Uterus contracting every 10 minutes. Duration of contraction 20 seconds.

7.50 p.m. 0.5 c.c. pituitrin given. Os admits three fingers.

8.0 p.m. Pulse 125. B.P. 115 mm. Hg. Uterus contracting every 12 minutes. Duration of contraction, 30 seconds.

8.20 p.m. Pulse 120. B.P. 115. Uterus contracting every 10 minutes. Duration of contraction, 30 seconds.

8.50 p.m. Pulse 117. B.P. 125. Uterus contracting strongly every 5 minutes. Duration of contraction, 30 seconds.

9.50 p.m. Pulse 115. B.P. 125. Uterus contracting every 5 minutes. Duration of contraction, 20 seconds.

10.50 p.m./
10.50 p.m. Pulse 116. B.P. 120. Uterus contracting every 5 minutes. Duration of contraction, 25 seconds.

11.50 p.m. Pulse 112. B.P. 120. Uterus contracting vigorously every 2 minutes. Duration of contraction, 20 seconds.

At 12.20 a.m. patient gave spontaneous birth to a still born child. The placenta was not born one hour after birth of child as it was considered not advisable to interfere as uterus was not contracting satisfactorily. Placenta was then expressed by Crédé's method and this was followed by severe haemorrhage. 0.5 c.c. Pituitrin was then injected, but had little effect.

20 mins ernutin was then injected and a hot intrauterine douche given, this effectually controlled the haemorrhage.

There was 30 ozs. blood lost in the third stage. The mother made an uninterrupted recovery.


Induction.

Mrs. C. Aet. 38. 3rd Gravida. 38 weeks pregnant.

Obstetric History. 1st baby induced at home (stillborn) 2nd " " " " " "

Pelvic Measurements. Interspinous 9 1/2"
     Intercrestal 11"
     External conjugale 7"
     Internal conjugale 3 3/4".

History. On 30th December patient was examined by Dr. Maxwell, who advised immediate induction as the foetal head could only be pushed into the pelvic brim with difficulty.

Treatment/
Treatment. Three bougies were inserted into uterus on 31st December at 12 p.m., pains started 54 hours later. When patient had been one hour in second stage, the foetal heart became slow and irregular, so forceps were applied and a living child delivered.

After waiting 1 hour, 20 minutes in third stage attempts at expressing placenta by Crédé's method unsuccessfully.

0.5 c.c. pituitrin was then injected into patient's thigh.

11 p.m. Pulse 96. B.P. 136 Hg. Uterus contracting weakly every 10 minutes, duration of contraction 30 seconds.

11.5 p.m. 0.5 c.c. pituitrin injected.

11.15 p.m. Pulse 92. B.P. 145 mm. Hg. Uterus contracting strongly every 2 minutes. Duration of contraction, 30 seconds.

At 11.15 p.m., ten minutes after injection of pituitrin, uterus was contracting vigorously and placenta was expressed by Crédé's method. Only 6 ozs. haemorrhage in third stage.

Case 5. Prolonged first stage.

Matilda C. Aet. 19. 1st Gravida.

Pelvic Measurements. Interspinous 9". Intercristal 10½". External conjugate 8".

History. Patient had been 36 hours in first stage and pains very weak and os uteri five shillings dilated. It was decided to give her injection of pituitrin.

4.0 p.m. Pulse 90. B.P. 105 Hg. Uterus contracting fully every 5 minutes. Duration of contraction, 40 seconds.

4.10/
4.10 p.m. 0.5 c.c. pituitrin injected. Os uteri 5/- dilated.

4.20 p.m. Pulse 90. B.P. 108 mm. Hg. Uterus contracting every 5 minutes. Duration of contraction, 30 seconds.

4.40 p.m. Pulse 80. B.P. 113 mm. Hg. Uterus contracting strongly every 3 minutes. Duration of contraction, 35 seconds.

Patient reached second stage at 4.45 p.m.

5.10 p.m. Pulse 64. B.P. 120 mm. Hg. Uterus contracting vigorously every 2 minutes, duration of contraction 40 seconds.

At 5.40 p.m. patient gave spontaneous birth to a living baby weighing 5 lbs. 11 ozs. after a second stage of 55 minutes and one hour and a half after injecting the pituitrin.

The placenta was born 35 minutes after the birth of the baby. There was only 8 ozs. haemorrhage in the third stage.

Case 6. Experimental, to test effects of Pituitrin.

Lydia W. Aet. 27. Second Gravida.

Obstetric History. Miscarriage at 5 months.

Pelvic Measurements. Interspinous 9 1/4" Intercristal 10 1/4"

External conjugale 7 1/2".

History. Patient had been in labour twelve hours, pains weak and os uteri five shillings dilated. It was decided to give her 0.5 c.c. pituitrin to watch its action.

6.40 p.m. Pulse 88. B.P. 95 mm. Hg. Uterus contracting feebly every 4 minutes. Duration of contractions, 30 seconds.

6.50 p.m./
6.50 p.m. P.5 c.c. pituitrin injected. Os uteri five shillings dilated and soft.

7.0 p.m. Pulse 90. B.P.115. Uterus contracting strongly every 2 minutes. Duration of contraction 40 seconds.

Patient reached second stage at 7.5 p.m.

7.20 p.m. Pulse 38. B.P. 122 mm. Hg. Uterus contracting vigorously every minute. Duration of contraction 20 seconds.

At 7.30 p.m. after a second stage of 25 minutes and forty minutes after injecting pituitrin, patient gave spontaneous birth to a living child weighing 7 lbs. The placenta was born 35 minutes later. There was 15 ozs. haemorrhage in third stage.

Case 7. Experimental to test effects of Pituitrin.

Mrs S. Aet. 33. Third Gravida.

Obstetric History. Two children born alive.

Pelvic Measurements. Interspinous 9
t Intercrestal 10
t External conjugale 7
t

History. Patient having weak pains and os uteri five shillings dilated. She has been 17 hours in first stage and it was decided to give her injection of pituitrin to watch its action.

3.5 p.m. Pulse 78. B.P. 115 mm. Hg. Uterus contracting feebly every 15 minutes. Duration of contraction, 30 seconds.

3.15 p.m. 0.5 c.c. pituitrin injected. Os uteri thin 5/-dilatation.

3.25 p.m. Pulse 76. B.P. 115 mm. Hg. Uterus contracting every 17 seconds. Duration of contraction 30 seconds.

3.45 p.m./
3.45 p.m. Pulse 72. B.P. 130 mm. Hg. Uterus contracting strongly every 5 minutes. Duration of contraction 30 seconds.

4.15 p.m. Pulse 86. B.P. 135 mm. Hg. Uterus contracting vigorously every 2 minutes. Duration of contraction 40 seconds.

Patient reached second stage at 4.25 p.m. and twenty minutes later, and an hour and thirty minutes after injecting the pituitrin, gave spontaneous birth to a living baby weighing 5 lbs. 12 ozs. The placenta was born ten minutes later.

There was 8 ozs. haemorrhage in the third stage.

Case 8. Prolonged Second Stage.

Mrs. F. Aet. 27. First Gravida.

Pelvic Measurements. Interspinous 9½"
Interocristal 10⅜"
External Conjugale 7¾".

History. Patient has been 1½ hours in the second stage and the foetal head is making no advance. The uterine pains are getting weaker. Foetal heart is regular and strong.

Patient was given injection of pituitrin.

11.25 p.m. Pulse 11. B.P. 145 mm. Hg. Uterus contracting every 3 minutes. Duration of contraction 30 seconds.

11.35 p.m. 0.5 c.c. pituitrin injected.

11.45 p.m. Pulse 92. B.P. 150 mm. Hg. Uterus contracting every 3 minutes. Duration of contraction 40 seconds.

12.5 a.m. Pulse 82. B.P. 160 mm. Hg. Uterus contracting strongly every 2 minutes. Duration of contraction 35 seconds.

12.35 a.m./
12.35 a.m. Pulse 84. B.P. 162 mm. Hg. Uterus contracting strongly every 1 minute. Duration of contraction 30 seconds.

At 12.40 a.m., one hour and five minutes after injecting pituitrin, patient gave spontaneous birth to a living baby weighing 8 lbs. The placenta was born twenty minutes later. 3 oz. haemorrhage in the third stage.

Case 9. Prolonged Second Stage in Induction Case.

Eva S. Aet. 19. 1st Gravida. 38 weeks pregnant.

Pelvic Measurements. Interspinous 8½"
Intercristal 9½"
External Conjugale -7"
Internal Conjugale + 4".

History. On January 3rd, Dr. Roberts saw patient and as the foetal head could only be pushed into the pelvic brim with difficulty he advised induction.

Treatment. On January 4th three bougies were inserted into uterus at 12.45 p.m. and 63½ hours later pains started on January 7th.

On January 8th, when patient had been three hours in second stage and foetal head making no progress, it was decided to give her injection of pituitrin.

10.50 p.m. Pulse 98. B.P. 130 mm. Hg. Uterus contracting every 5 minutes. Duration of contraction 30 seconds.

11 p.m. 0.5 c.c. pituitrin injected.

11.10 p.m. Pulse 96. B.P. 137 mm. Hg. Uterus contracting every 5 minutes. Duration of contraction 30 seconds.

11.30 p.m. Pulse 90. B.P. 150 mm. Hg. Uterus contracting strongly every 2 minutes. Duration of contraction 35 seconds.

12.0 p.m./
12.0 p.m. pulse 90. B.P. 150 mm. Hg. Uterus contracting strongly every 2 minutes. Duration of contraction 30 seconds.

At 12.5 a.m., one hour and five minutes after injecting pituitrin, patient gave spontaneous birth to a living baby weighing 6 lbs. 1½ ozs. Placenta born 18 minutes later. 6 ozs. haemorrhage in third stage.


Mrs D. Aet. 25. 1st Gravida. 40 weeks pregnant.

Pelvic Measurements. Interspinous 9"
Intercrystal 11"
External conjugale 7½".

History. Patient sent in to Queen Charlotte's Hospital by Dr. Newbing of Sutton on account of placenta praevia.


Per vaginum. Os uteri admitted one finger, placental edge felt on left side os internum. Membranes unruptured.

Treatment. Patient was having no pains so a full size Dr. Ribe's bag was inserted into uterus, the membranes being first ruptured. There was a good deal of haemorrhage during insertion of bag.

The bag was expelled thirty hours later, the mother having very feeble pains and the os uteri fully dilated.

When mother had been three hours in the second stage/
stage and foetal head was making no advance, it was decided to give her injection of pituitrin. The application of forceps was contraindicated as uterine pains were quite absent.

7 a.m. Pulse 100. B.P. 110 mm. Hg. No uterine contractions.

7.10 a.m. 0.5 c.c. pituitrin injected. Os uteri fully dilated.

7.20 a.m. Pulse 102. B.P. 115 mm. Hg. Uterus contracting every 15 minutes. Duration of contraction 30 seconds.

7.40 a.m. Pulse 100. B.P. 115 mm. Hg. Uterus contracting every 15 minutes. Duration of contraction 30 seconds.

8.10 a.m. Pulse 96. B.P. 112 mm. Hg. Uterus contracting feebly every 20 minutes. Duration of contraction 40 seconds.

9.10 a.m. Pulse 98. B.P. 114 mm. Hg. Uterus contracting every 20 minutes. Duration of contraction 30 seconds.

As patient had been 5½ hours in second stage and pains were still so weak it was decided to give another 0.5 c.c. pituitrin. Forceps delivery was withheld for fear of haemorrhage in third stage, as uterine pains were so feeble.

9.30 a.m. Second dose of 0.5 c.c. pituitrin given.

9.40 a.m. Pulse 96. B.P. 112 mm. Hg. Uterus contracting feebly every 25 minutes. Duration of contraction 20 seconds.

10.0 a.m. Pulse 96. B.P. 116. Uterus contracting strongly every 5 minutes. Duration of contraction 30 seconds.

10.30 a.m. Pulse 98. B.P. 120 mm. Hg. Uterus contracting vigorously every 2 minutes. Duration of contraction 30 seconds.

At 10.30 a.m., after a second stage of six and a half hours/
hours, patient gave spontaneous birth to a living child weighing 8 lbs. 7 ozs. Placenta born twenty minutes later, membranes adherent and removed with hand.

Severe haemorrhage after removal of membranes, 60 ozs. blood being lost. Haemorrhage was controlled by injecting 20 mins. ermitin and giving hot intrauterine douche.

Mother and child did excellently.


Mrs B. Aet. 24. 2nd Gravida. 40 weeks pregnant.

Obstetric History. 1st labour normal: child weighed 6 lbs.

Pelvic measurements. Interspinous 8 3/4"

Intercristal 10 1/2"

External conjugale 8".

Internal Conjugale -4.

Large sacral promontory.

History. Patient examined by Dr. Banister. Foetal head could only be pushed into brim with difficulty and as child seemed large, an induction was advised.

Treatment. Three bougies inserted into uterus at 12.30 p.m. When patient had been in first stage for 24 hours and os was five shillings dilated and uterine pains very weak, it was decided to give her an injection of pituitrin.

7.40 p.m. Pulse 74. B.P. 147 mm. Hg. Uterus contracting every 15 minutes. Duration of contraction 20 seconds.

7.45 p.m./
7.45 p.m. 0.5 c.c. pituitrin injected. Os uteri 5/- dilatation.

7.55 p.m. Pulse 74. B.P. 147 mm. Hg. Uterus contracting every 15 minutes. Duration of contraction 30 seconds.

8.15 p.m. Pulse 70. B.P. 155 mm. Hg. Uterus contracting every 10 mins. Duration of contraction 20 seconds.

8.45 p.m. Pulse 72. B.P. 155 mm. Hg. Uterus contracting every 5 minutes. Duration of contraction 30 seconds.

9.45 p.m. Pulse 100. B.P. 152 mm. Hg. Uterus contracting every 2 minutes. Duration of contraction 25 seconds.

10.45 p.m. Pulse 86. B.P. 152 mm. Hg. Uterus contracting every 2 minutes, duration 40 seconds.

11.45 p.m. Pulse 88. B.P. 150 mm. Hg. Uterus contracting every 2 minutes. Duration of contraction 35 seconds.

Patient reached second stage at 3.30 a.m. and at 3.50 a.m. gave spontaneous birth to a baby weighing 7 lbs. 8 ozs.

The delay was due to the large size of the child for the 3/4" conjugate, also due to a rigid perineum for the pituitrin brought on good pains.

The placenta was born twenty minutes later. 4 ozs. haemorrhage in third stage.


Anetta D. Aet. 24. 1st Gravida.

Pelvic Measurements. Interspinous 9 1/2".
Intercrystal 10 1/2".
External conjugale 6 1/2".
Internal conjugale 4".

History. Patient had been 73 hours in first stage and/
and foetal head making no advance, os uteri 5/- dilated, and uterine pains feeble. It was decided to give her injection of pituitrin.

3.45 p.m. Pulse 92. B.P. 117 mm. Hg. Uterus contracting feebly every 2 minutes. Duration of contraction 20 seconds.

3.55 p.m. 0.5 c.c. pituitrin injected. Os uteri 5/- dilated.

4.5 p.m. Pulse 90. B.P. 120. Uterus contracting every 2 minutes. Duration of contraction 30 seconds.

4.25 p.m. Pulse 90. B.P. 135 mm. Hg. Uterus contracting every 1 minute. Duration of contraction 30 seconds.

4.55 p.m. Pulse 87. B.P. 135 mm. Hg. Uterus contracting every 1 minute. Duration of contraction 20 seconds.

5.55 p.m. Pulse 88. B.P. 132 mm. Hg. Uterus contracting every 2 minutes. Duration of contraction 30 seconds.

6.55 p.m. Pulse 88. B.P. 135 mm. Hg. Uterus contracting every 2 minutes. Duration of contraction 30 seconds.

7.55 p.m. Pulse 86. B.P. 135 mm. Hg. Uterus contracting vigorously every 2 minutes. Duration of contraction 30 seconds.

Patient reached second stage at 8.15 p.m. and at 8.55 p.m., four hours after injection of pituitrin, gave spontaneous birth to a baby which weighed 6 lbs. 4 ozs. Placenta was born 25 minutes later.

6 ozs. haemorrhage in third stage.

Case 13. Experimental to test effects of pituitrin.

Mary R. Aet. 17. 1st Gravida.

Pelvic/
Pelvic Measurements.  
Interosseous 10"
Intercristal 11½"
External Conjugate 7½".

History.  Patient had been twenty-two hours in first stage and os uteri 5/- dilated.  It was then decided to give her 0.5 c.c. pituitrin.

4.10 p.m.  Pulse 82.  B.P. 130 mm. Hg.  Uterus contracting every 5 minutes.  Duration of contraction 30 seconds.

4.20 p.m.  0.5 c.c. pituitrin injected.  Os uteri 5/- dilated.

4.40 p.m.  Pulse 82.  B.P. 130 mm. Hg.  Uterus contracting every 5 minutes.  Duration of contraction 30 seconds.

4.50 p.m.  Pulse 76.  B.P. 145 mm. Hg.  Uterus contracting every 2 minutes.  Duration of contraction 30 seconds.

5.20 p.m.  Pulse 76.  B.P. 145 mm. Hg.  Uterus contracting every 2 minutes.  Duration of contraction 25 seconds.

6.20 p.m.  Pulse 78.  B.P. 143 mm. Hg.  Uterus contracting strongly every 1 minute.  Duration of contraction 20 seconds.

7.20 p.m.  Pulse 76.  B.P. 145 mm. Hg.  Uterus contracting every 1 minute.  Duration of contraction 30 seconds.

8.20 p.m.  Pulse 74.  B.P. 140 mm. Hg.  Uterus contracting vigorously every 2 minutes.  Duration of contraction 35 seconds.

Patient reached second stage at 11.55 p.m., seven and a half hours after injection of pituitrin.

After a second stage of two hours, twenty-five minutes patient gave birth to a living baby which weighed 6 lbs. 3 ozs.

The placenta was born twenty minutes later.

There was 4 oz. haemorrhage in third stage.

Case/

Bessie N. Aet. 24. 1st Gravida.

Pelvic Measurements. Interspinous 8 3/8"
Intercristal 10" External conjugate 7".

History. Patient has been 27 hours in first stage and os uteri size of half crown and very rigid. It was decided to give patient injection of pituitrin.

3.40 p.m. Pulse 86. B.P. 135 mm. Hg. Uterus contracting every 4 minutes. Duration of contraction 40 seconds.

3.50 p.m. 0.5 c.c. pituitrin injected. Os uteri size 2/6.

4.00 p.m. Pulse 86. B.P. 140 mm. Hg. Uterus contracting every 4 minutes. Duration of contraction 35 seconds.

4.20 p.m. Pulse 86. B.P. 155 mm. Hg. Uterus contracting every 2 minutes. Duration of contractions 30 seconds.

4.50 p.m. Pulse 84. B.P. 155 mm. Hg. Uterus contracting every 2 minutes. Duration of contraction 20 seconds.

5.50 p.m. Pulse 86. B.P. 150 mm. Hg. Uterus contracting every 1 minute. Duration of contraction 30 seconds.

6.50 p.m. Pulse 88. B.P. 152 mm. Hg. Uterus contracting every 1 minute. Duration of contraction 30 seconds.

7.50 p.m. Pulse 90. B.P. 150 mm. Hg. Uterus contracting every 1 minute. Duration of contraction 30 seconds.

Next morning at 11 a.m. patient was very exhausted, having been fifty three hours in first stage, the os uteri being three quarter dilated. It was thought advisable to give her morphine 1/6 gr. and Hyoscine 150 gr.

Patient reached second stage at 6.30 p.m. and as she/
she was very distressed. Application of forceps was indicated. The position of foetal head was left occipito posterior so the head was rotated manually and forceps applied and a living child weighing 7 lbs. 7 ozs. delivered. The placenta was born thirty minutes later. Only 12 ozs. haemorrhage in third stage.

Case 15. Caesarean Section. Cardiac Disease.

Mrs. B. Aet. 24. 1st Gravida. 35 weeks pregnant.

Pelvic Measurements. Interspinous 8\(\frac{1}{2}\)"
Intercrôstal 8\(\frac{3}{4}\)"
External Conjugale 7".

History. Patient has a double mitral murmur, a hacking cough, edema at bases of lungs and swollen feet. It was considered advisable to do Caesarean section under spinal anaesthesia.

Operation. Patient given 0.5 c.c. pituitrin just before the operation. 0.8 c.c. stovaine was then injected into spinal canal between the first and second lumbar vertebrae and in 15 minutes patient had complete anaesthesia below the ribs.

As patient was very excitable she was put under gas and oxygen.

Median abdominal incision was then made, the uterus exposed, incised, and the child and placenta removed. The uterus contracted well, and there was very little haemorrhage. The uterus was then sewn up with interrupted sutures silk worm gut and the patient then sterilized by removing a loop from each fallopian/
fallopian tube. Abdominal wall then stitched up in the usual way.


Mrs. T. Aet. 34. 1st Gravida. 40 weeks pregnant.

Pelvic Measurements. Interspinous $7\frac{3}{4}''$
Intercrinal $8''$
Diagonal conjugale $3\frac{1}{2}''$.

History. Patient had left leg amputated when aet. 17 owing to flail knee joint following acute poliomyelitis.
She has marked scoliosis and tilting of pelvis.

Patient given 0.5 c.c. pituitrin half an hour before the operation.

Operation. Median abdominal incision made and uterus exposed and incised, and child and placenta removed.
Uterus very flabby and bleeding freely. 20 mins. Ernutin then injected into flank and uterus then began to contract well and haemorrhage ceased. Uterus and abdominal wall then sewn up in usual way.
SUMMARY and CONCLUSIONS.

Whilst Resident Medical Officer at Queen Charlotte's I was constantly having inquiries from practitioners as to the action of pituitrin in midwifery, thus proving how interested they were in this drug. One question was invariably asked, namely, was it always safe to use pituitrin in suitable cases?

I may say I have used pituitrin in upward of sixty cases and its action has never given me the least cause for anxiety, nor have I ever seen it cause a rash, as described by some writers.

In all my cases I found that pituitrin had a definite action on the uterus, causing increased contractions, a rapid rise in blood pressure, maintained for from twelve to twenty-four hours, and that there was a marked slowing of the pulse rate.

I agree with Klotz and Hofbauer that pituitary extract has a definite diuretic effect and have never had to use a catheter or had any urinary trouble in cases in which it has been used.

In cases 1, 2 and 3 I think I have demonstrated the value of pituitrin in the treatment of ante-partum haemorrhage.

These cases cause more anxiety to the obstetrician than any other and the sooner the patient is having good pains the sooner his mind will be at rest and the/
the patient in safety. More especially was this the case in 1 and 2 where there was a considerable amount of concealed haemorrhage.

In cases 11, 12, 13 and 14 I have shown that pituitrin is not much use in the early part of the first stage in primipara, it was given in these cases more for watching its effect on the blood pressure, pulse and uterus than with the idea of hurrying on labour.

In case 5, a primipara, and case 6, a multipara, who however had only had a five months miscarriage before this pregnancy and had never been properly dilated up, pituitrin certainly hurried on labour, the child being born in case 5 ninety and in 6 forty minutes after the pituitrin was injected.

In no single case where pituitrin was used was there any difficulty with the placenta and in case 4, where the extract was given for adherent placenta, its action was very successful.

Cases 8, 9, 10 illustrate how effective pituitrin is in the treatment of prolonged second stage. There is no doubt that in the case of weak pains in the second stage, pituitary extract is of the greatest use, because by means of this product the application of forceps can certainly be avoided.

In my opinion this is quite sufficient for pituitary extract to occupy a due place in obstetrics.

I agree with Hofbauer in opposition to the views of/
of Foges, Hofstädter, Schmidt and Klotz that pituitary extract cannot replace ernutin in arresting post partum haemorrhage, as it does not act quick enough.

This I will say, however, that I have only seen one case of post partum haemorrhage where pituitrin was used in the first or second stages and that was in case 10, where the uterus was particularly inactive.

My experience of the use of pituitrin in cases of Caesarean Section is similar to that of Foges, Hofstädter, Schmidt and Stern, and it causes firm contraction of the uterus in the great majority of cases. Unfortunately I have only notes on two of these cases, one where the extract worked well and one where it failed.

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 beliefs.
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