TUBERCULOSIS AS A DISEASE OF THE NEWBORN*

CLIFFORD G. GRULEE, M.D., AND FRANZ HARMS, M.D.
CHICAGO

It seems to us that of all the chapters in medicine the most neglected is that of diseases of the newborn. We are only beginning to get here and there a little light on the clinical pictures here presented, and this shows us that the newborn infant is affected clinically by the same infections in a much different way from the older infant. It is for this reason that we wish to call attention to the subject of tuberculosis in the newborn, with the hope, not of adding a great deal to the literature, but of stimulating interest in a subject which has been so long neglected.

Much has been said and written about tuberculosis in children, and not a little about congenital tuberculosis. This has been a field which has been much studied by pathologists, but in which, as yet, the clinician has taken little interest. This is probably due to two causes: (1) the hopelessness of the case should the diagnosis be made, and (2) the extreme difficulty of making the diagnosis.

Though recognizing these facts, we feel that an attempt to add something to the clinical picture of tuberculosis may eventually be of practical as well as of scientific interest.

E. R. entered Cook County Hospital, obstetrical ward, Aug. 30, 1912, aged 20 years. She was transferred from the obstetrical ward to the woman's venereal ward because of a leukorrhea which, though suspicious, yet contained no organism which could be positively identified as the gonococcus. So far as the history shows, examination was negative except for an old, apparently healed, tuberculosis of the hip. It might be stated here that she left the hospital in good health and was known to be in apparently good health for several months after leaving the hospital, a notable fact in this case.

September 6 she gave birth to a baby, weighing 6 pounds, 8 ounces. This child was of a fair degree of nutrition and apparently at term. The temperature curve is best shown in the accompanying chart (Fig. 1). It will be noted that from the second day on the child ran an irregular temperature, varying between 98.6 F. and 105 F. During the first night the baby was very cross, and continued in that state for several days. The child did not get much from the breast and often refused to take the bottle feeding. Aside from warm packs for temperature and an occasional enema, no treatment was given. At 8:40 a. m. on the 13th the child had its first convulsion. It had two more convulsions before noon of that day. At that time the child was seen by one of us and the general examination revealed a child in a fair state of nutrition, apparently unconscious, with facial twitchings and eyes turned upward, first to the one side and then to the other. There were no râles distinguishable in the lungs; the heart area was not increased, nor were any murmurs detected. The liver was about 2 inches below the costal margin in the right mammary

* Received for publication Jan. 30, 1915.

[illegible]

Thorax: Pleural cavities contain a small amount of clear, straw-colored fluid. Pericardium contains a small amount of a similar fluid. Pleura and pericardium are smooth and shiny.

Lungs: Collapse only slightly. Surface is uneven, showing depressions—irregular—and of a bluish color. Everywhere crepitant. Lungs are studded with a few scattered nodules, yellow-white in color, firm, up to size of sago seed. Cut surface: Moist, red and shows similar nodules, peribronchial thickenings. Peribronchial glands markedly enlarged (Fig. 2).

Heart: Normal size. Musculature reddish-brown. In wall of left ventricle is a small white nodule, size of a pinhead. Aortic, pulmonic, tricuspid, and mitral valves are normal.

Fig. 2.—Tuberculosis of the newborn. *A*, tuberculous mesenteric and periportal glands. *B*, miliary tuberculosis of the spleen. *C*, tubercles in the lungs.

Abdomen: No free fluid. Peritoneum smooth and shiny. Ileocecal region is free. In region of gall-bladder is a massive growth, surrounding the gall passage, the size of a walnut, nodulated with masses up to size of a pea.

Liver: About normal size. Studded with a few nodules, both on the external and on the cut surface, similar to those described. Cut section: Lobules are very indistinct; parenchyma cloudy.

Pancreas: Head is imbedded in the mass surrounding the gall passage and is studded with similar nodules.

Spleen: Firm. Studded thickly with nodules up to size of sago seed (Fig. 2).

Kidneys: Fetal lobulation. Markings fairly distinct. A few nodules similar to those described.

Adrenals: Fairly large and show an occasional nodule.

Stomach: About normal size. Along lesser curvature are nodules up to size of small pea.

Intestines: Negative.

Mesenteric Glands: Enlarged, soft, red-gray. Microscopically, the nodules are seen to be made up of a coalescence of tubercles. A great number of tubercle bacilli are present.

Anatomic Diagnosis: Miliary tuberculosis of all organs, with tuberculosis of mesenteric lymph glands.

EPICRISIS

We have, then, the child born of a mother with supposedly a healed tuberculosis, whose only subjective symptom was a severe leukorrhea of unknown cause. The mother survived the child (an unusual thing in these cases) many months at least, and probably is still living. A baby born apparently at term and apparently healthy, had as early as fifteen hours after birth a high temperature, which continued irregularly until death. There was a distinct tendency to regurgitation, and on the seventh day generalized convulsions developed, which continued up to twenty-four hours before death. Death occurred on the eleventh day. On physical examination the child showed only an enlarged liver and enlarged spleen. At necropsy a generalized tuberculosis affecting most markedly the abdominal organs, and especially the periportal lymph-glands, liver and spleen was found. The tuberculosis was miliary in type, but the stage of the tubercles suggests that it had already begun *in utero*. Many tubercle bacilli were found in all sections of tuberculous areas (Fig. 3).

GENERAL CONSIDERATION

Tuberculosis of the placenta has been described by many authors. This is of importance in relation to tuberculosis of the fetus in proportion as the fetal or maternal portion of the placenta is involved. It is certain that in many cases only the maternal portion is involved, the fetal remaining uninfected by the tuberculous condition.

As to the relative frequency of tuberculosis of these two portions, it has been impossible for us to judge from the authorities consulted. It is worthy of note, however, that both placental tuberculosis and congenital tuberculosis are being reported with increasing frequency within the last few years.

The most exhaustive work on human congenital tuberculosis is that of Warthin and Cowie¹ published in 1904. They separate the authentic cases from those not sufficiently supported by evidence and find only five cases of certain congenital tuberculosis.

1. Warthin and Cowie: Jour. Infect. Dis., 1904, i, 140.

Cases of unquestioned tuberculous bacillosis have been reported by Bugge,² Londe³ (Case 5), Thiercelin and Londe,⁴ and Schmorl and Kockel.⁵ Nothing further need be said of this condition here except that it may form the basis for the development of cases of congenital tuberculosis which die after the first few weeks, if in fact such exist, about which there is a reasonable doubt.

Of the cases of tuberculosis of the newborn judged from a pathologic standpoint there are two forms, both of which of course are miliary in type: (1) pulmonary and (2) abdominal. (It should be stated here that all cases of this age reported as localized tuberculosis lack evidence necessary to be convincing.)

Fig. 3.—Showing tubercle bacilli in the liver tissue.

The first form is represented by the cases of Harbitz⁶ and Brindeau.⁷ In each of these the thoracic organs alone were affected and there was no involvement below the diaphragm. In the case of Harbitz the mother had an endometrial tuberculosis: in that of Brindeau no mention is made of the location of the tuberculosis in the mother. Brindeau's patient died on the twelfth day and showed large caseous nodules in the base of the lungs; Harbitz' patient died on the twenty-fifth day and showed miliary tuberculosis of the lungs with caseous peritracheal glands. There can be little doubt that the case of Brindeau is one of congenital tuberculosis. A doubt, however, may be raised as to that of Harbitz, because of the age to which the child lived, but

2. Bugge: *Beitr. z. path. Anat. u. z. allg. Path.*, 1896, xix, 433.

3. Londe: *Rev. de la Tuberc.*, 1893, i, 125.

4. Thiercelin and Londe: *Centralbl. f. Chir.*, 1894, xxi, 563.

5. Schmorl and Kockel: *Beit. z. path. Anat. u. z. allg. Path.*, 1894, xvi, 313.

6. Harbitz: *München. med. Wchnschr.*, 1913, ix, 741.

7. Brindeau: *Bull. Soc. d'Obst. de Paris*, 1899, ii, 235.

considering the presence of the endometrial tuberculosis it is altogether likely that the infection was congenital. In these cases one must look for a port of entry for the infection other than the umbilical vessels. In other words, placental infection need not be regarded as essential to this form. Much more likely would seem to be an aspiration of infected liquor amnii or vaginal secretions at the time of birth. While this might account for the location of the infection in the infant it would not coincide with the advanced nature of the lesion such as is seen in the case of Brindeau or perhaps in that of Harbitz. From the stage of the lesions it is altogether likely that the infection occurred *in utero*. If this be true, then the only plausible explanation is that it is due to an infection of the liquor amnii, an infection which might readily take place with an endometrial tuberculosis as in the case of Harbitz. There are two objections to this theory; the first is that the fetus is not supposed to respire *in utero* and hence the infected liquor amnii would not come in contact with the alveoli so as to produce lesions in the lungs. To explain the case of Harbitz it is only necessary to recall the recent work of Ghon,⁸ Wollstein and Bartlett,⁹ and others, which goes to show that the primary lesion may be in the bronchi (which are exposed to the liquor amnii) from which the neighboring lymph glands about the hilum are infected, and from these the lesion extends to the rest of the lung. Such an explanation, however, will not hold for the case of Brindeau. If we accept the recent work of Addison and How¹⁰ and of Ridella¹¹ it is altogether likely that the infant does respire *in utero*, in which case the infection of the deeper portions of the lungs would be readily explained. The other objection is that in both these cases the intestines have remained free. It is a well-known fact that the intestinal mucosa in extra-uterine life is quite resistant to tuberculous infection and it is quite likely that such is the case *in utero*, especially when we take into consideration that in its parasitic state the fetus does not use the intestinal canal for the purpose of supplying nutriment to the body.

The second or abdominal form might be termed the general miliary form. While the lesions are more marked in the abdominal cavity the thoracic viscera are always involved. We have been able to find in the literature ten cases of this form of tuberculosis¹² of the newborn other

8. Ghon: Der primäre Lungenherd bei der Tuberkulose der Kinder, Berlin and Vienna, 1912.

9. Wollstein and Bartlett: A Study of Tuberculous Lesions in Infants and Young Children, Based on Post-Mortem Examinations, AM. JOUR. DIS. CHILD., November, 1914, 362.

10. Addison and How: Am. Jour. of Anat., 1913, xv, 199.

11. Ridella: Ref., Ztschr. f. Kinderh., 1914 (Ref.), viii, 342.

12. The case of Strauss (Ztschr. f. Fleisch- u. Milch-Hygiene, 1910, xx, 129) quoted by V. Reuss (Die Krankheiten des Neugeborenen, Berlin, 1914, p. 452) proved on investigation not to be one of human tuberculosis.

than the one here reported (Sabouraud,¹³ Honl,¹⁴ Lehmann,¹⁵ Ustinow,¹⁶ Auché and Chambrelent,¹⁷ Stoeckel,¹⁸ Wollstein,¹⁹ Lobenstine,²⁰ Rollet,²¹ and Möller²²). Of these, only Wollstein's patient died of a disease other than the tuberculosis. In this instance the cause of death was broncho-pneumonia and at necropsy scattered tubercles were to be found. This case suggests a close relation with the bacillosis previously mentioned. In all of this group the most advanced lesions were to be found in the periportal glands and the involvement of the abdominal organs was greater than that of the thoracic. In many instances the placenta was found to be involved. We have here unquestionably infection through the umbilical vessels.

In all the cases of both these groups tubercle bacilli were found either in the tissues or by animal experiment.

The clinical data are very scant. The cases of Stoeckel,¹⁸ Sabouraud,¹³ Lehmann,¹⁵ Honl,¹⁴ Ustinow¹⁶ Auché and Chambrelent¹⁷ and Wollstein¹⁹ consist only in pathologic reports, the day of death being given in order, fourteenth, eleventh, first, fifteenth, uncertain, twenty-sixth and nineteenth. Of the other cases, two simply give besides the pathologic findings, the weight at birth and the day of death. In the case of Harbitz⁶ the child weighed 1,400 gm., was 47 cm. long, and died on the twenty-fifth day. In that of Rollett²¹ the child weighed 3,600 gm., was 51 cm. long, and died in forty-eight hours. The other three cases are somewhat more specific in their statements. That of Brindeau⁷ occurred in a baby whose birth weight was 2,150 gm. It was taken from the mother immediately. The child was cyanotic, somewhat edematous, and had a rectal temperature of 36 C. It remained cyanotic and died on the twelfth day. The spleen was normal in size, the liver somewhat enlarged and hard, and at necropsy was shown to weigh 190 gm. Miliary tuberculosis of the lung was found. The sections were very rich in bacilli. The second case is that of Lobenstine.²⁰ It occurred in a bottle-fed baby who died on the nineteenth day. At birth the child weighed 2,100 gm., at time of death, 1,650, showing a loss of 450 gm. The child was bottle-fed, showed a subnormal temperature throughout life, and had no cough nor diarrhea. An acute miliary tuberculosis was found at necropsy. The third case is that of Möller.²²

13. Sabouraud: *Compt. Rend. Soc. de Biol. de Paris*, 1891, xliii, 674.

14. Honl: Cited by Warthin and Cowie (Note 1).

15. Lehmann: *Berl. klin. Wchnschr.*, 1894, xxxi, 646.

16. Ustinow: *Arch. f. Kinderheilk*, 1898, xxv, 66.

17. Auché and Chambrelent: *München. med. Wchnschr.*, 1898, xlv, 616.

18. Stoeckel: *München. med. Wchnschr.*, 1904, li, 177 and 454.

19. Wollstein: *Congenital Tuberculosis*: *Arch. of Ped.*, 1905, xxii, 321.

20. Lobenstine: *Bull. Lying-In Hosp., City of N. Y.*, 1905, ii, 9.

21. Rollett: *Wien. klin. Wchnschr.*, 1913, xxvi, 1274.

22. Möller: *Arch. mens. d'Obst. et de Gyn.*, 1914, iii, 1.

The temperature was normal throughout. Respiration was short and labored, but there were no cyanotic attacks. The infant did not nurse well. The mother left the hospital with a tuberculosis of the uterus and died within two months of a general miliary tuberculosis.

From these meager data it is absolutely impossible to draw any definite conclusions as to the symptomatology of tuberculosis in the newborn. It is evident that Lobenstine's patient was a premature baby, or at least one congenitally debilitated, which would account very well for the subnormal temperature which existed throughout, since such an occurrence is not at all rare in infections of infants of this type. One would scarcely expect such a reaction in a baby of the size and vigor of the one we report. It is not at all impossible, too, that the early temperature in our case had nothing whatever to do with the tuberculosis, but was simply the so-called "inanition fever," which is so frequently encountered at this time. The enlargement of the liver, as mentioned by Brindeau, and present in our case, is a suggestive symptom, especially when combined with an irregular temperature existing from birth on. The combination of enlargement of the spleen, high, irregular temperature and enlargement of the liver, together with tuberculosis in the mother, is suggestive. In all cases except the one here reported and that of Möller the tuberculosis in the mother was as severe as that of the child, the date of death of the parent being only a few days before or after that of the child.

DIAGNOSIS

In the diagnosis of this affection very little can be expected from the ordinary tests. In the newborn the Pirquet test has proven negative almost without exception. Zarfl reports a positive *Stich-Reaction* in a baby, 17 days of age. Recently at the County Hospital one of us has been able to obtain a positive von Pirquet reaction in a premature infant, 16 days of age, whose mother was in the tuberculosis hospital. In another instance the reaction was positive on the nineteenth day. This, however, would give us little encouragement in the first few days of life, and hence the tuberculin reaction must probably be disregarded as a definite diagnostic means at this time. Since in many instances tubercle bacilli are found in the blood, a blood culture or the injection of blood into animals might be suggested. This offers three difficulties: first, that of obtaining blood from these young infants; second, the fact that the presence of the condition is rarely suspected, and, third, any animal thus experimented on succumbs to the tuberculosis only after the patient. It would seem, then, to be very difficult to arrive at a certain diagnosis in such cases, even though the case were suspected.

PROGNOSIS AND TREATMENT

As to the prognosis, tuberculosis of the newborn has been up to this time always fatal so far as we can tell. Sitzenfrey²³ reports four cases of tuberculosis of the placenta, however, in three of which the infants died at six weeks, three and six months, respectively; but the fourth remained alive during nine months' observation, and showed no symptoms of tuberculosis. It would seem, then, that the mere presence of tubercle bacilli in the placenta did not mean a tuberculosis of the fetus in all instances. The duration of life has varied from twenty-four hours to twenty-five days. It is very likely that children suffering with congenital tuberculosis may live as long as three to six months. The only clinical data on any case approaching this age is that given by Veszpremi.²⁴ The premature infant died on the thirty-seventh day, and from birth on had a temperature varying between 36.5 to 38.3 C. (from 97.7 F. to 101 F.).

Of course, treatment at present, in a condition of such extreme severity and of the nature of which tuberculosis of the newborn is, must necessarily be without results.

122 South Michigan Avenue—4800 North Western Avenue.

23. Sitzenfrey: *Die Lehre von der kongenitalen Tuberkulose mit besonderer Berücksichtigung der Plazentartuberkulose*, Berlin, 1909.

24. Veszpremi: *Centralbl. f. allg. Path. u. path. Anat.*, 1904, xv, 483.