

PLACENTAL TRANSMISSION.*

BY W. A. NEWMAN DORLAND, A.M., M.D.,

Instructor in Gynecology, Philadelphia Polyclinic; Assistant Demonstrator of Obstetrics, University of Pennsylvania.

When I was invited to read a paper before this association of medical men I was at first somewhat at a loss to determine just what would be the most opportune and acceptable subject for our evening's consideration. The difficulty lay not so much in a lack of suitable subjects; on the contrary, I have not the slightest doubt that any one of a score of subjects that I might select would give us a profitable and enjoyable mental repast. I recalled, however, that living as you do in the very atmosphere of practical medicine and surgery something that would carry you for the time being away from accepted detail into the more shadowy realm of interesting theory and speculation would lend an attractiveness to our meeting that might eventually bud into practical conclusions, such as would enrich our knowledge of the hitherto vague and undecided.

Guided by this impulse I have turned, therefore, to a question of more than passing interest; one that touches most intimately upon the welfare of the human race, since it closely concerns the life of every being called upon to pass through the precarious period of antenatal existence; a subject, moreover, upon which, so far as I am aware, no extant text-book of obstetrics satisfactorily treats, and yet one which within the last half decade is beginning to engage the attention of the thinkers in the obstetric branch of medicine. Thanks to the indefatigable labor of Grätzer, Ballantyne, Somma, and others, we are becoming better acquainted with the physiology and pathology of intra-

* Read before the Philadelphia Hospital Medical Society, March 5, 1900.

uterine life, and judging from the large number of papers that are annually appearing as the result of extensive scientific investigation and increased clinical and pathologic data, it will not be long before we shall be possessed of fairly considerable knowledge of these necessarily intricate matters.

It would be commonplace to state that the placenta is a peculiar foetal appendage destined for the time being—the last two trimesters of pregnancy—to assume the functions of the vital organs of the growing embryo. It is practically the foetal heart, lungs, and digestive tract; but were we to limit its functions even thus extensively we should probably be robbing it of other equally important rôles in the preservation of the foetal economy. Who as yet can determine the origin of the almost conscious power it shows in selecting from the maternal pabulum furnished to it those metabolites that are most essential for the foetal growth and well-being, and in rejecting other noxious elements that would jeopardize foetal existence? That this selective faculty, or as it has been termed, the *absorptive power*, of the placenta does exist is beyond all question or doubt; hence, has arisen the theory of placental transmission, whereby pathologists attempt to explain the development of certain diseases of early infancy and childhood. When we have made the statement, however, we have reached the limits of our positive information, and any attempt to explain the method by which the known fact is accomplished carries us into the realm of speculation. Again, who can say why this conscious organ will permit certain pathogenic germs or their toxins, or both, to pass through its meshes with great facility and others only exceptionally and apparently after a mortal resistance? Again, it is a known fact that a *materies morbi* can be transmitted readily from the foetus to the mother, as for example, the toxins that are active in the production of puerperal eclampsia, while similar toxins, circulating primarily in the maternal system, are strenuously resisted by the placental meshes as they endeavor to permeate into foetal tissues. Why do these cells refuse admission at one door and permit it at the other? And still again, why is it that certain drugs circulating in the maternal blood meet with an impregnable barrier when they encounter the choriodecidual interdigitations, while others leap the apparently trifling ledge as Remus is said to have vaulted the wall of Rome. It may be that by carefully studying the reported facts as they come from the pens of scientists and observant clinicians we can, by putting this and that together, arrive at some pretty definite conclusions.

In the first place, then, that certain drugs and poisonous substances

may be carried to the unborn foetus through the maternal vessels is an undoubted fact. As Fournier¹ has recently stated, the mediate treatment of a foetus through its mother is of great value in certain pathologic conditions, preëminent among which is syphilis. Many observers have demonstrated the introduction of drugs into the foetal system through the agency of the maternal circulation. Bureau² detected morphin in the blood of the placenta and umbilical vessels taken from a parturient morphinomaniac. Porak³ found that mercury showed great affinity for the placenta; lead and copper accumulated most in the foetal tissues; while arsenic was found chiefly in the skin of the foetus. With copper and lead abortion is not observed, but death of the young before birth is common. Mercury has the power of producing abortion. Lead-intoxication displays itself in the young by producing cerebral lesions and paralysis. Arsenic produces abortion from placental hæmorrhage. It is important to note that if the placenta is frequently and gravely attacked by syphilis, it is at the same time the elective organ of accumulation of mercury. As early as 1878 Porak found potassium iodid in the urine of the foetus forty minutes after it had been given to the mother; while Cathelineau and Stef found mercury in the ashes of a burnt foetus whose mother had been treated with that drug.

This transmissibility of drugs is a suggestive fact, and it can be safely asserted that intra-uterine medication, now practically in its infancy, is destined to become an important prophylactic agency during gestation.

In the second place, it is well known that certain diseases that are rampant in the maternal system find ready access into the placental circulation where they quickly accomplish their work of destruction and terminate the incipient human life. Such are the exanthemata, which appear to be especially prejudicial to foetal existence, and, in addition, assume an unwonted virulence in the presence of gestation whereby their morbidity and mortality are essentially increased. This is equally true of most germ-diseases.

Two theories have been advanced in explanation of this transmission, namely, the *parasitic* and the *leukocytic*.

(a) It would seem, as Rostowzew has indicated, that under the influence of the infection the epithelial coat of the chorionic villi loses impermeability, so that the bacilli pass directly through it. Such a result would lead at once to the suggestion that it is through bacterial action that the placenta surrenders its protective function and permits the osmosis of deleterious substances. If this assumption be true

we again see here the dominant influence exerted upon the human organism by bacteria, and we have one more proof to adduce in support of the germ-theory of disease. The disorganization of the delicate structure of the placental tissue, together with the abolishment of the physiologic function of the placental villousities through the action of bacteria, has recently been clearly demonstrated by Delore,⁴ who proves that this process does not partake of the nature of an inflammation but rather of a myxomatous and fibrous degeneration. As a direct result of these non-inflammatory changes the selective power of the placenta seems to be largely, if not totally, abolished, and germs and their toxins that would otherwise be arrested at the choriodecidual junction are transmitted into the fetal tissues. This evidence endorses the theory of Malvoz that transmission can only take place when there is a destruction of the villous epithelium as a result of some placental lesion.

(b) The older *leukocytic* theory at first sight seems equally plausible as the parasitic, and claims distinguished adherents both in this country and abroad. Grandin,⁵ in a paper read before the Medical Society of the State of New York, presents this view in the following well-selected sentences: "Given an instance where the woman is in health at conception, and for a certain period afterwards, and the chances are that the placenta intervening between woman and foetus is healthy. Now let this woman become diseased and at once the leukocytes in her blood-system carry the infection to the intervillous spaces. Here they are met by the barrier against disease established by the healthy placenta. This placenta contains healthy leukocytes with the property of resisting the entrance of diseased germs. The phagocytic action of these healthy leukocytes comes into play, destroys at once the leukocytes bearing disease, and thus the foetus is protected. Given, on the other hand, a woman diseased at the time of conception, or becoming so shortly afterwards, that is to say at a period when the placenta is in the course of early formation, then either we have at the outset a diseased placenta, or one which becomes diseased as it is forming. Such a placenta contains either no healthy leukocytes, or else they have but feeble resisting powers. The barrier interposed by the placenta is, therefore, ineffective to an absolute degree, or else the leukocytes within it resist feebly, or strongly, according to the intensity of the disease process endeavoring to gain access from the side of the woman. In this latter event disease is transmitted to the foetus, because the disease-bearing leukocytes from the side of the woman are stronger than and overcome the leukocytes in the placenta." Such is the leukocytic

theory, pregnant with suggestion, but beyond the possibility of proof. I must confess that my personal inclination is biased in the direction of the parasitic view; or it may be that both are correct, the parasites being the indirect cause of the transmission of disease by producing weakened or diseased leukocytes which in their turn are unable to cope with the toxins produced by the germs.

Most of our information as to the transmissibility of the acute infectious diseases from the mother to the child has been derived from the laboratory of the physiologist, where experiments have been conducted upon gravid animals. These experiments have been confirmed, however, from time to time by scattered clinical observations, and it will be interesting to note at this point the results that have thus far been obtained.

Typhoid Fever.—Manzoni and Charcelay in 1841, Weiss in 1862, Chantemesse, Straus, Chambrelert, Ernst, Durk, Satullo, Vidal, Frascani, and others have noted the passage of the typhoid bacillus through the placenta into the foetal tissues. Reher in 1885 examined the liver and spleen of a six-month foetus from a typhoid fever case, and obtained pure cultures of Eberth's bacillus. Neuhaus⁸ in 1886 obtained similar results from a four months' foetus; while Eberth in 1893, from a three-months' foetus, expelled with membranes intact, obtained pure cultures of the bacillus from the blood in the heart and other foetal organs. Janisewski⁷ reports the case of a woman eight months' pregnant and suffering with typhoid fever, as proved by bacteriologic examination of the stools, who gave birth to a foetus that survived for five days. At the autopsy no lesions were found except enlargement of the spleen, but cultures from the spleen, intestine, mesenteric glands, kidneys, and lungs produced typical typhoid bacilli. Freund and Levy⁸ record a miscarriage occurring in the fifth month of pregnancy and during the fourth week of a typical attack of typhoid fever. No abnormality was found in the foetus except a somewhat enlarged and slightly softened spleen. The intestines were normal. Cultures, however, made from the spleen and heart's blood, and from the placental blood, gave numerous colonies of the typhoid bacillus, while cultures from the other surface of the placenta and from the vernix caseosa were sterile. Fordyce⁹ examined a five months' foetus from a fatal case of typhoid fever, the maternal death occurring shortly after the miscarriage. Externally and internally nothing abnormal could be seen by the naked eye in the foetus or its appendages. The intestines seemed quite healthy; the liver and spleen not enlarged. Tubes inoculated from the kidneys, spleen, and intestinal contents gave pure

cultures of the typhoid bacillus; the blood was sterile. It was impossible to demonstrate bacilli in the tissues by microscopic examination. The Widal test was very successful in this case. Etienne¹⁰ records the examination of a fœtus which had been discharged in the fifth month of pregnancy on the twenty-ninth day of an attack of typhoid fever. The spleen and intestines of the child showed no signs of the disease, and the placenta was healthy. Culture-examination of the blood from the right side of the heart and from the spleen, liver, and placenta revealed an abundance of typhoid bacilli. Fränkel and Kinderlen have failed to discover the germs in the fœtal tissues in undoubted cases of maternal typhoid fever. It is worthy of note that in all of the cases recorded no macroscopic lesions of the fœtal organs were discoverable, although the bacilli were present in large numbers. Etienne explains this fact by supposing death to result from an acute blood-poisoning due to a large dose of the bacillus before local changes could occur. Freund and Levy, on the other hand, claim that the characteristic lesions are not found because the functions of the fœtal organs have not been established; hence they remain inert in the pathologic process.

From the foregoing cases we must inevitably conclude that typhoid fever undoubtedly can be transmitted to the embryo or fœtus, and usually with disastrous results, Sacquin reporting 310 cases with 199 abortions, and Martinet 109 cases with 66 abortions, a fœtal mortality of $63\frac{3}{4}$ per cent. In other cases the fœtus may survive, although manifesting the symptoms of the disease, while yet again it may be born alive and healthy as in a case recorded by Touvenaint,¹¹ and in a case of my own one year ago in which an eight months' fœtus was born in the third week of typhoid fever without showing any signs of the disease and ultimately becoming a plump and healthy infant.

Variola.—There is probably no exanthem that can be transmitted so readily to the fœtus as smallpox, although, strange to relate, the majority of fœtuses whose mothers are exposed to the infection do not contract the disease. Its virulence, however, has been shown conclusively by the high fœtal mortality and by the presence of the eruption or its scars upon the newborn child. Van der Willigen¹² records 80 cases of variola in pregnant women with a maternal mortality of 15 per cent, and a fœtal mortality of $36\frac{3}{4}$ per cent. Instances have also been recorded in which immune mothers have given birth to fœtuses bearing the scars of the disease, having evidently passed through an attack and survived without serious results to themselves or the mothers; and yet again twin pregnancies have been noted in which

one foetus was pock-marked and the other free from the scars. The proof of the placental transmission of this disease is to be found in the frequent death of the embryo and the cutaneous manifestations.

Scarlet Fever.—The infection of the foetus *in utero* by the scarlatinal virus is unquestioned, although of rare occurrence. Such cases have been noted by Gregory, Baillow, Hüter, Asmus, Stichel, Meynet, Tourtual, Leale, and Saffin. The foetus may perish *in utero* or it may be born with the typical scarlatinal eruption upon its body. Extensive desquamation simulating Ritter's disease may follow this rare foetal infection.

Measles.—S. Marx of New York, in all the literature of obstetrics, was able to find but six cases of antenatal infection with measles. Grandin explains this infrequency on the ground that the disease but rarely affects adults. Ballantyne¹³ reports the case of a woman who miscarried in the fifth month of her pregnancy while suffering from measles, the eruption at the time beginning to disappear. The foetus was born alive and was found to have the measles eruption upon the face, back, and legs. The foetus rarely dies from this disease, although Remy¹⁴ reports a case of miscarriage at five months and ten days, occurring during a mild attack of measles. The foetus lived for a few moments and died probably not so much from the disease as from the early expulsion from the uterus.*

Erysipelas.—The shedding of the skin by the newborn child is a comparatively rare condition known technically as dermatitis exfoliativa neonatorum, or Ritter's disease. There can be no doubt that some of the reported cases of erysipelas *in utero* have been in reality of the nature of the exfoliative dermatitis. Undoubted cases of intra-uterine erysipelas have, however, been reported, notably by Kaltenbach,¹⁵ Runge,¹⁶ Stratz,¹⁷ Lebedeff,¹⁸ and others, the specific germs of the disease being found in the foetal subcutaneous tissue, though absent in both the placenta and cord.

Recurrent Fever.—Grandin¹⁹ asserts that three cases have been recorded of recurrent fever affecting the foetus, in one of which the specific organism was found. The foetuses in two of the cases betrayed

* Since writing the above an interesting case intra-uterine transmission of measles has occurred in the practice of the writer. Three weeks before delivery at term the youngest child, three years of age, was nursed by the mother through a severe attack of measles. At birth the infant presented a beautiful eruption of the crescentic lesion thickly covering the chest and dorsum, which gradually faded and had disappeared by the third day. During the last two weeks the mother had noticed violent foetal motions which were probably the result of the systemic infection.

by violent motions that they were suffering from chills immediately subsequent to the maternal chills.

Pneumococcus Infection.—Intra-uterine infection with the diplococcus pneumoniae of Fränkel has been noted by Satullo, Netter, Talamon, Friedländer, Babès, and others. Delestre²⁰ reports the case of a woman who died of bilateral pneumonia immediately after labor, the child perishing on the third day from convulsions. Autopsy of the child disclosed a pneumonic spot at the base of the right lung and a meningitis, both caused by the pneumococcus. This diplococcus was also found in the blood, in the pericardial serum, in the cerebrospinal fluid, and in microscopic preparations of the lung, liver, and spleen. It is curious to note that in these cases of intra-uterine infection with the pneumococcus the specific lesions of pneumonia are generally absent notwithstanding the presence of the germs.

Streptococcus Infection.—Although of rare occurrence there have been recorded undoubted instances of septic infection occurring in the foetus *in utero* by Von Holst, Pyle, Satullo, Hanot, Luzet, Mars, Koubassoff, and others. Legry²¹ examined the lungs of a child which had suffered from imperfect respiration. The pleura showed fibrinous deposits and false membranes, and the pleural cavities contained a small amount of serosanguineous fluid. Bacteriologic examination of the membrane and fluid revealed the presence of streptococci-chains. Ricker²² reports the case of a woman who died in her sixth month of pregnancy of a disease diagnosed diphtheria. Careful bacteriologic examination revealed the streptococcus pyogenes, which was obtained in pure cultures from the placenta and liver of the foetus. No lesion was found in the foetus. Ricker also records a case in which the streptococcus was found in the blood of the umbilical vein of a stillborn child whose mother died shortly afterwards from the effects of a phlegmon of the arm, which was present at the time of the birth. In neither case was any lesion of the placenta discoverable. Chambrelent and Subrazes²³ inserted into the ears of a pregnant rabbit a bouillon-culture of the streptococcus. Some time after pure cultures of the streptococcus were obtained from the heart, blood, liver, and spleen of the mother, and from the interior of the embryos, which were the size of lentils and about twelve days old. They were infected with chains of streptococci. Bar and Renon²⁴ report the case of a woman who, while suffering from streptococcism in the eighth month of pregnancy, gave birth to a stillborn child, and perished herself fifty-three hours after labor. Although the foetus succumbed, cultures from the placental blood and from the liver, heart, and lungs remained sterile.

Anthrax.—Grandin as recently as 1896 stated that there is but one acute disease which the woman is not able to transmit to her child *in utero*, and that is anthrax. Undoubted cases, however, have been recorded by Wolf, Marchand, Koubassoff, Arloing, Straus, Chambrelent, and others. Rostowzew²⁶ had occasion to observe three cases of pustula maligna faciei in pregnant woman in the fourth, seventh, and eighth months. Anthrax bacilli were found in the foetuses, all of the mothers and their offspring perishing.

Tuberculosis.—Until recently it was supposed that the transmission of tuberculosis from the mother to the foetus was exceedingly rare, if it ever occurred, and Grandin²⁶ himself stated in 1896 that there was but one undoubted case on record. We now know, however, that this infection is more frequent than it is reported to be. Since Lehmann's²⁷ case of undoubted placental tuberculosis, the same clinician has observed²⁸ another case in which the foetus of a phthisical woman showed tubercle nodules in the liver, spleen, and lungs, with large numbers of tubercle bacilli. There was also tuberculous involvement of the bronchial, mediastinal, hepatic, mesenteric, and lumbar lymphatic glands, and of the left kidney. Kynoch²⁹ reports a case of a woman who died of acute tuberculosis in the third month of gestation. The placenta was found studded with gray tubercles, although there was no obvious tuberculous lesion in the foetus. Other authentic cases have been reported by Demme, Johnne, Sabouraud, Chauveaw, Charrin, Satullo, and others. Neil³⁰ recently quoted Osler to the effect that autopsy shows the lungs in the adult to be invariably affected in tuberculosis, while the other organs are involved in very small proportion, whereas the author finds that in children the lymph-glands, the bones, and the joints are mostly affected. The inference he draws is that the infection must have been transmitted from the mother by means of the vascular and lymphatic systems through the agency of the placenta.

Syphilis.—There is apparently no obstacle whatever to the transmission of the syphilitic virus from the mother to the foetus; in fact, it is a foregone conclusion that given an infected mother the foetus cannot escape early infection, if, indeed, it be not infected *ab ovo*. The literature teems with references to cases of inherited syphilitic infection, and I have made mention of this portion of the subject merely to make my paper complete.

The transmission of other germ-diseases through the placental meshes is recorded as follows: glanders by Cadéac, Löffler, and others; chicken cholera by Chambrelent; malaria by Taylor, Behrmann, Harris,

Bompiani, Negri, and others; articular rheumatism by Schäffer and Pocock; yellow fever by Bemiss; and diphtheria by Charrin.

From the foregoing review of the literature of the placental transmission of drugs and specific diseases, meager though it be, we are able to derive some very suggestive, if not conclusive, arguments.

1. While many drugs may be administered to the mother without any noticeable effect upon the foetus, there are certain substances that show a special tendency to traverse the placenta, and, entering the foetoplacental circulation, exert a positive influence for good or evil according to the condition that may be present in the given instance.

2. Maternal medication, therefore, is indicated in certain conditions, either in order to prevent the development of a similar condition in the foetus, or to counteract the effect of germs and their toxins already introduced into the foetal economy.

3. The drugs that have been found to affect the foetus *in utero* are notably opium, mercury, copper, lead, arsenic, and the iodides. In appropriate doses they may be administered to the mothers in suitable pathologic conditions with beneficial results to both mother and child.

4. Any morbid influence acting upon the mother either acutely, as in the case of the exanthemata, or more slowly, as in tuberculous and specific infection, will react deleteriously upon the product of conception, and either destroy it through its overwhelming toxic action, or render it feeble and less resistant to subsequent and post-natal invasion, or the disease will run an atypical course *in utero* with or without apparent vestiges at birth.

5. The entrance into the foetal structures is accomplished through the agency of the foetoplacental circulation. It is probable that access is gained through bacterial action, the germs rendering the placental villi less resistant to invasion, whereby both the microbes and their toxins pass the natural barrier at the choriodecidual junction.

6. As a rule, the infectious diseases do not manifest their characteristic visceral lesions in the foetus, probably because of the passivity of these organs during antenatal existence. The germs, however, may be detected in large numbers by bacteriologic and microscopic examination.

Bibliography.

¹ *La Sem. Méd.*, November 30, 1898.

² *Jour. de Méd. de Paris*, October 20, 1895.

³ *Nouv. Arch. d'Obstét. et de Gynéc.*, No. 3, 1894.

⁴ *Jour. de Méd. de Paris*, April 16, 1899.

- ⁵ *N. American Pract.*, August, 1896.
- ⁶ *Berl. klin. Woch.*, s. 389, 1886.
- ⁷ *Presse Médicale*, March 24, 1894.
- ⁸ *Berl. klin. Woch.*, June 27, 1895.
- ⁹ *Scottish M. and S. Jour.*, Vol. III., No. 1, 1898.
- ¹⁰ *Gaz. hebd. de Méd. et de Chir.*, No. 16, 1896.
- ¹¹ *Jour. de Méd. de Paris*, July 8, 1894.
- ¹² *Nederl. Tijdschr. o. Geneesk.*, No. 11, 1895.
- ¹³ *Edinburgh Med. Jour.*, March, 1893.
- ¹⁴ *Arch. de Tocol. et de Gynéc.*, June, 1894.
- ¹⁵ *Cent. f. Gynäk.*, No. 44, 1884.
- ¹⁶ *Cent. f. Gynäk.*, No. 48, 1884.
- ¹⁷ *Cent. f. Gynäk.*, Vol. IX., s. 213.
- ¹⁸ *Zeitsch. f. Geb. u. Gynäk.*, Bd. XII., H. 2, s. 321.
- ¹⁹ *Loc. cit.*
- ²⁰ *La Sem. Méd.*, February 9, 1898.
- ²¹ *Bull. de la Soc. Anat. de Paris*, December, 1893.
- ²² *Cent. f. allg. Path. u. Anat.*, VI., No. 2, 1895.
- ²³ *Jour. de Méd. de Bordeaux*, 1895.
- ²⁴ *Répertoire Univer. d'Obstét. et de Gynéc.*, September 25, 1895.
- ²⁵ *Medicine*, May, 1898.
- ²⁶ *Loc. cit.*
- ²⁷ *Deutsche med. Woch.*, No. 4, s. 87, 1894.
- ²⁸ *Berlin. klin. Woch.*, July 9, 1894.
- ²⁹ *Scottish M. and S. Jour.*, Vol. I., No. 2, 1897.
- ³⁰ *Med. and Surg. Bull.*, Alumni Assn. Univ. of Nashville, Tenn., May, 1898.