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THE RÔLE OF THE PITUITARY GLAND IN PREGNANCY AND PARTURITION.

I. Hypophysectomy.

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Technique.

It has been stated frequently that the invariable result of hypophysectomy during pregnancy is immediate abortion, yet the amount of experimental work which supports this conclusion is small. A series of hypophysectomies was therefore performed in pregnant animals to test the truth of this statement. Obviously, the operation must be done in such a way that no structure but the pituitary is injured, and that removal is complete. There are available a number of methods of approaching the pituitary. Amongst these are the nasal, the trans-dural, the buccal and the retro-pharyngeal; the first two are not convenient in the cat, and we have used only the two latter as fulfilling as nearly as possible the necessary conditions. That is to say, the removal is effected in full view of the operator, and at the same time the risk of damage to adjacent structures is reduced to a minimum.

One of us favours the buccal route, and the other the retro-pharyngeal. The buccal route permits of a more deliberate operation and gives, perhaps, the best view of the pituitary region, but it has the serious drawback that it is particularly liable to be followed by a severe nasal infection which may spread down to the lungs with fatal result. In any case, the post-operative period requires special care and skilled and conscientious nursing. With the retro-pharyngeal route these drawbacks are to some extent overcome, but the operation has to be conducted with considerable speed as retraction of the trachea cannot be indefinitely prolonged; the necessary retraction, moreover, somewhat interferes with the space available for manipulation.

It is not proposed to deal in this paper with the results in detail, or the full conclusions to be drawn from them. A new operative procedure is described, and some modifications of an operation already used by McLean.

I. The retro-pharyngeal route.

This will be described in detail, as it is, in many respects, a new one. Access is obtained by dissection of the neck, the pharynx is stripped from the base of the skull and the bone drilled over the pituitary fossa without exposure of any septic surfaces.

Anæsthetic. We have found an ordinary ether induction followed by ether and air administered by a pump through an intra-tracheal catheter to be the best method. The intra-tracheal catheter is essential to maintain an airway when the trachea is retracted. Experiments were made with various non-inhalation anæsthetics, but with all of them there is the common disadvantage that narcosis is prolonged and the return of the cough reflex delayed; this results in stagnation of secretions in the pharynx and a liability to infection which otherwise is avoided.

Pre-operative care. Only animals which have been some weeks in the establishment are used—a point which greatly assists convalescence. The day before operation only milk is given and on the morning of the operation nothing but water. Both at the beginning and at the end of operation the mouth and pharynx are thoroughly cleansed and swabbed with a 1 p.c. solution of mercurochrome. The skin of the front of the neck is shaved and purified by swabbing successively with 5 p.c. phenol solution, alcohol and iodine. A full surgical aseptic technique is used throughout.

Operation. The animal is tied out in the dorsal position and the chin well extended with a weighted hook. A skin incision about 3 in. long is made in the mid line of the neck, extending from $\frac{1}{2}$ in. below the jaw to the sternum. Skin flaps are dissected back, and towels fastened to skin edges with Michel's clips. The transverse vein under the chin is divided between ligatures, and the sterno-mastoid muscles are separated with the aid of a knife; this exposes the infra-hyoid muscles which are separated by blunt dissection from the carotid structures. The nerve to the infra-hyoids is isolated but not cut, but the nerve to the thyro-hyoid group has usually to be sacrificed. The hypoglossal and external laryngeal nerves are seen at the top of the wound but are not in any serious danger. The trachea and œsophagus are lifted up from the pre-vertebral fascia and held aside by a retractor, great care being taken not to compress the trachea so as to interfere with the air return. The pharynx is similarly separated for a short distance until the median fascial septum comes into view. This is then picked up with forceps and the fascia overlying the pre-tracheal muscles is incised just posterior to it. The separation proceeds

cranially, dorsal to this plane which eventually becomes continuous with the muco-periosteum covering the base of the skull. This muco-periosteum is separated from bone by swab dissection to just beyond the tip of the pterygoid bone, which can readily be felt with the finger; this is about ¼ in. beyond the large bullæ which lie immediately laterally to the pharynx. An occasional touch with a sharp-pointed knife may be necessary at the extreme lateral margins and care must be taken to avoid several small veins in this region.

The pharynx is now retracted by a specially designed retractor; this is about ½ in. wide and curved on the flat so as to fit round the hole to be made in the bone. When using it, it is imperative to avoid bruising the thin wall of the pharynx. The point selected to drill the bone is almost exactly opposite the pterygoid and not infrequently a small emissary vein may be seen issuing at the precise spot. We have been in the habit of using an ordinary dental burr driven by a foot-drill to pierce the bone, the hole being enlarged with the largest-sized burr in very much the same manner as a cavity in a tooth. Injury to the dura is easily avoided, and with a little trouble an opening at least as large as the pituitary fossa can be obtained. The cavernous sinuses lie one on each side of the pituitary fossa and joining them posteriorly is a large communicating sinus; the anterior side is comparatively free from blood vessels, so it is better to err in an anterior direction when drilling the bone.

The dura is incised at the central point between the sinuses, and the pituitary immediately bulges through it. A large-sized sucker attached to a water pump is applied, and a considerable portion of the pituitary thus removed; escape of cerebro-spinal fluid and some bleeding follows. The bleeding is controlled by application of crushed muscle. The portions of the pituitary lying circumferentially under the dura escape removal with the sucker, and are sought for with a small, curved, blunt-edged spoon. The pituitary is not shut off from the general cranial cavity by a "diaphragm" of dura as in some animals, so injury to the infundibulum cannot always be avoided. Should one of the large sinuses be injured the bleeding can usually be controlled in a few minutes by packing over a piece of crushed muscle; once or twice, however, it has been necessary to leave in a small muscle plug. The hole in the bone is filled with Horsley's wax, the superficial muscles are brought together with a running suture and the skin wound closed with interrupted stitches.

After-care. The wound is painted with Whitehead's varnish, but no dressing is applied. The cat is placed in a warmed cage on a bedding of cotton-wool—we have found this last point of no small importance in

obtaining healing by first intention which now almost invariably occurs. The stitches are removed after about a week.

Water is allowed immediately the animal comes round from the anæsthetic, but for the following 24 hours nothing else is permitted; thereafter milk is given, and at the end of 48 hours raw meat is usually taken. A sardine or other tasty morsel may assist in re-establishing the appetite. When this route is employed there is seldom any difficulty from sepsis of the pharynx or elsewhere, we have lost but few cats from this cause, and there is very little trouble in the post-operative period.

II. The buccal route.

Full details of the operative procedure in the removal of the pituitary by the buccal approach are given by McLean [1928]. The operation is performed with the cat on its back, the mouth held widely open; the soft palate is divided for about 2 cm., the muco-periosteum over the sphenoid is incised and retracted, and a hole drilled in the bone. The pituitary is seen at the bottom of the hole and is removed by suction under direct vision.

The modifications we have adopted are:

(1) *Anœsthetic.* Nembutal 844 has proved very satisfactory, as, in doses of 0·04 g. per kg., it gives adequate relaxation and the animal recovers consciousness in about 12 hours. It is given by intra-peritoneal injection as a 5 p.c. solution.

(2) *Nasal sepsis.* McLean's paper is mainly concerned with dogs, in which apparently nasal sepsis is infrequent. In the cat, however, nasal sepsis is only too easy to set up, and almost impossible to cure. We have, therefore, taken extreme precautions to avoid the entry of blood or mucus to the nose from the pharynx. For this purpose the posterior edge of the soft palate is pulled forward and a pledget of wool passed forward behind it, so that the posterior nares are plugged before the soft palate is incised. Further, to obtain a clear field and prevent the oozing of blood from the cut edges of the palate, we now use a solution of adrenaline 0·1 p.c. and 10 p.c. cocaine for local application to both surfaces of the soft palate before it is divided. The same solution is used to diminish the somewhat free bleeding from the muco-periosteum covering the sphenoid.

(3) *Whitehead's varnish.* This has been used to paint over the sutures (catgut 000) in the muco-periosteum and in the palate. We believe it gives better healing in what must be, whatever precautions are taken, a relatively septic cavity.

The actual removal of the pituitary, after it has been exposed through the mouth, is the same as that described above for the retro-pharyngeal route.

Results.

The earlier operations were followed in many cases by the delivery of normal-looking fœtuses in 2–3 days. It was at that time impossible to obtain pregnant cats whose date of impregnation was known, so that there was no evidence that the delivery was not occurring at the appropriate time. The greatest time which we have so far observed to elapse after operation before delivery occurred is 11 days. In only one of the series did the mother make any attempt to suckle her kittens, and in this case she abandoned the effort after 2 days; in all the other cases the mother ignored the kittens. Serial sections were made, in a number of cases, of the infundibular region of the base of the brain, and of the dura lining the pituitary fossa, to prove that the removal had been complete; details will be published later.

Table I.

Lateral pharyngeal				Buccal			
No.	Delivery or laparotomy	Days after operation	Fœtus alive or dead	No.	Delivery or laparotomy	Days after operation	Fœtus alive or dead
33	Laparotomy	10	1 A.	32	Delivery	3	1 A., 2 D.
36	Delivery	2	3 A.	35	Delivery	4	1 A.
42	Delivery	11	3 A.	43	Delivery	4	1 A., 2 D.
45	Laparotomy	5	3 A.	44	Delivery	5	4 A.
52	Laparotomy	5	5 A.	46	Delivery	8	1 D.*
56	Delivery	5	Fœtuses eaten	54	Delivery	2	3 D.*

* Premature.

Further experiments are in progress to ascertain whether the pituitary is essential to the continuance of pregnancy even during the earliest stages.

Conclusions.

1. Delivery can take place, apparently quite normally, in the absence of the whole pituitary.
2. Delivery does not necessarily follow immediately on removal of the pituitary.
3. Suckling has not been observed to take place.

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REFERENCE.

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