BLOOD GLUCOSE CHANGES IN THE NEWBORN

1. THE BLOOD GLUCOSE PATTERN OF NORMAL INFANTS IN THE FIRST 12 HOURS OF LIFE

BY

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(RECEIVED FOR PUBLICATION JANUARY 20, 1953)

Many investigations of the blood sugar levels of newborn infants have been made. The literature has been reviewed by Norval, Kennedy and Berkson (1949), who concluded that the values found varied widely. They considered this to be due to several factors, including the method of determination used, the source of the blood sample and the age of the infants.

Previous investigators have tended to estimate the blood sugar levels at birth, and subsequently at varying intervals throughout the first days and weeks of life. For example, Ketteringham and Austin (1938), using the modified Folin-Malmros method, made estimations at birth, at 3 to 6 hours and thereafter daily for the first three days of life. Hanley and Horn (1943) used the Jeghers-Myers modification of the Folin-Malmros method and made estimations at birth, at 1 hour and at 6 hours.

Both Ketteringham and Austin and Hanley and Horn have included in their results many infants, far from normal, who had been delivered by forceps or by other complicated manoeuvre, and often under ether anaesthesia which is known to raise the blood sugar level in the infant significantly.

It is evident that little is known concerning the detailed behaviour of the blood glucose levels of normal infants during the first critical hours when adaptation to a completely changed environment is taking place.

The purpose of the present investigation was to obtain a series of levels during the first 12 hours of life in full-term infants born of healthy mothers, uninfluenced by drugs known to affect the blood sugar, delivered spontaneously by the vertex, and themselves showing no abnormal features during the neonatal period.

These results will be used as a base line of normality in our subsequent investigations of the blood sugar levels of abnormal infants, whether asphyxiated, shocked or suffering from cerebral damage, or any other form of 'birth injury'.

Material

The subjects of this study were babies born at Southmead Hospital during the years 1950 and 1951. The primary selection was random, all babies born at an hour convenient to the clinical observer and to the laboratory staff being included. From this series, normal babies were selected by conformity to the following criteria: (1) mother unanaesthetized, but having in most cases received routine doses of analgesics; (2) spontaneous vertex delivery at full term; (3) no signs of asphyxia in the baby, regular respiration being established within three minutes of birth in all cases; (4) no observed abnormality of temperature, pulse rate, or respiration; (5) no signs suggesting cerebral damage, neither tense fontanelle, muscular twitchings, shrill cry nor abnormal muscle tone; (6) no clinical abnormality developing before discharge from hospital which could be attributed to birth trauma. (It was considered unnecessary to make a late follow-up study of these babies.)

Included in the series is one pair of twins (babies C6 and C7).

The analgesic routine included any of the following, depending on the duration of labour: (1) self-administered nitrous oxide and air from a Minnitt's machine; (2) pethidine hydrochloride in doses of 100 mg. by mouth, or by intramuscular injection, repeated in cases of prolonged labour; (3) a mixture, containing chloral hydr., gr. 20, pot. brom., gr. 20, nepenthe, minims 20, which might be repeated in prolonged labours.

Of these drugs, Larson (1949) has shown that morphia, the active principle of nepenthe, and pethidine ('meperidine'), are without effect on the blood glucose concentration in doses of the size of those used, and a search of the literature gives no

reason to attribute such an effect to chloral, bromide or nitrous oxide.

Method

The method used to estimate the blood glucose concentration was that of King and Garner (1947). An extensive experimental review of this method has been made in order to assess its range of error. The results of this investigation of its accuracy and consistency at the low concentration found in neonates are being published elsewhere by C. N. Chapman. The method is quick, and convenient and reasonable delay in analysis does not affect its accuracy. Only 0·05 ml. of blood is used and as frequent estimations were to be made this provided accuracy with small blood loss to the baby, an important point when nine samples had to be secured. In the preliminary investigation it was found that 95% of results were consistent to within 5 mg. per 100 ml., when the same sample of blood was subject to repeated analysis, and with this knowledge it was decided to omit duplicate sampling and analysis within the series.

The first sample was taken from the ear of the mother at the moment of crowning of the foetal head, or as near thereto as possible. The next sample was taken from the umbilical vein by the method of Hanley and Horn (1943). This was placed in a bottle containing the standard oxalate-fluoride blood sugar anticoagulant (Harrison, 1947), and a mixed sample withdrawn for analysis. Such samples are strictly comparable with the directly drawn capillary samples. Similar specimens were obtained from the umbilical artery in a number of cases. All subsequent samples were secured from a puncture of the ether-cleaned heel of the infant.

As delivery was thought likely to upset the pre-existing foetal equilibrium, it was decided to follow the variations of blood glucose at half-hour intervals for the first three hours of life. It was considered that any noteworthy change occurring later would be detected by investigations at three-hourly intervals.

On each occasion when a sample was taken the infant was assessed clinically, particular attention being paid to the temperature, pulse rate, respiration, muscle tone, muscle twitching or its absence, the tension of the fontanelle and the type of cry.

No fluid or feed was given to any infant during its first three hours of life, and subsequently, if any was given, it immediately followed the taking of a sample and was thus unable to influence the next sample, taken three hours later.

Results

The results of a study of 23 male babies are shown in Table 1. The value for the mother's blood glucose at the moment of delivery was not investigated at the beginning of the study, nor was that for the umbilical artery. Later, occasional lapses occurred when blood could not be taken at the exact time required, or a mishap occurred to the specimen. All the values estimated are recorded in Table 1.

The scatter of individual values about the mean is wide, from 49-118 mg. per 100 ml. in the umbilical artery, the most scattered, but even at two hours, where scatter is least, varying from 30 to 76 mg. per 100 ml., and the histograms (Fig. 1) show this. In view of the small numbers involved they correspond reasonably well with the normal distribution which Wooton, King, Maclean Smith and Haslam (1951) found random fasting adult blood glucose values to follow.

The mean values show a steady decline from the mother, 115·1 mg. per 100 ml., through the arterial side of the foetal circulation represented by the umbilical vein, 83·7 mg., to the venous side represented by the umbilical artery, 74·0 mg. per 100 ml. Once independent, not even this level is maintained by the baby, for by half an hour after birth a fall to 66·7 has occurred, and, by an hour, to 55·5 mg. per 100 ml. The mean values do not subsequently differ markedly from this.

A study of the histograms suggests that the results show less scatter as the baby gets older. Calculation gives the Spearman rank order coefficient of correlation between the standard deviation of each age series from its mean with the age of the babies in the series as −0·48, which indicates that there is a definite but not complete inverse correlation, and that the scatter of values is less as the babies grow older.

Table 2 and Fig. 2 give the results of a parallel study of 23 female babies. In this series, the mean blood glucose of the mothers is lower, 100·3 mg. per 100 ml., and this is true also of the blood in the umbilical vessels (75·7 and 60·5 mg. per 100 ml.). Stability appears to be reached earlier at half-an-hour, although this may only be because the maternal level was nearer to that at which the baby aims, and in any case is never so complete as in the male babies, the means varying from 46·5 to 58·0 mg. per 100 ml. as against 51·7 to 55·5 for the males, after the first hour.

Fig. 2 shows that although the means are more variable, the scatter around them is smaller than it was with the male babies, and the standard deviations, whose mean after the first hour is 11·4 as against 12·9 for the males, measure this. The coefficient of correlation for standard deviation with age is −0·92, almost perfect inverse correlation.

In adult life the blood glucose content does not appear to be influenced by the sex of the individual, and the results of this study show that this is true also of newborn babies. Table 3 is a consolidation of the two series into a larger series with 46 infants in each age group.

TABLE 1
BLOOD GLUCOSE OF NORMAL MALE BABIES

No.	Mother	Artery	Vein	½	1	1½	2	2½	3	6	9	12
C1	—	—	80	77	—	62	60	—	30	43	32	25
C3	—	—	65	49	35	35	46	46	43	60	30	10
C10	—	—	82	69	52	42	44	48	50	53	49	63
C14	—	—	90	56	51	51	51	51	48	49	49	57
C15	—	—	120	73	56	52	36	46	36	50	64	50
106	111	84	84	76	70	64	59	52	54	62	46	52
111	111	90	95	87	73	62	45	43	34	61	45	54
113	—	49	57	45	45	45	38	56	40	39	49	46
114	115	—	—	65	50	46	49	62	60	60	65	59
123	103	64	76	69	52	44	49	57	67	44	44	38
124	122	—	—	94	87	53	53	62	62	60	62	46
201	123	—	93	92	79	65	53	54	54	49	65	66
202	—	118	126	110	82	79	52	42	34	44	53	46
204	108	—	68	62	49	42	49	44	46	44	57	60
205	129	86	86	49	32	24	32	41	39	46	39	45
209	146	77	91	65	54	57	61	64	65	54	57	57
211	100	—	68	49	49	65	69	75	75	76	54	75
213	120	52	82	52	35	35	30	43	49	54	54	65
215	—	54	68	60	49	60	76	90	90	82	60	62
219	136	87	91	56	54	47	49	35	45	49	44	44
220	87	62	77	44	42	42	57	64	64	62	62	67
226	102	65	76	57	57	60	60	60	60	57	60	52
301	114	—	—	79	68	65	70	75	75	69	57	54
Mean	115·1	74·0	83·7	66·7	55·5	52·0	51·7	55·0	53·0	55·1	52·0	51·9
S.D.	15·1	20·1	17·0	17·5	15·0	12·9	11·8	13·3	15·4	10·7	10·2	14·1

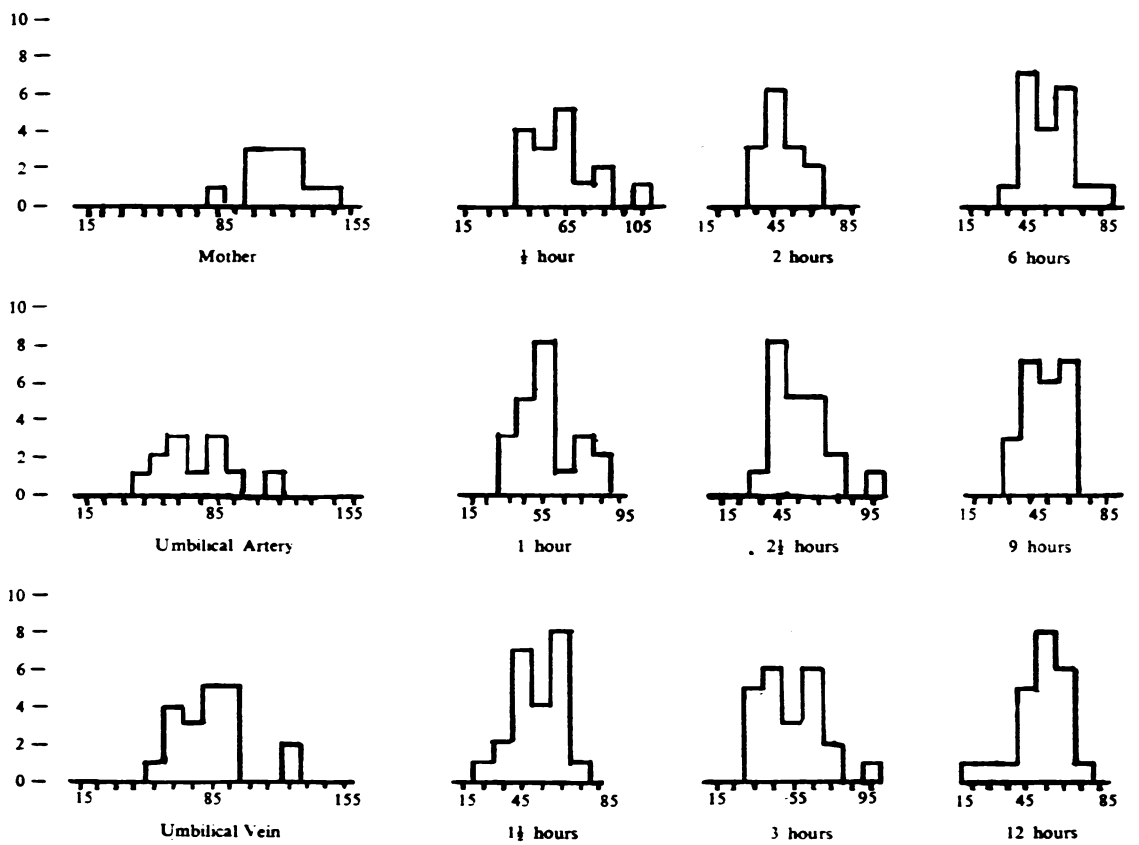

FIG. 1.—Histograms of blood glucose of male babies and their mothers. Vertical scale number in group, horizontal scales mid-group blood glucose.

TABLE 2

BLOOD GLUCOSE OF NORMAL FEMALE BABIES

No.	Mother	Artery	Vein	½	1	1½	2	2½	3	6	9	12
C6	—	—	70	52	50	46	57	56	55	62	59	52
C7	—	—	80	48	41	68	70	63	66	65	52	48
C8	—	—	83	40	21	21	35	55	64	65	73	75
C12	—	—	103	69	69	69	77	77	85	65	64	67
C13	—	—	90	62	37	29	37	37	37	32	36	34
102	95	—	69	35	35	42	46	68	70	48	48	48
103	68	40	52	68	72	62	48	46	52	48	46	41
104	—	—	54	27	44	49	50	46	46	46	46	46
107	106	—	82	64	52	46	52	54	68	62	43	60
112	95	—	79	46	38	45	49	44	45	62	37	47
115	90	—	—	49	38	49	38	72	65	60	56	52
116	76	47	49	48	46	49	54	56	57	52	44	44
119	104	57	76	46	37	49	53	53	54	45	61	52
120	106	49	57	70	49	52	54	62	61	54	54	52
126	75	—	70	54	61	61	65	65	65	46	40	54
127	127	54	87	44	32	32	52	52	54	70	52	40
128	81	57	61	49	52	46	34	34	34	40	49	49
203	—	70	84	60	42	50	57	54	56	53	44	45
206	100	70	76	47	24	19	38	46	52	57	57	60
210	118	—	91	84	70	74	68	74	62	64	50	54
221	114	—	92	68	60	60	60	60	60	65	65	57
223	154	107	107	68	54	54	70	61	62	57	54	60
225	95	54	54	46	46	54	60	65	65	70	57	46
Mean	100·3	60·5	75·7	54·1	46·5	48·9	53·2	56·5	58·0	56·0	51·6	51·8
S.D.	19·8	18·8	16·5	13·1	13·7	14·3	12·2	11·3	11·3	10·0	9·3	9·1

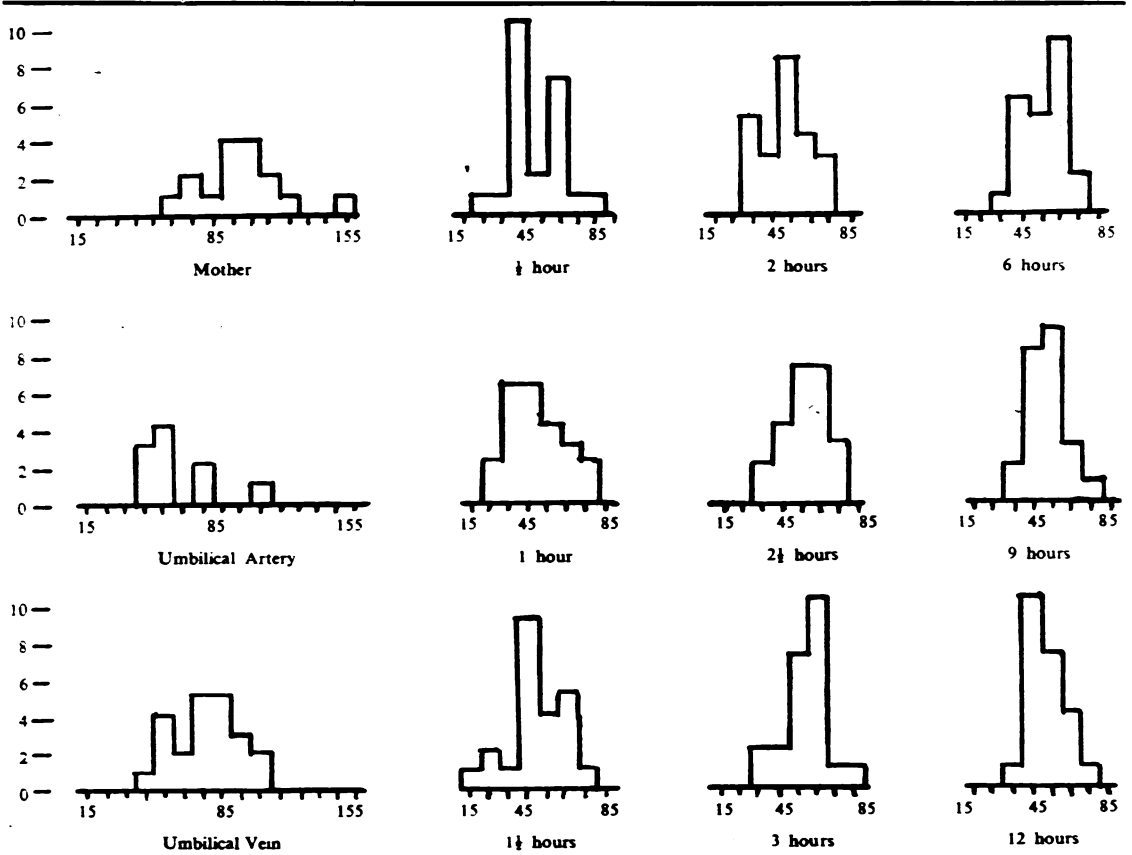

FIG. 2.—Histograms of blood glucose of female babies and their mothers. Vertical scale number in group, horizontal scales mid-group blood glucose.

TABLE 3
MEANS AND STANDARD DEVIATIONS IN TWO SERIES

	Means			Standard Deviations		
	Male Babies	Female Babies	All Babies	Male Babies	Female Babies	All Babies
M	115·1	100·3	107·5	15·2	19·8	23·1
A	74·0	60·5	67·9	20·1	18·8	20·1
V	83·7	75·7	79·6	17·0	16·5	16·7
½	66·7	54·1	60·4	17·5	13·1	16·6
1	55·5	46·5	50·7	15·0	13·7	15·8
1½	52·0	48·9	50·5	12·9	14·3	13·4
2	51·7	53·2	52·4	11·8	12·2	12·1
2½	55·0	56·5	55·8	13·3	11·3	12·0
3	53·0	58·0	55·5	15·4	11·3	13·6
6	55·1	56·0	55·5	10·7	10·0	10·6
9	52·0	51·6	51·8	10·2	9·3	9·7
12	51·9	51·8	51·8	14·1	9·1	12·0

No distinct pattern is apparent in the serial values for each baby after the initial fall from the maternal level has occurred. Some babies have an almost constant blood glucose level (e.g. C14, 104); others fluctuate widely (102, 215). With this in mind it was thought that a mean value for the relatively stable period from three to 12 hours was a more suitable basis for comparison with the birth weight of the baby than the single values used by previous workers. These data, birth weight and mean blood glucose values, are given in Table 4. The weights range from 2·6 kg. to 4·5 kg. and the mean glucose concentrations from 32 to 73 mg. per 100 ml. These results are presented diagrammatically in Fig. 3, which shows clearly that there is no correlation between them.

TABLE 4
BIRTH WEIGHT AND MEAN BLOOD GLUCOSE VALUE IN TWO SERIES

Male Babies	Mean Glucose	Weight (100 g.)	Female Babies	Mean Glucose	Weight (100 g.)
C1	32	31	C6	57	28
C3	36	36	C7	58	31
C10	54	29	C8	69	31
C14	51	42	C12	70	32
C15	50	31	C13	35	34
106	53	34	102	53	33
111	49	37	103	47	28
113	43	33	104	46	34
114	61	34	107	58	36
123	48	33	112	48	38
124	57	28	115	58	29
201	58	26	116	49	26
202	44	31	119	53	44
204	52	26	120	55	31
205	42	33	126	51	34
209	58	35	127	54	37
211	70	37	128	44	32
213	54	30	203	50	31
215	73	29	206	56	29
219	45	28	210	57	36
220	64	30	221	62	41
226	57	30	223	58	45
301	64	33	225	59	36

Discussion

In all the cases we have studied we have found the blood of the umbilical vein to contain less glucose than the mother's blood taken at almost the same time, and this can be assumed to be true of late foetal life also. This confirms the work of Morriss (1917), Ketteringham and Austin (1938) and Hanley and Horn (1943).

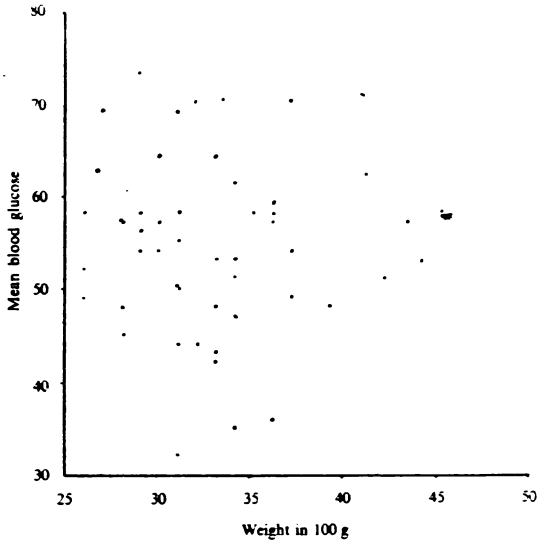

FIG. 3.—Scatter diagram showing birth weight and mean of blood glucose at 3, 6, 9 and 12 hours after birth.

In the values recorded for the umbilical artery the only surprising feature is that in five cases it has equalled that of its accompanying vein (cases 106, 205, 116, 223 and 225), at least within experimental limits. Hanley and Horn also report this in eight of their cases. It appears probable that on all these occasions blood was actually taken from the wrong vessel, an error by no means improbable, for there is considerable difficulty in taking blood from a contracted and pulseless artery in an often oedematous cord.

The apparent stabilization which we found to be progressive throughout the period studied is in accord with the results of McKittrick (1940), who reported increasing stability during the whole of the two-week period of his investigation. Norval, Kennedy and Berkson (1949) on the contrary, found no evidence of stabilization during the first week.

Greenwald and Pennel (1930) reported that the weights of the infants they studied bore no relationship to the infants' blood sugars, and Hanley and Horn (1943), give similar results. The results presented confirm this conclusion, and by having taken a mean blood glucose level as a basis for correlation, the effect of the fluctuation of the baby's blood glucose with the passage of time has been minimized. It had been thought that the failure of earlier workers

to recognize and allow for this fluctuation might account for their inability to detect any correlation of blood glucose with birth weight. This proved not to be the case.

The main result of this study, is however, to provide a background against which future blood glucose estimations can be considered. In the past the terms hypoglycaemic and hyperglycaemic have been applied to newborn babies whose blood glucose level was within the range of twice the standard deviation, either side of the mean, a range which includes 95% of the results of a normal distribution. In numerical terms we would suggest that all values between 30 and 75 mg. per 100 ml. are quite likely to be found in normal babies if the blood glucose is estimated by the method we have used, and the baby is between 1 and 12 hours old. Within the first hour, the baby's blood glucose is largely dependent on the widely variable blood glucose of its mother, and this might contain in itself important considerations from a clinical point of view.

Our object in this work was to determine a basis for extended studies of the clinical and biochemical indices of birth injury, and we realize that our strict criteria of normality restrict this basis to a limited number of babies and one type of delivery. It is proposed to publish shortly results relating to certain other types of delivery and later to 'injured' babies, where 'injured' will be interpreted in the widest sense. Work is also in progress to establish the mechanisms by which the physiological adjustments to birth are controlled.

Summary

Previous work on the blood glucose level of newborn babies is reviewed briefly, and the absence of intensive serial study noted.

Results are presented to show the changes which took place in 46 normal babies, born spontaneously to normal, unanaesthetized mothers.

It was found that during the first hour after delivery, the babies' blood glucose fell from 79 mg. per 100 ml., as found in the umbilical vein, to a mean value of 52 mg. per 100 ml., and that this level was maintained with varying constancy by individual babies.

From a total of 356 estimations it is concluded that the normal blood glucose range for babies between 1 and 12 hours old is 30 to 75 mg. per 100 ml.

This range appears to narrow slightly but progressively during this period.

There is no difference in blood glucose between male and female babies.

There is no relationship between the birth weight of these full term babies and the mean of its blood glucose at 3, 6, 9 and 12 hours.

The authors have pleasure in acknowledging their indebtedness to Professor A. V. Neale, who directed their attention to the problems of carbohydrate metabolism in the period immediately following birth and in whose department they were successive 'Cow and Gate' research fellows; also to the Obstetric and Paediatric Staff of Southmead Hospital, Bristol, for the clinical facilities, and especially to Dr. F. J. W. Lewis, Pathologist in Charge, Southmead Hospital, who took great interest in their work throughout, in whose department one of them was assistant clinical pathologist during part of the time when this study was in progress, and who made available the services of Mr. C. N. Chapman, who undertook a considerable number of the actual chemical estimations of the blood sugar, and whose separate paper on the experimental analysis of the accuracy and technique of this method has been prepared.

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