CONGENITAL TUBERCULOSIS

BY

MARY R. HUGHESDON, M.B., D.C.H.

Late Casualty Medical Officer, Children's Hospital, Birmingham

The clinical features and pathological findings in the form of tuberculosis acquired in intra-uterine life or during birth have been described and discussed by a number of authorities. Zarfl in 1930 gave a good review of the subject. The incidence of this condition has been differently estimated by reviewers of the published literature, the discrepancies being due to varying criteria of the evidence necessary to determine whether the infection may be accurately considered as having occurred before severance of the umbilical cord at birth. Warthin and Cowie (1904), Péhu and Chaliér (1908), and Whitman and Greene (1922) gave figures of the number of published cases up to the time of writing. In 1935 Beitzke analysed the details of all published cases and classified them according to the site of the primary complex. He found sixty-one cases of proven congenital tuberculosis with morbid anatomical lesions, and forty cases where tubercle bacilli were found in the foetus without histological changes. His criteria of proof of congenital tuberculosis in the infant were: (1) the tuberculous nature of the lesions in the infant must be proved; (2) a primary complex in the foetal liver is proof of the congenital nature of the tuberculous changes since it can only have arisen from tubercle bacilli in the blood of the umbilical vein; and (3) if there is no primary complex in the liver the infection is only congenital if (a) tuberculous changes are found in the foetus in utero or at birth or a few days after birth, (b) in a child who lives longer than a few days if extra-uterine infection can be excluded with certainty, the child being immediately separated from the mother and kept in an environment free from tubercle bacilli.

Since Beitzke's analysis in 1935 the following cases have been published and are here classified in tabular form on the basis of his criteria (see Table).

The total number of cases described between Beitzke's analysis in 1935 and the year 1945 is thirty-five. Of these, eleven are considered to be proven cases of intra-uterine or intra-partum tuberculous infection. Seven of these were cases of transplacental infection via the foetal blood stream, one with a primary complex in the liver only, four with primary complexes in both liver and lungs, one with miliary tuberculosis and no definite primary complex, and one with a tuberculous bacillaemia and no morbid anatomical lesion. Of the remaining four, three were cases of aspiration of infected amniotic fluid into the lungs and in one the primary focus was possibly in the skin, arising from direct contact with tubercle bacilli in the

amniotic fluid. Fifteen of the cases described are considered to be probable but not definitely proven cases of congenital tuberculosis. Of these, twelve probably arose by transplacental blood-stream infection, one by aspiration and two by ingestion of infected amniotic fluid. The remaining nine cases of the series are possible cases of congenital tuberculosis, though as the original papers were not available in this country during the war more exact classification has been impossible.

Thus, during approximately the last seventy years, there have been described in the world literature about 115 proven cases of congenital tuberculosis, including both cases with morbid anatomical lesions and those in which only a tuberculous bacillaemia occurred (just over 100 cases accepted by Beitzke in 1935 and eleven cases, classified in the Table, which have occurred since 1935).

Only four cases of congenital tuberculosis have been described in the British Isles up to the present time. Andrewes (1903) described a case which was accepted by Beitzke in 1935. Morley (1929) described a case which is not mentioned by Beitzke but which conforms to his criteria and was possibly unknown to him. This child died at the age of forty-two days with primary foci in the liver and advanced caseation in the coeliac lymph nodes; there was also a primary complex in the lungs. Price (1937) described a certain case and Davin-Power (1941) a probable case, both of which have been included in the Table.

Four further cases of congenital tuberculosis which occurred in a children's hospital in England will now be described.

Case reports

Case 1. P. J., a male infant aged twelve days, was admitted to hospital in July, 1932, with a history of having coughed for five days.

He was a full-term infant; the delivery was a normal one and no abnormality was noticed in the placenta on the customary naked-eye examination. The birth weight was 8 lb. and he seemed perfectly normal and lusty at birth. He was breast-fed until the seventh day and subsequently was given a dried milk mixture, but never took his feeds well. On the sixth day he began to cry almost continuously and 'snorting' breathing was then noticed. From the seventh day onwards he was noticed to be increasingly jaundiced. On the eleventh day he began to cough up thick white sputum and there was some respiratory distress.

On admission to hospital the infant was emaciated and slightly jaundiced. There was some umbilical

TABLE
CASES OF CONGENITAL TUBERCULOSIS PUBLISHED DURING AND SINCE THE YEAR 1935

Author	Condition of mother	Length of pregnancy (months)	Placenta	Birth weight of child (g.)	Length of extra-uterine life (days)	Tuberculin test	Pathological findings in the child	Presence of tubercle bacilli in the child	Remarks
Bertoye (1936)	Phthisis. Died on day of delivery.	9	2 grey lesions on the surface.	3,150	53	Intradermal (0.1 mg.) negative at 2 weeks. Cutaneous reaction negative 3 days before death.	Caseating primary foci and miliary tubercles in lungs; some caseation in a tracheo-bronchial lymph node. Subcapsular lesion in one kidney.	+	The child was separated from the mother at birth. This was a PROBABLE case of congenital tuberculosis, arising by transplacental blood-stream infection, with primary complex in the lungs. (Post-natal aerogenous infection cannot be excluded with certainty.)
Beskow (1939)	Generalized tuberculosis and salpingo-oophoritis. Died 8 days after delivery.	9	Not examined.	3,320	18	—	Intestinal tuberculosis with caseating mesenteric lymph nodes. Miliary tubercles in both lungs with normal-sized but caseous hilar lymph nodes.	+	There was some contact with the mother, but in view of the early death this was a PROBABLE case of infection by ingestion of liquor amnii containing tubercle bacilli, with primary intestinal complex.
Büeler (1943)	Died 56 days after delivery. P.M. showed bilateral phthisis, intestinal tuberculosis, tuberculous endometritis and miliary tuberculosis.	8½	—	2,130	48	Pirquet negative on 18th day.	Multiple caseating foci in all lobes of both lungs, with caseating tracheo-bronchial lymph nodes. Two intestinal ulcers; little caseation in mesenteric lymph nodes. Miliary tubercles in lungs, liver, spleen and kidneys.	+	The child was separated from the mother at birth. A CERTAIN case of congenital tuberculosis arising by aspiration of infected liquor amnii. (Although B.C.G. was given by mouth the distribution of lesions cannot be explained by the possible virulence of this strain.) Multiple primary foci in the lungs. The intestinal ulcers were possibly also primary, or could have resulted from swallowing of infected sputum.
Caussade et al. (1938)	Tuberculous. Died 28 days after delivery.	8	Macroscopically normal.	1,800	40	Cutaneous reaction negative.	Seven primary foci in the liver with large caseous lymph nodes in the porta hepatis. Mesenteric nodes enlarged to less extent and caseating. Miliary tubercles in lungs, spleen and tracheo-bronchial lymph nodes. (Intestine normal.)	+	A CERTAIN case of transplacental tuberculosis, with primary complex in the liver. (Although B.C.G. was given by mouth the T.B. recovered from the child were a human strain.)

Ciaccia (1938)	Phthisis. Died 10 days after delivery.	8	Macro- scopically normal.	2,300	60	Pirquet and Mantoux be- came +ve be- tween 30th and 50th day.	Caseating mediastinal and thoracic lymph nodes, with small foci throughout both lungs. Numerous caseous nodules in liver and spleen. Caseating pericardial node; Caseating cervical lymph node. Extensive caseation of mesen- teric lymph nodes. Millary tubercles in suprarenals. (No mention of lymph nodes in porta hepatis.)	+	The child was separated from the mother at birth and symptoms were observed soon after. This was a PROBABLE case of transplacental tubercu- losis with primary complex in the lungs and possibly also the liver. However, post-natal aerogenous infection cannot be excluded with certainty.
Conrad (1939)	Phthisis. Died 2 weeks after delivery.	—	—	2,820	46	—	Millary tubercles in liver, lungs and spleen (microscopic). No primary focus found.	+	The child was separated from the mother at birth. This was a PROBABLE case of trans- placental tuberculosis.
Davin-Power (1941)	Tuberculous meningitis. Died 3 days after de- livery.	8	Not ex- amined.	2,640	112 (about)	—	Caseating lesions in lungs, mediastinal lymph nodes, liver, spleen, pancreas and mesen- teric lymph nodes. Millary tubercles in lungs and kidneys. (No mention of lymph nodes in porta hepatis.)	—	The child was separated from the mother at birth. This was a PROBABLE case of trans- placental tuberculosis with primary lung complex, though post-natal infection cannot be excluded with certainty.
Erlich (1935)	Phthisis. Died 10 days after delivery.	(Born prema- turely.)	Not ex- amined.	2,200	31	—	Caseating lesions in lungs, mediastinal lymph nodes, liver and seventh left costal carti- lage. Millary tubercles in spleen, intestine and left kid- ney. (No mention of lymph nodes in porta hepatis.)	+	The child was separated from the mother at birth. This was a PROBABLE case of trans- placental tuberculosis, with primary lung complex. (Post- natal infection cannot be definitely excluded.)
Gallerani (1937)	—	—	—	—	37	—	' Primary liver and gland tuber- culosis. (Unfortunately only an abstract of this paper was obtainable.)	—	In the absence of further details this must be considered a possible case of transplacental tuberculosis.
Gané et al. (1939)	Tuberculous.	9	—	1,980	53	Pirquet negative on 28th day.	Generalized millary tubercu- losis; nodular tuberculosis in lungs. (Only an abstract of this paper was obtainable.)	—	The child was separated from the mother within 1 hour of delivery. This was a POSSIBLE case of congenital tubercu- losis.
Gonzalez Warcalde (1941)	—	—	—	—	—	—	(Neither the original paper nor an abstract could be obtained.)	—	A POSSIBLE case of congenital tuberculosis.

TABLE—continued

Author	Condition of mother	Length of pregnancy (months)	Placenta	Birth weight of child (g.)	Length of extra-uterine life (days)	Tuberculin test	Pathological findings in the child	Presence of tubercle bacilli in the child	Remarks
Gonzalez Warcalde (1942)	Phthisis. Died 48 days after delivery.	9	Not examined.	—	(Still-born.)	—	(Anasarca; serosanguinous tumour of head. Serosanguinous fluid in pleural, pericardial and peritoneal cavities. Congestion and oedema of brain.) Primary foci in lungs; smaller foci in liver. Similar foci in spleen and kidneys. Extensive caseation of mediastinal, hepatic and splenic lymph nodes.	+	A CERTAIN case of transplacental tuberculosis, with primary complexes in the lungs and liver.
Gournay and Regnard (1941)	Phthisis. Died 14 hours after delivery.	7½	Macroscopically normal.	1,800	54	Negative at birth. Positive on 34th day.	Multiple lung lesions, from miliary foci to caseating broncho-pneumonic areas. Caseating lesions in liver and mesenteric lymph nodes. Miliary tubercles in spleen and mesentery. Tuberculous meningitis. (No description of mediastinal lymph nodes or of those in porta hepatis.)	—	The child was separated from its mother and other tuberculous persons from birth. This was a PROBABLE case of transplacental tuberculosis. Possibly there were primary complexes in both liver and lungs.
Grénet et al. (1935)	Phthisis and tuberculous meningitis. Died 3 days after delivery.	8	Macroscopically normal.	2,600	65	Cutaneous reaction negative at about the 50th day.	Miliary tubercles in lungs, liver and kidneys. Caseating areas in spleen. Mesenteric and one mediastinal lymph node enlarged but not caseating. Basilar meningitis. No primary focus found.	+	The child was separated from the mother at birth and received B.C.G. by mouth during the 1st week of life. This was a PROBABLE case of transplacental tuberculosis.
Guilbeault et al. (1939)	Phthisis and miliary tuberculosis. Died soon after delivery. P.M. showed caseous endometritis.	—	—	3,000	18	—	Miliary tubercles in lungs, liver, spleen and kidneys. Skin pustules. Caseating right inguinal lymph node. (No description is given of microscopic appearances in the skin or lymph node. Possibly the skin infection was a primary tuberculous one resulting from tubercle bacilli in the amniotic fluid.)	+	The child was separated from the mother at birth and post-natal aerogenous infection was excluded by x ray of the chests of all contacts. B.C.G. was given subcutaneously on the ninth day but the T.B. isolated from the child was a human strain. This was a CERTAIN case of congenital tuberculosis, either transplacental or arising by infection of the skin from the liquor amnii.

Gustina and Cleveland (1936)	Clinically and radiologically healthy at time of delivery. (Pleural effusion 7 years previously.)	—	—	24	Mantoux negative 48 hours before death.	Massive bronchogenic lesions in both lungs, with areas of caseous pneumonia. Cascating peribronchial lymph nodes. (No lesions elsewhere.)	+	A PROBABLE case of congenital tuberculosis caused by aspiration of infected amniotic fluid. Post-natal infection cannot be excluded with certainty.
Hamne and Gellerstedt (1938)	Phthisis and generalized tuberculosis. Died 2 days after delivery.	8	Not examined.	68	—	Intestinal ulceration, with cascating mesenteric lymph nodes. Cascating foci in liver and spleen. Miliary tubercles in lungs. (Mediastinal lymph nodes and those in porta hepatis normal.)	+	A PROBABLE case of congenital tuberculosis arising by ingestion of infected amniotic fluid. Although the child was separated from the mother at birth a post-natal infection from contaminated milk cannot be eliminated with certainty.
Jacobsen (1936)	Pleural effusion during pregnancy. Died of miliary tuberculosis 6 weeks after delivery.	9	A few white infarcts.	17	—	Skin vesicles and pustules. Numerous millet-sized tuberculous foci in the enlarged liver. Miliary tubercles in spleen and lungs. (No mention of lymph nodes.)	+	The infant was separated from the mother at birth. A CERTAIN case of transplacental miliary tuberculosis, with no definite primary complex.
Keyser (1940)	—	9	Macroscopically normal.	34	Negative.	Disseminated infiltrations in both lungs (radiologically). (Only an abstract of this paper was obtainable.)	+	A POSSIBLE case of congenital tuberculosis. More exact classification is impossible without further details.
Kraus (1935)	Phthisis, intestinal tuberculosis, caseous endometritis and miliary tuberculosis. Died 25 days after delivery.	9	Macroscopically normal.	18	—	Extensive caseous pneumonia in all lobes of both lungs, with cascating mediastinal lymph nodes. The lower lobes of the lungs were most heavily involved. Miliary tubercles in liver, spleen and kidneys.	+	The child was separated from the mother at birth. A CERTAIN case of congenital tuberculosis arising by aspiration of infected liquor amni.
Latienda and Franco (1944)	—	—	—	—	—	Two cases. (This paper was not available.)	—	TWO POSSIBLE cases of congenital tuberculosis.
Montaux (1943)	—	—	—	—	—	(Neither the original paper nor an abstract was available.)	—	A POSSIBLE case of congenital tuberculosis.
Moss and Stoesser (1940)	Tuberculous endometritis and cervicitis. Miliary tuberculosis. Died 4 months after delivery.	7	Not examined.	38	—	Many primary foci in lungs with enlarged mediastinal lymph nodes. Tuberculous nodules in thymus. Microscopic tubercles in liver and spleen.	+	The infant was separated from the mother at birth. A PROBABLE case of transplacental tuberculosis with primary lung complex; the infection reaching the lungs via the ductus venosus.

TABLE—continued

Author	Condition of mother	Length of pregnancy (months)	Placenta	Birth weight of child (g.)	Length of extra-uterine life (days)	Tuberculin test	Pathological findings in the child	Presence of tubercle bacilli in the child	Remarks
Price (1937)	Phthisis. Alive 6 months after delivery but more recently moribund.	—	—	—	49	—	Caseating foci in liver, spleen and lungs. Caseous lymph nodes in porta hepatis and at hilum of spleen. Enlarged sub-diaphragmatic lymph nodes. One caseating mediastinal lymph node.	+	A CERTAIN case of trans-placental tuberculosis in view of the primary complex in the liver. There was also a primary lung complex.
Reiche and Wheelock (1939)	Tuberculous endometritis. Alive 2 months after delivery.	—	Not examined.	2,324	19	Mantoux 1 in 1,000 negative.	Innumerable small nodules throughout both lungs with very numerous tubercle bacilli. Microscopic changes only in tracheo-bronchial lymph nodes. (Other organs normal.)	+	The child was separated from the mother at birth. A CERTAIN case of congenital tuberculosis due to aspiration of infected liquor amnii, in view of the distribution of the lesions and the masses of tubercle bacilli in the lungs.
Robillard and Imprescia (1942)	Miliary tuberculosis. Died a few weeks after delivery.	33 weeks.	Macroscopically normal.	1,675	1	—	Caseating tubercles in both lungs; enlarged caseating hilar lymph nodes. Numerous tubercles in liver, spleen, pancreas and adrenals. Portal lymph nodes enlarged and caseating. Less numerous lesions in kidneys and mesenteric lymph nodes. Tiny tubercles on serosal surface of intestines.	+	A CERTAIN case of trans-placental tuberculosis, with primary complexes in the liver and lungs.
Scheidegger (1936)	Died 24 months after delivery. P.M. showed genital tuberculosis, tuberculous peritonitis and miliary tuberculosis.	—	Not carefully examined.	—	12	—	Large caseating foci in liver, spleen and lungs. Mediastinal lymph nodes and those of porta hepatis caseating and calcifying. Miliary tubercles in other organs.	+	A CERTAIN case of trans-placental tuberculosis, with primary complexes in the liver and lungs.
Schwarzenberg et al. (1939)	—	—	—	—	—	—	(Neither the original paper nor an abstract was obtainable.)	—	A POSSIBLE case of congenital tuberculosis.
Siegel and Singer (1935)	Died of tuberculosis 18 hours after delivery.	7	Contained a large tuberculous area.	—	36	—	Post-mortem revealed no demonstrable pathological lesion.	+	A CERTAIN case of trans-placental tuberculous foetal bacillaemia. (Culture of heart blood.)

copyright.

Terplan and Hosterman (1936)	Chronic phthisis and Pott's disease.	—	Macroscopically normal.	—	About 42	—	(Death occurred from pneumococcal meningitis following purulent otitis media.) Numerous caseous tubercles in liver and lungs. Extensive caseation in periportal and periaortic lymph nodes. Early caseation in tracheo-bronchial lymph nodes. Few tubercles in mesenteric lymph nodes. Miliary tubercles in spleen and other organs. (Microscopic appearances are not described.)	—	A PROBABLE case of transplacental tuberculosis in view of the primary foci in the liver with advanced changes in the corresponding lymph nodes. Proof is lacking as the presence of tubercle bacilli was not confirmed.
Trillat et al. (1936)	Died 1 day after delivery. P.M. showed tuberculous changes limited to the right lung.	9	—	3,150	53	Mantoux 1 in 100 and 1 in 10 negative at 2 weeks.	Caseating foci in both lungs with consolidation of right lower lobe. Miliary tubercles confined to the lungs. Enlarged tracheo-bronchial lymph nodes, one caseous.	+	The child was separated from the mother at birth. A PROBABLE case of transplacental tuberculosis with primary lung complex. The lesions could also have been caused by aspiration of infected amniotic fluid. (Post-natal aetogenous infection has not been excluded with certainty.)
Vosskühler (1937)	Phthisis.	—	—	—	18	—	Caseating foci in lungs. Caseating mediastinal lymph nodes. Caseating foci in spleen. Miliary tubercles in liver. Caseating lymph nodes at liver hilum and along lesser curvature of stomach. Peripancreatic nodes also caseous. (No primary liver focus found.)	—	The tuberculous nature of the lesions was not proved. A PROBABLE case of transplacental tuberculosis; there was probably a primary liver complex together with the primary lung complex.
Vosskühler (1941)	Phthisis. Died 8 days after delivery.	—	—	—	24	Mantoux 1 in 100 positive on 21st day.	* Extensive bilateral non-confluent tuberculous pneumonia. No primary complex. (Only an abstract of this paper was obtainable.)	+	In the absence of further details this can only be considered a POSSIBLE case of congenital tuberculosis.
Zarfl (1936)	Phthisis. Died 10 days after delivery.	7	Macroscopically normal.	2,050	43	Pirquet negative. Subcutaneous reaction (1 mg. O.T.) negative.	Many caseating foci in lungs with enlarged and caseating tracheo-bronchial lymph nodes. Microscopic tubercles in liver and spleen.	+	The child was separated from the mother at birth. This was a PROBABLE case of congenital tuberculosis. The primary lung complex was caused either by aspiration of infected amniotic fluid or possibly by transplacental blood stream infection.

sepsis and the liver and spleen were both considerably enlarged. He died on the day of admission.

Family history. The mother of this infant had a symptomless tuberculous lesion at the apex of the right lung which was discovered during pregnancy and thought to be quiescent. Her general health was good throughout the pregnancy. Three months after delivery she became ill and was found to be suffering from bilateral phthisis. She died four months later from extension of the pulmonary disease.

The father had no symptoms or signs of tuberculosis. The mother's sister had died in a sanatorium previously, but had no contact with the infant. There had been one previous pregnancy a year before which had resulted in miscarriage.

Post-mortem findings. The body was that of a fairly well-developed, slightly jaundiced baby; there were no external lesions. Two caseating lymph nodes, the size of peas, were present in the superior mediastinum. The thymus was of average size. The pleurae were healthy. There were caseating lymph nodes at the hilum on both sides. Throughout both lungs miliary caseating foci were seen, but no primary pulmonary focus was found. The peritoneum was normal. The mesenteric lymph nodes were not grossly enlarged and were not caseating. No lesion was found in the intestinal tract. The stomach was normal. The pancreatocolic lymph nodes formed a large caseating mass. The liver showed a moderate enlargement and scattered caseating foci, the size of grains of rice; the gall bladder was not grossly distended and bile

was expressed into the duodenum. The spleen was considerably enlarged, 45 g. in weight, and showed caseous foci. The kidneys showed no gross abnormality on naked-eye examination. The urinary bladder and the ureters were normal. The adrenals showed congestion of the medulla. The meninges and brain were normal in appearance. Thyroid and pituitary were macroscopically normal.

Histology. LIVER. There was one sharply demarcated area of necrosis about 1.5 mm. in diameter. It consisted of a granular material, which stained a pale bluish colour with haematoxylin, and much nuclear debris. There was neither specific granulation tissue nor lymphocytic infiltration nor fibrosis around this focus. Besides this focus there was a diffuse necrosing process resembling acute yellow atrophy.

PANCREATICO-LIENAL LYMPH NODE. Very extensive, almost complete and uniform caseous necrosis.

SPLEEN. Numerous sharply demarcated areas of necrosis, 0.4 to 2 mm. in diameter, consisting of granular eosinophilic material, pyknotic nuclei and nuclear debris.

KIDNEY. A single sharply demarcated necrotic area was seen, 0.2 mm. in diameter.

CERVICAL LYMPH NODE. Numerous areas of caseation, not sharply demarcated.

BRAIN AND LEPTO-MENINGES. Mononuclear infiltration of the meninges; oedema of the brain.

Bacteriology. A moderate number of acid- and alcohol-fast bacilli was seen in liver sections stained by the Ziehl-Neelsen method. Films were made

FIG. 1.—Case 1. Diffuse necrosis of the liver; 'acute yellow atrophy' type.

FIG. 2.—High-power view of Fig. 1.

from caseating lymph nodes and showed numerous acid- and alcohol-fast bacilli.

Comment. The tuberculous nature of the foetal lesions in this case was proved by the presence of tubercle bacilli. The death of the child at the age of twelve days with widespread and advanced tuberculous changes and the situation of the largest caseating lymph nodes in the abdomen makes it certain that the infection occurred in utero. The largest caseating foci were found in the liver. Unfortunately the records contain no reference to the lymph nodes in the porta hepatis, but the pancreatico-lienal group of nodes showed enlargement and advanced caseation and it may be assumed that they formed the 'second station' in the primary hepatic complex which originated by transplacental blood-borne infection via the umbilical vein.

The caseating lymph nodes at the hila of the lungs indicate that there was also one or more primary pulmonary focus, although none of the minute caseating lesions could be identified as such. There was no massive involvement of the lungs to suggest that aspiration of infected amniotic fluid had taken place and the route of infection was almost certainly again transplacental by the foetal blood stream. There was spread via the lymphatics to lymph nodes in the superior mediastinum and in the neck. The miliary foci in the spleen and kidneys must have occurred by blood-stream dissemination secondary to the primary complexes.

This was, then, a case of transplacental tuberculosis with primary foci of disease in the liver and lungs. A notable feature of the case was the histologically unspecific character of the necrotic changes and the association with diffuse necrotic changes in the liver of the acute yellow atrophy type.

Case 2. M. L., a male infant aged forty-four days, was admitted to hospital in May, 1943, with a history of bleeding and discharge from the nostrils for the past week.

He was a full-term infant and the labour was a normal one. Nothing abnormal was noticed about the placenta at the maternity home, where the usual naked-eye inspection had been made. The birth weight was 7 lb. 14 oz. and the baby was fed on a dried-milk mixture. He took his feeds well, gained weight and seemed healthy until the onset of the nose-bleeding.

On admission to hospital he was a moderately well-nourished baby weighing 8 lb. 2 oz. There was a slight jaundice of the skin and conjunctivae and a purulent blood-stained discharge from both nostrils. Two pin-head-sized ulcers were present on the mucous membrane over the hard palate. The liver and spleen were enlarged and there was a small amount of fluid in a right inguinal hernial sac. There was one enlarged lymph-gland in the right axilla. There were no abnormal physical signs in the chest.

A Wassermann reaction was negative. Blood examination showed: Haemoglobin 68 per cent.,

FIG. 3.—Case 1. Circumscribed granuloma of liver, unspecific in character.

red blood cells 3,360,000 per c.mm., total white blood cells 9,600 per c.mm., polymorphs 55 per cent., metamyelocytes 4.5 per cent., myelocytes 1.0 per cent., eosinophils 0.5 per cent., mononuclears 6.0 per cent., lymphocytes 33.0 per cent., normoblasts 35 per 100 white blood cells, reticulocytes 6.6 per cent.; anisocytosis and polychromasia were marked.

The infant continued to take his feeds well and his temperature was never higher than 99.4° F. (rectal). The stools were loose but not unduly frequent. He never coughed. On the third day after admission he had a small blood-streaked vomit and on the fourth day, i.e. the forty-eighth day of life, he had two further vomits and then died.

Family history. The mother of the infant was aged forty and had been quite well previous to this pregnancy. She had had four healthy children and no miscarriages or stillbirths. During this pregnancy she did not feel at all fit and at the fourth month she had a right-sided pleurisy. At the sixth month her chest was x rayed at a tuberculosis dispensary, but no treatment was considered necessary. There was no puerperal pyrexia or cause for anxiety in her condition during the confinement. Two months after the death of the infant (four months after delivery) an x ray of her chest showed a small round focus at the right apex, without cavitation, and some opacity due to pleural thickening at the right base. At this time she had some cough, but there had never been any sputum.

FIG. 4.—Case 2. Liver with caseating lymph nodes at the porta hepatis and along the lesser curvature of the stomach. (Natural size.)

The erythrocyte sedimentation rate was 17 mm. in one hour (Micro-Landauer 50 mm. column). There were no signs or history of tuberculous disease elsewhere and nothing to suggest miliary spread. She weighed 8 st. 3 lb., about 10 lb. under her highest known weight, and was carrying on her household duties as usual.

The father was admitted to a sanatorium suffering from pulmonary tuberculosis during the sixth month of the pregnancy and was discharged home with sputum positive for tubercle bacilli when the infant was three weeks old, so that there was exposure to infection from the father from the third to the sixth week of life.

The mother's father had also been in a sanatorium several years previously; he saw the infant on several occasions, the exact dates of which could not be ascertained, so that there was exposure also to this possible second source of infection.

Post-mortem findings. The body was that of a normally developed infant in poor nutritional condition. One hempseed-sized and one pin-head-sized abscess were present in the skin of the right thigh. A few lentil-sized excoriations were present in the skin of the abdominal wall and on the legs. Two lentil-sized, superficial, clean ulcers were situated in the mucous membrane of the hard palate. The tonsils were flat, hempseed-sized, and showed no evidence of inflammation. Larynx, trachea, oesophagus, thyroid and parathyroids were normal. The cervical lymph nodes were not enlarged, and there was no macroscopic evidence of tuberculosis. The thymus was atrophic. About 5 to

10 c.cm. of thin blood-stained fluid were present in each pleural cavity. All lobes of both lungs were studded with millet- to hempseed-sized sharply demarcated yellowish-white nodules. The tracheo-bronchial and bifurcation lymph nodes slightly enlarged. In the bifurcation node there was a hempseed-sized caseated area. Millet-sized caseated nodules were present in the lymph nodes of the posterior mediastinum and one bean-sized, and there was an extensively caseated lymph node on the upper surface of the diaphragm. The pericardium was normal. The heart muscle was pale and friable. The intima of the aorta and pulmonary artery was moderately jaundiced. The ductus arteriosus was patent. About 20 c.cm. of clear yellow fluid were present in the abdominal cavity. The umbilical vein and arteries were obliterated, with no evidence of inflammation. The liver was very considerably enlarged, three to four fingers' breadths below the costal margin; its colour was reddish-brown, the surface smooth, and its consistence firm. The surface and cut surface were studded with millet-sized yellowish-white nodules and less numerous nodules of hempseed- to lentil-size. The spleen was 11 by 7 by 3.5 cm. in size and 90 g. in weight; it was hard, and there was extensive fibrinous perisplenitis. Numerous yellowish-white nodules were present on the cut surface, varying from millet-seed to small pea-size. Occasionally there was softening and formation of a small cavity in the centre of such a nodule. The kidneys were soft; irregular reddish hyperaemic patches were seen on the cut surface. No naked-eye

evidence of tuberculosis was found. The urinary bladder and ureters were normal. Stomach, duodenum, small and large intestines were normal. There were several enlarged and completely caseated lymph nodes at the porta hepatis, the largest being pea-sized. There was a lentil-sized caseated lymph node at the neck of the gall bladder and a chain of caseated hempseed- to lentil-sized nodes along the lesser curvature of the stomach up to the cardia. A second similar chain was formed by the pancreatico-lienal lymph nodes. The mesenteric lymph nodes were slightly enlarged and showed on the cut surface tiny areas of caseation. The cranium, meninges and brain were normal. Both tympanic cavities and mastoid antra were filled with dirty greenish-grey pus.

Histology. LIVER. The liver was studded with necrotic areas of varying size. These were sharply demarcated, but no lymphocytic rings, epithelioid cells, giant cells nor fibrous capsules were seen in the periphery. Only where the borders of such a necrotic area touched an interlobular space some proliferation of fibroblasts was noticed. The necrotic areas consisted of an amorphous material with nuclear debris and included a few polymorphonuclear leucocytes and a few elongated oval nuclei. In some of the interlobular spaces there was a cellular infiltration. This was diffuse and consisted mainly of lymphocytes without epithelioid cells or giant cells. Many liver cells were loaded with bile pigment. Here and there a tiny haematopoietic focus was seen in a dilated liver capillary.

LUNGS. There were fairly sharply demarcated areas of necrosis with no lymphocytic rings, epithelioid cells, giant cells nor fibrous capsules. In some of the necrotic areas the outlines of the interalveolar septa were still discernible, especially with elastic tissue stain, and it could be seen that the foci had developed from a pneumonic exudate undergoing caseation. In the neighbourhood of such foci there was a considerable infiltration of the interalveolar septa with large mononuclear cells,

and such cells were also seen within the alveoli.

PORTAL LYMPH NODE. Complete and uniform caseous necrosis of the whole node was present.

TRACHEO-BRONCHIAL AND MESENTERIC LYMPH NODES. Numerous tiny areas of caseation, mainly in the marginal lymph follicles. In one of the nodes two larger caseating areas were seen.

KIDNEY. There was an occasional area of caseous necrosis about 150 μ in diameter and occasional epithelioid cell tubercles of the same size, very occasionally one with a Langhans' giant cell.

In some areas small interstitial cellular infiltrations were seen consisting of lymphocytes, large mononuclear cells, plasma cells, and a few polymorphonuclear leucocytes.

PANCREAS. Normal.

THYMUS. Atrophy of cortical tissue.

SPLEEN. There were large areas of caseous necrosis, surrounded by a hyperplastic pulp.

HEART. Atrophy of muscle fibres. In the sub-endocardial tissue a single epithelioid cell tubercle with a giant cell was seen.

Bacteriology. Acid- and alcohol-fast bacilli were seen in sections from the portal, mesenteric, tracheo-bronchial lymph nodes, the liver and the spleen. A direct smear from the right middle ear showed polymorphonuclear leucocytes, acid- and alcohol-fast bacilli, a few Gram positive lanceolate diplococci and a few Gram negative bacilli; that from the left middle ear showed many pus cells, many acid and alcohol-fast bacilli and some Gram negative bacilli.

Comment. There were multiple primary foci in the liver of this child with enlargement and caseation of lymph nodes in the porta hepatis and along the lesser curvature of the stomach. Although the lesions in the lungs were numerous their distribution did not suggest that they had arisen by aspiration of infected liquor amnii and it is probable that these

FIG. 5.—Case 2. Caseous foci in the lungs. Small areas of caseation in the bifurcation nodes. A larger completely caseated node on the diaphragm (arrow).

primary foci with the corresponding caseating mediastinal lymph nodes also arose by blood-stream infection from the umbilical vein. A superimposed post-natal aerogenous infection occurring before the development of tuberculin sensitivity in response to the initial blood-borne infection cannot be excluded with certainty however. The lesions in

FIG. 6.—Case 2. Lung: area of caseous necrosis. Mononuclear exudate in adjacent alveoli and monocytic infiltration of interalveolar septa.

the spleen, kidneys and heart must have been due to a secondary blood-stream dissemination, while those in the remaining abdominal lymph nodes were probably a direct extension of infection along lymph channels from the portal and pancreaticolienal group of nodes. The middle ear lesions might have been produced either by aspiration of infected liquor amnii into the naso-pharynx, with ascension of infection along the Eustachian tubes or by a blood-stream dissemination. The latter is more probable in this case, where there was no other evidence of the presence of tubercle bacilli in the amniotic fluid and there were no caseating lymph nodes in the neck to suggest that the middle ear lesions were primary foci, as described by Baar and Evans (1941) in their review of primary tuberculosis of the middle ear. (One such case of primary tuberculosis of the middle ear probably arising by aspiration of infected liquor amnii has been described by Zarfl (1924).)

This was, then, an undoubted case of congenital transplacental tuberculosis with primary complexes in both liver and lungs.

The absence of epithelioid cells, Langhans' giant cells and lymphocytic rings from the primary foci in the lungs and liver of this child as well as from the lesions in case 1 is interesting in view of similar findings reported by Zarfl (1913) and by Pagel and Price (1943) in very early primary tuberculous foci in the lungs of young infants dying from other causes. In case 2, as in the cases of Zarfl and of Pagel and Price, the histological changes in the lungs consisted of a non-specific 'alveolitis' with exudate. Reichle and Wheelock (1939) also described foci of non-specific pneumonia in an infant dying at nineteen days of an aspiration type of congenital tuberculosis. The alveolar exudate in their case contained very large numbers of tubercle bacilli. These were all cases of infection in very early infancy or during foetal life and death occurred after only a short interval. The fact that there was no tubercle formation in these young infants, who are known to possess very poor natural resistance to the tubercle bacillus and also probably died in the pre-allergic period, before the development of any acquired immunity, is in accordance with the view that the cellular response and histological changes in tuberculous infections are determined by the state of natural and acquired immunity of the host (Ranke; Baar, 1936). Tubercle formation has been produced experimentally as a first response to infection in previously uninfected animals and according to Rich and McCordock (1929) the response of the allergic animal to infection differs in an essentially quantitative rather than qualitative way from that of the non-allergic one; however, typical epithelioid cell tubercles are not normally seen before allergy has developed (Pagel, 1939).

The mother of the child M. L. had minimal tuberculous disease, and this is unusual, since in the great majority of cases described the mothers of infants with congenital tuberculosis have been severely ill and have died of their tuberculosis within a few weeks of delivery. Grulee and Harms (1915) reported a case where the mother was alive several months after delivery and was clinically healthy apart from an old healed tuberculosis of the hip. In Whitman and Greene's (1922) case the mother suffered from pulmonary tuberculosis and was alive thirteen months after delivery and in Chiari's (1932) case also the mother had pulmonary tuberculosis and was alive two-and-a-half years after delivery. In a few cases to be mentioned later the mothers appeared to be completely healthy. In the case of M. L. there was definite evidence of activity of the mother's tuberculosis during pregnancy in the form of pleurisy and a tuberculous maternal bacillaemia must have been the source of the infection of the umbilical vein blood via the placenta.

Case 3. A. E., a female infant aged thirteen months, was admitted to hospital in September, 1941, with a history of cough, irritability and loss

of weight during the previous eight weeks. There had been occasional vomiting and the stools had been loose and slimy for about a month.

She was a full-term infant and the delivery was a normal one which took place in the obstetrical ward of a general hospital. No abnormality was seen in the placenta at the usual naked-eye inspection. The birth weight was 6 lb. 10 oz. and the infant was breast-fed. At one month old she became jaundiced, the stools were white and the urine dark in colour. This state of affairs lasted for three months, after which she did well for a time. At four months old the first tooth was cut and at six months she sat up. At seven months she was ill for three weeks with a respiratory infection which was diagnosed as broncho-pneumonia.

On admission to hospital the child was pale, sallow and ill. She was slightly dehydrated and had a loose cough and a haemorrhagic nasal discharge. The weight was 16 lb. 13 oz. There were numerous rhonchi and râles present over both lungs. The liver and spleen were both enlarged and palpable two to three fingers' breadths below the costal margin. There was a lentil-sized nodule in the anterior abdominal wall. The superficial lymph nodes were not enlarged.

A Mantoux reaction (old tuberculin 0.1 mg.) was positive. The Van den Bergh reaction gave a prompt biphasic response. Blood examination showed: haemoglobin 78 per cent., red blood cells 4,710,000 per c.mm., total white blood cells 16,000 per c.mm., polymorphs 76 per cent., lymphocytes 18 per cent., monocytes 5 per cent., and plasma cells 1 per cent.

The child remained ill and died on the sixth day after admission. The temperature only reached 100° F. on two of these days, remaining for the most part below 99° F.

Family history. Both parents were alive and well three-and-a-half years after the death of the child. They were not conscious of any ill health. Shortly after the death of the child they were examined at the Anti-tuberculosis Centre and no signs of tuberculosis found; x rays of their chests showed no abnormality. Again in January, 1944, there were no physical signs or x-ray evidence of tuberculosis in mother or father. Except for 'biliousness' the mother was well during the pregnancy and puerperium. No member of the family was known to suffer from tuberculosis.

The mother has had six pregnancies in all; three children and one miscarriage at the second month preceded the child A. E. and one apparently healthy baby has been born since. Of the elder children two are apparently healthy and the third had a small pleural effusion with a positive Mantoux reaction in 1943.

Post-mortem findings. The body was that of a normally developed pale child in poor nutritional condition. There were no external lesions. Tonsils, larynx, pharynx and trachea were normal. The veins of the oesophagus were moderately dilated. Thyroid and parathyroids were normal. The cervical lymph nodes were macroscopically normal. The thymus was atrophic. The pleura on the right side was normal; on the left side there was a circumscribed fibrinous pleurisy over the upper lobe. Both lungs were studded with millet-sized yellowish-white nodules. On the left side there was a walnut-sized completely caseated focus

at the base of the upper lobe. In the centre of this focus there was liquefaction of the caseous material with formation of a few small cavities. There was an open communication between these cavities and the bronchial tree. A second sharply demarcated, completely and uniformly caseated focus was present in the anterior part of the lower lobe near to the interlobar cleft. The broncho-pulmonary, hilar, tracheo-bronchial, bifurcation and para-tracheal lymph nodes were enlarged. The largest node was at the bifurcation; it was about hazel-nut-sized, completely caseated and extensively softened. Complete caseation and some liquefaction were also found in the left paratracheal lymph nodes. The other lymph nodes of the mediastinum showed smaller areas of caseation. The pericardium, the heart and the great vessels were normal. The peritoneum was normal. The liver was 19.5 by 11 by 7 cm. in size, and weighed 190 g. Its anterior margin was rounded, the colour yellow, the surface finely granular and the consistency hard. Four caseated nodules, three in the left and one in the right lobe, were seen. The nodules were hempseed- to lentil-sized; one of them showed a pin-head-sized cavity in the centre. On the cut surface the normal structure of the liver was completely obliterated. The spleen was considerably enlarged, 9 by 6 by 3 cm. in size, 60 g. in weight, and fairly hard. Numerous millet- to hempseed-sized nodules, yellowish-white in colour, were seen on the cut surface. One single millet-sized caseated nodule was seen in each kidney. The urinary bladder and ureters were normal. The stomach and duodenum were normal. Several greyish-white nodules and superficial ulcers were seen in the Peyer's patches and solitary follicles of the small intestine. The large intestine was normal. The lymph nodes at the porta hepatis were considerably enlarged, the largest the size of a walnut, completely and uniformly caseated, partly softened. Enlarged and extensively caseated lymph nodes were also seen along the lesser curvature of the stomach and in the pancreatico-lienal and para-aortic groups. The mesenteric lymph nodes were slightly enlarged and showed small areas of caseation. The adrenals and the pancreas were normal. The cranium, the meninges, the venous sinuses and the brain were normal. There was pus in the right tympanic cavity and mastoid antrum.

Histology. LIVER. The section showed 'lobuli' of various sizes and shapes without definite relationship to the central veins and separated by broad strands of connective tissue. The liver cells showed very severe fatty changes of the infiltrative type, which were more advanced in the peripheral zones of the pseudolobuli. In one section a large caseated area was seen surrounded by connective tissue. Within the latter Langhans' giant cells were seen. In all other places the connective tissue was unspecific in character.

LUNGS. There were many fairly sharply demarcated nodules of necrosis. These nodules were not surrounded by a fibrous capsule and a definite ring of lymphocytes was absent. Langhans' giant cells were frequently seen in the peripheral parts of the necrotic areas and in the surrounding tissue. In one section the lung tissue was overcrowded by scavenger cells lying in the alveoli, in the inter-alveolar septa and in the connective tissue surrounding the bronchi and blood-vessels.

SPLEEN. There were many nodules of necrosis with much nuclear debris.

KIDNEY. Fatty degeneration of the epithelium of the convoluted tubules. No tuberculous changes were seen in the sections examined.

PORTAL LYMPH NODE. The whole node showed uniform caseous necrosis. In the periphery there was a capsule of unspecific granulation tissue.

Bacteriology. A film from a portal lymph node showed a moderate number of acid- and alcohol-fast bacilli. From the pus from the middle ear haemolytic staphylococcus aureus was cultured, but no tubercle bacilli were seen.

Comment. The primary complex in the liver and portal lymph nodes here again leaves no doubt that this is a true case of congenital tuberculosis, though the length of life of the child was unusually long. Chiari (1932) described a very similar case where the child lived to the age of twenty-six months. The next greatest length of life recorded up to the present is that of a case described by Sitzenfrey (1909), where the child lived to six months.

The post-mortem findings in the case of the child A. E. suggest that the primary complexes in the liver and lungs originated at approximately the same time, since there was an almost equal degree of enlargement and caseation of the portal and mediastinal groups of lymph nodes. The hepatic lesions were certainly produced by blood-borne infection from the umbilical vein; the obstructive jaundice occurring at the age of one month suggests that the nodes in the porta hepatis were already at this time large enough to press upon and obstruct the common bile duct. The two large primary pulmonary foci probably also originated by trans-placental blood-borne infection, though a superimposed aerogenous infection occurring shortly after birth and before the development of a tuber-

culin sensitivity cannot be excluded with certainty. The smaller disseminated lesions in the lungs, spleen and kidneys must have been produced by a miliary spread via the blood stream secondary to the established primary foci. The ulcers of the small intestine were obviously of comparatively recent origin and had resulted from the swallowing of sputum containing tubercle bacilli.

A remarkable feature of this case is that no evidence of active tuberculosis could be found in the mother; presumably she had a small focus in a lymph node or in the abdomen which broke down during pregnancy and spread either directly to the endometrium and placenta or into the blood stream, with subsequent infection of the foetal blood in the umbilical vein. Three cases of congenital tuberculosis occurring in children of apparently healthy mothers have been reported previously. In Morley's (1929) case there was no clinical or radiological evidence of tuberculosis in the mother, and in the cases of Söderström (1932) and of Straus (1895) the mothers appeared clinically free from tuberculosis.

Another interesting feature is the association with portal cirrhosis of the liver in this case and the presence of diffuse changes (mentioned above) in case 1, which, when healing, may result in cirrhosis of the liver.

Case 4. K. W., a female child aged twenty-seven months, was first seen in the out-patient department in April, 1944, when she was brought up on account of 'frequent bronchitis' and recent anorexia and irritability.

She was a full-term infant and the labour was a normal one. No information about the placenta is available. The birth weight was 7½ lb. She was fed from birth on a dried-milk mixture and subsequently on a normal mixed diet.

When first seen she weighed 21 lb. There was coryza with some redness of the throat and a mild stomatitis; temperature 100° F. The general condition of the child suggested a diagnosis of Pink disease, the muscle tone being poor and the hands and feet pink and slightly swollen. There was a pink macular rash. She was irritable but had no photophobia. There were no abnormal physical signs in the chest, abdomen or cardiovascular system. Six days later bilateral otitis media developed and paracentesis was performed. Three days later again the child was admitted to the hospital as she became increasingly fretful and the temperature rose to 101·8° F. There was some discharge from both ears and tenderness over the right mastoid process. No abnormal physical signs were found in chest, heart or abdomen. A total of 16 g. of

FIG. 7.—Case 3. Liver with enlarged lymph nodes in the porta hepatis.

FIG. 8.—Case 3. Steato-cirrhosis of liver.

sulphathiazole was given during the next six days; the otorrhoea ceased but the child continued fretful and vomited several times daily. The temperature varied from 97° to 100·6° F. On the sixteenth day after she was first seen she was noticed to have a loose cough. The general appearance was still that of Pink disease. The throat was congested and there was some stiffness of the neck. There were no abnormal physical signs in the chest, heart or abdomen. Lumbar puncture showed a clear fluid under increased pressure. The cerebrospinal fluid findings were: white blood cells 190 per c.mm. (all lymphocytes), protein 120 mg. per 100 c.cm., chloride 608 mg. per 100 c.cm., sugar 18 mg. per 100 c.cm.; in the direct smear (Ziehl-Neelsen) a few acid- and alcohol-fast bacilli seen. A Mantoux test (old tuberculin 0·1 mg.) gave a positive reaction.

The temperature rose and varied from 98° to 102° F. until death, which took place twenty-one days after the child was first seen, the age at death being twenty-seven months and two weeks.

Family history. This child was the second in a family of three, the other two of whom were living and apparently well. The parents were living and stated that they were healthy; unfortunately it was not possible to investigate them further as they failed to attend the Anti-tuberculosis Centre. It is not known whether the mother had had any miscarriages.

Post-mortem findings. The body was that of a pale female child in poor nutritional condition. There were no external abnormalities. The tonsils were pea-sized, each with two millet-sized, yellowish-white soft areas. The larynx was normal. The oesophagus showed post-mortem acid digestion in its distal part. The thyroid and trachea were normal. The thymus was atrophic. There were numerous miliary tubercles in the pulmonary and costal pleurae, especially on the left side. There was a lentil-sized, sharply demarcated, completely and uniformly caseated focus at the base of the lower lobe of the right lung, in its posterior part. All lobes of both lungs were studded with miliary tubercles. There was one pea-sized completely caseated lymph node in the right inferior part of the posterior mediastinum in close vicinity to the base of the lower lobe of the right lung. Several lentil-sized completely or partly caseated tracheo-bronchial lymph nodes were present on the right side. An occasional pin-head area of caseation was seen in some of the left tracheo-bronchial and

paratracheal lymph nodes. The pericardium was normal. The heart muscle was very pale. A single sub-endocardial tubercle was seen in the left ventricle. The peritoneum was normal. In the right lobe of the liver there were two completely caseated and sharply demarcated foci, in size between that of a hempseed and that of a lentil. There were also very numerous miliary tubercles in the liver and a few bile duct tubercles. The spleen was enlarged. There was a tuberculous perisplenitis and the cut surface of the spleen was studded with miliary tubercles. Numerous miliary tubercles were also seen in the kidney. The renal pelvis, the ureters and the urinary bladder were normal. The stomach was normal. There were submucous tubercles and pea-sized tuberculous ulcers in the lower jejunum and in the whole ileum. The large intestine was normal. There was a group of pea-sized completely caseated lymph nodes at the porta hepatis and several lentil-sized completely caseated peripancreatic lymph nodes. The mesenteric lymph nodes were hempseed- to lentil-sized and showed tiny areas of caseation.

The skull and dura mater were normal. There was a grey gelatinous exudate in the cisternae chiasmatis, interpeduncularis and pontis. Numerous miliary tubercles were seen in the arachnoid of the Sylvian fissures and over the vertex of the brain. There was a moderate degree of hydrocephalus. The brain showed oedema. The whole brain was dissected in slices of about 5 mm. thickness; no tuberculoma was found. The sinuses of the dura mater were normal. There was some blood, but no pus, in the right tympanic cavity. The left middle ear was normal.

Histology. LUNGS. The primary focus showed a large area of caseous necrosis with granular deposits of lime salts in the central part. The necrotic area was surrounded by a narrow band of fibrous tissue. Within the latter here and there a giant cell of the Langhans' type was seen. In some parts a cluster of lymphocytes was attached to the fibrous capsule. There were numerous epithelioid cell tubercles with Langhans' giant cells in the interstitial tissue in sections from all lobes. Many

FIG. 9.—Case 4. Primary tuberculous complex of lung.

of these tubercles showed a central area of caseation.

LIVER. The primary focus had the same structure as that of the lung. There were also many epithelioid cell tubercles with Langhans' giant cells in the tissue of periportal spaces, some of them with central caseation, some without. Occasionally a cellular infiltrate of unspecific character was seen in a periportal space.

SPLEEN. Very numerous extensively caseated miliary tubercles. Some of the Malpighian bodies showed large germinal centres.

KIDNEY. An occasional caseated miliary tubercle was present. In the vicinity of one such tubercle an unspecific interstitial cellular infiltrate was seen.

HEART MUSCLE. Fibres thin, striation indistinct.

PANCREAS normal.

Bacteriology. Acid- and alcohol-fast bacilli were found in direct smears from the tracheo-bronchial and portal lymph nodes.

Comment. In this case again there was an undoubted primary complex in the liver; two caseated primary foci with caseating lymph nodes in the porta hepatis. On the basis of Beitzke's (1935) criteria, then, this was a certain case of congenital transplacental tuberculosis. The primary focus in the right lung may have arisen also by blood-borne infection via the umbilical vein or may have been an independent air-borne infection which took place during the first few weeks of extra-uterine life. The primary foci in liver and lungs were of approximately the same size and were both completely caseated; the corresponding lymph nodes were similarly of equal size and equal degree of caseation, so that it must be assumed that the lesions in liver and lung were of very similar age.

The tuberculous intestinal ulcers might have arisen by ingestion of infected amniotic fluid, but in that case the mesenteric lymph nodes would probably have shown a greater degree of enlargement and caseation; more likely the intestinal infection was a comparatively recent one caused by the swallowing of infected sputum.

The miliary tubercles in the lungs, heart, liver and spleen of this child and the meningeal infection arose from a secondary invasion of the blood stream by tubercle bacilli from one of the components of the primary complexes. Although this sequence of events is common in post-natal primary tuberculosis in childhood, tuberculous meningitis is a very rare occurrence in the congenital form of tuberculosis. Zarfl (1930) wrote that in no case of congenital tuberculosis had infection of the meninges been found. The case reported by Chiari (1932) died with generalized miliary tuberculosis and tuberculous meningitis secondary to primary complexes in the liver and lungs and resembled the present case also in the long survival of the child and the comparatively good health of the mother, who had symptomless tuberculous lesions at both lung apices. Since 1935 tuberculous meningitis has been reported in two probable cases of congenital tuberculosis (Gournay and Regnard, 1941; Grénet et al., 1935) but in no certain case.

The mother of the child K. W. was subjectively healthy and was alive two years after delivery, though unfortunately no detailed investigation was possible.

This case, which survived to the age of twenty-seven-and-a-half months (one month longer than

FIG. 10.—Case 4. Primary tuberculous complex of liver.

FIG. 11.—Case 4. Primary focus in lung.

the case of Chiari (1932) mentioned above) is the oldest child in whom congenital tuberculosis has so far been reported.

Discussion

The fact that four cases of congenital tuberculosis have been observed in one children's hospital during the last twelve years suggests that intra-uterine or intra-partum infection of the foetus with tubercle bacilli may occur more frequently than the total of 115 proved cases reported in the world literature between 1873 and 1945 suggests. Gofton (1937), in a survey of tuberculosis in slaughtered calves up to the age of six months, found an incidence of congenital tuberculosis of 0.42 per cent., compared with 1.47 per cent. of post-natal tuberculosis. It is possible that transmission of the disease to the human foetus may occur on a similar scale (though it is not suggested that congenital tuberculosis is at present of any practical importance in the epidemiological problem of the control and treatment of tuberculosis in man).

Infection of the foetus may evidently take place when the mother's tuberculous lesion is minimal or even undetectable by present methods of investigation and this is consistent with the view that tuberculous bacillaemia may occur at any time during a period of activity of an existing tuberculous focus, however small. Loewenstein (1935) cultured the blood of fifty-nine parturient women suffering from pulmonary tuberculosis, together with blood from the umbilical vein, and found that in eleven cases

FIG. 12.—Case 4. Miliary tubercle in liver.

both maternal and foetal blood contained tubercle bacilli. The frequent incidence of tuberculous lesions in the placenta has been shown by Schmorl and Geipel (1904), who found such changes in nine out of twenty, and by Sitzenfrey (1909), who found them in six out of twenty-six placentae from tuberculous women. Such lesions are liable at any moment to release tubercle bacilli into the foetal blood spaces of the placenta, with subsequent infection of the foetus via the umbilical vein. Alternatively, tubercle bacilli may be liberated from a lesion in the placenta or membranes into the amniotic fluid and the foetus may be infected by inhalation or ingestion of the fluid. It is not certain whether tubercle bacilli can be carried over into the foetal blood stream through a healthy placenta.

It has been suggested by several authors that congenital tuberculosis is not necessarily fatal if the infection is a mild one and that cases may survive undiagnosed into late childhood or adult life. Cases 3 and 4 here reported seem to lend weight to this hypothesis. Dying as they did at the ages of thirteen and twenty-seven months respectively, it was not until the post-mortem examinations that there was any suspicion that their tuberculous infections had arisen *in utero*, or at latest intra-partum. If infected children can survive the most dangerous first twelve months of extra-uterine life it would seem reasonable to suppose that their resistance to the tubercle bacillus is sufficiently great

to allow of a possibility of the lesions healing, with subsequent complete recovery. Evidence of healing was present in case 4, which showed calcification in the primary lung focus, and in the case reported by Chiari (1932), where there was calcification in the primary foci and lymph nodes. Calcification has also been reported by Feller (1930), Harbitz and Kjelland Mördre (1913), Scheidegger (1936), Thorn (1894), Whitman and Greene (1922), and by Zarfl (1930).

The true incidence of congenital tuberculosis can only be estimated by routine post-mortem examination of children dying from all causes.

Summary

A review is made of the cases of congenital tuberculosis published between 1935 and 1945.

Four cases of congenital transplacental tuberculosis which occurred in a children's hospital in England between 1932 and 1944 are described. One died at the age of twelve days, the second at forty-eight days, the third at thirteen months and the fourth at twenty-seven months. In all four cases there were primary complexes in both liver and lungs.

It is suggested that congenital tuberculosis may be commoner than has hitherto been supposed and may not be invariably fatal.

I wish to thank Dr. Baar for his post-mortem reports and photographs and advice, and also Dr. Braid and Dr. Neale for permission to publish two of these cases.

REFERENCES

- Andrewes, F. W. (1903). *Trans. path. Soc. Lond.*, **54**, 142.
- Baar, H. (1936). *Acta paediatr.*, **18**, 322.
- Baar, H. S., and Evans, R. (1941). *J. Laryng.*, **56**, 159.
- Beitzke, H. (1935). *Ergebn. ges. Tuberk. Forsch.*, **7**, 1.
- Bertoye, P. (1936). *Rév. Médecin.*, **53**, 631.
- Beskow, A. (1939). *Nord. med.*, **4**, 3527.
- Büeler, R. (1943). *M Schr. Geburtsh. Gynäk.*, **115**, 329.
- Caussade, Melnotte and Niemann (1938). *Rev. Méd. Nancy*, **66**, 265.
- Chiari, H. (1932). *Virchows Arch.*, **285**, 779.
- Ciaccia, A. (1938). *Sperimentale*, **92**, 54 (translation, Royal Society of Medicine).
- Conrad, C. E. (1939). *Sih. med. J.*, **32**, 169.
- Davin-Power, M. (1941). *Brit. med. J.*, **1**, 13.
- Erich, M. (1935). *Bull. Soc. Pédiat. Paris*, **33**, 578.
- Feller (1930). (Quoted by Beitzke.)
- Gallerani (1937). (Abstract *Zbl. ges. Tuberk. Forsch.* (1938), **48**, 534.)
- Gané, T., Toma, I., and Petresco, S. (1939). (Abstract *Amer. J. Dis. Child.* (1939), **58**, 1109.)
- Gofton, A. (1937). *Edinb. med. J.*, **44**, 333.
- Gonzalez Warcalde, J. (1941). *Rev. med. Cordoba*, **29**, 499. (Not available.)
- (1942). *Prensa med. argent.*, **29**, 771. (Abstract R.S.M.)
- Gournay, J. J., and Regnard, M. (1940). *Paris méd.*, **1**, 65.
- Grénet, H., Metzger, M., Héraux, A., and Mézard, J. (1935). *Arch. Méd. Enf.*, **38**, 229.
- Grulee, C. G., and Harms, F. (1915). *Amer. J. Dis. Child.*, **9**, 322.
- Guilbeault, A., Bernier, A., Bertrand, A., and Manseau, G. (1939). *Un. méd. Can.*, **68**, 610.
- Gustina, J., and Cleveland, W. G. (1936). *Arch. Path.*, **22**, 570.
- Hamne, B., and Gellerstedt, N. (1938). *Acta paediatr.*, **20**, 380.
- Harbitz and Kjelland Mördre (1913). (Quoted by Beitzke.)
- Jacobsen, E. (1936). *Ugeskr. Laeg.*, **98**, 418. (Translation R.S.M.)
- Keyser, E. (1940). (Abstract *Amer. J. Dis. Child.* (1941), **62**, 191.)
- Kraus, E. (1935). *Cbl. allg. Path. u. path. Anat.*, **63**, 273.
- Latienda, R., and Franco, E. F. P. (1944). *Arch. argent. fisiol.*, **20**, 308. (Not available.)
- Loewenstein, E. (1935). *Beitr. Klin. Tuberk.*, **87**, 57.
- Montaux (1943). *Rev. Soc. pédiat. Rosina*, **8**, 15. (Not available.)
- Morley, R. H. (1929). *Arch. Dis. Childh.*, **4**, 227.
- Moss, A. J., and Stoesser, A. V. (1940). *J. Lancet*, **60**, 142.
- Pagel, W. (1939). *Pulmonary Tuberculosis* by Kayne, G. G., Pagel, W., and O'Shaughnessy, L., London.
- and Price, D. S. (1943). *Amer. Rev. Tuberc.*, **47**, 614.
- Péhu, M., and Chalié, J. (1908). *Arch. Méd. Enf.*, **11**, 1.
- Price, D. (1937). *Brit. J. Tuberc.*, **31**, 264.
- Ranke, K. E. (see Zimmerli, E., and Simmonds, F. A. H. (1930). *Tubercle, Lond.*, **11**, 241, 304 and 345).
- Reichle, H. S., and Wheelock, M. C. (1939). *Arch. Path.*, **28**, 799.
- Rich, A. R., and McCordock, H. A. (1929). *Bull. Johns Hopk. Hosp.*, **44**, 273.
- Robillard, G. L., and Imprescia, S. Z. (1942). *N.Y. St. J. Med.*, **42**, 1955.
- Scheidegger, S. (1936). *M Schr. Kinderheilk.*, **65**, 1.
- Schmorl and Geipel (1904). *Münch. med. Wschr.*, **51**, 1676.
- Schwarzenberg, J., et al. (1939). *Rev. chil. Pédiat.*, **10**, 339. (Not available.)
- Siegel, M., and Singer, B. (1935). *Amer. J. Dis. Child.*, **50**, 636.
- Sitzenfrey (1909). (Quoted by Siegel and Singer.)
- Söderström, H. J. (1932). *Acta tuberc. scand.*, **6**, 306.
- Straus (1895). (Quoted by Beitzke.)
- Terplan, K. L., and Hosterman, O. (1936). *Arch. Path.*, **22**, 569.
- Thorn (1894). (Quoted by Beitzke.)
- Trillat, Éparvier, Bertoye and Bertrand (1936). *Bull. Soc. Obstét. Gynéc., Paris*, **25**, 724.
- Vosskübler (1937). *Beitr. path. Anat.*, **98**, 349.
- (1941). (Abstract *Schweiz. med. Wschr.* (1941), **48**.)
- Warthin, A. S., and Cowie, D. M. (1904). *J. infect. Dis.*, **1**, 140.
- Whitman, R. C., and Greene, L. W. (1922). *Arch. intern. Med.*, **29**, 261.
- Zarfl, M. (1913). *Z. Kinderheilk.*, **5**, 303.
- (1924). *Wien. med. Wschr.*, **74**, 1113.
- (1930). *Beitr. Klin. Tuberk.*, **74**, 380.
- (1930). Engel, S., and Pirquet, C., 'Handbuch der Tuberkulose,' Leipzig.
- (1936). *Z. f. Kinderheilk.*, **58**, 266.