BLOOD SUGAR LEVELS IN BABIES BORN OF DIABETIC MOTHERS

BY

GEORGE M. KOMROWER

From St. Mary's Hospitals, Manchester, and the Department of Child Health of the University of Manchester

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Many observers have reported upon the blood sugar levels determined during the first days of life of normal infants; and it is generally agreed that there is considerable variation in the figures of different babies, and also some instability of the levels in each individual infant under investigation, the figures being invariably lower than those in older persons (Creery and Parkinson, 1953; Greenwald and Pennell, 1930; Hartmann and Jaudon, 1937; Ketteringham and Austin, 1938; McKittrick, 1940; Norval, Kennedy and Berkson, 1949; Smith, 1951; Wachter, 1949).

There is less information concerning the blood sugar levels of the infants born of diabetic mothers, but the evidence suggests an early and rapid fall to a low level followed by a slow rise to more normal levels (Haslewood and Strookman, 1939; Joslin, Root, White and Marble, 1952; Miller and Ross, 1940; Oakley, 1953; Pedersen, 1952; Peel and Oakley, 1950; Reis, DeCosta and Allweiss, 1950).

It has been possible to make some observations on 21 normal infants and 40 infants born of diabetic mothers, and figures are produced for comparison. Twenty-five of the 40 'diabetic' babies were given 50% glucose at set intervals during the first eight hours of life, a total of 2 g. of glucose being given in all, but no further feeding was attempted until the infants demanded. This regime, based on the work of Reis and his colleagues in Chicago (1950), was employed as part of an M.R.C. investigation into pregnancy in diabetes: the remainder were not given glucose and feeding was only begun when the infants cried hungrily.

The majority of the 'diabetic' babies were delivered by Caesarean section in the thirty-seventh to thirty-eighth week, the mothers being given 30 g. glucose within two hours of the operation.

Blood sugar estimations were made on the cord blood (umbilical vein), and on heel blood obtained at half hour, one hour, two hours, four hours, 12 hours and 24 hours. The method of estimation was a modification of the method employed by Haslewood and Strookman (1939),

namely, 0.1 ml. of whole blood is pipetted into 3.70 ml. of isotonic sodium sulphate-copper sulphate solution in a conical centrifuge tube; 0.2 ml. of sodium tungstate is added, and the mixture is well shaken. The precipitated proteins and copper tungstate are spun down in the centrifuge; 0.5 ml. of the supernatant fluid (≈ 0.0125 ml. blood) is mixed with 1 ml. of the mixed copper reagent in a $\frac{3}{4}$ in. diameter test-tube. The tube, stoppered with cotton wool, is placed in a boiling water-bath for exactly 10 minutes. After immediate cooling, 3 ml. of the phosphomolybdic acid reagent are added. The colour is compared with that produced by 1 ml. of a standard glucose solution in benzoic acid, treated in the same way as the blood filtrate. Duplicate readings were made as often as possible but as it was not feasible to obtain the full amount of blood on all occasions several of the results have been discarded.

The normal infants were born in the thirty-ninth or fortieth week by ordinary forces and suffered no complications in the neonatal period. They were not fed for 12 hours, when they were offered glucose saline; if this was taken satisfactorily the child

TABLE 1
NORMAL CONTROLS

No.	Weight (lb. oz.)	Cord Blood	Blood Sugar (mg. %)									
			Hours after Birth									
			$\frac{1}{2}$	1	2	3	4	6	8	12	24	
1	7 11 $\frac{1}{2}$	110	95	102	133							99
2	4 1	69			75		94	77		125		90
3	5 15	83		91	49		68	45		47		
4	8 0	86	77	81	77			62		59		
5	5 10			75				118		81		
6	8 0	53		58	65			65				
7	5 5	85					26	36				28
8	5 5	77			24		32	30				30
9	7 5	109						98				
10	6 15	116		125						116	120	
11	7 14	111		104	82		98	77				
12	7 11	75		94	65		77	70				
13	7 7	123	78	69	60		52	55				
14		178	95	120			67	100				86
15	7 8	95	168				122					
16	6 4	67								33		90
17	6 0	50								80		
18	5 12	117		125			127			116	80	
19	5 12	115					78					
20	7 12	86		95						100	100	
21	7 12	76	69		118		60			75		

was put to the breast at 15 hours and routine feeding begun (Table 1). These babies showed a wide scatter of blood sugar levels at any one interval of time (Fig. 1), but the bulk of the results lay around the mean (Fig. 1). The graph does not show any sudden

infant usually stabilized slowly at a rather lower level than that of the normal infant (Figs. 2 and 3).

A comparison has been made between the infants given glucose (25 in all) during the first eight hours (D + g) and those (15 in all) who were left un-

FIG. 1.—Normal controls.

rise or fall of blood sugar and it suggests that the majority of newborn infants soon attain a reasonably stable blood sugar level. The infants concerned had normal births with uncomplicated neonatal periods: in spite of the fact that four of the results were below 30 mg. % no symptoms suggesting hypoglycaemia were observed.

The results obtained in the babies born of diabetic mothers showed considerable variation with a marked drop in blood sugar level during the first two or three hours of life. Once this drop occurred the

disturbed (D - g). It can be seen that there is no significant difference between the average figures plotted (Fig. 4), although the figures in the D + g group are slightly higher. It is felt, therefore, that there is no indication for the routine administration of oral glucose solutions to the infants born of diabetic mothers. One is lead to this decision by the figures recorded and by the knowledge that these children behave as premature babies and must be treated as such: many of them require oxygen during the first hours of life because of respiratory distress; in

addition drowsiness and a poor cough reflex are often found and one is of the opinion that the early routine administration of fluid solutions with the resulting disturbance of the child might give rise to

in these babies and to determine whether this state contributes to the high mortality rate.

Several workers have commented upon the remarkable absence of any unusual symptoms in

FIG. 2.—Babies born of diabetic mothers given glucose (D+g.)

more harm than good. It has, therefore, been decided to reserve the oral glucose solution for those babies presenting the clinical signs of hypoglycaemia.

The final and main purpose of this study is an attempt to assess what constitutes hypoglycaemia

premature or new-born babies presenting with very low blood sugar levels (Joslin *et al.*, 1952; Norval *et al.*, 1950; Oakley, 1953; Pedersen, 1952; Sheumack, 1949; Smith, 1951). In a recent paper Oakley (1953) estimated the blood sugar levels at two-hourly intervals in a series of 35 children, of whom 17

received 50% glucose. He does not give his results in detail but says that very low levels were estimated in children who survived satisfactorily: in three

symptoms of hypoglycaemia were not observed in the first 24 hours of life, and suggests that the onset of any severe symptoms (cyanosis, twitching, grunt-

FIG. 3.—Babies born of diabetic mothers not given glucose (D—g.)

infants who died the blood sugar levels dropped to 35 mg., or less, per 100 ml. Pedersen (1952) in a comprehensive study of blood glucose levels in the infants born of diabetic mothers, says that clinical

ing respirations) demands a thorough examination of the child in order to exclude complications such as atelectasis, cerebral haemorrhage, infection and heart disease.

FIG. 4.—Comparison of the average mean in Figs. 1-3.

TABLE 2
BABIES BORN OF DIABETIC MOTHERS GIVEN
GLUCOSE

No.	Weight (lb. oz.)	Cord Blood	Blood Sugar (mg. %)											
			Hours after Birth											
			½	1	2	3	4	6	8	12	24			
1	4 13	178	173	83	54		112		161	82	85			
2	6 4½	300		159	126		60		73		91			
3	7 3	81		37										
4	7 10	241	128		46	36	73		40	48	128			
5	7 2	50	70							55				
6	2 5	192	135											
7	5 11	190	112		73			82		108				
8	6 8	197		205	120									
9	6 3	67			165		65							
10	6 14	85		82	45		51							
11	7 12	92	98		117	60	139							
12	6 12	91		40	38			60						
13	4 4½	140	116	90	56	48	100	164		M				
14	8 4	141	70	32	26	22	18 H			38				
15	10 5	130	52	36	10 N	27	38	45	57	80				
16	6 15	110		92	18	15 H	28	53	75	92				
17	7 2	90	25	16	14 H	18	18	17						
18	5 15	90												
19	7 11	92	72	69	64	93	94	75		50				
20	7 10	80	40	30		38			47		60			
21	4 5	135	55	58		40		44	55		46			
22	6 4	204		85		105					65			
23	6 4½	65	104											
24	7 0	165	126	136	191		123	113		90				
25	6 12½	63	36	24	21		20 N	30	33	29				

M = death; H = hypoglycaemia; N = no symptoms.

It can be seen (Tables 2 and 3) that the blood sugar levels in our cases frequently fell below 40 mg. %, a level which Hartmann and Jaudon (1937) suggested was (Tables 2 and 3) indicative of moderate hypoglycaemia, and many were below 35 mg. %. In spite of the most careful clinical observations we saw only four children in whom the symptoms suggested hypoglycaemia; in these infants pallor, a sudden drop in temperature, shallow respirations and occasional twitching were noted. The recorded blood sugars in three cases were as follows: 14 mg., 18 mg. and 18 mg. % respectively; the other infant experienced a rapid drop of 226 mg. % in one hour. There were, in contrast, infants with levels of 10 mg., 15 mg. and 20 mg. % who were symptom free.

It is our belief that, in spite of the low blood sugar levels recorded in the first hours of life of the babies of diabetic mothers, the clinical picture of hypoglycaemia is very rare as all infants are more capable of accommodating themselves to sudden reductions and low levels of blood sugar than are their elders.

In this series of 'diabetic' babies there have been seven deaths and Table 4 describes the pathological diagnoses and the recorded blood sugar levels. In each case there was an obvious cause of death, intracranial haemorrhage being the commonest factor. The infant Sefton did have a rapid fall of blood sugar in the first hour, but as his cord haemoglobin was 75% and his condition desperate from birth, it is our opinion that the subcapsular

TABLE 3
BABIES BORN OF DIABETIC MOTHERS NOT GIVEN
GLUCOSE

No.	Weight (lb. oz.)	Cord blood	Blood Sugar (mg. %)											
			Hours after Birth											
			½	1	2	3	4	6	8	12	24			
1	6 9	55		85	50		65		59					
2	6 0	85		51	48		49		69					
3	5 8½	142												
4	8 2	97	73	54	23		47							
5	9 6	210		50	46		78				75			
6	5 7													
7	12 6	180	140	30										
8	3 11	110	100	52		60	140		M	48				
9	8 2	73	52	50										
10	7 6	182	157	45	66	82	90	50	25					
11	8 12	290	76 H	20 N		30	45	44	65	50				
12	8 8	169	156	55					58					
13	6 12½	128	66											
14	7 7	170	30			30	15 N							
15	4 10½	108	61	40					34	46				

M = death; H = hypoglycaemia; N = no symptoms.

TABLE 4
DETAILS OF NEONATAL DEATHS

Initials	Maturity	Blood Sugar Levels (mg. %)							Lived	Anatomical Diagnosis	Weight (lb. oz.)
		0	$\frac{1}{2}$	1	2	4	8	12			
C.G.	36 weeks	140	116	90	56	48	100	164	13 hours	Hyaline membrane Haematoma liver Follicular ovarian cysts	4 4
Sefton	35 "	140	-30						10 "	Subcapsular haematoma liver Prematurity	5 7
S.W.	33 "	73	52	50	15	20			6 $\frac{1}{2}$ "	Intra- and peri-ventricular haemorrhage Hyaline membrane Atelectasis Prematurity	3 11
Stephen	36 "	169	156	55			58		20 "	Hyaline membrane Atelectasis lung	8 8
M.D.	31 "	No sugars done (too ill)							15 "	Intraventricular and subarachnoid haemorrhage Subcapsular haematoma liver Asphyxia	4 7
W.H.	32 "	No sugars done (too ill)							3 "	Intraventricular cerebral haemorrhage Prematurity	5 9
D.B.	36 "	192	135						5 days	Tiny baby (twin) Meningo-myelocoele	2 5

bleeding occurred before birth, and that the subsequent lowering of the blood sugar was not a major contributory factor to death. (In this case respiration was never properly established and gentle rocking was employed together with oxygen therapy for several hours.)

The low figure in the case S.W. was associated with symptoms suggesting hypoglycaemia, but in view of the necropsy findings it is unlikely that death was hastened by the hypoglycaemia. There is no evidence that this condition contributed to death in any of the other cases recorded here.

Summary

Estimations of the blood sugar level during the first 24 hours of life were made on 21 normal infants and 40 infants born of diabetic mothers. Twenty-five of the latter 40 babies were given 50% glucose in the first eight hours of life.

The normal infants showed a wide scatter of blood sugar levels but there was no dramatic rise or fall in the figures in any one case.

The babies of diabetic mothers revealed a rapid drop in the first hours of life with a slow rise towards the end of the first 24 hours. There were considerable variations in the figures obtained.

The administration of a 50% oral glucose solution did not make any appreciable difference to the blood sugar levels obtained compared with the group of infants to whom glucose was denied.

The clinical picture of hypoglycaemia in infancy is described and the fact that it is an uncommon finding is stressed.

It is suggested that few, if any, babies born of diabetic mothers die as the result of hypoglycaemia.

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REFERENCES

- Creery, R. D. G. and Parkinson, T. J. (1953). *Archives of Disease in Childhood*, **28**, 134.
 Greenwald, H. M. and Pennell, S. (1930). *Ibid.*, **39**, 281.
 Hartmann, A. F. and Jaudon, J. C. (1937). *J. Pediat.*, **11**, 1.
 Haslewood, G. A. D. and Strookman, T. A. (1939). *Biochem. J.*, **33**, 920.
 Joslin, E. P., Root, H. F., White, P. and Marble, A. (1952). *The Treatment of Diabetes Mellitus*, 9th ed. London.
 Ketteringham, R. C. and Austin, B. R. (1938). *Amer. J. med. Sci.*, **195**, 318.
 McKittrick, J. B. (1940). *J. Pediat.*, **16**, 151.
 Miller, H. C. and Ross, R. A. (1940). *Ibid.*, **16**, 473.
 Norval, M. A., Kennedy, R. L. J. and Berkson, J. (1949). *Ibid.*, **34**, 342.
 — (1950). *Ibid.*, **11**, 1. 36, 177.
 Oakley, W. (1953). *Brit. med. J.*, **1**, 1413.
 Pedersen, J. (1952). *Diabetes and Pregnancy. Blood Sugar of Newborn Infants*. Copenhagen.
 Peil, J. and Oakley, W. (1950). *Trans. XII Brit. Cong. Obstet. Gynec.*, 1949, 161. London.
 Reiss, R. A., DeCosta, E. J. and Allweiss, M. D. (1950). *Amer. J. Obstet. Gynec.*, **60**, 1023.
 Sheumack, D. R. (1949). *Med. J. Aust.*, **2**, 553.
 Smith, C. A. (1951). *The Physiology of the Newborn Infant*, 2nd ed. Oxford.
 Wachter, H. E. (1949). *J. Mo. med. Ass.*, **46**, 837.