

*Stated Meeting, February 6, 1877.*

*The President, DR. T. G. THOMAS, in the Chair.*

DR. PAUL F. MUNDÉ opened the discussion on

THE INFLUENCE ON THE FŒTUS OF MEDICINES, PARTICULARLY NARCOTICS, ADMINISTERED TO THE MOTHER DURING PREGNANCY AND LABOR,

by reading the following paper :

“For some time past, Mr. President, I have been waiting for an opportunity to bring this topic before the Society. During the past summer, I was called to attend a lady in her second confinement at Long Branch, who had, during that whole pregnancy, been addicted to the use of morphine, having gradually reached the large amount of twelve to sixteen hypodermic syringefuls of Magendie’s solution, or twelve to sixteen grains of morphine in the twenty-four hours. There was nothing abnormal about the pregnancy, the voluntary movements of the child being felt with the usual distinctness, although the latter as well as the uterine contour were not accessible to the touch on account of the enormous tympanites existing during the last weeks of gestation. The labor progressed normally, but the contractions were painful and inefficient, and the administration of chloroform, at the imperative wish of the patient, perhaps, retarded them somewhat more. However, the child was finally born after a labor of about twelve hours; was lively, and immediately cried lustily, and appeared to be no worse either for the chloroform or the morphine (several syringefuls of which had been taken as usual, during the night, prior to my arrival at two A.M.; the baby was born at nine A.M.). It was not nursed, as the mother said she had had no milk in her former confinement, but mainly because I thought it decidedly unsafe for the mother, with her opium habit, to nurse her child, although one might have supposed that the latter had become accustomed to the drug. It was given to a wet nurse, thrived finely, and has as yet had no illness of consequence.

I should not have thought much about the peculiar features

of this case, quietly assuming the gradual habituation of the foetus in utero to the morphine, had I not, during the past fall, found that this very subject of the influence of narcotics on the foetus had been discussed at a meeting of the Leipzig Obstetrical Society in Feb., 1876, and that the opinions of the members participating in the debate differed both as regards the transmission of narcotics to the foetus in utero, and the practical deductions to be drawn from recent published investigations. It therefore occurred to me, that it would be interesting to learn the views and experience of the members of this Society on the matter, to the accomplishment of which end, the second question asked by Dr. Mattison at the conclusion of his case reported at the last meeting, presents a fitting opportunity.

The literature of this subject of placental osmosis is exceedingly scanty. The regular text-books on Obstetrics merely give the physiological theories of the placental circulation or gaseous interchange; not one of them refers to the transmission of medicinal agents to the child through the maternal blood. Schroeder alone mentions the investigations of Reitz (*Centralbl. f. d. med. W.*, 41, 1868), who after injecting cinnabar into the blood of a pregnant rabbit, found the red particles of that chemical, in the blood of the foetus, particularly distinct in the capillaries of the pia mater; S. therefore considers the transmigration of maternal blood cells into the blood of the foetus easily conceivable.

The older journals contain only investigations on normal placental respiration by Müller, Pflüger, Schwartz, Kraemer, Hecker, Veit, and others, who all leave the question more or less undecided; in those of later date, I have been able to find but five separate papers, all, as it happens, by German authors (of other countries there are absolutely none on record), Gusserow of Zürich, Zweifel of Strasburg (two), Benicke of Berlin, and Fehling of Leipzig. Gusserow<sup>1</sup> injected tincture of iodine and a solution of ferrocyanide of potassium into the stomach of pregnant rabbits, guinea pigs, and dogs, but was unable to find any traces of the drugs in the liquor amnii, or in the urine of the foetus, even when the dose had been given five days before. On the other hand, he was able to detect iodine in the liquor amnii and in the urine of the new-born infant after administering iodide of potash for some time (about two weeks) to the mother before her delivery.

A discovery which, if confirmed, is likely to prove of great practical importance, was made by Zweifel<sup>2</sup> in 1874, who, in five cases where chloroform had been inhaled during labor,

<sup>1</sup> *Arch. f. Gyn.* III., 2, 1870.

<sup>2</sup> *Berl. kl. Woch.*, May, 1874.

found traces of the agent in the placenta and in the urine of the new-born infant, thus showing that that vapor, at least, is rapidly transmitted to the foetus.<sup>1</sup> In a later paper<sup>2</sup> he reviews the subject of foetal respiration and details the result of a number of experiments made on pregnant rabbits. He opened the abdomen and uterus, shut off the supply of air from the mother, and immediately the foetus began to respire violently. Both the umbilical arteries and the vein became purple in color, and asphyxia supervened. As soon as air was again admitted to the mother the color in the umbilical vessels commenced to grow brighter, and in five seconds the vein was bright red and the foetus made vigorous respiratory movements. He therefore considers that by these experiments 'the proof of the respiration of the foetus through the placenta is conclusively furnished, and that this respiration is subject to exactly the same conditions as that of the animal after birth.'

Benicke<sup>3</sup> reported the results of his experiments with salicylic acid to the German Medical Association in 1875. He gave the agent to twenty-five women during labor, and found it in the urine of the children immediately after birth, the shortest time after its administration being forty minutes. He therefore concludes, in contradiction to Gusserow, that the osmosis between the mother and the foetus is an exceedingly active one. Paul Ruge and A. Martin<sup>4</sup> report precisely the same observation with salicylic, but iodide of potash was found by them only in small quantities after prolonged use of the drug by the mother.

The most instructive, and for our purpose the most practical, paper is that by Fehling,<sup>5</sup> who details experiments on two rabbits and one dog, into whose jugular vein woorara was injected with the intention of producing the specific effect of the poison on the foetuses. The latter, however, utterly failed to show the influence of the drug, and even those rabbit foetuses, whose mother had been anaesthetized to apnoea with chloroform, persisted in moving actively and respiring freely when the uterus was opened.

Judging from this last experiment, and also from universal practical experience, Fehling concludes that Zweifel's observations on the rapid passage of chloroform into the foetal system are still open to question. As for the placenta, that organ

<sup>1</sup> I find Ch. Hüter reported as having found chloroform in the blood of new-born infants, but no practical deduction seems to have been drawn from this observation, and it apparently passed into oblivion.

<sup>2</sup> Arch. f. Gyn. IX. 2.

<sup>3</sup> Zeitschr. f. Geb. u. Fr. I. 3.

<sup>4</sup> Ibid, 2.

<sup>5</sup> Arch. f. Gyn. IX. 2.

he says would first have to be cleared of all maternal blood and coagula before the detection of chloroform in its substance could be considered positive proof of Zweifel's statement.

Probably none of us, who have frequently administered chloroform in obstetric practice, can, if we eliminate operative cases, tedious labors, and all cases where asphyxia would be likely to ensue from the dystocia itself, remember a case where the foetus was the worse for the chloroform. Fehling mentions eleven such cases, and all the children were born in a lively condition, and none had jaundice, as Zweifel reports of his cases.

Scarcely less difficult to determine than the injurious effect on the foetus of chloroform inhalations, according to Fehling, is that of hypodermic injections of morphine, because all the cases in which morphine was used were for that very reason more or less abnormal cases, and the asphyxia of the new-born child might therefore be as well ascribed to the dystocia as to the morphine. Still, Fehling admits that in certain cases where the foetal heart-sounds were perfectly regular and rhythmical, and the child was rapidly and easily extracted with the forceps, its asphyxiated condition might have been due to the administration of morphine to the mother—a supposition confirmed, he thinks, by the presence of hemorrhagic effusion into the brain and medulla oblongata, discovered at the autopsy.

Of sixty-eight cases collected by Fehling from his own observations, in which morphine was administered hypodermically, among those where the labor terminated spontaneously, four children were born dead and six asphyxiated; four other children, three of which were easily delivered by the forceps, and one by podalic extraction for breech presentation, were born alive but died unexpectedly within a few hours after birth, without apparent cause. The cerebral organs of all these children presented the hyperæmic appearance above mentioned. They were all, but one, healthy, vigorous infants; the labors had been easy, and the conviction that the morphine had caused the asphyxia almost involuntarily forced itself upon Fehling; nor do the figures mentioned by Kormann,<sup>1</sup> who was one of the first to recommend hypodermics of morphine in obstetric practice, contradict this opinion, for, although he declares never to have witnessed any injurious effects from the morphine in the foetus or new-born child, he states that of his fifty-four cases, six children were still-born and six died soon after birth.

In the discussion which followed the reading of this paper

<sup>1</sup> *Mon. f. Geb.*, 32.

before the Leipzig Obstetrical Society, Henning and Ahlfeld mentioned having seen cases in which the morphine undoubtedly proved injurious to the child; Leopold reported a case from his own practice and one by Higginbotham, where morphine was given for some time during pregnancy without injuring the child—a circumstance which was explained by Fehling and Weickert on the ground that the foetus acquired the opium habit with its mother. Fürst also called attention to the innocuousness to the foetus of laudanum enemata, given during pregnancy. All the members agreed in recommending caution in hastily ascribing hyperæmia of the brain and meninges, etc., of the child to the use of morphine during labor, as these symptoms are observed after various other modes of death.

All the above investigations clearly show that there exists an active and constant interchange of nutritive and other material between the mother and the foetus through the medium of the placenta; and that all substances, be they gaseous, dissolved, or otherwise suspended in the maternal blood, pass from the placental sinuses through the double epithelial septum, dividing the maternal from the foetal vessels, into the finest ramifications of the foetal villi and thus into the systemic circulation of the foetus, who in exchange, in all probability, transmits to the mother a portion, at least, of the effete products of his tissue-changes. The rapidity with which this transmission of maternal substances may occur is almost instantaneous, for, according to Vierordt, the time required for the blood to complete the circuit of the human vascular system is but 23.1 seconds.

Fehling tells us that the easily diffusible substances—those which are most readily taken into the circulation and detected in the excretions of adults, such as the salines, salicylic acid, and chloroform—are also those which are most rapidly transmitted to the foetus; while others which are more slow in their action on the adult, such as woorara, and probably also morphine, do not so readily pass to the foetus.

The reason why different observers have not witnessed the same results, some having detected the substance given to the mother in the foetal blood or excretions, and others not, is explained by Fehling on two grounds: The relation of the dividing septum to the fluids in which it is bathed, which, in the one case favors osmosis, in the other retards it; and 2: The quantity of the substance contained in the maternal blood.

On the permeability of the materno-foetal placental septum by certain substances, and on the amount of the latter contained in the maternal blood, will thus, in a great measure, depend the susceptibility of the foetus in utero to these substances. To prove, therefore, what drugs and how much of each drug can

be given to the mother to insure its transmission to the foetus, should be the first aim of future investigations on this subject.

We have been told, what would indeed seem most plausible, that the volatile vapor chloroform is readily transferable to the foetus, although the injurious effects one would naturally expect therefrom are by no means apparent, notwithstanding the daily use of the agent in obstetric practice. We have further seen, that there are at least some cases in which asphyxia or death of the foetus, is fairly attributable to the hypodermic administration of morphine to the mother during labor. But there our knowledge of the transmissibility of special medicinal agents ends—if we except a few successful experiments with the iodide of potash—and even as regards chloroform and morphine, there still exists a wide diversity of opinion.

With reference to the influence of medicinal agents on the infant during pregnancy still less can be said, nor is that period for obvious reasons so favorable for therapeutic action on the foetus as, particularly, that of lactation. We all know that by giving the mother tonics and various nutritive medicinal agents we aid in securing a vigorous and healthy offspring; we also know that, by putting a syphilitic mother under specific treatment during her pregnancy, we are preserving the child from premature death, or for a time at least, from venereal disease. But still we do not know why the foetus in utero is not poisoned by a drug given to the mother in a dose adapted to her, it is true, but large enough to be fatal to the child after birth. Of course the explanation is, that the child gradually becomes accustomed to the poison (as doubtless in the cases of Leopold, Higginbotham, and myself); but why was the *first* dose not injurious? How many times have I administered opium and morphine during pregnancy, even to the complete narcotism of the mother; and when questioned by the patient whether the child would not be injured by the drug, have invariably and positively answered No, without having any other ground for my belief than previous experience, and the silence with which this subject is passed over in the text-books! And still it seems as though something definite should be known on this subject; as though some scientific explanation should be given for the immunity of the foetus in utero to opium during pregnancy, while during labor the child appears to become, to some extent, susceptible to the drug, until after birth there is no medicine by which it is more easily or fatally affected.

There must be some difference in the transmission of drugs to the foetus in utero, and to the child after birth, or its nervous organization must be less impressible (to narcotics, at least) before birth. How else could we explain the case quoted in the

"Annales de Gynécologie" for August, 1876, where the newborn child of a woman accustomed to the daily use of opium in large quantities—an ounce or more a week—died in a few hours after taking the breast for the first time? But if the fœtus in utero is admitted to absorb freely the substances circulating in its mother's blood, what is the difference between that species of absorption and that from the mother's milk?

The immense importance of further elucidating this matter need scarcely be pointed out, covering, as it does, not only the transmission of drugs to the fœtus, but also the much more important question of the transmission of the germs of disease: syphilis (Kassowitz<sup>1</sup> says that syphilis cannot be transmitted, from the mother to the fœtus, or vice-versa during gestation; that the syphilis-germs do not pass through the materno-fœtal septum, and that the child will be syphilitic only if the mother had the disease before impregnation, or the disease emanated from the father alone), variola, morbus maculosus Werlhofii (one case by Dohrn), nephritis (several cases by C. Ruge), malaria, and other maternal affections.

In view of the difficulty attending experimental investigations in this as in other kindred topics, the publication of individual professional experiences is the most ready way of furthering the inquiry, as well as the careful observation of and recording, in all future cases, of the effects on the fœtus of any drug given to the mother during pregnancy and labor.

The period of lactation was, by oversight, not included in the subject for discussion, and still the knowledge of the effects of drugs on the fœtus through the mother's milk is even of greater practical value than during pregnancy or parturition. Every physician knows that certain drugs act on the nursing child when given to the mother, and therefore draws indications as to their use or avoidance. But a systematic series of investigations has, to my knowledge, never been made as to what remedies pass more or less readily into the mother's milk, in what quantity they do so, and in what amounts they must be given, either to act on the child, if so desired, or not do so, if likely to prove injurious. According to recent investigations by Lewald,<sup>1</sup> iron passes very readily into the milk, as also bismuth, oxide of zinc, lead, arsenic, antimony, iodine and its compounds, quinine and mercury; narcotics and alcohol, he thinks, cannot be eliminated by the milk, which opinion, I am sure, can easily be shown to be incorrect; indeed, the case above mentioned so proves it, as far as opium is concerned.

There would seem to me to be several points specially worthy of investigation in this matter of materno-fœtal osmosis, such

<sup>1</sup> Lyon Médical, June 20th, 1875.

as, *first*, the influence on the foetus of the remedies frequently administered to the mother during parturition, principally chloroform, chloral (which has recently been so warmly recommended), opium, belladonna, ergot; *second*, if I may be permitted to hazard a suggestion, the question whether the vaccination of a pregnant woman would not secure her child against variola after its birth; *third*, whether the syphilitic child of a woman who was syphilitic before that child was conceived (Kassowitz), could not be cured of the disease by subjecting the mother to antisymphilitic treatment during lactation; *finally*, whether a child which was not born syphilitic, because its mother did not become infected until after impregnation (also Kassowitz), could be permitted to nurse its syphilitic mother with impunity, if the latter be either specifically treated, or not treated at all, since the transmission of the syphilitic virus through the lacteal secretion, is, I believe, by no means proved."

DR. FORDYCE BARKER made the following remarks:

"MR. PRESIDENT:—I regard the subject which we are discussing this evening as one of great practical importance to all engaged in obstetrical practice, but it is one which up to the present time has received but little attention from writers. A young man, anxious to settle the question, whether it be safe for the foetus to administer narcotic drugs to women during pregnancy and parturition in such full doses as the condition of the mother would otherwise require, would find but little in obstetrical literature to aid him in deciding the question.

As I understand it, this discussion originated in the report of a most interesting case, read at the last meeting, in which a primipara in labor was seized with convulsions, for the arrest of which one grain and one-third of morphia were introduced hypodermically into the maternal system, within a period of three hours, the first hypodermic injection being five hours, the second four hours, and the third two hours before the birth of the child. The child was asphyxiated at birth, remained so for nearly an hour, during which time artificial respiration was most assiduously kept up. In the subsequent fifteen hours the child had nine convulsive seizures, with arrest of respiration, and

<sup>1</sup> An observation made by a veterinary surgeon, named Silvain, in France, in 1857 (*Récueil de Méd. Vétér.*, *N. Y. Med. Record*, Jan. 1, 1876), would certainly give plausibility to this hypothesis. He vaccinated a number of ewes, several of which were pregnant. On the twentieth day following the operation, a lamb born of one of the vaccinated ewes presented on the inside of the left thigh the three marks which had been made on the mother, at the same place, and on the same leg, when the lamb was yet a foetus. She had been delivered twelve days after vaccination, and on the twentieth day the pustules were in both, ewe and lamb, in the period of desquamation.



only a fluttering pulsation over the precordial region. The child was only kept alive by artificial respiration. Previous to delivery the mother had three convulsions, but none after the labor was completed. It is a most interesting fact that both mother and child recovered.

The question has arisen whether the convulsions of the child were due to the hypodermic injections of morphia, and naturally there has grown out of this inquiry the larger question as to the influence on the infant of medicine, particularly narcotics, administered to the mother during pregnancy and labor.

Now, in discussing this subject it will be wise for us to inquire what positive knowledge we have which will aid us in answering this question.

The first question which naturally suggests itself in reference to the case reported is, whether opium poisoning will cause convulsions in a young infant. In many works on *Materia Medica*, as for example in the U. S. Dispensatory and in the recent work of Bartholow, convulsions are not mentioned as among the phenomena of opium poisoning. But other writers, as, for example, Pereira, Stillé, and Anstie, do speak of convulsions as a result of opium poisoning. Experiments seem to have demonstrated that in the lower orders of animal life, as in fishes, amphibians, reptiles, and birds—in short, where there is a low degree of brain development—convulsions are the common result of opium poisoning. So also in infants it produces the same result, as clinical observation has abundantly established, while in more advanced life convulsions from this cause are very rare. It is said by some authors, I know not on what evidence the assertion is made, that among certain races of man, who have a low degree of brain development, as the Negro, the Malay, and the Javanese, convulsions are the common result of opium poisoning.

I think, therefore, we must all admit that opium poisoning may cause convulsions in an infant.

Then the next question which is suggested by this discussion is, what maternal influences may be transmitted to the foetus in utero. I think all will concede that we have abundant evidence that certain diseases are directly communicated from the maternal system to the foetus, as, for example, the specific exanthemata, small-pox, scarlet fever and measles, and certain specific poisons, as syphilis. Then, also, I believe most fully that emotional causes and mental impressions affecting strongly the maternal system may modify the development and the vitality of the foetus, even to the extent of destroying life. I could give some striking illustrations of this fact, which have come under my personal observation.

It seems to me that a careful study of the literature of the subject will convince every one, that in no way is the effect of such influence more frequently and demonstrably evident than by convulsions in the new-born infant. Guersant and Blache relate the case of a woman of very irascible temper, especially when pregnant, who lost three of her children shortly after birth by well marked convulsions. Convulsions in the new-born infant are not of rare occurrence when the mother has suffered from eclampsia during labor. Depaul describes one case where the labor proceeded naturally, without any symptom to excite anxiety, until the head began to distend the perineum and appear at the vulva, when the woman was suddenly seized with convulsions and immediately died. The child was delivered living by the forceps, but died some minutes after in convulsions. Prestat, Schmitt, Cazeaux, Hervieux, and many other authors whom I do not at the moment recall, mention cases where the infant after birth has had convulsions like those of the mother. I have published three such cases. In two, the mother had severe convulsions during labor, but recovered. In both, the child was born alive, but died a few hours after birth from convulsions, precisely identical in character with those of the mother. In the third case, the child had three convulsions within two hours after birth, but after this time it did well.

I make this brief allusion to the etiology of convulsions in the new-born infant, only for the purpose of showing that in the case reported there existed a well-known cause for the phenomena in this child after birth; and therefore it seems to me unphilosophical and illogical to ascribe them to a cause which in the literature of our profession has hitherto been unknown to produce such a result, unless we can find in science some explanation why this should be the more probable cause.

It is, then, pertinent to ask whether either clinical observations or experimental investigations have in any way shown that opium or its preparations, introduced into the maternal system, may act injuriously on the fœtus or cause convulsions in the infant after birth. What evidence is there, based on clinical observations, that any drugs administered to the woman will exert their direct specific influence on the fœtus in utero? I suppose it to be an accepted opinion of the profession that blood diseases may be communicated by the maternal to the fœtal system, and, to a certain extent, a vague belief prevails that a specific treatment administered to the mother may act directly in curing the fœtal disease. I think it probable that a large majority of the profession hold the opinion that syphilis in the fœtus is amenable to specific treatment of the mother,

or at least that such specific treatment acts directly on the fœtus. But I think it would be difficult for any one to find any direct evidence of this in the recorded literature on this subject, and from one case which came under my own observation, I have been disposed to call in question the soundness of this belief. A lady who had been married for seven years, but never pregnant, came under my care for uterine disease. A few months subsequently she became pregnant, and at about the full term of gestation gave birth to a dead hydrocephalic child. I found that the child had a very large liver, and, as there was also marked evidence of peritonitis, I expressed to the husband privately my suspicion that the death of the fœtus was due to syphilis. He confessed that at a former period he had been treated for syphilis by Dr. Sturgis. I advised him to again put himself under the care of Dr. Sturgis, and I emphatically urged him to avoid impregnating his wife for some time to come. But only a few months after I found this lady to be in the third month of pregnancy. From this time to the end of gestation she was constantly under anti-syphilitic treatment. She gave birth to a living and apparently healthy child, which a few days after began to have snuffles and lose flesh, and a syphilitic eruption appeared on the face. The child was treated by mercurial inunctions, and is now about three years of age. The health of the mother was good, and she never manifested the slightest symptom of syphilis. In this case, specific treatment of the mother, continued for six months, does not seem to have materially influenced the syphilitic fœtus, which was cured in a comparatively short period by direct treatment after birth.

We know that thousands of women have been kept profoundly under the influence of anæsthetics for hours during labor, and that the infant when born has been as active and lively as if no such agent had been administered to the mother. For more than twenty-five years I have given chloroform to every woman whom I have attended in labor, who has had sufficient pain to require such relief, and I have never had the slightest reason to suspect that the child was in any way affected by the use of this agent. Twenty-one years ago, this coming month, I kept one woman twenty-six hours profoundly and continuously under the influence of chloroform, using in that time three and a half pounds of chloroform—a part of which, of course, was wasted in inhaling from a towel. This lady was a vigorous, plethoric primipara. She was seized one morning, without any premonitory symptoms, with convulsions. This was before hypodermic injections were used in this country. I bled her very largely, but she had two more con-

vulsions before I could procure chloroform; although there were evident threatenings of a recurrence whenever she was allowed to partially come out from under the influence of the anæsthetic, yet she had no return of the convulsions. It was twelve hours after the first, before there were symptoms of approaching labor, and, for reasons which I need not stop to detail now, I did not deem it wise to force labor. She was at last delivered by forceps of a very large, active child, who is now a most clever, promising student of medicine. Since that time I have often kept women in labor, eight, ten, or twelve hours under the influence of chloroform, but I am confident that no child born under such circumstances ever manifested in the slightest degree any effect due to this agent. I am aware that Zweifel, within a year or two, has stated that he has found chloroform in the urine of the new-born infant when the mother had inhaled the vapor during parturition; but the clinical experience of thousands of observers in all parts of the world has so positively demonstrated the innocuousness of this agent upon the fœtus in utero that the observation of Zweifel carries no weight with practical men.

Clinical observations in regard to the effect of opium and its preparations on the fœtus when administered to the mother are much more limited in number and much less conclusive as to their results. More than twenty years ago I was struck by the remark in Pereira's *Materia Medica* that wet nurses and pregnant women must employ opium with great caution, as its use by them may endanger the life of the child. As regards its danger in pregnant women, I especially noticed the remark because I had previously attended a notorious opium-eater twice in her confinements, and I had curiously observed the fact that the children, when born, seemed in no way affected by the mother's habits. Since that time I have attended twice another lady, who had acquired the habit of daily using a very large quantity of McMunn's Elixir. After a terrible struggle she conquered her unfortunate habit, and since then I have attended her in a third confinement, and I was quite unable to distinguish any difference in the children at birth, as regards the influence of the opiate. Pereira, in a foot-note, gives Ramsbotham as his authority for the statement as to the danger to pregnant women from the use of opium. I had the curiosity to look up the passage referred to in Ramsbotham, and I find all he says on this subject is, that he had heard that in a woman, who was accustomed to habitually use opium in large doses, it was observed that her children at birth were dull and stupid.

All will remember that for a time it was almost universally

believed in the profession that the use of opium was contra-indicated and even hazardous in uræmia. For some years I supposed that Dr. Metcalfe and myself stood almost alone, in this city, in the opinion that opium was a safe and most important agent in the treatment of uræmic convulsions, but I have since ascertained that at the same time Dr. Loomis and Dr. Lente were equally strong in their convictions on this point. I first made use of the hypodermic injections of morphia in the treatment of puerperal convulsions in the spring of 1859. The patient resided in Brooklyn, and was under the care of the late Dr. Horatio S. Smith. She was supposed to have passed the eighth month of pregnancy, when one evening, without any symptoms which had attracted the notice of her husband, she was suddenly seized with convulsions, and Dr. Smith, whose residence was very near, was called in. I saw her late at night, and she was then in a comatose state, having had three severe convulsions. She was evidently too anæmic to bear venesection, there were no signs of uterine action, and she was too feeble as, we both thought, to bear the shock of labor, and so we made no attempt to bring it on. On careful examination which was made several times, I could not detect the sounds of the fetal heart or the placental bruit, and I therefore was positive that the child was dead. With some hesitation Dr. Smith consented that I should make a hypodermic injection of fifteen minims of a solution of morphia sixteen grains to the ounce of water. Four hours after the first injection, she began to grow restless and there were some convulsive twitchings of the muscles of the face, and the same quantity of morphia was again injected hypodermically. I left her profoundly under the influence of morphia, and perspiring most profusely, with the understanding with Dr. Smith that if she rallied and recovered strength sufficient to render such a course feasible, I should be notified, and we would then bring on labor. I heard nothing of the case until about ten days afterwards, when I received a letter from Dr. Smith saying that our patient had no more convulsions, but after the effects of the morphia passed off, she constantly improved in her general condition, until the day before, when, in an easy labor for a primipara, she gave birth to a healthy living child, and both mother and child were then doing well. With the humor characteristic of the man, Dr. Smith closed his letter by saying, 'Now own up handsomely that you were wrong, for you said the child was dead.'

Since that time, I have, in a considerable number of cases, made use of hypodermic injections of morphia in convulsions occurring before labor, and the child has been born alive, with no symptoms indicating that it had been affected by the

morphia, and there are certainly several physicians in this city who can vouch for this fact. I have never made use of hypodermic injections of morphia in the treatment of convulsions during labor, as I think that I have good reason to prefer the treatment, under these circumstances, which I have elsewhere described. But in convulsions, occurring before and after labor, I believe hypodermic injections of morphia to be often the most effective and useful measure that we can adopt.

All this may be said to be negative evidence, only proving that in some fortunate cases the fœtus is not affected injuriously by large doses of morphia administered to the mother. But then, I ask, have we any positive evidence proving the contrary, viz., that the child has been affected by morphia administered to the mother before delivery? I know of none. I have found none such recorded, neither have I ever heard of any. I know that Dr. Lusk, and others whom I now do not recall, have given morphia hypodermically, in the treatment of convulsions during labor, and the child has been born alive.

Next I would ask, whether any experiments have demonstrated that the fœtus can be affected injuriously by the most powerful agents introduced into the maternal system, except such as interrupt the utero-placental circulation. My friend, Dr. Mundé, has already anticipated me in referring to the experiments of Fehling, published in a recent number of the *Archiv für Gynækologie*.

I therefore will only briefly refer to some of the results which Dr. Fehling obtained. He introduced into the jugular vein of a pregnant rabbit sufficient curare to completely paralyze the animal, including the nerves of respiration and circulation, but life was supported by a tube in the trachea. After a time, the length of which I do not recollect, he opened the abdomen, and found the young entirely unaffected by this most powerful and rapid of known poisons. In another experiment he chloroformed an animal until there was an entire suspension of respiration, and all reflex action ceased, but artificial respiration was kept up for eighteen minutes. He then opened the abdomen, and the young were found unaffected by the chloroform.

So then, in conclusion, I will ask permission to read the following propositions, which I wrote out before coming here this evening, and which tersely express my convictions on this subject:

1st. There is no evidence which can be accepted in science, that narcotic drugs, administered to the mother, ever produce their *specific* effects on the *fœtus in utero*.

2d. Therefore, such drugs should be used without fear of

their effect on the foetus, whenever they are necessary for the health or the life of the mother."

DR. WM. M. CHAMBERLAIN said<sup>1</sup>: "Prof. Gusserow, of Strasburg, in the third volume of the *Archiv für Gynækologie*, carefully considers the subject of the exchanges which pass between the mother and the foetus.

He regards the human ovum, like that of the bird, as comparatively independent, possessing a respiration of its own, deriving oxygen from the placenta as we obtain it from the atmosphere; having a calorific function of its own, whereby its body is some two degrees (F.) warmer than its mother's; and a secretory function, whereby sebum is deposited on the surface in the vernix caseosa, urine in the bladder and in the liquor amnii, and the meconium in the intestines.

He reviews the literature of the subject, which he finds somewhat voluminous, but inconclusive.

He collates cases of maternal poisoning, in which the foetus did not share, and some in which it did; cases in which the child was born with the small-pox, when the mother had not been infected, and cases of twins where one child had variola and the other was free of it at birth.

He concludes that there is evidence of a certain amount of exchange between the two organisms, but that the details are not well made out.

He therefore institutes a series of experiments, first upon animals, and then upon the human subject, to determine in what time, to what extent, and in what portions of the ovum substances, with which the mother's organism may be impregnated, reappear. These experiments may be summarized as follows:

Three guinea-pigs, at term, were injected with solutions of iodine of such strength that an intense reaction of color appeared promptly in the urine. At the end of an hour they were killed, and neither in the urine or the tissues of the foetus, or the liquor amnii was any iodine reaction to be found.

Three rabbits were injected two, four, and five days successively with iodine in the same way. The reaction, which was very marked in the mother's secretions, could not be found in any part of the ovum. Finally, two pregnant bitches were in like manner treated with ferrocyanide of potash, but no transfer to the pups could be shown.

Proceeding to the human subject, he gives in detail the results of experiments upon fourteen different pregnant women who took iodide of potassium in various amounts, from a

<sup>1</sup> Meeting, Feb. 20th.

scruple to a drachm per day, for periods varying from three days to five weeks before delivery. The results were somewhat various; generally, moderate iodism was induced in the mother, as appeared by the reaction of the urine, and by slight diarrhoea. In no case did he recognize any noxious effect upon the child. The liquor amnii was examined during labor, and the child's urine, when it could be obtained, directly after birth, and before suckling.

These fourteen cases may be divided as follows: In six cases no iodine was found in either. In three cases, the child's bladder being empty, the liquor amnii contained iodine faintly. In four cases the child's urine showed iodine, and the liquor amnii did not. In one case the child's urine contained iodine, and the liquor amnii was lost. The six entirely negative cases were those in which the drug was given for less than a week, or in which its administration was necessarily interrupted. The proper appreciation of the series would seem to be that when the mother's secretions had been for several days impregnated with the drug, it began to appear in those of the child, and the bearing of these experiments upon the question now before us evidently is, that if a salt, so soluble, so diffusible, and so patent in its reactions as iodide of potassium, only very slowly and very slightly affects the system of the child, then an alkaloid like morphia, possessing these properties in a much less degree, and administered only a few hours before delivery, would probably not exercise any dangerous influence upon the foetus.

My own views upon this subject have probably been much influenced by a case, which I reported to the Society ten years ago, of a woman who throughout gestation, parturition, and lactation took by the mouth an average of twenty grains of the morphine salt every day. The child did not show any appreciable effects."

DR. PEASLEE continued the discussion as follows:

"I had hoped, before taking any part in this discussion, to have heard some argument, or learned some facts, on the affirmative side of this question, since it is one of very great practical importance, and I have always endeavored, during my professional career, not now a short one, not to err in the direction of incautionness. Meantime, I maintain the negative view of this inquiry, both from *a priori* considerations, and from such facts as I have acquired from my own experience and otherwise.

The two divisions of this inquiry are: 1. Do medicines in general affect the foetus in utero, by absorption into its blood, when administered to the mother during gestation and during



parturition? 2d. Do narcotics especially affect the fœtus in utero, by such absorption, when given to the mother in the conditions just mentioned?

1. *Of Medicines in General.*—The fœtus in utero is isolated from the mother so far as is possible consistently with its nutrition and development, the maintenance of its temperature, and its protection from injury. To secure the first-mentioned object alone, a constant surface of indirect contact exists after the third month between the mother and the fœtus, viz., that afforded by the placenta, and which corresponds to one-third or less of the internal surface of the uterine cavity. At all other points, the liquor amnii isolates the fœtus from the mother, except so far as, in consequence of its movements, or otherwise, the fœtus may temporarily touch the uterine surface, but without any results requiring to be considered here.

Of this indirect contact of the fœtus with the mother, through the placenta, the immediate results are, (1), the absorption from the mother's blood into that of the fœtus of all the elements, oxygen included, which are required for the development of the latter; and, (2), the elimination from the latter of its carbonic acid gas and its elements from dis-assimilation into the blood of the mother. For, the fœtus having no vascular connection with her, derives no part from her of its blood as such.

That this absorption of blood-elements is very slowly effected is shown by the fact that, during all the last six months of gestation, only an average of about seven pounds of fœtal blood and tissues are developed. Indeed, no less than four, and probably five, layers of tissue are interposed to secure this result between the mother's and the fœtal blood: 1st, the comparatively thick walls of the lacunæ, entering into the structure of the maternal portion of the placenta; 2d, a layer of connective tissue (perhaps hypothetical); 3d, a pavement epithelium covering the tufts of the fœtal placenta; 4th, a layer of embryonic connective tissue; and, 5th, the walls of the placental vessels, mere capillaries at first, but finally becoming larger and thicker. If to these anatomical facts we add the physiological one, that the blood but slowly circulates through the maternal lacunæ, we easily account for the slowness of absorption from the mother's blood; and understand why those elements alone, probably, enter the blood of the fœtus for which there is a physiological necessity, except certain agents in a gaseous form. We, however, know that certain pathological agents, as the cause of syphilis and of the exanthemata, are transmitted from the mother to the fœtus; but these agencies have no recognized analogy with the action of medicines, and therefore no further

notice of them is required here. It is, however, certain that certain gases, not normally present in the mother's blood, do traverse the intervening tissues and enter that of the fœtus. I very generally observe that sulphuric ether administered (in vapor) as an anæsthetic during parturition is given off from the lungs of the new-born for some hours after birth; a fact of which I shall make application farther on. Chloroform thus administered, has also been found in the urine of the new-born child (Zweifel).

*A priori*, therefore, I think that mere solutions in the mother's blood of abnormal substances, whether medicinal or otherwise, are not absorbed into the fœtal blood in any appreciable amount; or if appreciably, a long time is required to produce any effect upon the fœtus. Salicylic acid may, however, prove to be an exception to this general proposition (Fehling).

And what are the *facts*? Does any therapist know of a medicine which, administered to the mother during pregnancy for any length of time, will produce diuresis in the fœtus, and thus at will increase the amount of the liquor amnii? Does anybody know of a cathartic which, acting from the mother, will expel the meconium from the alimentary canal of the fœtus, and then, if continued, produce a diarrhœa, or tenesmus and tormina after the canal is evacuated? And does any practitioner ever hesitate to prescribe diuretics and cathartics during pregnancy, whenever required, from any apprehension of any such effects as I have mentioned? I confess I never have myself.

Dr. Mundé has detailed the experiments of Gusserow and others in the administration during pregnancy of different iodine preparations—since these are remarkable for their facility of absorption; the results being precisely as the preceding view would lead us to expect. For, 1. There was no trace of iodine in the fœtal urine, unless the former had been for a long time (several weeks at least) taken by the mother; 2. Only in less than one-half of these cases even could it be detected at all; and, 3. It was never diluted if the drug had been given for less than a week. Finally, only the slightest amount, and never sufficient to produce any characteristic effect, was detected in any instance.

As a general proposition, therefore, I do not believe that medicines in general have any appreciable effect by absorption upon the fœtus in utero, even when administered for a considerable length of time (several weeks at least) to the mother; the effects of mercurial treatment of the mother upon a syphilitic fœtus, when long continued, being, however, an exception to this

rule. Still less, therefore, do I believe that remedies in general can affect the foetus by absorption when taken by the mother merely during the process of parturition, even though unusually prolonged.

2. *Of Narcotics in Particular.*—Nor do I admit that narcotics especially affect the foetus in utero by absorption when administered to the mother during gestation or parturition. The improbability of their absorption into the foetal blood has already been shown, while considering the general question. I have, however, mentioned as exceptions, sulph. ether, and chloroform, administered anaesthetically, in gaseous (vapor) form, during parturition. But inasmuch as even these are never transmitted to the foetus in amount to produce any injurious or even any apparent effect, far less probable is the assumption that narcotics in solution would be absorbed in quantity to produce appreciable effects. And what are the *facts* of experience here? Does any physician know of a narcotic which, given to the mother, will even put a foetus asleep o' nights, in cases where the mother is kept awake and in distress by too forcible and continuous foetal movements? Does any physician know of any narcotic which can kill the foetus in utero in any doses, without first killing the mother? If such an agent were generally known, not one-half of the children now born alive, would ever see the light. The abortionist's occupation would indeed, be gone, for every woman could herself destroy her offspring in utero, whenever she might choose to do so. The Creator has wisely guarded against such destruction of foetal life by the anatomical and physiological conditions I have already specified. On the other hand, we know that drugs which have a certain reputation for destroying the foetus can never be relied upon to effect that object; and that they not very seldom kill the mother, and apparently without affecting the foetus at all. And when they do effect the object intended they merely excite the uterus to contraction; no appreciable amount, whatever the dose, being absorbed into the foetal blood.<sup>1</sup>

I have, therefore, never hesitated to administer narcotics to pregnant women whenever they have needed them, and in such doses and as long as they were required. I have, I think, frequently saved the lives of mothers by this practice, and I have certainly never destroyed a foetus in this way, so far as I suspect or believe. I have arrested puerperal convulsions by full hypodermic injections of morphia, and the children have lived and done well. I have also had cases thus treated in which the

<sup>1</sup> Fehling attempted to destroy the foetus in utero, by injecting woman into the jugular vein, in two rabbits and a bitch; but with no effect upon the foetus, though the parents were nearly killed.

fœtus was born dead. But I have also had cases of fœtal death, in connection with convulsions, where no narcotics had been administered. All know the danger to the fœtus of a single puerperal convulsion, and consider themselves very fortunate to save it, under any management of the case, if several have occurred. If the attempt has been made to arrest them by the administration of chloroform or ether, no one accuses these agents if the child is born dead; though they are doubtless far more absorbable than other narcotics, for the reason before given; and both should be entirely discontinued in practice if the latter are really injurious to the fœtus in rational doses.

And if the use of narcotics more or less prolonged in pregnancy does not appreciably affect the fœtus in utero, what reason is there for the belief that they may do so, if given in a single dose, or repeated a few times, during the 24 or 48 or even 96 hours of parturition? I perceive none at all. If we assume in advance that every fœtus born dead after the administration of a narcotic in a case of convulsions, is killed by the narcotic, we may doubtless get cases enough to confirm the assumption. But how shall we reconcile with it the far greater number of cases in which the fœtus or the new-born, dies in precisely the same way, so far as can be known, though no narcotic has been given? In conclusion, I will say that I have never avoided the use of an efficient opiate to control excitement and procure sleep when required in tedious labors; and I think I have thus conducted many a case to a natural termination and a safe result for both mother and child, which would otherwise have resulted disastrously to the latter at least. And I have still to acquire the facts substantiating the proposition, that narcotics administered during parturition to the mother, even in doses fatal or nearly so to her, will produce any appreciable *narcotic* effect upon the fœtus in utero. If the mother be kept for hours in a state of coma or semi-asphyxia by a narcotic, the fœtus may be born asphyxiated or even dead. But it is not the absorption of the narcotic which affects the fœtus, but the state of the mother's blood and circulation. Such doings, however, are not contemplated, I suppose, in the question before us."

DR. W. R. GILLETTE detailed his experience in a number of cases as follows:

"That certain narcotics administered to the mother during parturition may affect the fœtus in utero, or the new-born child, has long been a matter of my firm belief. I had considered it a determined point that opium, or its preparations, were danger-

ous agents to the child, when given in sufficient doses to the mother to produce a decided degree of narcotism, as evinced in partial anæsthesia, a contracted pupil, a slowed respiration, and a dusky, darkened facies. From remarks made by members of this Society who are rich in obstetrical experiences, it seems that they are decidedly of the opinion that no such potency exists, and that in pregnancy and parturition opium is as safe an agent to administer, and as free from danger to the unborn infant, as ether or chloroform. In discussing this question, we had better treat it from the stand-point of our personal experiences, cutting loose from all theories or hypotheses which are founded upon the altogether insufficiently understood physiological relations existing between the woman and the foetus in her uterus. The question is one of supreme importance to the profession and the community, and it can only be satisfactorily solved by a recourse to experimental observations, which are at the hand and within the power of every one who practises the obstetric art. As an advance in this direction toward the solution of the question, I submit, with the advice of several members of this Society, some cases which have by their fixed and startling similarity of symptoms still further convinced me that this special narcotic, morphia, *when administered to the degree of producing its physiological phenomena* in the mother, will invariably produce a relative condition of narcotism in the new-born infant.

The first case is that of a physician's wife, whom I was called to attend in confinement some months ago. She had borne one child ten years previously, which she had lost, and she looked upon her present confinement with great delight and hope. The labor was normal in every respect. The vertex presented in the L. O. A. position. The first stage was six hours, and presented nothing abnormal. The second stage, of ten hours' duration, was characterized by vigorous, normal pains, which the patient bore badly. I proposed an anæsthetic, chloroform or ether, but the husband would not permit it, on the ground that his wife had valvular lesion of the heart. I maintained that, granting his position, so much the more reason was there why, by the administration of ether or chloroform, we should relieve voluntary muscular effort and pain, and thereby remove a proportionate degree of strain from the circulation. He insisted upon the hypodermic use of morphia, and administered ten drops. The foetal heart at this time was beating with perfect regularity and frequency.

The injection not having relieved the pain very markedly in half an hour, he administered six drops more. Labor advanced

rapidly, but the patient now slept between pains, and was hardly aroused by some pains at all. The head was advanced to the inferior strait, and then, upon examining the foetal heart sounds, I noticed they were extremely rapid and irregular. I at once proposed forceps, and expressed the opinion that the foetus was dying. This was refused, and in half an hour the child was born easily, but limp, flaccid, with dropped jaws, and making no voluntary or respiratory movement. I immediately separated it from the mother, and commenced efforts for its resuscitation, which were successful to the extent that the child breathed about five times a minute, a shallow, gasping respiration, and the heart fluttered back into a partial existence. I will not recite the further restorative procedures in this case; they were all, the galvanic battery included, kept in operation for three hours, and then the child died, so markedly and typically representing death from opium poisoning, that it could not but be admitted by the father that his practice was wrong. If it were necessary, I could relate two more cases almost identical with this, and where the children were born by easy labors, only to die by the morphia which had been administered to the mother to the degree of partial narcotism. I hasten now, however, to briefly relate some observations that were noted with more care and exactitude, and which from my former experience were hardly necessary for my own belief, but which I am convinced will give the discussion a broader and more active interest. I was assisted in these observations by Dr. Estabrook, a gentleman of experience, to whom I am indebted for his great care and patience.

CASE I.—Aet. 22; primipara, U. S. Was taken in labor 10 P.M., and continued comfortably in the first stage until 4:30 P.M. of the next day, when the second stage fairly commenced and lasted until 7:30 P.M. (3 hours). Labor was normal in every respect, the vertex presenting in L. O. A. position. At 4:30 P.M., Magendie's solution of morphia  $\text{m}x.$  was given hypodermically. Respirations at this time were 24 per minute, between pains. At 5 P.M., half an hour after, the patient was asleep, respiration between pains 18, pulse 80, full and strong, and pupils contracted down to less than half their normal size. The child was born at 7:30 P.M., did not cry on delivery, made two (2) inspirations during first minute, and became deeply cyanosed. The pulse was full, strong, and 70 per minute. The pupils were contracted to a fine point. Artificial respiration was maintained for 10 minutes, after which voluntary respirations rose to 6 per minute; pulse 90. The child was now left to its own efforts, of course being watched. At 8:15 (three-quarters of an hour after birth), respirations were 28, pulse

126, and the cyanotic appearance which had characterized it nearly gone. The child was asleep, however, and did not wake to cry, during the process of washing. The next day it was strong and well.

CASE II.—Aet. 18; Ireland; primipara. Vertex presenting L. O. A., and labor in every respect normal. First stage twelve hours long; the second, one and a half hour. At commencement of second stage, 10 A.M., gave  $\pi x$ . Mag. sol. hypodermically. At this time mother's respiration between pains, 28. At 11 A.M., one hour after administration of morphia, respirations 22, pulse 76, full and strong, pupils strongly contracted. Sleeping between pains, and sometimes not aroused by them. Child born at 11:40 A.M., made no attempt at respiration for one minute, then breathed from five to ten times per minute, until 11:50 (ten minutes), when it gave a feeble cry. Pupils contracted strongly, unaffected by light, and surface was cyanosed. Half an hour after delivery, respirations 28, pulse 126, cyanosis nearly gone. At 1 P.M., breathed regularly, but could only be made to cry with difficulty. Its recovery was complete.

CASE III.—Aet. 34; Ireland; second pregnancy. Labor began at 5 P.M.; second stage at 12:15 A.M.; normal in every respect. Respirations 24 (between pains), pulse 70. At 12:30 A.M., gave her hypodermically Mag. sol.  $\pi xi$ . The patient was crying out bitterly with each pain. At 2:15 A.M., respirations 20, pulse 62; patient was sleeping between pains, and scarcely aroused by them. Pupils contracted strongly. The child was delivered at 2:30 A.M., and during *first five* minutes no attempt at voluntary respiration was made at all. Heart beating 40 per minute. Artificial respiration was maintained twenty minutes, during last ten minutes of which twelve voluntary efforts at respiration were made. At the end of twenty-five minutes the respirations were 28, and pulse 90 per minute. The child was deeply cyanosed, and the pupils so contracted as to be scarcely perceptible. At the end of an hour respirations were 46, somewhat irregular, pulse 120; the child was still asleep, though easily roused. It convalesced perfectly.

CASE IV.—Aet. 23; U. S.; primipara; labor normal in all respects. First stage commenced 5 P.M.; second stage, 3 A.M., following morning, and ended at 4:30 A.M. Gave hypodermically at 3:30 A.M., Mag. sol.  $\pi x$ , with effect of reducing respirations 4 per minute, strongly contracting the pupils, and producing sleep, which sometimes continued during pains. Child born at 4:30 A.M., made no voluntary respiration during first three minutes, and required artificial respiration to be maintained fifteen minutes. At the end of this time respirations were but 22, irregular, and pulse 100; pupils very small,

and cyanosis marked. It remained in this condition, and uttered no cry, until two hours after birth. The child refused to nurse from birth, remained cyanosed, respirations irregular, sometimes as high as sixty or seventy per minute, and then falling to twenty or thirty. The pulse averaged about one hundred. On the second day after birth, after remaining in this condition, it went into convulsions and died. On autopsy the only changes found were an intense cerebral congestion, particularly at the base of the brain, and a slight colitis.

CASE V.—Aet. 27; Ireland; primipara; labor normal, commencing 7 A.M.; second stage 8 P.M., and ended 11:10 A.M. Gave Mag. sol.  $\text{Mx}$ . at 9 P.M., which produced marked contraction of the pupils, and sleep; not much effect on the pulse and respiration. Child born at 11:10 P.M., did not breathe for nearly one minute; then respired and gave a feeble cry. After this breathed six times per minute. The pupils were strongly contracted. Respirations, which were kept up artificially, as in all the cases, soon rose to 24, and in half an hour were 44 per minute. The child convalesced.

CASE VI.—Aet 33; England; fourth child; labor normal; commenced 8 P.M.; second stage, 11:30 P.M., and ended at 1 A.M. (one hour and a half). Gave Mag. sol.  $\text{Mx}$ . at 11:30 P.M., with well-marked narcotic effect, *i.e.*, marked contraction of the pupil, diminished respirations, and sleep between pains, and during same. At 1 A.M. the child was born, uttered no cry, and only respired six times the first minute. The pulse was 90, the pupils contracted markedly, and the surface was cyanosed. At end of half an hour, artificial respiration having been maintained at intervals, the respirations rose to 36, the pulse to 126, and the cyanosis disappeared. It slept unremittingly for two hours, and convalesced perfectly.

It seems hardly necessary to review these cases. There is such a similarity of symptoms pertaining to both mother and child, that no comment is needed. They selected, were all normal labors. The foetal heart sound was invariably taken before the administration of the morphia, and found to be normal in frequency and rhythm. The morphia was administered in doses which *insured an effect*, and this, the cases almost uniformly relate to be slowness of respiration, contraction of the pupils, somnolence, and in some instances anæsthesia during uterine contractions. In no instance was the labor delayed by the morphia; on the contrary, it will be observed that the labors were of average duration and ease. The children were uniformly born in a condition, it seems to me, which in the adult we would recognize as narcotism. The respirations were absent or delayed, and were only revived and maintained by artificial move-



ments. The pupils were contracted, the surface cyanosed, the circulation slowed, and the whole body limp, flaccid, with jaws dropped and eyelids half closed. Their manner of resuscitation in no respect resembled the release from asphyxia which sometimes besets the new-born child. The child asphyxiated from the ordinary accidents of its birth, when once it has been made to fully respire, when once its lungs have taken in oxygen, maintains a rapid and uniform respiratory action, which is almost invariably ushered in with a cry. It needs no further watching. Our cases, however, presented very different clinical phenomena, namely, absence of all tonicities, absent or infrequent respirations, and slow and irregular pulse. They could only be revived and their lives maintained by continued artificial respiration. So depressed were they that it was not considered safe to leave them unwatched until two hours had elapsed. The somnolence, contracted pupils, and continued cyanosis were particularly marked. These are unusual and abnormal phenomena in the neonatus. In my observation the child is not disposed to sleep until one or two hours after its birth. Our narcotized children, however, were very somnolent, even after respiration was restored, and in some instances they slept through the entire process of washing and dressing. It may be thought in objection that the pupils of the new-born child are always contracted. This is not the case; on the contrary, the pupils are usually dilated. This at least is my observation, and I know of no other observations upon this point. We know, in support of this, that the new-born child will gaze with a steadiness at a flame or blaze of light which would dazzle the sight of an adult. There must be less sensibility of the organs of vision at this age, as there is of the nerves presiding over the other special senses.

The whole group of symptoms point, through my interpretation, to the depressing effect of the narcotic upon the cerebrospinal centres of the child, and it will be remarked, upon carefully noting the above cases, that the more marked the symptoms of narcotism were in the mother, the greater was the degree of depression in the child, and consequently the greater was the difficulty in rallying it.

I have made two observations of the effect of atropine on the neonatus, when administered to the mother in the second stage of labor, which I will also report.

CASE I.—Primipara; age 18. Labor commenced 3 A.M., March 5th. Os uteri fully dilated at 12 M., at which time  $\frac{1}{16}$  grain of atropine was given hypodermically. At 1.30 P.M. pupils were slightly dilated,  $\frac{1}{16}$  grain was again given hypodermically, with effect of widely dilating pupils, and produc-

ing decided dryness of throat. Labor pains continued very strong, but owing to disproportion between the size of head and pelvis no advance was made, and at 4:30 P.M., the forceps was applied and a living child delivered. Child began to cry vigorously immediately. Pupils were *markedly* dilated in a mere rim of iris, and refused to respond to light.

CASE II.—Multipara; 10th child, age 38. Second stage of labor commenced at 5 P.M., March 5th, when  $\frac{1}{8}$  grain of atropine was given hypodermically. Child was born at 5:30 P.M. (one-half hour), at which time pupils of mother were markedly dilated and slight dryness of throat complained of. Pupils of child were not at all dilated, and responded promptly to light.

These cases apparently contradict each other, but it will be noted that in the first case the foetus was under the influence of the drug (as evidenced by the mother's symptoms) *three* hours; while in the second case it was only under the influence (*via* the mother) thirty minutes. Perhaps this latter fact will explain why the atropia failed in the latter case. It may require a larger time for this especial drug to effect its influence upon the foetus, or it may require a much larger dose. This latter I think is the case, inasmuch as it is a therapeutical fact that children tolerate a much larger dose of belladonna relatively than adults.

I hope to continue the observations with this agent, and shall take pleasure in reporting the results to the Society.

DR. JACOBI thought that Dr. Gillette's fears had caused him to give more weight to these experiments than they deserved. Morphia does not act as a ferment, but is used up in producing its effects on the woman, so that little is left to affect the child. Again, when the one-third of a grain given is diluted in the blood of the woman the proportionate amount which can go to the child is so infinitesimal as not to be capable of affecting it.

The discussion was still farther continued<sup>1</sup> by Dr. WARD, who stated that he had had no experience with morphia, but that he had used chloral in large doses in very many cases of labor, but had never observed any effect on the child.

DR. SKENE said that he had nothing which might be considered as positive evidence on either side. He entertained the belief, however, that morphia, when given hypodermically to the mother, would produce its specific effects on the foetus in utero.

One case had made a very decided impression on his mind. He was attending a lady who had borne several living children.

<sup>1</sup> At the meeting, March 6th, 1877.

She was very nervous, and the labor was tedious, and finally she became so restless as to be nearly unmanageable, complaining of severe pain in one side of the abdomen whenever a pain came on. He gave 10' m. of morphia solution hypodermically to quiet her. When he gave it he was certain that the child was still alive. The labor was soon ended, but the child was dead. Dr. Skene had read Dr. Mattison's case, and felt sure that that child had suffered from the effects of morphia. Although well aware that morphia given by the mouth or rectum did not affect the child, he was convinced that when thrown suddenly into the circulation by the hypodermic syringe it would affect the foetus. Whether it was possible to destroy the child before killing the mother was another question.

DR. PEASLEE did not see why morphia should produce its effects any more certainly when given by the skin than when given by the mouth. Morphia does not act upon the mother in any case till it has entered her blood, and except that it enters more rapidly, when applied hypodermically, and affects her more promptly, the result is the same. When the mother already experiences a certain measure of effect from morphia the result to her and to the foetus, if any, is, he maintained, the same by whichever of the two methods it was made to enter her circulation.

DR. MUNDÉ agreed with DR. GILLETTE that the pupils of a new-born child are always dilated; that is, larger than those of an adult under the same conditions.

DR. PEASLEE admitted that the pupil was generally not contracted, but knew that it was sometimes contracted when morphia had not been given. He had recently seen a case where a little ether only had been given. The first stage had been very long, the second lasting four hours—on the whole a tedious labor. The child did not breathe at all, and resembled as nearly as possible Dr. Gillette's fourth case. Here he observed the pupils immediately after birth, and they were decidedly contracted. Dr. Peaslee said that if the mother were asphyxiated by morphia the child would certainly be affected, and that by the morphia, but it would not be narcosis, but asphyxia, and that was not the point.

DR. THOMAS said: "In renewing the discussion, gentlemen, which has now occupied the time of three meetings of this Society, allow me to refresh your memories with a statement of its origin, its progress, and its present position.

Four weeks ago Dr. Mattison, of Brooklyn, wrote to several obstetricians of this city, relating to them a case of ante-partum convulsions, in which he had employed morphia hypodermically, and in which the child was born so decidedly asphyxiated that artificial respiration had to be lengthily kept

up to ward off the occurrence of fatal consequences. The chief object of his inquiry was this: Was it possible that the alarming foetal condition was due to the morphia transfused into the maternal blood, or might it be regarded as pretty certain that it was due to causes purely connected with the process of parturition in a woman affected as this one was? Amongst others, I was addressed in reference to the matter, and seeing in it elements of great moment to the interests of the lying-in chamber, I, with Dr. Mattison's consent, brought this communication before you. This was the '*fons et origo argumenti.*' At the meeting at which Dr. Mattison's letter was read, one of our fellows, Dr. Mundé, moved that the subject of discussion for the ensuing meeting should be:

*'The Influence on the Infant of Medicines, Particularly Narcotics, Administered to the Mother during Pregnancy and Labor.'*

This discussion was opened by Dr. Mundé, who favored us with an exhaustive report of the literature of the subject, chiefly derived from German sources, consisting of experiments in the laboratory and at the bedside. He was followed by Dr. Fordyce Barker, who, drawing upon his large and varied experience, gave us a full recital of his views. These, as you remember, were decidedly opposed to the belief that drugs administered to the mother could affect the foetus in utero, his remarks being ended with a formula proposed for the adoption of the Society embodying this conclusion.

At the informal conversation which succeeded the regular meeting, so decided was the influence exerted on the negative side of the question by the efforts to which I have alluded, that I found myself standing almost alone in the advocacy of the view that narcotics, administered hypodermically to the mother in large dose, would affect the foetus in utero. One member of the Society declared that he had used these drugs, and still used them, even during parturition, without fear; another, that he would not, even in the case of his own wife, hesitate to employ them; and many others, that if such a result could occur it would long ago have been recognized. Dr. Gillette, whose large experience as an obstetric practitioner we all know, alone shared with me the conviction to which I have just now expressed adhesion.

Thus stood the discussion at the end of the first meeting devoted to it, and it was carried over to the next. At this Dr. E. R. Peaslee fully reviewed the subject, and thoroughly treating it both from a physiological and clinical stand-point, came to the conclusion that although certain drugs did pass from the mother to the child when administered for a long time,

those administered for a short period never affected the foetus in utero. Dr. Peaslee was followed by Dr. Chamberlain, who amplified the reports of experiments by Gusserow upon the pregnant woman, already alluded to by Dr. Mundé. At this point in the discussion a paper was read by Dr. Gillette, whose report of some experiments upon this subject is fresh in your memories. Although impressed with the fact from his past experience that the hypodermic use of morphia upon the parturient woman does affect the foetus in utero, he was emboldened by the positive convictions which he had heard from men of large experience to try the effect of this mode of medication again, and then reported the results of cases in which its effects had been carefully watched. He was followed by Dr. Jacobi, who endeavored to prove by a resort to mathematical calculations, based upon the proportionate amounts of circulating fluid in mother and foetus, that the portion distributed to the latter could not be sufficient to materially influence it. This brought us to the end of that meeting, when the discussion was again adjourned to that in which we now take part.

This evening we have had the pleasure of hearing further remarks by Drs. Peaslee, Gillette, Skene, and others, and now as the opinions of members appear to be rendered, and no one offers to continue the discussion, I propose, with your permission, to express my own views in reference to the point at issue.

I think, gentlemen, indeed, I may say that I feel certain that, without a dissenting voice, you will agree with me that at the present moment the question presents itself to us under two aspects.

1st. Is it possible for a drug to pass from the blood of the pregnant woman through the placenta into the blood of the foetus in utero?

2d. Is there any danger that such a passage from mother to child, during pregnancy or the act of parturition, could exert an injurious influence upon the latter?

The first question need not at all detain us. It is answered by the reports made by Gusserow and others, and reported here by Mundé and Chamberlain. The experiments which have been made put the question entirely at rest in the affirmative. It matters not if in one hundred experiments the substance injected into the maternal blood is *not* discovered in that of the foetus in ninety-nine cases. If it be so discovered in the hundredth, the question is answered. Not the question of frequency or of probability, mark you, for that does not concern our present inquiry, but merely that of possibility—whatever happens is possible, and that such passage from maternal to foetal blood happens is abundantly proven.

Now, as to the second question. Remember how this question was excited, bear in mind how the particular fœtus whose case brought it before us was poisoned, if poisoned at all, and I think that you will agree with me that at no time during this discussion would you as a body have felt willing to say to any of the participators in the debate, except Gillette and Skene, 'rem acu tetigesti.' A great deal of negative testimony has been laid before us, numbers of instances in which narcotics have been freely administered by mouth and rectum without observable influence on the fœtus, general deductions from general experience, but who beside these two gentlemen have the power to report to us that they had used morphia hypodermically near or during labor, that they had closely watched the result upon the fœtus, and that no influence had been exerted? Not one! It has been asked to-night, why should morphia administered hypodermically to the pregnant woman more decidedly affect the fœtus in utero than that given by the mouth? For myself I answer, 'I don't know,' but this is the question most germane to our subject: 'Does morphia hypodermically administered to pregnant women exert an injurious influence upon the fœtus?'—not how, nor why, nor how often,—but simply, does it or does it not do so? To this limit the question narrows itself when bereft of all the *entourage* which general discussion throws around it. To this question we may speak with some show of evidence at our disposal; to this I am able alone to speak from personal observation, and to this I shall chiefly confine myself.

I have characterized a good deal of the evidence deduced as "negative evidence." Do not understand me as undervaluing such evidence; a great deal of our knowledge rests upon such. But I do say that, when weighed against positive evidence, it should always be entirely overbalanced. Suppose that the question of the danger of ordinary vaginal injections of warm water was under discussion; you can readily imagine the display of a large amount of evidence scouting the possibility of danger from so simple and common a therapeutic resource. Yet, every man here knows that in very rare cases from this arise uterine colics, and even pelvic peritonitis. The same remark applies to vaccination, passage of the male catheter, lancing the gums of infants, the use of Thudicum's douche, and many other apparently harmless therapeutic measures. Now a thousand instances cited in which they did no harm are of value by themselves; but when opposed by one hundred, in which they unquestionably did great harm, their value vanishes as the mist does before the sun. With all due respect for my able opponents, I feel that they have proven that, as a rule, drugs

(narcotic or others), given cautiously by mouth or rectum, do not affect the foetus in utero as a rule. I admit that this is proven, and were this all the evidence before us I would willingly yield the point at issue; but this is not all. What I have called positive evidence is now to be pitted against this, and it is for you to decide which, 'when weighed in the balance, is found wanting.'

On a point like this no man, unless he has some grounds upon which to base his conviction, has a right to an opinion in opposition to the views which are generally accepted. Let me, therefore, give you a reason for my strong convictions with regard to this matter in the very inception of this discussion. I had obtained enough positive evidence to convince me years ago, and I obtained it in this way:

Some years ago, when the hypodermic syringe was first used here, I conceived the idea that anæsthetics might be given up in labor and hypodermic injections take their place. I proceeded very cautiously at first, giving morphia hypodermically in very much smaller doses than the gentlemen who have previously spoken, and with an entirely different object. I used five drops of Magendie's solution of morphia when the efforts of the uterus were very violent and the woman was in absolute pain—never thinking of the child, my faith in the innocuousness to the woman being perfect. All the labors were natural, and accomplished within a reasonable time. Two of the children delivered were free from any opium influence, but four gave such distinct evidences of it that I was convinced of the possibility of the transmission of morphia thus administered to the foetus in utero. Might not these children have been asphyxiated from other causes? you may ask. I can only express my decided belief that they were narcotized, and leave my evidence in your hands, saying, in conclusion, that in one of the children artificial respiration had to be persevered with for more than an hour before the child could be considered out of danger. Its condition was just that described in one or two of his cases by Dr. Gillette to-night.

Now mark you, gentlemen, during the fifteen years which have elapsed since that time, I have gone on using this means during pregnancy and labor, but I have done so very cautiously. It is always well to know the danger attending the means which we employ for good. Knowing the dangers attending vaccination, the vaginal syringe, the male catheter, and Thudicum's douche, I still employ them all. Knowing their dangers teaches me to avoid the evil while I avail myself of the good that is in them.

Of the effect of morphia given to the mother during preg-

nancy upon the child, I know of little positive evidence. Dr. Skene presents his experience with one case to-night—a healthy woman pregnant with a vigorous child—morphia administered hypodermically for neuralgic pain in the mother—foetal movements soon ceasing, and a still-born child the sequence, though, perhaps, not the consequence, I admit. Over twenty years ago Dr. Ezra R. Pulling, well known to most of you as a careful, conscientious, and capable observer, made a careful clinical study of the foetal heart. Two cases, in which it appeared decidedly affected by narcotics exhibited by the mouth, I here present. That they are by no means conclusive I freely admit; I present them merely for what they are worth.

CASE I.—April 16th, 1855.—B. Nolan, residing at 27 Mulberry Street, about eight and a half months advanced in gestation, applied for relief from facial neuralgia, for which I prescribed a placebo. I found the foetal pulsations two inches below and one and a half inches to the left of the umbilicus unusually strong. Three successive examinations, at intervals of ten minutes, showed an average frequency of 141, the extreme variation being but two beats per minute.

April 21st, five days later, I was sent for, and found her under the influence of a strong narcotic. She had applied to a druggist, who had given her a mixture containing sulph. morphæ gr. iii., the whole of which she had taken in thirty-six hours. Three examinations, made in the same way as the foregoing, showed the frequency of the foetal pulse to vary from 119 to 124, the average being 122. I may mention that she remained under the influence of the narcotic about eight hours after I was called.

An examination twenty-four hours later showed the foetal pulsations to range from 124 to 128, averaging 126; force about the same as in the preceding observation.

This woman had an easy labor at term. The child was feeble, but ultimately did well. I was unable to hear the foetal heart during labor, not seeing her till near its termination.

CASE II.—June 3d, 1855.—Mrs. Barclay, of 36 Cherry Street, at the commencement of the ninth month of her first pregnancy, complained of "false pains." The frequency of the foetal pulse was 133. It was most distinct near the median line. I prescribed ten drops of laudanum every sixth hour. On visiting her at the end of twenty-four hours I found that she had so far exceeded my instructions as to take about ninety minims of the tincture, and that she was considerably narcotized. The foetal heart was 118 (single observation).

My notes do not show anything special in reference to her confinement, which occurred at term.



You have before you now in evidence that narcotics sometimes, when administered in large doses to the pregnant woman, affect the foetus in utero, the following cases:

8	by	Dr. Gillette,
2	"	Pulling,
1	"	Skene,
4	"	Thomas,
1	"	Mattison.

The doubts attaching to Skene's and Pulling's cases I admit. I cannot admit, so long as I rely upon the evidence of my own senses and my ability to differentiate narcotism from asphyxia, the slightest doubt as regards my own cases; while in Dr. Mattison's case I think we have as strong evidence as could be obtained under the circumstances.

But what are you going to do with Dr. Gillette's cases? He experimented nine times, seven times with morphia and twice with atropia. In all his cases the labors were normal, accomplished in a reasonable time, and without manual or instrumental aid. In every case in which the morphia was used the child showed opium poisoning more or less profoundly. The respiration was slow, the heart-stroke feeble, and the pupil contracted. Dr. Peaslee says contraction of the pupil is often natural to the neonatus. Admitted; but see the effect of atropia—pupil widely dilated, iris scarcely discernible. The second case in which atropia was used was terminated in a half hour after its employment by the forceps.

Were all these results upon the foetus coincidences? If so, the occurrence of such coincidences is more remarkable than that of foetal poisoning by means of the mother's blood. I see but two methods of dealing with these cases; first, to declare that the experimenter has grossly blundered in his deductions; or, second, to admit that if there be any value to be accorded to clinical evidences these cases go to prove that large doses of narcotics, hypodermically administered to the pregnant woman, may affect her child injuriously. It is true that Dr. Peaslee tries to meet these cases by the assertion that the dose was large enough to cause asphyxia in the mothers, and that thus the children were affected. But note the fact that in no solitary case did the respirations go below 18 to the minute. Does that look like dangerous opium poisoning? In my own cases certainly nothing bordering on narcotism happened; the patients did not show to any great extent the effects of the drug, for I sat by the bed and conversed with them, and there were no marked results of the opium visible, the effects simply showing themselves in a diminution of the size of the pupil and the pain. Again, take the case of Dr. Skene, where the

patient was doing perfectly well, and the foetal heart beating. The Doctor uses a hypodermic injection of morphia, and the child, without any assignable cause, dies.

I am perfectly willing to admit the force of the remark of Dr. Peaslee at the last meeting, that where morphia is administered during labor and the child dies, it is not a logical deduction that morphia killed the child. But let us suppose that in a large number of cases in which morphia has been used the child does show distinctly the evidences of opium poisoning, is the deduction still an unwarrantable one?

In conclusion, let me say that although I may appear to speak strongly upon the subject, I have no wish to deal with it in a dogmatic spirit. I do not claim, even with the powerful testimony which has been adduced here by Dr. Gillette, that the matter should be looked upon as entirely settled. But this I do feel, and feel strongly, that with the light which we at present have, this Society should not let its dictum go forth in favor of the negative side of this question; that it cannot, with the evidence now before it, even if it desired to do so, endorse the conclusions arrived at by some of those who have advocated that position."

DR. PEASLEE.—"In regard to the right to form an opinion on this subject, I hold that every one has that right if he has facts on which to base it, however he acquired them—otherwise not. I have the facts of my own experience and that of others, and judge therefrom. Dr. Gillette has added also certain experiments, and these being made known become at once the property of the whole profession, and I, or any one else, can base an opinion upon them with the same right as himself. I noted at the last meeting that I adopted the negative side of this question because I possessed no facts which proved the affirmative to be the true view. And I must now add that with the aid of the experimental facts which Dr. Gillette has adduced, I still adhere to my former position. Dr. Thomas has very truly remarked that one positive fact is worth more than any number of negative ones. But what are the positive facts in Dr. Gillette's investigations, except that he gave the mothers the morphia and the children were born more or less asphyxiated? It is not positively proved that they were asphyxiated by the absorption of the morphia from the mother into the foetal blood. Some may consider this as probable, and Dr. Gillette does so. I do not, since I can account for the condition of the children by a supposition to me much more probable than that. Several substances have been shown to enter the foetal blood from that of the mother, especially ether, chloroform, and salicylic acid, as we have already seen. But in no

instance was the amount absorbed sufficient to produce any perceptible effect, injurious or otherwise, upon the fœtus. The woorara even did not affect the fœtus at all. I am not, therefore, prepared to admit the affirmative of this question till (1) the narcotic is actually detected in the blood or the urine of the new-born, and (2) there are symptoms also in the latter which are clearly due to the morphia detected. Then we shall have something *positive* to base our decision upon, and till then I must wait. Dr. Gillette has had a positive experience, with at best but a doubtful result, so far as this question is concerned. His two experiments with atropine also lead to no positive conclusion as to the question whether that narcotic is absorbed from the mother's blood into that of the fœtus.

If the question be whether it be possible to injure the fœtus in utero by narcotics given in excessive doses, there can be no difference of opinion. For if the dose kills the mother the fœtus will die of course, and if it nearly kills her, the fœtus cannot entirely escape injury. I should not myself think of producing the narcotic effects upon the mother during parturition which Dr. Gillette produced. Indeed, in a labor perfectly normal in every respect, I suppose no one of us would administer morphia at all. But with the knowledge I possess up to the present time I should still, as heretofore, prescribe morphia during labor in what I considered a sufficient dose to effect the object I had in view, as already explained in my previous remarks. I should never use it as an anæsthetic during labor, of course."

DR. GILLETTE said: "It has been deemed perfectly safe and proper to use the drug to produce a certain degree of anæsthesia, and it is utterly impossible to produce anæsthesia in a woman in labor with the ordinary dose of five or six drops. In the cases which I report, the drug did not produce any asphyxia at all. I cannot understand a case of asphyxia in which the respirations are not below eighteen in the minute. It is well known that opium, if given under certain circumstances, causes flushing of the surface; and this is not because of any want of oxygenation of the blood, but is the physiological effect of the drug, causing dilatation of the capillaries. I cannot agree with Dr. Peaslee that any effect on the woman could occur, with the doses which I used, sufficient to interfere with oxygenation in the fœtus. The oxygenation is peculiar and rapid in the new-born child, and once air is admitted into its lungs the danger is over. It is also noticed that the respiration is uniformly maintained when once simple asphyxia is removed. Now, in these cases of asphyxia, if you choose to call it asphyxia, the respirations were infrequent and came very

slowly. The children were somnolent, the pulse was slow, and they showed every indication of oppression of ~~some~~ nerve centre."

DR. PEASLEE considered that the lividity or leaden color after the use of narcotics is always a sign of imperfect action of the blood, whether the frequency of the respiration be diminished or not.

DR. GREENE: "I think that I speak the feelings of the majority of the members of the Society when I say that we are under a debt to Dr. Gillette for his interesting and valuable paper, with all its information, and I therefore move him a vote of thanks."

DR. PEASLEE remarked: "Though I do not adopt his conclusions, I feel very much obliged to Dr. Gillette for his interesting communication, since there are very few, I think, who would have performed these experiments under the same circumstances."

The motion was unanimously carried.