

Infantile Diabetes

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Diabetes mellitus in infancy has been recognized since 1789 when Rollo reported the first authentic case. There have been subsequent reports through the nineteenth and twentieth centuries, but the condition is not common in the first year.

In a review made in 1934 at the Children's Memorial Hospital,¹ of 65 cases of diabetes occurring before the age of 13 years, only one patient was found to have had diabetes before the first birthday, while 11 patients had

onset of the condition in the second year. By 1949, out of a total of 202 cases seen at this hospital there were 6 cases (3 per cent) in which diabetes developed in infancy.

Schwartzman, Crusius and Beirne² tabulated and reviewed 57 cases of infantile diabetes up to 1947. In this series the onset of diabetes occurred before the age of one year in 0.5 per cent. Joslin, Root, White, and Marble³ reported seven cases occurring below the first year of life in a study of 1,430 diabetic children (0.5 per cent incidence) in agreement with the findings of the former group. John⁴ recently reported two diabetic infants in a series of 500 patients with juvenile diabetes (or 0.4 per cent occurring in the first two decades of life).

Guest⁵ reported a most interesting family of three consecutive siblings who were found to have diabetes

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under the age of one year, two at three months and one at nine days of age.

We are reporting the following cases to call attention to the clinical picture and the difficulties in making a correct diagnosis of diabetes mellitus in acutely sick children and to point out the important therapeutic measures. We feel that through the analysis of these case reports, an awareness of the possibility of diabetes will make for earlier diagnosis and treatment. In view of the high mortality, the need for earlier recognition is apparent. In our cases the correct diagnosis was made before admission in only one instance.

CASE REPORTS

Case 1. A ten-month-old baby boy was admitted to the Children's Memorial Hospital on January 27, 1927, with a history of vomiting and polyuria beginning two days before admission. Restlessness and labored respirations developed the next day. Examination revealed a comatose, pale, well-nourished infant with deep, rapid respirations, rales in the bases of both lungs and abdominal tenderness. There was an acetone odor to the breath. The temperature was 101° F. A diagnosis of ketosis was made. Glycosuria was discovered later; it was controlled with small doses of insulin.

After the fifth hospital day, he developed a severe diarrhea and vomiting, pneumonia and otitis media. He died on the twelfth hospital day of pneumonia, otitis media and acute intestinal intoxication.

Autopsy revealed gross atrophy of the pancreas, fatty changes in the liver and kidneys, broncho-pneumonia of the right upper lobe, emphysema and hypostatic edema and hyperemia of the lungs.

Case 2. A baby girl, aged 4¾ months, was admitted to the Children's Memorial Hospital September 18, 1942, with a history of vomiting and polyuria for three days. Rapid respiration and fever were noted the day of admission. In three days there was a weight loss of 2½ pounds.

Examination revealed a dehydrated infant with rapid respirations and acetone breath. She responded to stimuli. The chest was clear. The liver was enlarged. The temperature was 102° F. A diagnosis of renal anomaly and acidosis was made.

Later, the urine revealed sugar graded 4 plus, acetone, and diacetic acid. Blood sugar was 875 mg. per 100 cc. Non-protein nitrogen was 57 mgm. per cent and the carbon dioxide combining power was 10 volumes per cent. The leucocyte count was 36,000.

The treatment included the use of 700 cc. of one-sixth molar solution of sodium lactate, 300 cc. of saline solution with 5 per cent glucose and 44 units insulin. The sugar in the urine remained 4 plus, although the test for acetone became negative. The blood sugar fell to 420. The patient became less responsive. The temperature rose to 106° F., and she died seventeen and one-half hours following admission.

Autopsy revealed mild congestion of the bases of both lungs, fatty infiltration of the liver and a small pancreas. Microscopic study of the pancreas revealed pleomorphism of the islets with shrunken cells and pyknotic nuclei.

Case 3. A seven-month-old baby boy was admitted to the Children's Memorial Hospital December 12, 1943. The birth weight was 3½ pounds. A sibling, six years of age, had diabetes. The day before admission, he became restless and developed a high fever (104° F.) and abdominal distention. Initial physical examination revealed a dehydrated, acutely ill child. The eyeballs were rolled upward. The skin was dry. The anterior fontanelle was depressed, the respirations were rapid and there was an acetone odor to the breath. Dullness was elicited over the base of the right lung together with showers of fine rales at both bases. A diagnosis of broncho-pneumonia was made. Later, the blood sugar was 434; the test for carbon dioxide combining power was 20 volumes per cent. The urine contained sugar graded 4 plus; acetone was negative.

The treatment included 30 units of regular insulin; 400 cc. of one-sixth molar solution of sodium lactate; 600 cc. of saline solution containing glucose, followed hours.

The respiration became irregular and shallow and the infant was placed in an oxygen tent. The fever increased from 104° to 105° F. The respiration became very slow and coma developed. Later, gasping respirations were followed by long periods of apnea. The blood sugar twenty hours after admission was 105, the nonprotein nitrogen was 42 and the carbon dioxide combining power was 26 volumes per cent. Two and one-half hours later the respirations increased to 60 per minute and the baby was again gasping. His color became poor and he expired about twenty-four hours after admission.

Autopsy revealed a hemorrhagic broncho-pneumonia and a cloudy swelling of the liver. Microscopic examination of the pancreas with Goodpasture's stain revealed a normal number of islets. An abundance of

eosinophilic alpha cells were present. Occasional beta cells were identified.

Case 4. A baby girl, aged 11½ months, entered the Children's Memorial Hospital March 7, 1946, with a history of frequency of urination, fussiness, failure to gain and slight drowsiness for one month. Coryza and blepharitis were noticed six days before admission. Because of her failure to gain weight, a urinalysis was made; it revealed sugar, graded 4 plus. The birth weight was nine pounds, eight ounces. The father was six feet, eight inches tall.

The initial physical examination revealed a severely ill baby of good development and nutrition but with poor tissue turgor. The infant was restless. The respirations were 30 per minute and of the Kussmaul type. Acetone was present on the breath. The lungs were clear. The throat was mildly infected. The blood sugar was 288.

Treatment with insulin and fluids was followed by return of respiration to normal. Ketone bodies disappeared 18 hours after admission. Because of the fever of 101° F., penicillin was prescribed. Recovery was essentially uneventful. The patient was discharged from the hospital on a weighed diet and six units of protamine zinc insulin, with four units regular insulin in the morning and two units of regular insulin at night.

On November 30, 1949, she was 42 inches tall and weighed 44 pounds. The daily dosage of insulin then was one dose of 18 units of a mixture containing regular and protamine zinc insulin in a ratio of 2:1.

Case 5. A baby girl, 10 months old, was admitted to the Municipal Contagious Disease Hospital of Chicago December 15, 1948, with a history of croup for two days associated with anorexia and fever. Penicillin had been given orally for two days. Respiration became rapid and she vomited once. She had been brought to the hospital with a suspicion of meningitis.

The physical examination revealed a febrile infant with respirations of 48 per minute which were deep and grunting along with a flaring of the alae nasi. The temperature was 103° F.; the pulse rate was 160. Dullness was noted over the lower chest on the right but no rales were heard. The examination of the spinal fluid did not show cells or organisms; the tests for protein and sugar were normal. A specimen of urine, obtained the morning following admission, contained sugar graded 3 plus, but she was receiving glucose solution intravenously at the time. She was treated with chemotherapeutic agents for pneumonia and responded

after the first twenty-four hours. On the third hospital day she was lethargic and the breathing was still labored in spite of treatment. Fluids were discontinued. The blood sugar was subsequently found to be 500. and the urinary acetone and diacetic acid were both graded 4 plus. Another specimen of urine, obtained four hours later, still contained sugar graded 4 plus.

Twenty units of regular insulin were given subcutaneously and, in three hours, 15 units more were administered. 500 cc. of one-sixth molar solution of sodium lactate was administered intravenously. Within 12 hours the infant responded to stimuli and the respiration was essentially normal in rate and depth. Orange juice and a weak formula were offered and were accepted readily. On the eighth hospital day, the child was transferred to the Children's Memorial Hospital. At this time the blood sugar was 362; the hemoglobin was 10 gm.; the red blood cell count was 4,260,000, the white cell count 7,800 per cu. mm. A six hour feeding schedule was established. Feedings consisted of whole boiled milk, vegetable, cereal and fruit. She remained afebrile and alert and was discharged on the thirteenth hospital day. Four units regular insulin twice daily and 6 units globin insulin once daily have controlled the glycosuria. There have been no subsequent complications.

Case 6. A baby boy, aged 12 months, was admitted to the Children's Memorial Hospital February 4, 1949, with a history of restlessness, anorexia for three days and a fever of 101° F. The day prior to admission he vomited twice and his respiration became heavy and rapid. The following morning, after vomiting twice, he was rushed to the hospital.

The physical examination revealed a well-developed comatose infant boy in shock and not responding to stimuli. The temperature was 103° F. rectally, and the respiration was 42 per minute, deep and regular; there was flaring of the alae nasi. The pulse, thready and weak in quality, was 136 per minute. Fine rales were heard at both lung bases with suppression of the breath sounds at the right base. Bronchial breathing was heard in the left axilla.

He was treated for pneumonia immediately with penicillin. Plasma and 250 cc. of one-sixth molar solution of sodium lactate were given intravenously. Supportive measures initially produced a good response. Within six hours after admission the chest had cleared remarkably with only a few rales remaining; however, the respiration remained deep and rapid and the patient was still comatose. A urinalysis revealed sugar graded 4

plus, acetone and diacetic acid. The carbon dioxide combining power of the plasma was 15.5 volumes per cent. The plasma chloride was 373 mg. per 100 cc. Twenty units of regular insulin were given subcutaneously. The same dose was repeated in three hours. After six hours, ten units were administered. At that time the urine showed sugar graded 2 plus, acetone and diacetic acid graded 4 plus. A total of 300 cc. of normal saline solution followed by 400 cc. of 5 per cent solution of dextrose in water were given intravenously.

Fifteen hours following admission the urine showed sugar 3 plus, and acetone and diacetic acid 4 plus. Ten units of regular insulin were then given. Response was noted shortly and the patient awakened. The sugar urine was only 1 plus, with acetone and diacetic acid 3 plus. Four units of regular insulin were given three hours after the last injection. Three hours later, 21 hours after admission, the patient developed severe, near fatal, insulin shock with apnea and cyanosis. He was revived by artificial respiration and rapid intravenous injection of a 10 per cent solution of dextrose in water. He was then placed upon a six hour management with intravenous feedings until he was able to eat, which was on the fourth hospital day.

On the seventh hospital day he developed a mild upper respiratory infection with a slight elevation of temperature. The insulin requirement rose from 4 units in twenty-four hours to 18 units in twenty-four hours. He was discharged alert and active on the twenty-first hospital day. Three doses of crystalline insulin per day have controlled the glycosuria. There have been no subsequent complications.

COMMENT

The age of onset of the disease in these six cases was 4½ months, 7, 10, 10¼, 10½, and 12 months. A family history of diabetes was recorded in two cases—one patient having a sibling with diabetes, the other a paternal uncle. The father of one child approached gigantism (*Case 4*). Four of these patients were of German extraction.

The pathological findings in *Case 1* revealed a gross atrophy of the pancreas, in *Case 2*, pleomorphism of the islets of Langerhans with shrunken cells and pyknotic nuclei, and in *Case 3*, a normal number of islets without apparent reduction of eosinophilic alpha cells but only an occasional beta cell.

The initial symptoms presented by diabetic infants are listed below in the order of frequency:

Fever, 100%	Anorexia and vomiting, 66%
Pulmonary signs and symptoms, 100%	Restlessness, 66%
Accelerated respiration, 100%	Polyuria, 66%
Rales and signs of pneumonia, 66%	Loss of weight, 33%

The susceptibility of infants with diabetes to severe respiratory infections leads to the predominance of fever and pulmonary signs and symptoms. This has not been recognized adequately in the past. Therefore, we wish to emphasize the need for consideration of diabetes when such symptoms are present. Special attention should be given when respiratory symptoms and signs improve or subside after the use of antibiotics and replacement fluid therapy but when hyperpnea and coma persist.⁶ Early urinalysis and blood sugar determinations should be performed to establish an early diagnosis.

The administration of penicillin accelerated recovery in *Case 4* and probably prevented death in *Cases 5* and *6*. It is possible that all three patients who expired might have recovered from the diabetic acidosis and infection had penicillin been available to supplement insulin.

Adequate insulin therapy must always be prescribed. Severe hypoglycemia must be prevented. In *Case 6* insulin shock was almost fatal. It is probable that hypoglycemic shock caused death in *Case 3*, since the last blood sugar of 105 was recorded two and one-half hours before death and two hours before apnea was noted.

SUMMARY

Six cases of infantile diabetes are reported. In all cases, severe respiratory infections complicating diabetes dominated the clinical picture.

Attention is directed to the prominence of respiratory signs and symptoms. Penicillin therapy has favorably influenced the prognosis in infantile diabetes.

REFERENCES

- ¹ Newcomb, Alvah L.: Diabetes Mellitus in Children. *J. Pediatrics*, 4:617, May 1934
- ² Schwartzman, Joseph; Crusius, Margaret E.; Beirne, Donald P.: Diabetes Mellitus in Infants Under One Year of Age. *Am. J. Dis. Children*, 74:587, November 1947.
- ³ Joslin, Elliott; Root, Howard; White, Priscilla; Marble, Alexander: Treatment of Diabetes Mellitus, Philadelphia, Lea and Febiger, 1940, pp's. 42, 48, 607, 672.
- ⁴ John, Henry J.: Diabetes Mellitus in Children, *J. Pediatrics*, 35:723, December 1949.

⁵ Guest, George M.: Infantile Diabetes Mellitus: Three Cases in successive siblings; two with onset at three months of age and one at nine days of age. *Am. J. Dis. Children*, 75:461, March 1948.

⁶ Farrell, Harry W.; and Newcomb, Alvah L.: Acute Onset of Infantile Diabetes Mellitus with Infection. *Quart. Bull. of Northwestern Univ. M. School*, 24:40 Spring 1950.

DISCUSSION

ROBERT L. JACKSON, M.D. (*Iowa City, Iowa*): Recognized diabetes mellitus in infants is rare. In the past 26 years, 492 diabetic children with onset under 16 years of age have been observed in our clinic. Of these, 5 had onset during infancy (one per cent) and 24 had onset of their disease between the first and second year of life, making 5.8 per cent with onset under two years of age.

Of the 5 children with onset under one year of age, all responded satisfactorily to treatment; 3 have maintained a fair to good level of control, (as defined by us in our publication) for as long as 19 years and are living and well; one has maintained fair to poor control and has had frequent insulin reactions with possible central nervous system damage; the other patient was observed for 3 years, but her present status is unknown.

Of the 24 children with onset between the first and second year of life, 7 have maintained a good to excellent level of control for as long as 27 years and all are living and free from degenerative changes; 12 have maintained a fair level of control for as long as 25 years and are living, some have early signs of degenerative changes; the remaining 5 patients have maintained a fair level of control, one died, two have had central nervous system damage, and the exact state of the other two is unknown.

Anorexia, vomiting and diarrhea are very common symptoms of sick infants. The most common causes of illness in infants are infections of the respiratory and gastrointestinal systems. Inadequate intake or excessive loss of water, electrolyte and other nutrients deplete the infant's stores more rapidly than the older child or adult. Consequently, dehydration, ketosis and acidosis are frequently encountered in the nondiabetic infant. Urine specimens are more difficult to obtain from infants because of lack of bladder control and difficulty of

collecting specimens, especially in baby girls. Therefore, routine urine examinations frequently are not done. The onset of diabetes mellitus in infants and young children is relatively abrupt because of the severity of the disease. Diabetes symptoms may not be elicited as a detailed history too frequently is not taken; the symptoms of an infection may overshadow those of diabetes. It is easy to understand why the existence of diabetes mellitus, when it does occur in infants, may be overlooked.

The diagnosis is simple, providing the physician considers the possibility, and examines the urine and blood for sugar content. There may be suspicion of a small amount of sugar in the urine because of a false positive Benedict's test, from the relatively high content of reducing substance such as creatine and uric acid. However, a strongly positive reduction test always is found in infants and children with untreated diabetes. When the urine causes a mild reduction, the test should be repeated and the cause of the positive test should be found. Galactosuria in infants, in our experience, is much more common than glycosuria. Infants with definite galactosemia and galactosuria do not thrive and have an enlarged liver and a high incidence of cataracts. This inborn error of metabolism easily is treated by eliminating lactose in the diet. The diagnosis also is easy if the condition is thought of and laboratory procedures are done to identify the nonfermentable sugar. Seventeen infants with this condition have been observed in our clinic in the last 16 years as compared to only 5 infants with diabetes.

During acidosis and ketosis relatively large amounts of insulin will be needed to control diabetes, but, with improvement, the maintenance dosage will decrease rapidly to as little as three or four units a day. In measuring small doses for infants and younger children, we have found it desirable to employ a tuberculin syringe which will permit varying the dose by 0.4 units when using U 40 insulin or 0.2 units when using U 20 insulin.

Because of the lability of these very young patients and the decreased reliability of reduction tests of their urine (because of other reducing substances such as creatine), great care must be taken to avoid overdosage with insulin. There is the ever-present danger of irreparable damage to the central nervous system.