

**An experimental inquiry into the effect upon the mother of poisoning the
foetus / by W.S. Savory.**

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Dr John Percy
with the author's Compliments

AN
EXPERIMENTAL INQUIRY
INTO THE
EFFECT UPON THE MOTHER
OF
POISONING THE FŒTUS.

BY
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EFFECT UPON THE MOTHER

OF

POISONING THE FŒTUS.

THE structure of the placenta and the character of its circulation,—the close and intimate relation which exists there between the foetal and maternal blood,—is naturally appealed to in explanation of the well-known effects produced in the child by various morbid and other peculiar conditions of the maternal system occurring during pregnancy. This intimate relation between the two circulations at the placenta is looked to for an explanation, not only of the transmission of obvious and fully-developed disease from the mother to the foetus, as variola and syphilis, but also of those more subtle and obscure changes which are likewise understood to be capable of affecting the child.

Although the influence thus exercised by the mother upon the foetus has been known to everyone for ages past, and is continually illustrated by striking examples, it is only comparatively recently that the converse relation—the influence of the foetus upon the mother—has received any attention.

The subject has been most ably brought before the profession by Dr. Alexander Harvey, in a very interesting series of philosophical papers “On the Fœtus in Utero as

inoculating the Maternal with the peculiarities of the Paternal Organism.”*

In these well-known essays, he advances some excellent observations, and cites many cases to show “that an explanation offered by Mr. M^cGillivray, of Huntly, is the true one, viz.: that while, as all allow, a portion of the mother’s blood is continually passing by absorption (and assimilation) into the body of the fœtus, in order to its nutrition and development, a portion of the blood of the fœtus is as constantly passing, in like manner, into the body of the mother; that as this commingles there with the general mass of the mother’s own blood, it inoculates her system with the constitutional qualities of the fœtus; and that, as these qualities are in part derived to the fœtus from its male progenitor, the peculiarities of the latter are thereby so engrafted on the system of the female, as to be communicable by her to any offspring she may subsequently have by other males.”

Now although we are in possession of absolute facts which furnish clear and convincing evidence of the direct transmission of what may be termed accidental matter from the mother to the fœtus, not only of certain diseases, but also of foreign substances,—as camphor and oil, in the experiments of Majendie and D. Williams,—yet we have no such conclusive facts in support of the converse proposition. However strong the argument from analogy may be, supported as it is by the record of cases of extreme interest, yet demonstrative evidence is wanting of the direct absorption of foreign matter from the fœtus by the mother. Indeed, the only experiments in reference to this point with which I am acquainted were attended by a negative result.

In his *Compendium of Physiology*, Majendie briefly says, “I have often injected very active poisons into the vessels of the cord, directing them towards the placenta; but I have never seen the mother suffer from the effects of them.”

* Monthly Journal of Medical Science for October, 1849, and September, 1850.

And this negative result may be supposed to depend upon the fact that, after all, the communication between the maternal and foetal blood is only an indirect one, and is therefore limited. It may reasonably be believed to be one office of the cells which intervene between the foetal and maternal vessels to regulate or control such transmission,—to exercise a selecting influence on the materials absorbed, as some other cells in all probability do. It is commonly supposed that the office of these cells is solely connected with the transmission of materials from the mother to the foetus, one set selecting and separating, and the other elaborating and absorbing them.* Therefore, even if an interchange to a certain extent be admitted, there is still no proof that poisons or other morbid materials, whether arising from within or from without, must necessarily pass from the foetus to the mother.

But in whatever way the argument may be supported, it is certain that two very opposite opinions are expressed by physiologists on this subject. Dr. Harvey, after quoting this sentence from Mr. M'Gillivray, "I am quite aware that many physiologists maintain that, in the highest species of animals, the blood cannot be returned by the foetus to the mother during utero-gestation," endorses it with the following statement: "That this opinion is very generally held by physiologists in this country is quite certain. Dr. Alison, for instance, after observing (on the authority of Majendie and of Dr. David Williams, of Liverpool), that camphor and oil injected into the blood of pregnant animals are soon detected in the blood of the foetus; but that poison, injected into the umbilical arteries, although mixing with the blood on its way from the foetus to the placenta, does not affect the mother; and that fatal hæmorrhage in the mother does not apparently diminish the fulness of the vessels of the foetus, adds, 'so that it would seem that the transmission of fluids is almost entirely from the mother to the foetus.'

* Kirkes's Physiology, 3d edition, p. 681. Carpenter's Manual of Physiology, 3d edition, pp. 154-5 and 526.

Again, Dr. Kirkes, referring to Professor Goodsir's observations as to the intervention of two distinct layers of cells between the foetal and maternal portions of the placenta, speaks of the one being 'probably designed to separate from the blood of the parent the materials destined for the blood of the foetus,' while the other 'probably serves for the absorption of the material secreted by the other set of cells, and for its conveyance into the blood-vessels of the foetus,' no idea, seemingly, being entertained of a converse process.* Moreover, the view taken by most physiologists of the destination of that portion of the foetal blood which is transmitted to the placenta, appears to be exclusively that of *renovation* or *aeration*, by coming into relation with the oxygenated blood of the mother, nothing being said as to *re-absorption* into the maternal system." In a note, he adds, "In his History of Medicine, Dr. Alison expresses himself even more strongly on the subject: 'The experiments of Majendie and others have proved that any substance which may be circulating in the blood of the mother finds ready access to that of the foetus, but that there is little or no transference of fluids in the opposite direction.'"

Those authors who express a contrary opinion cannot refer to any facts in support of it.

As the question at present stands then, the only demonstrative evidence is that yielded by the experiments of

* It is, however, only fair to add that, in the later editions of his work, Dr. Kirkes, in a note, expresses the following strong opinion:—"Although, in the text, mention is made only of the passage of materials from the blood of the mother into that of the foetus, yet there can be no doubt of the existence of a mutual interchange of materials between the blood of both foetus and parent, the latter supplying the former with nutriment, and, in turn, abstracting from it materials which require to be removed."

The most recent expression of Dr. Carpenter's opinion is to this effect. After giving the common account of the function of the placenta, as furnishing materials for the nutrition of the embryo, and as a respiratory organ, he adds, "And it is probable, too, that the placenta is to be regarded as an excreting organ; serving for the removal, through the maternal blood, of excrementitious matter, whose continued circulation in the blood of the foetus would be prejudicial to it."

Majendie, and these gave a negative answer. All the rest of the evidence which has been adduced on either side is devoid of proof—is indirect and inconclusive.

This subject was brought before the notice of the Hunterian Society by Mr. Jonathan Hutchinson, in a paper on “The Communication of Syphilis from the Fœtus to the Mother,” read there in the latter part of 1856.* It was followed by a very interesting discussion, and it then occurred to me that it should be brought to the test of experiment. I could find no such evidence on record, excepting the experiments of Majendie already referred to, and these had yielded a negative result. But the nature of these experiments appeared to me objectionable, for it seems almost impossible to open the vessels of the cord and inject directly into them without interfering to a fatal extent with the fœtal circulation.

This was the general plan of my experiments:—

By opening the abdomen and uterus to expose and isolate a living fœtus. Then to inject into it, with the least possible amount of violence, some substance capable of ready absorption, and the operation of which is marked by obvious and unmistakable effects. To be sure that no trace of the substance came into direct contact with the maternal tissues. To place the fœtus thus injected in a condition most favourable for the continuance of the circulation, and then to watch for symptoms of the operation of the poison upon the mother.

The poison I selected from some others was strychnia, for these reasons:—

It is extremely active in very minute doses.

It is easily dissolved, and therefore readily absorbed.

Its absorption is rapidly followed by its operation on the system.

The symptoms of its operation are striking and characteristic.

* The paper is printed in the Medical Times and Gazette, Dec. 20, 1856, and Jan. 10, 1857.

This question in relation to the transmission of syphilis had previously been often suggested by various authors, but it is much more fully discussed by Mr. Hutchinson.

Its effects are not materially counteracted, nor its symptoms masked, by the influence of chloroform.

After some experiments with strychnia, dissolved in various menstrua, as alcohol, benzole, &c., I preferred, as the most eligible, a solution of strychnia in diluted acetic acid. In this way I obtained a very convenient solution of the acetate of strychnia of sufficient strength.

Twenty-four grains of strychnia were dissolved in seven drachms of distilled water, by the addition of one drachm of acetic acid. Twenty minims of this solution therefore contained one grain of strychnia.

A certain quantity of this solution was introduced, usually, into the abdominal cavity through the parietes by means of an Anel's syringe. This little instrument is very convenient for the purpose. The abdominal wall can be easily pierced by its fine point without any violence. The quantity of fluid injected can be accurately calculated, and, when withdrawn, the minute puncture is so closed by the natural elasticity of the tissues, when the foetus is far advanced in development, as to prevent the escape of any portion of the solution.

The subjects of my experiments were dogs, cats, and rabbits. Dogs, from their size, are the most convenient, and furnish the most satisfactory results.

From a considerable number of experiments I select the following ones as fair examples.

Experiment I.—A pregnant bitch, a common, smooth-haired terrier, weighing about twelve pounds, was rendered insensible by chloroform. The abdomen was opened in the median line, and the uterus was partially drawn out. It was carefully divided over a foetus. The amnion was punctured, and the foetus, lively and vigorous, was allowed to escape. It was received upon a napkin, and remained connected with the mother only by the cord. The foetus was supported so as to avoid stretching the cord. The abdominal wall was cautiously punctured with the point of

the syringe, and ten minims of the solution (half a grain of strychnia) were injected into the cavity. When the syringe was withdrawn no fluid escaped. The puncture was so minute that nothing exuded even upon pressure. The fœtus, which struggled slightly after the operation and then became tetanic, was suffered to remain where it lay, not in contact with the mother.

An incision was then made in another part of the uterus, over a second fœtus, which was only partially exposed, and not drawn out. The side of the chest was wiped dry, the point of the syringe was inserted between the lower ribs, and about the same quantity of the solution was injected into the thorax. The piston was slightly retracted before the pipe was withdrawn, and not the least trace of moisture appeared. The part where the puncture was made was carefully watched for some seconds by Mr. Crowfoot and myself, and we both were fully satisfied on that point. That portion of the uterus which had only partially extruded was now carefully replaced, without any protusion of the fœtus, then the rest of the uterus, and lastly the fœtus first operated on was returned into the abdomen, and the wound was closed by sutures.

The bitch lay on her side motionless, and breathing tranquilly, for eight minutes from the time of the first operation. In about nine minutes slight spasms appeared. These gradually increased in intensity, and continued with scarcely any intermission for eighteen minutes. In twenty-eight minutes from the time of the injection the dog was dead.

Five minutes after her death the abdomen was re-opened. There were two other fœtuses, besides those two which had been injected; four in all. While the two which had received the strychnia revealed no signs of life, the other two were still alive and vigorous. They lived for some time after separation from the mother, and one, which was suffered to escape from its membranes, respired and otherwise displayed such evident signs of full development, such as crying, that any doubts of the near approach of natural labour, which could have been entertained after a mere inspection of the

fœtuses, were completely set at rest. The parts were found in the abdomen as they had been replaced, and the fœtus, which was operated on in the uterus, still remained there.

Now I am satisfied that in these experiments none of the solution escaped from the fœtus through the puncture, because I ascertained that if proper precaution had been adopted in the injection, none escaped upon pressure.

Moreover I had learned from another set of experiments, that when the solution is allowed to come into direct contact with the maternal tissues, as when injected into the uterine or peritoneal cavity, or when allowed to escape from the fœtus, its symptoms are never delayed for a period at all approaching the length of time which elapsed between the closure of the abdomen and their manifestation in these experiments. The usual period is two minutes, and this is rarely extended to five. The animal is in most instances dead before that period.

But that this source of fallacy did not arise, I have more than once unintentionally obtained still better evidence in another way. Some of my experiments, the earlier ones more especially, were attended with a negative result. Fœtuses were injected and returned into the mother, but no visible effects on her of the poison followed. Prolonged exposure and rough manipulation when the fœtuses were small and feeble, had been fatal to their circulation. But I now see the importance of the negative results which these experiments yielded. The solution could not have escaped from them, or in any way have come into contact with the maternal tissues.

More recently I have performed the following experiment.

Experiment II.—I removed two fœtuses within a day or two of their full term from the uterus of a cat immediately after its death from chloroform, having previously placed ligatures on the fœtal portion of the cords. They both were lively. I injected ten minims of the solution into the abdominal cavity of each by perforating the walls with the point of the syringe

in the usual manner. When the syringe was withdrawn the punctures remained dry, and the spots were scarcely visible. No fluid exuded upon pressure. Then, without in any way securing those punctures, I introduced the two fœtuses alive and tetanic into the abdominal cavity of another cat under chloroform, and allowed them to remain there for more than twenty minutes. Not the slightest symptom of strychnia was produced in the cat.

We are naturally reminded by the negative result of these experiments of the impunity with which a mother may carry a dead and decomposing fœtus. In neither case is there any longer a circulation.

In the following experiment the possibility of the fallacy occurring, which has just been alluded to, was prevented.

Experiment III.—A cat, far advanced in pregnancy, was rendered insensible by chloroform. The abdomen was opened and the uterus exposed. It was divided at a part to which a placenta was not attached, and a vigorous fœtus extracted in its membranes, which were removed from it. It was supported on a napkin, and into the abdominal cavity about ten minims of the solution were injected. The portion of integument around the puncture was then carefully pinched up and secured by a ligature, so as to prevent the possibility of any escape of the solution. A second fœtus was then extracted and treated exactly in the same manner. Both, with the portion of the uterus, were then returned into the abdomen, which was closed with sutures.

For ten minutes from the period of the first injection the cat lay on her side breathing tranquilly. Then slight spasms ensued in the hinder extremities; these gradually increased, and at length passed into violent and general ones. In seven minutes more the cat was dead.

The abdomen was then re-opened, and the ligatures placed upon the punctures in the fœtuses were found still perfectly secure. Both the injected fœtuses were yet alive. Within a few minutes after they were injected they exhibited decided

spasms, and these continued, for a long period after the death of the mother, frequently to recur. The other fœtuses were not affected.

In the next experiment, the fœtuses, after being injected, were not returned into the abdomen.

Experiment IV.—A pregnant rabbit, within a day or two of her full term, was rendered insensible by chloroform, and the uterus was exposed by the usual longitudinal incision, and protruded considerably. It was carefully divided over a fœtus, which was immediately expelled, and received on a napkin; remaining connected with the mother only by the cord. The point of the syringe was inserted through the abdominal wall, and about five minims of the solution were injected. None escaped. Five other fœtuses—all but one—were removed and injected in a similar way; from five to ten minims of the solution being thrown into each. The punctures remained dry. In one case the cord gave way. The fœtuses were all fully developed, and very vigorous. Almost immediately after the injection, decided tetanic spasms appeared in all, but each survived, and moved actively for some time after. None of the fœtuses were replaced after injection; indeed, it would have been impossible to do so, owing to their size. They were allowed to lie outside the mother, and remained connected with her only by the umbilical cords.

At the end of fifteen minutes from the time of the first injection decided tetanic spasms appeared in the mother, and, after repeated attacks, she died rigid in three or four minutes more. During the spasms of the mother, two or three of the placentaë became detached.

The following experiment is a still more striking one.

Experiment V.—A large bitch, far advanced in pregnancy, was rendered insensible by chloroform. The uterus was exposed and opened to a small extent, at a spot as far as possible from the attachment of a placenta. Through this,

by means of very gentle pressure, a fœtus, enclosed in its membranes, was readily expelled. The membranes were divided, and the fœtus, now only connected by the cord, was placed in a large but shallow vessel of water, conveniently arranged, the temperature of which was about 100°—that is, as nearly as possible the temperature of the fluid in which it is naturally immersed. Into the abdominal cavity of the fœtus, which was kept distant from the mother the entire length of the cord—some two or three inches—twenty minims of the solution (one grain of strychnia) were injected, the fœtus being raised from the water for that purpose. In about two minutes, the fœtus, which was vigorous and lively, exhibited decided spasms, and these continued to recur at frequent intervals.

Another fœtus, removed in the same manner, and placed in the same water, was similarly treated, and similarly affected. In about five or six minutes a ligature was placed on each cord, and the fœtuses were separated, by dividing the cords on the fœtal side of the ligature. Little or no blood escaped from them. Three other fœtuses were subjected to the same process, and after a few minutes likewise removed. The quantity of the solution injected into each varied from twenty to twenty-five or thirty minims. Into one nearly forty minims were thrown. They all exhibited tetanic spasms, which in the majority continued, though feebly, after division of the cord. The protruded portions of the uterus, which still contained three or four fœtuses, and such portions of the intestines as had escaped, could be only partially replaced, owing to the contracted state of the abdominal muscles.

The mother continued to breathe placidly under the influence of chloroform for thirty minutes from the period of the first injection, and for fifteen minutes after the last fœtus had been removed. At the end of that time very slight twitchings were visible: these became more and more marked, and passed at length into a decided spasm. The spasms, preceded by twitchings, gradually increased in

intensity, occurring at intervals of about two minutes. For fifteen minutes I watched some six or seven, to remove any doubt of their character, and then as the effects of the chloroform were rapidly subsiding, I did not choose to prolong the experiment further, and the dog was killed.

In this experiment, all direct contact between the injected *fœtuses* and the mother was prevented. No communication whatever existed between the injected *fœtus* and its mother, except through the cord and placenta. It cannot be doubted that the poison passed from the blood of the *fœtus* to the blood of the mother at the placenta.

These experiments, more especially the latter, are very delicate ones, and unless certain conditions concur, they are very likely to fail. When *fœtuses* are removed from the uterus and exposed, they soon become feeble; the circulation very rapidly declines: and, of course, they perish the more quickly in proportion, as they are young and small. Therefore, in order to ensure success, it is most important that the *fœtuses* be well developed, near their full term, large and vigorous. It is more difficult, but, nevertheless, quite possible, to succeed when the *fœtuses* are much younger. For the same reason and to facilitate the necessary manipulation, the larger the mother is the better. In dividing the uterus, care must be taken not to wound the placenta. This may be avoided by gently raising up the uterine wall between the thumb and forefinger before cutting it—in this way the absence of placenta can be ascertained. It is also as well to avoid, if possible, dividing the larger veins. For this and for other reasons, the most convenient part of the uterus for division is towards the constricted portion between two adjacent *fœtuses*,—as the placentæ are circularly attached around the dilated portions in which the *fœtuses* are contained,—and at a point most distant from its attachment. In operating on the *fœtus*, traction of the cord must be most rigidly avoided, for, besides interfering with its circulation,

it is very likely to tear a portion of the placenta from the uterus.

All these remarks apply with increased force to the last experiments where the fœtuses remain exposed, for, when they are returned in a feeble condition to the abdominal cavity, the warmth of the mother often greatly restores them. In the latter experiments, the more fœtuses that can be injected the better, and, in a few minutes after the injection of each, it is as well to detach it, for its circulation has then probably almost ceased, and, by retaining it, the experiment is complicated and the risk of accidental contact of the fœtus with some part of the mother, or separation of the placenta, is increased. But this more delicate and difficult experiment is doubtless most obviously free from objection.

One or two points in these experiments appear worthy of notice. The great length of time the fœtus survives after the injection of strychnia, is remarkable. I think this may be thus explained. When strychnia kills rapidly, it produces death principally by affecting the muscles of inspiration; thus fixing the chest and so suspending respiration. When strychnia kills quickly, it kills by apnœa. This kind of death the fœtus in utero of course escapes, and in it death is probably produced by exhaustion, as in ordinary cases when strychnia kills more slowly.

Again, in my experiments, after the mother has died from the effects of strychnia, I have carefully watched for any appearance of tetanus in those fœtuses which still remained untouched in the uterus. And although the effect of strychnia is so striking in the fœtus when directly injected, I have never observed any of its symptoms in those which I had not poisoned. This fact is most interesting in relation to the present inquiry, and may probably be explained by the short time the mother survives its effects.

A similar remark applies to chloroform. Although, in my experiments, the mother was invariably reduced to a state of profound insensibility, yet the fœtuses, when exposed, were always active and lively.

I submit, then, that proof is no longer wanting of the direct and rapid transmission of matter from the fœtus to the mother through the blood in the placenta.

Although it has hitherto been the custom, when considering the close and intimate relation between the fœtal and maternal blood, to speak only or especially of the effect produced in the fœtus by morbid materials present in, or other unnatural conditions of the blood of the mother, to say the least, it must be admitted that there is an equally free and direct transmission of matter—though for many reasons a less obvious one—from the fœtal to the maternal blood.

When the influence which the fœtus in utero thus exercises upon the mother shall be fully recognised, it will soon become more clearly understood. At present it is impossible to estimate the importance of the subject. While standing only on the very threshold of the inquiry, enough is visible to tempt any one beyond. Why should not the investigation of this question lead to results which, although more difficult to obtain, are perhaps not less worthy of research, than those useful and extensive ones which have already been disclosed by the study of hereditary transmission of disease?

THE END.

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