

## CONGENITAL TUBERCULOSIS WITH THE REPORT OF A CASE.

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At the present day, undoubtedly more than ever before, the subject of tuberculosis is attracting world-wide interest. The usual methods of its propagation are now well understood; but we are still ignorant of the exact part played by heredity in its production. There are two common theories with regard to the latter.

First: The theory of an hereditary predisposition (we omit purposely the theories of Baumgarten and von Behring).

Second: The theory of direct bacterial infection in utero.

In support of the first theory.

(1) Direct bacterial transmission is far too unusual to account for the frequency of the disease in the young.

(2) A predisposition to the disease may be derived almost as frequently from the father as from the mother; while in the case of the true congenital transmission no authentic case of direct transmission from the father is on record.

(3) The predisposition may be handed down from a parent, grand-parent, etc., having only a mild form of the disease; while in those cases in which direct bacterial infection takes place, the parent (the mother) suffers usually (not always according to Schmorl) from a severe type of the disease—most frequently from a general miliary tuberculosis.

In support of the second theory.

The first undoubted case of congenital tuberculosis was described by Johne in 1885, and occurred in a calf foetus of eight months, found in the uterine cavity of a cow which died of phthisis, the uterus and placenta being normal.

Since then numerous cases have been described by other veterinarians, until in 1898 more than sixty cases of calves with congenital tuberculosis had been reported, and Klapp estimated that 2.63 per cent. of all calves born of tubercular cows are tuberculous.

Human cases of congenital tuberculosis are much less frequent, Schmorl and Birch-Hirschfeld being the first to describe the case of a seven-months foetus born of a tuberculous mother and showing tubercle bacilli in its liver and the placenta, no histological changes of tuberculosis being present.

Sabouraud was the first to describe a well authenticated case of congenital tuberculosis in which miliary tubercles were found in the liver and the spleen of the infant. Doubtful cases have been reported since the year 1825, but in the absence of convincing microscopical examinations, these must remain doubtful. Hauser, reviewing the literature in 1898, found 18 cases which he considered as undoubted tubercular infection of the foetus, or at least as cases of transmission of tubercle bacilli into the foetal circulation, and which were classified as follows: Nine with extensive tuberculosis of the foetal organs, 5 in which tubercle bacilli without the presence of tubercles were found in the foetal organs, and 4 cases of placental tuberculosis.

The literature has been critically reviewed within the last year by Warthin and Cowie, whose stricter classification has served to separate the undoubted from the doubtful cases, the criteria required being "the presence of characteristic anatomical changes and of tubercle bacilli, the development of the lesions within such a short time after birth as to preclude the possibility of extra-uterine infection, and the exclusion of syphilis." From this point of view the undoubted cases of congenital tuberculosis have been reduced to six, accepting three of Hauser's nine (Howe, Sabouraud and Lehmann), and adding those of Ustinow, Auché and Chambré-lente and Veszpremi. So that the case here reported is the seventh of undoubted congenital tuberculosis to be reported.

The four cases of placental tuberculosis mentioned by Hauser are all accepted in Warthin's stricter review, and two reported by Warthin and

that of Auché and Chambrelente added.

To these the cases of Runge and Warthin and Cowie, as well as our own, must now be added.

Veszpremi, unfortunately, was not able to examine the placenta in his case.

Hauser omitted a second case of Lehmann's, Schmorl and Geipel add nine cases in 1904.

There are, therefore, nineteen cases of placental tuberculosis recorded up to the present time. Finally, the five cases mentioned by Hauser in which tubercle bacilli without the histological lesions of tuberculosis have been found are augmented to twelve in Warthin's classification.

In Congenital Tuberculosis which parent is the Infecting Agent.

Not a single indisputable case of direct bacterial infection from the father is on record; even though experiments have proven, beyond a doubt, that the semen may contain tubercle bacilli in advanced general tuberculosis, or severe tuberculosis of the testes.

Method of Transmission in Congenital Tuberculosis.

The infection is transmitted in all cases through the placenta or decidua basalis, from the maternal blood (although the ovary may be the seat of the tuberculosis it has not been positively demonstrated, that direct infection has taken place through an infected ovum). The placenta shows in all cases, tubercular changes; but the degree of infection of the child does not necessarily depend upon the degree of those changes.

Character of the Involvement of the Child.

(1) There may be bacterial infection without definite lesions.

(2) There may be both tubercular changes and tubercle bacilli.

As further evidence that direct intra-uterine infection may take place (although rarely), we would now refer to an additional case of this character, but recently occurring in the service of Dr. J. W. Markoe at the Lying-In Hospital.

History.—Mrs. L. A. (Hospital No. 4,918), para VII.; aged, 33 years; was admitted into the hospi-

tal on December 7, 1904.

She was in the ninth lunar month of pregnancy, and was suffering from pulmonary tuberculosis.

Physical Examination.—The patient was very poorly nourished and of poor color. She looked far gone with the disease, and had a severe cough with considerable expectoration. At the apices and bases of both lungs, there were impaired resonance and broncho-vesicular breathing, together with many crepitant and subcrepitant rales. There was considerable sibilant breathing in the intra scapular region.

The abdomen was the usual size for the ninth month of pregnancy. The foetus was apparently active. Examination of the sputum, showed the presence of tubercle bacilli.

The urine contained a trace of albumen, a few casts and gave a positive diazo reaction.

During the following three days the patient gradually went down hill.

The breathing became more labored; the cough more troublesome. The temperature ranged between 100° and 104° F.

On the fourth day after admission, she went into labor, spontaneously, and delivered herself in a few hours of an eight months' child. After the labor, she failed rapidly and died on the sixth day.

The Child.—This was a male; poorly nourished; weight 2,100 grammes. It was fed by the bottle, on modified milk; and did badly from the start. After gradually losing weight and running continually a subnormal temperature, it died on the nineteenth day.

At no time was there any cough or diarrhoea.

At the time of death its weight was 1,650 grammes, a loss of 450 grammes from its birth weight. The child was not allowed near its mother or any other tubercular cases.

The pathological report of the case as made by Dr. Martha Wollstein is as follows:

The placenta measured 16 cm. in diameter and 3 cm. in thickness; its cord was implanted eccentrically. There was no marginal rim of infarcts and no large infarct at any point. A triangular area

measuring 5 x 7 ctm., with its base at the placental margin and its apex near the insertion of the cord, was yellow in color, soft in consistency and suggested cheesy material. There were two small yellow tuberculous areas in another cotyledon. Grayish nodules were numerous over the membranous surface, but, on comparison with a normal placenta, these did not seem to be miliary tubercles. The triangular cheesy area extended to and involved the membranes, the maternal surface of which was more roughened here than at any other point. The foetal surface of the membranes was apparently roughened, as though covered with a fibrinous exudate over this area of 2 ctm. by 3 ctm. in diameter. Over the two other cheesy masses the foetal surface was in a similarly roughened condition.

Smears from the yellow area stained with carbol-fuchsine and Gabbet blue showed many tubercle bacilli, some of them in small groups of four to six.

On microscopic examination of the placental sections the chorionic membrane was found to contain areas of necrosis in which nuclear fragments were very numerous, few cells being preserved. The central portions of these areas resembled cheesy material, and giant cells in small numbers were found at the edge of the cheesy centre; epithelioid cells were not present. The areas were irregular in shape, passing gradually into the normally preserved chorion without any limiting zone, and involving the amnion, whose covering epithelium was completely destroyed and its free (foetal) surface covered with granular fibrin and nuclear fragments. Large vessels in the chorion contained thrombi of agglutinated red blood cells, staining bright red with eosin and not always filling the lumen of the vessel completely.

Many intervillous spaces contained fibrinous masses similar to those seen in normal placental sections. But in other cases the spaces contained masses which were more homogeneous, almost hyaline in appearance, and surrounded by leucocytes whose nuclei were almost all fragmenting. These masses either filled the space between two villi completely or touched only one villus. But where it came in contact with the villus, the epithelial cells were wanting, although present immediately

beyond the point of contact. This point is of interest as regards the question as to whether or not a normal syncytium is an efficient bacterial filter, and thus a protection to the foetus. Certainly the agglutination thrombi had destroyed the syncytium in this case, while in no section were the syncytial cells affected over a villus whose adjacent spaces were empty or filled with normal blood cells or with fibrinous masses.

Many villi were normal. Some contained small cheesy tubercles in their stroma beneath an adherent thrombus, and others were fused together into necrotic masses in which the villus outlines were more or less completely lost, cheesy matter and a few giant cells occupying the center. These tuberculous areas were readily distinguished from small white infarcts, of which a few were present in the sections. Tubercle bacilli were found in the tubercles in the chorion, in the cheesy masses in the villi and in the intervillous spaces, both free and in the thrombi. Warthin and Cowie call attention to agglutination red blood cell thrombi in the intervillous spaces of the placenta in their case.

Schmorl has recently described placental tuberculosis as occurring in four forms, dependent upon the localization of the tubercle bacilli; on the periphery of the villi, when the tubercles form in the intervillous spaces; in the interior (stroma) of the villi; in the basal decidua; in the chorion, involving the amnion as well. The first form is the most frequent one, and occurs specially in placentae which are fully formed; the third variety, on the other hand, occurs in the early months of pregnancy. The second variety is very rare, as a primary placental lesion (Schmorl having found it but once), though, as in our case, tubercles in the substance of the villi often occur secondarily to their formation in the intervillous spaces. The rarity of this form of primary placental tuberculosis would argue against the villus involvement while the syncytium remains normal. The case here described illustrates the intervillous and chorionic localization of tubercle bacilli, with secondary involvement of the villous stroma. Schmorl describes one case in which the tuberculous area in the chorion had perforated the amnion and tubercle bacilli were found

on the surface of that membrane. Thus, says Schmorl, there is the possibility of gastro-intestinal infection of the foetus by means of the tubercle bacilli in the liquor amnii. In this connection, the case of Herrgott and Haushalter, in which guinea pig inoculations with amniotic fluid gave positive results, is of great interest; and it is to be regretted that no such fluid was obtainable in our case, where the placental lesion points to infection of the amnion and liquor amnii.

The umbilical cord showed no tuberculosis on gross or microscopic examination. Nor were tubercle bacilli found in the vessels of the cord in the sections.

The uterus, removed three hours after death, measured 16 cm. in length and was very flabby. Its peritoneal surface was covered with young, translucent tubercles in large numbers. On opening the organ a large shred of apparently necrotic placental tissue presented itself. This was but slightly adherent, and beneath, as well as around it there were cheesy areas varying from 1 to 5 cm. in diameter. There were several small cysts on the cervical mucosa, but no signs of tuberculosis were visible. The placental site in the upper portion of the anterior uterine wall was covered with shreds and small clots, of which that above mentioned was the largest. The tubes and ovaries were normal in size and appearance. Tubercle bacilli in large numbers were readily found in smears from the endometrium and from the large necrotic mass. Microscopical examination showed the uterine lining to have the structure of the decidua at term. At many points cheesy degeneration had occurred throughout its entire thickness, extending into the muscle coat to an irregularly varying depth; while small tubercles, with cheesy centers, were scattered throughout the middle and inner muscular coats, even at some distance from the cheesy endometrium. Tubercle bacilli were demonstrated in the cheesy areas and also in decidual sinuses which were not adjacent to a cheesy mass.

The foetus was a male, 19 days old, small and poorly nourished. It presented no skin lesions. The dried cord stump was still adherent.

**Brain.**—No hemorrhage and no tubercles. Ventricles normal.

**Heart.**—Valves normal. Foramenovale open. Muscle anemic.

**Lungs.**—No pleurisy, no atelectasis. A few small broncho-pneumonic areas were scattered through both upper and lower lobes. In the right upper lobe, near the upper part of the posterior border, were two small, gray tubercles, each 3 mm. in diameter. No other tubercles were present. The bronchial lymph-nodes were not enlarged; red in color.

**Spleen.**—Weighed  $8\frac{1}{2}$  grams and measured  $4\frac{1}{2} \times 2$  cm. It was firm, dark red and showed small, grayish tubercles on the surface and in its substance.

**Liver.**—Was moderately fatty, and deeply congested, but not enlarged in size. Small tubercles were scattered over the surface and throughout all the lobes. One cheesy tubercle 2mm. was present in the right lobe. The round ligament contained fluid blood. No enlarged lymph nodes in the hilus.

**Stomach.**—Normal.

**Intestines.**—The mucosa in the colon and lower ileum was congested. The Peyer's patches and solitary follicles were swollen, but none were ulcerated. Mesenteric lymph-nodes were enlarged, but not cheesy.

**Peritoneum.**—Contains no fluid. The mesentery is studded with small grayish nodules which outline the lymph vessels.

**Kidneys.**—The boundary zone of each kidney contains from 3 to 5 small tubercles. No other lesions present. Weight, 17 grams. Supra-renals and pancreas normal.

**Pathological Diagnosis.**—Acute miliary tuberculosis of lungs, liver, spleen, kidneys and mesentery. Broncho-Pneumonia. Fatty Liver. Hyperplasia of lymph-nodes.

**Microscopic Examination.** Lung. — Tubercles with cheesy centers and surrounded by mononuclear round cells, but no giant cells, were found around the small blood vessels. The surrounding lung tissue shows alveoli filled with desquamated epithelium,

fibrin, and pus cells, which also infiltrated the alveolar walls. All blood vessels were deeply congested.

**Spleen.**—No tubercles could be demonstrated in any section.

**Liver.**—The tubercles were very small and devoid of giant cells. They were situated at the periphery of the lobules around the portal vessels. The connective tissue was nowhere increased and the bile-ducts were normal.

**Kidneys.**—The tubular epithelium showed a moderate amount of parenchymatous degeneration, and in the boundary zone around a blood vessel two small blood tubercles were present.

**The Mesenteric Lymphnodes.**—Hyperplasia of their lymphoid cells and of the lining cells of the sinuses, but no tubercles are present. The blood vessels are congested. No bacilli found in any sections.

**Colon.**—The covering epithelium has disappeared. The glands are normal and the solitary follicles are congested, but show no signs of tuberculosis.

It is evident that the tuberculous infection in this case was haematogenous in character. From the gross appearance of the mesentery at autopsy, it seemed probable that, in addition, there had been infection by means of the amniotic fluid. Such was apparently not the case, though again it is to be regretted that no animal inoculations were made with the mesenteric lymph nodes.

Smears from the heart's blood and umbilical vein were negative for tubercle bacilli. In smears from the liver a few tubercle bacilli were found after looking through a number of smears.

A portion of the right lobe of the liver was removed by sterile instruments into a sterile glass covered dish and cut into small pieces with sterile knives. The fluid thus expressed was injected into a healthy guinea pig. For 48 hours afterward the animal seemed ill, but then recovered its appetite and seemed lively, although a nodule appeared in the right groin near the point of injection, and the pig lost weight. On the 35th day it was chloroformed to death. The node in the right groin measured 2 x 5 cm. in diameter, and had a softened cheesy center, smears from which showed large numbers of

tubercle bacilli. Smaller tubercles were found on the parietal peritoneum near the largest node. The spleen was much enlarged and studded with cheesy tubercles. The liver contained many gray tubercles.

None were present in any other viscus.

Sections from the liver and spleen confirmed the evidence of tubercles in these organs; tubercle bacilli were also found in them. The lesions in the foetus of our case were very few and recent, considering that the child lived 19 days. The fact recalls the case of Doleris and Bourges, in which the child of a tuberculous mother died five weeks after birth and no tubercles were found in its organs, although the heart's blood inoculated into a guinea pig, gave a positive result.

Warthin calls attention to this case and his own in relation to latent congenital tuberculosis and immunity of the foetal tissues, the virulence of the bacilli present, having been proven by inoculation into guinea pigs.

Summing up the pathology of our case in the light of Schmorl's work on tuberculosis of the placenta, and considering the advanced stage of the tuberculous lesion in the endometrium, we may assume that the basal decidua was first affected, the tubercle bacilli travelling from the decidual sinuses to the covering of the villi, localizing there and causing thrombi in the adjacent intervillous spaces, destruction of the covering epithelium, entering the villous stroma and finally reaching the chorion.

Thus all four varieties of placental tuberculosis are illustrated in this case.

That the foetus was infected comparatively late might be argued from the early stage of the tubercles in the child which had lived for 19 days.

In conclusion we would add a word or two as to the early management of infants, born of tuberculous mothers.

(1) They should not be allowed to nurse the mothers, but should be fed, either on the milk of a wet-nurse or on modified cow's milk.

(2) They should not be allowed near the mothers nor in the room with other tuberculous individuals.

(3) They should be kept in as pure an atmosphere

as possible, and especial care should be given to the maintenance, close to the normal of the body-temperature.

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