ON
THE ACTION OF DIGITALIS
UPON
THE UTERUS.

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LAST October, in the Burton Ward of St. George's, a case of most severe menorrhagia, which had nearly proved fatal, was cured by the infusion of digitalis, administered almost by accident. The circumstances are sufficiently striking to deserve a full account of the case.

Catharine Mackenzie, æt. 48, a widow, was admitted on the 18th of September, 1854. She stated that her health had been good, and that the uterine functions had been performed naturally, until twelve months previously, when she fell from a ladder, about twelve feet high, and got considerably bruised about the lower part of the back. A week after this blood began to flow from the vagina; at first in small quantities, but it soon became profuse and accom-

panied with pain; and so it continued, without intermitting for a single day, until her admission.

She was first treated in another department of the hospital without benefit; and when she was transferred to Dr. Lee, her case was regarded in the most unfavorable light.

She was perfectly blanched, and was scarcely able to stand, on account of weakness and vertigo. There was a discharge of blood from the vagina, so copious that none of the ordinary appliances were sufficient to keep it within bounds; it poured into the bed; and during micturition it passed from the vagina in gushes. There was slight pain about the sacrum. The ankles were œdematous; the tongue flabby and rather coated; the pulse 80, not very unnatural. On examination, the uterus was found in a perfectly healthy condition, though slightly anteverted; the os was quite soft and smooth, and there was no organic disease of any kind within reach.

Nothing was made out which could give any particular direction to the treatment. Sulphuric acid and sulphate of magnesia were given, but with no effect, except as an aperient.

Three days after this the patient complained of pain in the region of the heart; and said that during the night she had had several attacks of shortness of breath, in which she thought she should have died. On examining the chest, the signs of pericarditis were at once perceived, and the patient was referred to Dr. Nairne.

On the 28th of September all acute symptoms had subsided, and the only unnatural sound in the chest was a regurgitant aortic murmur. The hemorrhage was more profuse than ever, and the patient was extremely low. Four grains of acetate of lead, with half a grain of opium, were given three times a day, and wine was ordered.

On the 2d of October a violent attack of purging and vomiting, with much coldness of surface, made a change of treatment necessary. The discharge was not in the least diminished. On the following day medicine was given con-

taining sulphuric acid and chloric ether. This seemed to do rather harm than good ; and, on the 5th, the acetate of lead was recommenced, with the same result as before. Sulphuric acid was again given, conjoined with etherial and alcoholic stimulants, which had now become indispensable, on account of the excessive faintness and weakness of pulse which had resulted from the loss of blood. On the 9th, tannic acid was prescribed, but it proved as ineffectual as the previous medicines.

The condition of the patient was now hazardous in the extreme. She was evidently sinking. The blood passed during micturition was apparently nearly as copious as the urine, and enough escaped into the bed to make it necessary to change the sheets several times a day. There was a loud diastolic murmur heard all over the central portion of the heart; and the pulse was 94, jerking and extremely weak. Another vaginal examination was instituted, but no additional light was thrown upon the source of the hemorrhage. With a vague idea that the cardiac derangement might, in some way, lie at the root of the evil, a trial of digitalis occurred to me. In such a case any chance was worth seizing; and Dr. Lee consented to the experiment. On the 10th the medicine was commenced; half an ounce of the infusion being given three times a day. On the morrow the improvement was remarkable. The discharge was comparatively scanty; the appetite had returned; and the patient expressed herself immensely relieved. During the night the discharge totally and finally ceased.

From this time the improvement was most rapid. On the 13th the digitalis was exchanged for iron; and on the 31st the patient left the hospital, tolerably strong, and declaring herself perfectly well. And there is reason to believe that she so remains; for she has never come back to the hospital, though she promised to do so at once in case of a relapse.

It now became a question whether this sudden discontinuance of the hemorrhage was to be regarded as a mere accidental coincidence, or was to be attributed to the action

of the digitalis. And supposing that the change was in consequence of the medicine, it remained to be discovered in what way the medicine operated; whether directly or indirectly; whether upon the general circulation first and secondarily upon the uterine; or whether upon the uterus especially, in some manner hitherto unexplained. It is the object of this paper to answer these inquiries.

Since the occurrence of the aforesaid case patients have been admitted into the Burton Ward labouring under menorrhagia, arising from different causes; in age they have varied from 19 to 64; and in other particulars they have differed as widely. Many of the cases have been of a kind to get well without much medical interference; these have always been allowed to do so. In every case requiring active remedies, admitted since October, 1854, the administration of digitalis has constituted the sole treatment. The discharge has invariably been extinguished; the time of its cessation varying with the strength of the medicine. In cases where the medicine was given in the largest doses, the discharge has not appeared after the second day; where the remedy has been given in a more dilute form, the hemorrhage has never outlasted the fourth.

The effects which follow the administration of a large dose—an ounce and a half of the infusion, for instance, are such as to establish beyond question the powerful influence of digitalis upon the uterus. A few minutes after the draught is swallowed, the patient complains of acute pains in the back and hypogastrium, which she compares to the pains of the first stage of labour; a quantity of blood, solid and fluid, is then ejected; and the discharge is absent until, after several hours, the pain subsides, and the bleeding returns with diminished force. After each repetition of the remedy, the cessation becomes longer, and the recommencement more feeble, until after three or four doses the discharge ceases.

It is not my purpose at present to dwell upon the *modus operandi* of the drug; I merely wish to show that its effects are immediate and well marked. When a morbid action

gradually subsides, after a course of treatment, the amelioration may be quite independent of the medicine swallowed ; but when each draught is followed by a temporary removal of the disease, we have no choice but to admit that the recovery is in consequence of the treatment. A case may be here introduced which will serve to illustrate some of the preceding statements.

A married woman, named Mary Lee, 37 years of age, the mother of a large family, was admitted on the 18th of January. She gave the following account of the progress of her disorder :

“ Ever since the last labour, which occurred nine years ago, the menses have been profuse, and mostly mixed with coagula. Eleven months ago, after much hard work, with insufficient food, the hemorrhagic discharge became nearly continual : and she came to St. George’s, at first as out-, latterly as in-patient, undergoing treatment for four months without much temporary or any permanent advantage. Short irregular intervals have occurred until within the last eight weeks, during which period the discharge has been excessively copious, and has not intermitted for a single day.”

When she was admitted she was in a state of the most extreme anæmia ; the heart’s beats were very feeble, but without murmur ; the pulse was 70, and extremely weak and small. The discharge was constantly flowing into the bed ; besides which, whenever urine was evacuated, great quantities of blood gushed from the vagina. The quantity of sanguineous fluid thus voided was estimated at four pints in the day and night ; of this a great portion was urine ; but it seemed that about a quarter of the amount was pure blood.

Half an ounce of the infusion of digitalis was now ordered three times a day, in an ounce of water, commencing on the 18th. On the morning of the 22d, the discharge ceased somewhat suddenly. No other effect was observed from the medicine ; the pulse was reduced only two beats ; it remained quite regular, and of about the same character

as before. On the 24th, the medicine caused vomiting, and the pulse became reduced from 68 to 60, still remaining regular. Whereupon the digitalis was exchanged for a solution of citrate of iron.

The patient progressed favorably until the 12th of February, when a little sanguineous discharge reappeared, which was merely supposed to indicate the return of the monthly period. But on the following day the patient was fainting with loss of blood, which was pouring out with nearly its former profusion; the pulse then numbering 72. The infusion was now given at the rate of an ounce and a half three times a day. The effect of the first dose was to cause pain, which supervened in about five minutes, chiefly referred to the back, but also affecting the lower part of the belly, and said accurately to resemble pains in the first stage of labour. This lasted acutely for about half an hour, and then gradually diminished, not entirely disappearing for some hours. The accession of the pain was immediately followed by the forcible expulsion of a quantity of blood, mostly coagulated; after which the bleeding ceased, and remained absent so long as the pain endured.

Except that each recurrence of the discharge was scantier than the preceding, the same phenomena occurred after each repetition of the medicine, until the fifth dose, after which no blood was passed. The medicine was continued until the 18th, when the patient was attacked with vomiting, looseness of the bowels, and a sensation of heat about the mouth and throat; and the pulse, which had been gradually increasing in rate, was found to have reached 92. The unpleasant symptoms presently subsided; iron was prescribed; and the patient speedily acquired a condition of health to which she had been long a stranger.

A vaginal examination was now made, and the uterus was found in a perfectly natural condition. There was a little thickening of the os, such as is generally observed in women who have borne many children. It is to be regretted that circumstances prevented an examination immediately before the administration of the foxglove; but perhaps it

would not be too much to assume that the uterus was then in the same state as it was some months previously, when the symptoms were much the same. The body and neck were then so distended, and the os so open, that a fibrous tumour was suspected to exist.

After a due interval the natural catamenial discharge appeared, no coagula were passed, and the evacuation was scanty, and lasted but two days. The patient then left the hospital in a state of perfect health, and resumed her former laborious occupation. She was seen very recently (September 17th); she was perfectly well, and the menses had never shown the slightest tendency to transgress their natural limits.

"It is not necessary to dwell longer upon individual cases; it is enough to repeat that, so far as regards a speedy cessation of the discharge, the result has been the same in *every* case subjected to the treatment. I should here mention that the digitalis has always been given in company with wine and good diet. Owing to the kindness of Dr. Barclay, I am enabled to confirm my assertions by the results of his practice. Dr. Barclay writes, "The cases in which I have employed it" (*i. e.* the digitalis) "were such as seemed to me to be instances simply of functional derangement, which did not require the interference of the accoucheur; and I can say with confidence, that this mode of treatment has been more satisfactory in its results than any other I have hitherto adopted. Cases, indeed, have not been wanting which have resisted the influence of tonic and astringent remedies, which have yielded readily to this."

Before quitting the first part of my subject, I may allude to the results of a few experiments upon the sanguineous discharge resulting from organic disease of the uterus. It seems that in these cases the remedy acts with somewhat less certainty than in the preceding, a larger dose is required, and the effect is sometimes transient.

In a case of polypus, where violent hemorrhages were apt to occur, one of the attacks was suddenly cut short, while at its height, by the administration of an ounce of the infusion. The discharge ceased within an hour of the taking of the first dose, and never occurred again, although the tumour was allowed to remain untouched for three weeks. Where hemorrhage resulted from a fibrous tumour distending the uterus, the same dose produced the same effect, except that it was less permanent. In a case of advanced cancer of the os uteri, with continual and profuse sanguineous discharge, an ounce and a half of the infusion was found to cause total cessation of the hemorrhage within a quarter of an hour, the suspension generally lasting for about twelve hours. This sequence was observed as often as the experiment was made. In the same case it was found that half an ounce of the same preparation was perfectly ineffectual. Where severe attacks of bleeding depended upon rigidity of the uterus, with a roughened and tubercular state of the os, the hemorrhages were found to cease after five or six half-ounce doses. The advantage here was merely temporary.

Taking into consideration the preceding facts, I think we are justified in believing that digitalis cures, with more certainty than any remedy hitherto employed, cases of menorrhagia not connected with organic disease; and that, where organic disease gives rise to the symptoms, the action of the medicine is scarcely less manifest, although the advantage may be temporary.

I shall now consider the *manner* in which digitalis influences the uterus so as to produce these effects. The alteration must depend on some change, either in the local organism or in the general circulation. That the change is not in the latter is evident from the fact, that hemorrhages from other parts of the body are not controlled like those from the uterus. Moreover, it was found, that on the cessation of the hemorrhage, the pulse was not uniformly slower or weaker than when the treatment was com-

menced. It was found to have become slower in only seven of the sixteen observations, and even then the retardation was generally very slight. Then as to the *force* of the circulation, the pulse was not found to have become perceptibly weaker, except in one solitary instance. Thus it seems that the peculiar uterine influence is quite independent of any change in the heart's action or general circulation. It must, therefore, depend on some change wrought by the medicine in the local organism.

As far as I know, there are but two kinds of action which could be thus established in the uterus which would serve to account for the phenomena. Contraction of the capillary vessels, or the firm closing up of the uterus itself, might either of them prevent the effusion of blood from the lining membrane.

That constriction of the vessels is the change induced is a theory which cannot be upheld. Such an effect would probably not be confined to the uterus, but would be equally observed in other parts of the body. Hemorrhage from the lungs, bowels, and kidneys, would be amenable to the remedy. Besides this, it will be seen that there are certain particulars in the effect of the medicine which are not compatible with the supposition.

All the facts point to the conclusion that the digitalis acts by causing muscular action in the uterus itself. A short time, generally about ten minutes, after a considerable dose of the medicine is swallowed, the patient complains of severe pain in the region of the sacrum, which passes into the hypogastrium, and in every respect resembles the pain of the first stage of labour; very shortly after this a considerable quantity of blood, generally partly coagulated, is forced out of the uterus. No more discharge is then observed for several hours, so long as the contractile pain continues; and the same effect is noticed after each subsequent dose until the hemorrhage is abolished. In the case of Mary Lee, given at page 5, this succession of events was observed four times. Other cases have occurred at the hospital, in which the same effects were noticed.

A patient, named Ellen Morling, who was affected with very severe uterine hemorrhage, was ordered an ounce and a half of the infusion three times a day. The first dose was taken in the evening; very shortly afterwards pain came on in the back, and along the inside of the left thigh, precisely resembling, in character and position, the pain of her last labour. Within fifteen minutes of the taking of the medicine, a clot, said to have been as large as an egg, was expelled, and the discharge totally ceased until the following morning, when it recommenced. Another dose was then administered, and the same results were observed to follow with more quickness; a mixture of solid and fluid blood had been expelled, and the discharge had totally ceased, within five minutes. The discharge reappeared a short time before the third dose was given in the afternoon. The effects were the same, but more immediate; scarcely any interval was said to have existed between the taking of the draught and the expulsion of the contents of the uterus and suspension of the discharge; the pain was more severe than it had previously been. On the following morning the discharge reappeared in very small quantity; the remedy was given in half-ounce doses, and the cure presently completed.

The chain of symptoms here observed—the labour-pains, the expulsion of the contents of the uterus, the suspension of the discharge, seem to be the precise effects which might be expected to result from forcible contraction of the uterus; and it is not easy to suggest any other explanation.

A striking confirmation of this theory was supplied by a case which, at first sight, seemed contradictory. A patient, named Ann Cage, was brought into the Burton Ward, suffering from the symptoms of malignant disease of the uterus. She had a profuse sanguineous discharge. Hemorrhage, under similar circumstances, had previously been suspended by digitalis, and now the medicine was given in the same doses as before. An ounce and a half of the infusion was ordered twice a day. The first dose was ineffectual; it was repeated after two hours with no better

result. After two more repetitions of the medicine, the discharge was still flowing with unabated profusion, and it became manifest that the symptom was not amenable to the remedy. This was the first and only exceptional case. On making a vaginal examination, an irregular fungoid tumour was found attached to the anterior lip of the os uteri. This was extremely vascular, and its surface was the source of the discharge. The entire disease was external to the cavity of the uterus; the organ itself was healthy. If the medicine possessed a merely astringent action, its effect would be the same whether the cancer were within or without the cavity of the uterus.

Before concluding this portion of my subject, I may give the results of some experiments upon the recently impregnated uterus, which, if not sufficient in themselves to establish the stimulant effect of digitalis upon the organ, are valuable as tending strongly to confirm the conclusions previously formed.

E. Waters, being, as she supposed, very near the termination of her fifth pregnancy, had an attack of vague abdominal pains, which presently passed off. On the following day no pain whatever was experienced, and there was no sign of impending labour; whereupon an experimental dose of 20 drops of tincture of digitalis was administered. In fifteen minutes slight uterine pain was experienced; and in fifteen minutes more the patient was unmistakeably in labour. Within nine hours the child was born. Ten minutes after that event 50 drops more of the tincture were given. This was followed, in ten minutes, by a most marked increase in the uterine pains; and for the next twelve hours the after-pains were excessively frequent and severe, more so than she had ever before known them.

Mary Macaulay was delivered of her first child on the 1st of August. After-pains were complained of on the following day. On the 3d and 4th they were completely absent. On the evening of the 4th, half an ounce of the infusion of

digitalis was given, and severe pains were felt through the night. The medicine was continued three times a day until the 7th. During the whole of that period the pains were frequent, and latterly they were very acute. When the medicine was discontinued they at once subsided.

Harriet Killick was delivered of her sixth child on the 18th of August. In previous labours she never had after-pains severely, and they never lasted beyond the second day. An hour after the completion of the labour, the patient being free from pain at the time, one ounce of the infusion was administered, and ordered to be repeated twice a day. A quarter of an hour after the first dose acute labour-pains came on, as severe as while the child was in the uterus. This subsided after two hours, and the patient was free from pain until the second dose was taken. This was followed by another attack of pain, which, however, was not so severe as the previous. When the medicine was taken for the third time, the patient had been for hours without uneasiness of any sort. In a quarter of an hour she was seized with after-pains of the same character as previously, but of much greater severity. "She thought she should have been torn to pieces." The patient now declined to take any more of the medicine, and had no further attacks of pain. It was observed in this case that there was almost a total absence of sanguineous discharge, although in all previous labours it had been profuse.

In four other cases the pain of uterine contraction was observed to depend on the administration of digitalis. The particulars are not given, as the cases very closely resemble those already narrated.

In these experiments the fact sought to be established is simply the connection between the pain of uterine contraction and the absorption of digitalis into the system. It is not expedient to multiply cases, as the experiment seems not devoid of cruelty, and, if it were recklessly enforced,

might well be productive of danger. These cases seem quite sufficient to prove that the drug has the action upon the uterus which has been previously attributed to it. It stimulates the nervous system of the organ, and excites the muscle to contract. It stimulates the ganglia in which the motor power of the uterus resides. This fact is not without significance. It may help us, eventually, to a more general and philosophical view of the action of foxglove than we have yet attained. It will be seen that this effect upon the uterus is precisely analogous to the influence exerted by the same medicine upon the heart. In a lecture given by Dr. Bence Jones before the College of Physicians, and printed in the 'Medical Times,' the action of digitalis upon that organ is very fully explained. It is therefore not necessary, in this place, to do more than repeat the conclusions there arrived at. It is there shown that the medicine acts as a stimulant upon the musculo-motor system of the heart, although that effect is at first masked by an action of the same kind upon the pneumogastric nerves. "It may safely be assumed that in man digitalis acts on the nerves that regulate the heart's action, first as a stimulant, and in large doses as a sedative."

The operation of foxglove upon the other involuntary muscular organs yet requires to be accurately observed. It is by no means impossible that its effects upon the heart and uterus may turn out to be merely portions of an action which occupies a wider field than has hitherto been supposed.

In concluding, I wish to express my regret that I am unable to give any comparative statement of the manner in which the uterus is affected by the various preparations of digitalis; but I cannot now supply deficiencies, as my opportunities for observation have drawn to an end.

I cannot sufficiently express my obligation to Dr. Lee, for allowing me to make free use of the cases in his ward.

It is to his kindness that this paper owes its existence. I am, moreover, indebted to Dr. Barclay for valuable suggestions, and to Dr. Bence Jones for invaluable counsel and encouragement.