ON THE USE OF PITUITARY EXTRACT IN OBSTETRICS*

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Although the first use of pituitary in obstetrical practice was made in England, but few papers dealing with its action have been published in English, while in Europe it has been so extensively used that a study of the large number of papers and cases now published enables one to formulate, with considerable precision, rules for its employment. This is especially true after one has given it, with success and failure, in one's own experience. This forms the justification for this paper.

In 1895, Oliver and Schaefer, in their series of experiments with organ extracts, followed up their papers on the striking effects produced by the injection of extracts of the adrenal by showing that extracts of the pituitary also produced a rise in blood-pressure. In 1898, Howell showed that it was the posterior lobe which possessed this property. This was confirmed by Schaefer and Vincent, and in 1901 Schaefer and Magnus showed that the extract of the infundibular portion increased very markedly the flow of urine. At this point the matter rested until 1906, when Dale, in the course of some observations on the action of ergot, noted that the extract of pituitary brought about a marked uterine contraction. This observation, however, was entirely lost sight of until Blair Bell and Hicks, led by some experiments which they had on hand, obtained from Dale some pituitary extract and produced with it marked contractions of the uterus in pregnant rabbits.

In consequence of the results obtained, Blair Bell was led to use it in some obstetrical cases. He presented his observations before the Liverpool Medical Institution, November, 1909, and his paper was published in December. In it he refers to its use in two cases of post-partum hemorrhage, and one case in which it was used in the expulsive stage of labor. In September, 1910, Aarons of Edinburgh read a paper at the International Congress in St. Petersburg, in which he reported success in its use in six cases of post-partum hemorrhage.

On June 25, 1909, Frankl-Hochwart and Fröhlich of Vienna reported on some experiments which they had made with pituitary extract. They were led to join forces in the study of the action of pituitary on the vegetative nervous system, as both of them had previous experience with

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the pituitary gland under pathological conditions, and from what was known of the pharmacological action of the extract they were led to infer that it would produce uterine contractions. In this respect their hopes were answered, and they found that pregnant rabbits showed a very marked increase in uterine movement after the administration of pituitary. The effect on blood-pressure was by no means marked, although it was found to be considerable when injected into dogs. They also observed, as they had expected, very marked effects on the urinary bladder and were able to show that it not only stimulated, but increased the irritability of both the nerves to the bladder and to the uterus.

In conclusion, they suggested that it should be used in obstetrics, and it was not long before the advice was acted on. In January, 1910, Foges and Hofstätter tried it in some cases to arrest post-partum bleeding. They showed that it had little effect on blood-pressure, but quite promptly brought about uterine contractions. They had several failures, three at least in which no effect whatever was produced.

Early in 1911 Hofbauer published the first series of cases in which it was used to increase labor pains. In his twelve cases the effects were always exceedingly striking, the movements coming on or increasing in force within a few minutes. He saw in no case any indication of tetanus uteri, but in several cases regular storms of contractions, bringing on a very rapid delivery. The publication of this exceedingly optimistic paper has led to pituitary being very widely used, and at least seventy-five papers dealing with the use of pituitary in labor have been published. An examination of the literature has disclosed a total of at least 1,650 cases in which it has been administered. A complete list of references is appended. The author has avoided, as far as possible, counting any case twice. The latest paper and the highest number of cases by any author being taken to include those previously reported.

My attention was attracted to the advantages of pituitary extract in obstetrics from the results seen in animal experimentation in the pharmacological laboratory. In the course of researches which have been in progress in this laboratory, and for demonstrations for student classes, pituitary has been used a considerable number of times to increase uterine movements. The accompanying curve (Fig. 1) is shown as very typical. As may be seen from this tracing, the uterine movements have been very markedly increased in both rate and amplitude, while the tone, as judged by the elevation of the line joining the bases of the waves, has not been raised, save at first where an irregular tetanus may be seen. In none of the cases in which it was employed has a true tetanus uteri, i. e., a very marked rise in tone with comparatively slight superimposed movements, been seen. Hahl and Malinowsky have recorded the variations in intra-uterine pressure with a bag, after the method of Westermarck, and in

Figure 1

Figure 2

two cases reported by Hahl, there was some rise in tone, the movements being shorter and stronger, at shorter intervals and with increased intra-uterine pressure; and Malinowsky shows a good tracing of a uterine tetanus. In other cases no increase in tone occurred, but only of movements. Such tetani are, however, not uncommon with ergot preparations, but apparently much less so with pituitary. Cases have, however, occurred. In one of the cases published by Rieck a tetanus evidently occurred, and is very well described by him. When it took place after the second injection, which was given six hours after the first injection, the patient stated that she felt the individual pains, but the examining hand could detect no contractions or relaxations.

Lieven also reports a case in which the uterine tetanus was so marked that the child's heart-rate fell steadily to 82, and there was a marked passage of meconium. Spaeth reports a similar case. He was, however, so unfortunate as to see the child die. Seitz and Roemer have each stated that they have also seen tetanus occur. Hamm, too, in one case which was brought to him after the child was dead and the patient had been in labor for a considerable period of time, injected pituitary, and regular movements set in. These, however, died away, and a second injection was given, which was followed in seven minutes by a tetanic constriction which lasted eight minutes, then regular movements for one or two hours, which gradually died away. A third injection produced another tetanus of eleven minutes' duration, then regular movements; and the fourth, tetanus of seventeen minutes, followed by regular movements, which led to delivery. He states that he has frequently seen the fetal heart-rate fall to 80; but in view of the rapidity of delivery in most cases, does not consider this dangerous. The above incident shows quite clearly, however, that the use of pituitary is not without some danger to the child, though danger to the mother seems very slight. In consequence, the fetal heart sounds should be, if it is at all possible, kept constantly under observation. This danger seems undoubtedly greatest when the drug is administered during the first stage.

A study of the literature has disclosed that the majority of observers, and especially those with the larger series of cases, have found that for the production of abortion, pituitary alone is insufficient. We might quote in this connection Schiffmann, who, out of seven cases, had three complete failures. Hell, Fischer, Nagy, Hirsch, Voigt, Merkel, Sellheim and Trapl have all pronounced against its use for this purpose.

Nor has it been of any great service in initiating premature labor. Trapl, Schiffmann, Fischer, Nagy, Hirsch, Voigt, Foges and Hofstätter, Merkel and Sellheim may be quoted in support of this statement. Nevertheless, successful cases have been observed in which one or two injections sufficed; and in the production of both abortion and premature labor, it

has proved in almost all cases a useful aid to other methods, such as dilatation by mechanical means.

Practically all observers are unanimous in declaring that it is of the greatest value in overcoming uterine weakness supervening after dilatation of the soft parts, and during the expulsive stage of labor. The effect, as a rule, is very prompt. The pains set in with great vigor in fifteen to twenty minutes or less, and are strong, rapidly leading to delivery; sometimes in a few minutes, and frequently within the hour. As mentioned above, pituitary has been used in at least 1,650 cases, but it is difficult to estimate in how many of these cases it was given during this phase of labor. Not more than a dozen failures during this stage are recorded. The total number of complete failures reported is less than fifty, and these failures are largely amongst those cases in which it was used for production of abortion or premature labor, without other means being employed, or post partum. Several observers have found that it produces movements that are so rhythmical and strong as to be of the greatest value in converting abnormal into normal positions. There is, of course, no general agreement as to what constitutes failure; and as details in all the longer series of cases are not given, it is impossible to express the results recorded in the literature in a more exact fashion. Hofbauer, in his last forty cases, reports no failures; Cahn, out of eighty-seven cases, three; Aubert, 15 per cent. of failures; Foges and Hofstätter, out of sixty-three cases, three failures. These figures seem very typical; but it must be noted that other observers, with as large a series or larger, say nothing of failure.

Its action in these cases is well illustrated by the following cases, selected from amongst those seen by me.

CASE 1.—Primipara, 23 years of age. Labor pains began about 3 a. m. When examined at 9 a. m. the cervix was soft and easily dilatable; but the pains were feeble, and during the course of the pain there did not appear to be any advance of the head, which was in the first position. The patient was seen several times through the day; and the soft parts, including the vagina and perineum, became gradually softened; but still the pains were very feeble, did not advance the head and caused the patient no distress whatever. At 4:30 p. m. 1 c.c. of infundibular extract, prepared by Messrs. Burroughs, Welcome & Co., was injected. Strong expulsive pains began in five minutes. The contractions were regular and continuous. The head descended quickly and the child was born at 4:45 p. m. The uterus was well contracted. The placenta separated and was expelled in five minutes. Without pituitary, one would undoubtedly have used forceps in this case, as the patient was becoming rather tired, and would apparently have gone on for hours without delivering herself.

CASE 2.—III-para, 25 years of age. This was the third pregnancy in three years, and she had not been feeling very strong during the latter weeks. Labor began at 9 p. m. The pains were only slight all night, but sufficient to dilate all the soft parts. They occurred every five minutes, but seemed to have no expulsive power. The patient did not appear to help herself very much, and as she was becoming tired, one had to consider interference. It was decided to try pituitary before forceps. One c.c. of the infundibular was injected at 7:20 a. m. In five

minutes strong rhythmical contractions occurred, which caused a rapid expulsion of the child in less than ten minutes. The placenta was expelled in five minutes.

Pfeifer, Sterne, Zinsser, Jaeger, Mory and Hamm have seen failure to produce delivery, owing to failure of the soft part to dilate. Hamm, indeed, saw physiological stricture develop in four cases where it was used to produce premature labor.

In the two cases of failure seen by me, the difficulty appeared to be that the soft parts did not become dilatable. No ill effects were produced, but forceps had to be applied.

CASE 3.—Primipara, 23 years of age. Labor began at 9 a. m. There were feeble pains all day, which became more severe at 10 p. m. The head was in the first position. Dilatation was progressive and the head descended. Then the pains became feeble, and had little expelling power. One c.c. of infundibular extract (B., W. & Co.) was injected. Stronger pains came on within twenty minutes, but the perineum did not relax, nor did the patient seem to help herself. Finally the forceps were applied and delivery effected. The uterus was well contracted, and the placenta was expelled within ten minutes.

CASE 4.—Primipara, 28 years of age. There were feeble pains throughout the day, which became more regular about 11 p. m. When seen at 2:30 a. m. the pains were occurring at about five-minute intervals. The patient was very nervous and did not help herself very much. The cervix was well dilated, and the pains were not very strong. One c.c. of infundibular extract was injected. In about twenty minutes the pains, as judged by the patient's sensations, became more severe; but the contractions were not appreciably quickened, nor did they advance the head, which was in the first position and fairly low down, although not bulging the perineum. After waiting some time, and as the patient was becoming tired, forceps were applied and delivery effected at 6 a. m. The uterus contracted well, and the placenta was expressed in ten minutes.

In this case the injection of pituitary extract did not seem to increase at all the expulsive power of the uterus; but there appeared to be a distinct lack of voluntary efforts on the part of the patient.

Several observers warn their colleagues not to employ pituitary after delivery of the child and before that of the placenta. Rieck reports a case of retention of the placenta. Hirsch, Voigt, Foges and Hofstätter, Rieck, Merkel, Seitz, Kroemer, have all found it not so valuable post partum; and several of these express a preference for ergot. In view of the greater frequency with which the latter in laboratory experience produces tetanus uteri, this is easily understood. Sellheim reports that out of twelve cases in which he used it, eleven were failures.

Several observers state that they have found it of no value in uterine atony; e. g., Anderes; and this condition probably explains the cases of complete failure to reawaken pains when they have prematurely ceased, such as reported by Zinsser (five out of sixty-five cases), Hamm (one case in forty).

In addition to the action of pituitary on the uterus, its action in increasing the movements of the urinary bladder are important. Jaschke and Franz have employed it as a postoperative tonic for this purpose;

and several of those who have used it in obstetrics have noted that the bladder was well emptied without the use of a catheter.

That in pituitary we have a drug which will increase the flow of milk, was shown by Mackenzie and confirmed by Ott and Scott, and may be illustrated by the curve produced in Figure 2. In this experiment the method employed was that of Mackenzie. A lactating cat was anesthetized, the skin removed from over two mammae, their nipples cut off, and the gland deeply incised. An injection of pituitary produced the prompt response shown in the tracing. In all, some 5 c.c. of milk were secreted. After an interval of thirty minutes a further injection produced an increased flow. The effect of an intravenous injection is evidently very marked, but brief. Whether single or even daily injections will lead to a permanent increase in milk production is not decided. The cases advanced in support of this view by Reynolds are not sufficiently numerous, nor were the observations recorded with sufficient care to be convincing.

CONCLUSIONS

1. Pituitary is of great value in cases of weakness in uterine movements after the soft parts are well dilated. Failure in these cases is rare, probably less than 1 per cent. The later in labor, but before delivery, the more striking the effect. The danger to the child and mother is very slight.

2. As an addition to some mechanical method, e. g., the Champetier de Ribes' bag, it is of great value in bringing on premature labor or abortion. In the former case it may be sufficient in itself, but there is some risk of tetanus of the cervix, or of the uterus, especially when repeated injections are required.

3. For delivery of the placenta its use is accompanied by the danger of tetanus uteri and retention.

4. In post-partum hemorrhage a considerable percentage of failures may be expected.

When a need for a uterine stimulant arises in cases conforming to the above indications, I believe that pituitary is of the greatest value, and will act as in Cases 1 and 2, which are typical of others in my experience.

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