Congenital Syphilis in Newborn

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In six cases of congenital syphilis in newborn at Los Angeles County-USC Medical Center over a seven-month period the clinical findings fell into two categories related to the time of onset of symptoms. Infants ill in the nursery presented evidence of transplacental infection; infants who became ill later showed the "classic" findings of rash, rhinorrhea and pseudoparalysis.

No single clinical symptom was present in all cases but all symptomatic infants had radiographic evidence of bone disease. Respiratory distress was present at the onset of symptoms in three of four infants with neonatal disease, and all three had evidence of interstitial pneumonia in chest radiographs.

Serologic testing may be difficult to evaluate in the newborn period, but more recent and specific tests are helpful in diagnosis. Penicillin remains the drug of choice. The only death occurred at five hours of life in a premature infant. Growth and development in surviving infants appeared normal.

DURING THE PAST DECADE, the reported incidence of syphilis in the United States has risen sharply. The increase in congenital syphilis has paralleled that of adult cases. Brown et al estimated there were twice as many cases of congenital syphilis in 1962 as in 1957. The Los Angeles County-University of Southern California Medical Center has experienced a similar rise in incidence. In the seven-month period from October, 1968, to May, 1969, six cases of congenital syphilis were treated, as against three in the previous 12-month period.

The six recently treated cases are reported to illustrate the wide range of clinical symptoms seen in early infancy. In four of the infants the condition was diagnosed shortly after birth. The two remaining patients were discharged asymptomatic from the nursery and returned with symptoms when two to three months of age.

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Reports of Cases

CASE 1: A girl, birth weight 2,960 grams, gestational age 34 weeks (above the 90th percentile; Denver Intrauterine Growth Curve* [I.U.G.C.]), was born to a 34-year-old Mexican-American (M-A) woman, gravida 9, para 8. Pregnancy was uneventful with the exception of a mild episode of "flu-like" illness with rash lasting 15 days during the last month of pregnancy. A Venerae Disease Research Laboratory (VDRL) serologic test for syphilis on blood drawn in the first trimester of pregnancy was positive but the mother was lost to public health follow-up.

At birth the infant was depressed, with an Apgar score of 5, and a heart rate of 80. In the nursery, she was cyanotic and had grunting, rapid respirations. The liver was palpable 4 cm below the right costal margin and the spleen 2 cm below the left costal margin. The extremities were moderately edematous and the face was puffy. There was a left facial palsy and left upper arm weakness. A radiograph of the chest showed a diffuse infiltrate in the right lung field and questionable cardiomegaly. Kolmer and VDRL tests performed on cord blood were positive (Table 1). The infant was given fluids intravenously and penicillin and digitalis parenterally. On the second day, a generalized fine petechial rash developed over abdomen and back. There were large ecchymotic areas, and bleeding around vena puncture sites. Visible jaundice appeared with a total bilirubin of 5.3 mg per 100 ml, of which 1.2 mg was direct. Clinical findings are summarized in Table 2. Radiographs of the long bones showed the typical lesions of congenital syphilis. The patient remained severely ill, requiring supplemental oxygen and parenteral fluids for six days, then gradually improved. Penicillin and digitalis were discontinued at two weeks of age, and the infant was discharged from the nursery in good condition at three weeks of age.

When last seen, at two months of age, the baby was alert and active. No residual neurological or physical abnormality was evident. The mother returned to Mexico and the infant was lost to further follow-up.

CASE 2: A girl, birth weight 2,330 grams, gestational age 38 weeks (10th to 25th percentile I.U.G.C.), was born to a 25-year-old M-A woman, gravida 3, para 2. Pregnancy history was normal. The mother had had one prenatal clinic visit in the first trimester and a VDRL test on a specimen drawn at that time was negative. At birth, the infant had a wrinkled appearance, decreased subcutaneous fat and generalized poor muscle tone. On the fifth day she became tachypneic, the respiratory rate rising to 100. At this time the spleen was palpated 2 cm below the left costal margin and small shotty lymph nodes were felt in the left axilla. Radiographs of the chest revealed a diffuse infiltrate in the right lung field. Radiographs of the long bones showed changes consistent with congenital syphilis. Kolmer and VDRL tests on cord blood were positive (Table 1). Before these results were available, parenteral kanamycin and ampi-
cillin were given, with clinical improvement. The baby was discharged from the nursery on completion of two weeks of this therapy.

When last seen, at three months of age, she was alert, gaining well and developing normally. Radiographs of long bones at this time showed healing of the destructive bone lesions.

CASE 3: A girl, birth weight 2,950 grams, gestational age 40 weeks (25th to 50th percentile I.U.G.C.), was born to a 23-year-old M-A woman, gravida 2, para 1. The mother had had no prenatal care and was admitted to the hospital in active labor. Pregnancy was normal. The infant had peeling skin and meconium-stained nails and umbilical cord. She had generalized poor muscle tone, a weak grasp reflex and an incomplete and sluggish Moro reflex. There was shortening of the right leg and click on rotation of the right hip. Radiographs of the bones showed the classic changes of congenital syphilis, with lesions in the acetabulum and right femur. The spinal fluid was clear, contained a very few round cells and had protein content of 113 mg per 100 ml and sugar of 45 mg per 100 ml. The infant was treated with parenteral penicillin and was discharged at two weeks of age.

When last seen, at three months of age, she was alert, active and growing well. The right leg remained shorter than the left with limitation of movement. Radiographs showed healing of the destructive bone lesions with flattening of the acetabulum.

CASE 4: A girl, birth weight 2,211 grams, gestational age of 34 weeks (50th to 75th percentile I.U.G.C.), was born to a 20-year-old primigravida M-A woman. The mother had had no prenatal care and was admitted in active labor with vaginal bleeding. At delivery the infant was severely depressed, with an Apgar score of 2. On arrival at the nursery the infant was limp, cyanotic and gasping. The lungs were filled with crackling rales and thick mucus was suctioned from the trachea. The abdomen was greatly distended. The liver was palpated 9 cm below the right costal margin and the spleen 4 cm below the left costal margin. Radiographs of the chest showed bilateral diffuse pulmonary infiltrate and bone changes in the clavicles consistent with congenital syphilis. Results of Kolmer and V.D.R.L. tests on cord blood were positive (Table 1). Intravenous fluids and parenteral penicillin were started by one hour of age, but the infant died at five hours.

At post mortem examination,* enlargement of liver and spleen were noted. All the lobes of the lung were poorly aerated. Focal gumma formations were found in the lungs and the liver. The air spaces contained large numbers of fibroblasts and histiocytes. The portal triads of the liver showed fibrosis and acute cholangitis. There was extramedullary hematopoiesis in the lungs, liver, spleen, kidneys and adrenal glands. Fibrosis and extensive endarteritis were found in the pancreas, thymus, gastrointestinal tract, lungs and portal areas of the liver. Darkfield examination of the lungs was positive for Treponema pallidum.

CASE 5: A baby girl, birth weight 2,500 grams, gestational age 38 weeks (10th to 25th percentile I.U.G.C.), was born to a 30-year-old woman, gravida 7, para 5, ab 1. The mother had recently arrived from Mexico and had had no prenatal care. Pregnancy was normal and delivery uncomplicated. The infant was normal at birth, was discharged from the nursery in good condition before a report of positive results of tests for syphilis on the mother’s blood, and was lost to follow-up.

At two and one-half months of age the baby was returned to the hospital out-patient department with complaint of rash on the palms. She was returned again the following week with a complaint of tenderness and decreased movement of the left leg. She was irritable, had purulent rhinorrhea with crusting around the nares, scaly vesicular rash of hands and feet and tenderness of the left leg. Long bone radiographs showed multiple destructive bone lesions consistent with congenital syphilis. Results of Kolmer and V.D.R.L. tests were positive (Table 1). Spinal fluid examination showed clear fluid with 5 lymphocytes per field, protein 127 mg per 100 ml and sugar 68 mg per 100 ml. The infant was admitted to hospital, treated with parenteral penicillin for two weeks and was discharged in good condition.

When seen one month later she was alert and active, with normal growth and development. Radiographs of long bones showed healing of lesions.

CASE 6: A boy, birth weight 3,320 grams, gestational age 38 weeks (75th percentile I.U.G.C.), was born to a primigravida who had come from Mexico eight months before delivery and had had no prenatal care. Pregnancy and delivery were uncomplicated. The infant was normal at birth and was discharged before the mother’s serologic tests were reported positive for syphilis. The infant

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was referred for evaluation to the hospital clinic at two weeks of age. He was alert, active and well nourished. The skin in the inguinal area was reddened but not macerated. Radiographs of the long bones were normal. Results of Kolmer and VDRL tests were positive. The baby was returned to the clinic at three weeks of age, and Kolmer and VDRL tests done then were reported as negative. He was discharged from the clinic without treatment at one month of age.

At two and one-half months of age he was admitted to the hospital with redness and limitation of movement of the right upper arm. He had been well until, two days before admission, the mother “pulled his arm” when bathing him. On admission he appeared alert and well nourished. The spleen was palpated 3 cm below the left costal margin. Radiographs of the long bones showed multiple destructive lesions consistent with congenital syphilis. Kolmer and VDRL tests were positive (Table 1). After treatment with parenteral penicillin for two weeks the baby was discharged in good condition.

When last seen, at four and one-half months of age, he was alert, active and developing normally.

**Discussion**

The clinical features of congenital syphilis are related to the time of onset of symptoms. The classically described triad of pseudoparalysis, rhinitis and maculo-papular rash which alerts the physician to the clinical diagnosis has not been present in the nursery in our patients. Rather, the infants who were ill from birth presented with non-specific signs and symptoms which are associated with transplacental infection of various kinds. Consequently, the clinical diagnosis was more difficult in the early cases, and yet prompt recognition of congenital syphilis is particularly important, as it is one of the few transplacental infections for which effective treatment is available. Infants who were sick in the nursery had signs and symptoms present at birth, and all were severely ill. The disease was most severe in the premature infants.

Syphilis has been the most frequent transplacental infection encountered in our nurseries in the last four years. In descending order are rubella, herpes virus hominis, and cytomegalic inclusion disease. Toxoplasmosis has occurred rarely. The typical bone lesions seen in congenital syphilis have been the greatest aid to early diagnosis. Except for the bone lesions, none of the clinical manifestations in the cases presented are limited to congenital syphilis.

According to previous reports, in the nursery congenital syphilis presents most often as a hemolytic disorder with anemia, jaundice and hepatosplenomegaly or as a bleeding disorder with thrombocytopenia. Three of our four patients had splenomegaly, two had hepatomegaly and evidence of hemolytic anemia. The hemolytic anemia is clinically indistinguishable from that caused by other transplacental infections or hemolytic disease secondary to blood group incompatibility and is characterized by anemia, reticuloctyosis and distortion of red blood cell morphology. Previous reports have emphasized the presence of jaundice which may be so severe as to require exchange transfusion. The bilirubin often has a high direct component and is associated with abnormal liver function. Jaundice was not prominent in the infants presented. Only one of them had jaundice and it was minimal and not prolonged, but it was clearly differentiated from physiologic jaundice by the high direct component and the accompanying hepatomegaly.

The frequency of respiratory distress and radiographic signs of interstitial pneumonia in the infants with neonatal disease was an unexpected finding. Respiratory distress was the most common symptom, the most troublesome in management, and the direct cause of death in the one infant who died.

Transient nonspecific neurologic findings occurred in the four patients with clinical disease in the nursery. All were considered to have poor muscle tone. Two of the four infants had decreased movement of an extremity—in one case probably related to delivery rather than infection. In the one case in which spinal fluid examination was done in the nursery, there was elevation of the protein content. Although the neurologic findings were transient, spinal fluid examination should have been performed in all cases of congenital syphilis, for such information is necessary in evaluating any future neurologic difficulty.

Generalized lymph node enlargement has been reported to be a frequent and characteristic finding in congenital syphilis. Lymphadenopathy was not prominent in the infants presented. Only one infant had axillary adenopathy, and it minimal.

One of the most consistent clinical findings of transplacental infection is intrauterine growth failure. Congenital syphilis has long been known to be associated with prematurity by weight. Two
of the four under-sized infants presented here were truly premature, with gestational age of 34 and 35 weeks. They were the most severely affected. None of the infants showed significant growth failure as judged by Denver Intrauterine Growth Curve, although the two who were born at term had clinical evidence of intrauterine malnutrition in the peeling skin, decreased subcutaneous tissue, and meconium staining.

In summary, the infants with clinical disease in the nursery did not present with the “classical” triad of congenital syphilis but had the generalized nonspecific findings of transplacental infection described above.

In contrast, the remaining two infants, who appeared normal in the nursery, later developed the “classical” signs of congenital syphilis—rhinorrhea, rash and pseudoparalysis. Rhinorrhea is reported to be present in half of the cases of congenital syphilis. It begins as a benign appearing mucoid discharge and rapidly progresses to an unrelenting sero-sanguinous exudate. The rash of congenital syphilis is characteristically described as being scaly-vesicular with predilection for the hands and feet, particularly the palms and soles. Reddened macerated “diaper rash” is also commonly found, occurring primarily over the anal and buttock area and proving to be resistant to conventional treatment. The third entity of the triad, pseudoparalysis, is seldom found in an infant except in congenital syphilis. In addition to the triad of congenital syphilis, the nonspecific symptoms of irritability, anemia and failure to thrive, with secondary infection, emphasize the generalized nature of the disease.

In all the cases presented herein there was radiographic evidence of bone disease. This was the only constant finding in both the infants who were ill in the nursery and those who became ill later. This finding coincided with clinical symptoms: the bone radiographs were normal in an asymptomatic infant and showed disease when the infant became ill (Case 6). The radiographic changes remained after the patients were clinically well. Healing was slow, and bony changes were evident up to two months after evidence of active disease had disappeared.

Serologic diagnosis of congenital syphilis can be misleading unless several factors are considered. The infant's cord blood mirrors the mother's to a large extent. Positive results of serologic tests in the newborn do not mean disease is present; it may reflect a biologically false positive maternal reaction or inactive maternal disease. The infant's serologic tests may be falsely negative if the maternal infection has been recent. Several recent articles have reviewed methods of serologic diagnosis of syphilis.

Invasion of Treponema pallidum produces antibodies of two basic types: (1) antibodies known as reagins, which are not specific to the treponema organism, and (2) antibodies to the treponema organism itself. The non-treponemal antigens produce two varieties of antibodies: univalent antibodies (Kolmer and Wasserman), detected by complement fixation tests and bivalent antibodies (VDRL and Kahn) detected by flocculation test (Table 3). Either test may be reported quantitatively or qualitatively. The univalent complement fixation antibody passes through the placenta but the bivalent flocculation antibody may not. This would account for the differences of reaction between mother and newborn with various tests. Since the half-life of passively transferred reagin is approximately 32 days, at one month of age, a 50 percent reduction in quantitative titers or reagin antibody occurs. The infant's blood titer should return to normal within three months if the positive reaction is due to passively transferred reagin and no intrauterine infection has occurred. In Case 6, in which the Kolmer was reported as positive at two weeks and negative at three weeks, a laboratory error should have been suspected and the test repeated before the infant was discharged to follow-up. These tests are obviously not specific for syphilitic infection in the immediate newborn period, although they have the advantage of being practical and widely available.

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<th>Table 3.—Sero-Diagnosis of Congenital Syphilis</th>
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<td>I. Non Treponemal Antigen Tests</td>
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<td>A. Flocculation Tests (monovalent antibodies)</td>
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<td>VDRL</td>
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<td>Kahn</td>
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<tr>
<td>B. Complement Fixation Tests (bivalent antibodies)</td>
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<td>Kolmer</td>
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<td>II. Specific Treponemal Antigen Tests</td>
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<td>A. Treponema Pallidum Immobilization (TFI)</td>
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<td>B. Specific Treponemal γM Flourescent Treponemal Antibody Absorption (γM-FTA-ABS)</td>
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ponema pallidum immobilization test (TPI)\textsuperscript{12} and fluorescent treponemal antibody absorption test (FTA-ABS).\textsuperscript{13} The TPI antibody develops more slowly than non-treponemal antibodies, and the TPI test is less sensitive in early syphilis. The FTA-ABS test is more specific and more sensitive than the TPI.\textsuperscript{18} Since these antibodies do cross the placenta these are tests for maternal infection but are not specific for newborn infection.

The fetus has been shown capable of producing antibodies in response to intrauterine infection.\textsuperscript{14} The antibodies produced in utero reside in the \(\gamma M\) globulin fraction and since IgM does not cross the placenta, detectable antibodies at birth are believed to be the result of fetal production. Cases of intrauterine infection often have elevated levels of IgM in the cord serum.\textsuperscript{15} In the present series, both clinically ill newborns in which IgM levels were obtained (Table 1) showed significant elevation. Elevation of IgM is not specific for congenital syphilis and has been found in other intrauterine infections such as toxoplasmosis, rubella and cytomegalovirus.\textsuperscript{15} A specific FTA-ABS test using fluorescent-labelled antihuman IgM to demonstrate only syphilitic antibodies produced by the infant has been reported by Scotti and Logan\textsuperscript{16} and by Alford et al.\textsuperscript{17} This test was performed in four of the cases herein reported (Table 1) and was positive in all.

Treatment for congenital syphilis is simple and effective. Procaine penicillin G in aqueous suspension, 150,000 to 200,000 units per kilogram of body weight divided into ten equal daily intramuscular injections is our recommended therapy. The relapse rate is reported to be 5 percent.\textsuperscript{18} Kanamycin and ampicillin, although effective in the management of one of the patients in the present series, are not the drugs of choice for therapy of congenital syphilis.

Although the infants may be desperately ill and die in the nursery, all the surviving infants in this series did well after discharge from the hospital. On follow-up all babies were growing normally and were alert without evidence of neurologic sequelae. Hemoglobin levels returned to normal rapidly although hepatosplenomegaly persisted up to two months after treatment. Despite treatment, interstitial keratitis, neural deafness and Clutton's joints may develop years later,\textsuperscript{4} and for this reason prolonged follow-up of all cases is important.

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