SOME ASPECTS OF STARVATION IN THE NEWBORN BABY

BY

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Most babies begin to take milk feeds within two or three days of birth and thereafter their intakes of milk steadily increase during the first week and a large proportion of the materials they derive from the digestion of such feeds is retained. This normal process may be hindered by the repeated vomiting exhibited by some premature babies, in the absence of any apparent organic cause except their prematurity, and also by vomiting associated with organic intestinal obstruction by duodenal or jejunal atresia or volvulus of the midgut. Even when the obstruction has been relieved by operation, because of post-operative delay in gastric emptying or intestinal ileus another five or six days may elapse before an intake of milk is achieved; during this time starvation may be almost complete, being relieved only by small quantities of dextrose administered by intravenous infusion, which provide only a small fraction of the total calorie requirements of such babies. There have been few studies of deprivation of this degree, though Rickham (1957) reported a newborn baby who was almost completely starved for 10 days after birth and was submitted to two operations for duodenal cyst and intestinal obstruction.

During a series of metabolic studies of newborn babies we have been able to observe a premature baby who, because of vomiting, was not fed milk for 10 days after birth. Another baby, with jejunal atresia and meconium obstruction, was submitted to two operations and was not fed milk for 16 days after birth.

Methods

These babies were nursed throughout in incubators at a temperature of 85° F. (29·4° C.); humidity was not measured. The methods of collection and analysis were as described by Stevens, Hughes, and Wilkinson (1962).

Case Reports

Case 1 (Table 1). Male, 3 lb. 5 oz. (1·5 kg.), 32 weeks' pregnancy; cyanosed at birth, responded to sucking out, vomited small amounts of bile-stained fluid repeatedly from 48 hours after birth. On admission, 66 hours after birth, his condition was good but there was some abdominal distension and meconium had not been passed. After admission there was no more vomiting and evidence of organic obstruction was not found, some dilated loops of intestine could be seen and felt in the abdomen, peristalsis was visible but an upright radiograph showed gas shadows throughout the small and large intestine, and radiograph after barium enema did not show any sign of Hirschsprung's disease; diagnosis, intestinal inertia due to prematurity.

Metabolic balance study started six hours after admission. The baby was kept in an incubator at 85° F. (29·4° C.), nothing being given by mouth until 60 hours after admission when 10 ml. 0·18% saline in 4·3% dextrose every hour was started, alternately by bottle and nasogastric tube. Aspirations were small and not bile-stained, except for 12 ml. on 7th day of life. On the 8th day there was a sudden deterioration in general condition, the pulse rate falling to 60 a minute and the temperature to 91·2° F. (32·9° C.), but the condition improved soon after oral saline was stopped and the tube was removed. Six hours later oral feeds were started, 5 ml. 5% dextrose every hour increasing to 15 ml. which was continued for three days. On the 10th day, 3 ml. of olive oil was administered per rectum, and meconium was first passed on 10th day. On the 11th day feeds of half strength expressed breast milk, 15 ml. three-hourly started, increased to three-quarter strength after 24 hours and given in increasing volumes until 17th day of life, when full strength feeds were given. The infant continued to make good progress, but body temperature remained subnormal throughout, in spite of remaining in incubator. He vomited occasionally after feeds and during the night. Streptomycin 15 mg. i.m. was given six-hourly from the 8th to the 15th day. He was sent home on 22nd day of life, and subsequent progress gave no further cause for anxiety.

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TABLE 1
CLINICAL COURSE OF CASE 1

<i>Plasma electrolytes and blood urea</i>																				
Sodium (mEq/l.)	135	155			149	146	146	143	143								141			
Potassium (mEq/l.)	—	6.7			8.5	5.8	5.4	4.4	4.7								5.9			
Chloride (mEq/l.)	—	114			124	109	—	107	112								103			
Bicarbonate (mM/l.)	—	17			15	19	21	28	24								19			
Urea (mg./100 ml.)	79	75			50	37	30	21	24								19			
Bilirubin (mg./100 ml.)	7.6	14			12.9	14	—	12.8	12.6								—			
Haemoglobin (%)	134				147		135										137			
Plasma protein (g./100 ml.)							5.0										5.0			
P.C.V. (%)						67														
<i>Oral feeds (ml.)</i>																				
5% dextrose						81	100	120												
4.3% dextrose				65	225	153														
0.18% saline																				
1-strength E.B.M.*									120											
1-strength E.B.M.										120	160	200	200	240	227	225	240	300	300	
Full-strength E.B.M.																				
Age in days	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	

Note: Case 1 was admitted at the end of the 2nd day of life. * E.B.M. = expressed breast milk.
—, no estimation.

TABLE 2
CLINICAL COURSE OF CASE 2

<i>Plasma electrolytes and blood urea</i>																				
Sodium (mEq/l.)	141	141	138	134	133	129		141	143	143	133	138	141	133			138	—		
Potassium (mEq/l.)	6.6	7.0	6.8	6.7	6.6	6.1		6.2	5.6	5.6	5.9	5.2	3.5	5.5			6.3	6.5		
Chloride (mEq/l.)	101	103	108	95	102	108		95	91	92	92	93	93	95			92	88		
Bicarbonate (mM/l.)	—	23	45	—	24	—		36	31	29	32	31	33	31			35	37		
Urea (mg./100 ml.)	29	37	—	34	37	27		28	77	37	34	31	30	25			53	60		
Haemoglobin (%)	152		128		123			110	93		99						110			
P.C.V. (%)					63				45											
Plasma protein (g./100 ml.)																	4.7			
<i>Intravenous fluid (ml.)</i>																				
Blood		30						25			20									
Plasma																		100		
M 6 lactate							128	67												
4.3 dextrose			127	115	126	128	111	29	99	114	93	112	37							10
0.18% saline																				
<i>Feeds orally or by ileostomy (ml.)</i>																				
5% dextrose												35	60	60	335	340				
1-strength E.B.M.*																	225			
1-strength E.B.M.																	100	340	255	
H.T.F.† + aminosol																	50	345	15	
Age in days	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	

Note: First operation was at the end of the 3rd day and the second operation was at the end of the 10th day.

* E.B.M. = expressed breast milk. † H.T.F. = Humanized Trufood. —, no estimation.

Case 2 (Table 2). Male, 6 lb. 12½ oz. (3.083 kg.), born after normal pregnancy, prolonged difficult labour, had blue asphyxia but recovered well. At first he fed well from the breast, but from the 2nd day vomited bile-stained fluid repeatedly, only two small pellets of whitish-brown material being passed from the anus. He was admitted three days after birth, and was ill, jaundiced, with distended abdomen and loud bowel sounds. At operation, jejunal atresia 34 in. (95 cm.) from duodeno-jejunal flexure; 24 in. (60 cm.) of normal terminal ileum contained small pellets of greenish sticky meconium. Dilated terminal jejunum was resected with an end-to-end anastomosis between ileum and jejunum. At first the post-operative condition was satisfactory but only white pellets of meconium were passed. After three days, aspirations became thicker and

green, the abdomen was distended and the bowel sounds louder; abdominal distension continued to increase for seven days after first operation. On the 10th day of life the abdomen was reopened through the previous incision. The anastomosis had broken down because of distension of bowel with inspissated meconium, and a localized abscess had formed; above this level the jejunum had perforated. The anastomosis was taken down, the proximal end of the ileum was brought to the surface of the abdominal wall as an ileostomy, and the distal end of the jejunum was anastomosed to the side of the ileum near the ileostomy. Intramuscular injections of 10 mg. hydrocortisone were given daily from 11th to 16th days.

Little fluid was drained from ileostomy, but 5 ml. 5% dextrose solution was injected into ileostomy and by

FIG. 1.—Case 1: sodium, potassium, and nitrogen balances, calorie intake, weight, fluid intake, and urine output during the 19 days of study.

In Figs. 1 and 2 intake has been plotted up from the baseline and output down from the intake line; negative balance shows below the baseline and positive balance is indicated by the clear area above the baseline.

FIG. 2.—Case 2: sodium, potassium, and nitrogen balances, calorie intake, weight, fluid intake, and urine output during the 13 days of study.

mouth every hour from 3rd day after second operation and the quantity was later increased. On 18th day of life, ileostomy began to discharge and the wound to break down. Oral and ileostomy feeds of milk were begun on the 17th day of life, seven days after second operation, and two days later amino acid solution was added to feeds. A fistula developed from the small intestine above the ileostomy, the wound gaped, and the general condition became very poor. The infant died after 20 days.

Metabolic Studies

Details are given in Figs. 1 and 2 and Tables 1 and 2.

In *Case 1* these lasted from the 3rd until the 21st day of life and can be divided into two periods; eight days of starvation mitigated only by 4.3% dextrose in 0.18% saline or 5% dextrose solution followed by 11 days when milk feeds of gradually increasing strength and volume were provided. In *Case 2* the balance study lasted from the 4th to the 16th days; from the 4th to 15th days an intravenous infusion of 4.3% dextrose in 0.18% saline was maintained to which sodium lactate was added on the 9th and 10th days. From the 13th to 16th days 5% dextrose solution was given by mouth and by ileostomy.

Urine Volume. In *Case 1*, the volume of urine passed was consistently low, even for a small premature infant, especially during the administration of saline on the 5th and 6th days, but rose when dextrose alone was given on the 8th and 9th days. During the period of establishment of milk feeds, the urine volume remained above 35 ml./24 hours. The largest output was 108 ml. on the 14th day. *Case 2* weighed 3.00 kg. on admission but he passed volumes of urine which exceeded 50 ml./day on only three occasions and were of the same order as those passed by *Case 1* who weighed only half as much.

Nitrogen Balance. In *Case 1*, since he took no milk until the 11th day and a stool was not passed until the 10th day, for the first nine days the negative balance was related entirely to losses in the urine. These losses were high, averaging 176 mg./24 hours during the first three days, more than twice the amount excreted in the urine when milk feeds were first started. As soon as milk was given, the nitrogen balance became positive and absorption was over 80% from the 12th day. The intake was at first small and retention did not reach 70% until the intake rose to 292 mg. on the 15th day. From the 12th day body weight increased and there was little variation in urine nitrogen.

Case 2 took no milk during the balance study, and the negative nitrogen balance reflects the large losses of nitrogen (in the urine 85.4%, gastric aspirations 13%, faeces 1.6%). The nitrogen loss in the urine was much larger than in *Case 1*, though the daily volumes of urine were similar. The urinary nitrogen was particularly high on the three days before the second operation, associated with intra-abdominal infection. Urinary nitrogen output declined during the four days following the first operation but rose during the four days after the second operation at which time it appeared to be proportional to the urine volume; on the 15th and 16th days both the urinary

volume and the urinary nitrogen output fell. The total loss of nitrogen during the 13 days was 4.663 g. equivalent to 29 g. protein.

Potassium Balance. In *Case 1* from the 3rd to 6th days, the potassium output in the urine fell from 1.32 to 0.22 mEq/24 hours and then remained between 0.14 and 0.21 mEq/24 hours until milk feeds began. The potassium: nitrogen ratios for the urine losses fell from 6.8 on the 3rd day of life to 2.1 on the 8th day. For 8 days, until milk was fed, the total loss of potassium was 3.79 mEq and of nitrogen was 935 mg. (potassium: nitrogen ratio 4:1).

In *Case 2* the potassium balance was negative throughout the balance study, the largest loss in the urine, 1.69 mEq on the 10th day, just before the second operation was associated with a large output of nitrogen. The urinary loss of potassium exceeded 0.6 mEq/day on only two other days and the total over 13 days was only 7.11 mEq. During the last two days of the study and on the 6th, 7th, and 8th days before the administration of sodium lactate, more potassium was lost in the gastric aspiration than in the urine. On the day potassium was first fed to *Case 1*, absorption exceeded 80% and the balance was positive. The average urinary loss of potassium which had been 0.18 mEq/24 hours during the last 4 days before feeding rose to 0.38 from the 11th to 14th days. Further increases in potassium intake from the 15th to the 21st days (mean 1.79 mEq/24 hours) were accompanied by increases in the urinary potassium excretion to an average of 0.58 mEq/24 hours. During the last seven days, 60% of the intake was retained compared with 76% for nitrogen.

Sodium Balance. In *Case 1* the urinary output was highest on the 3rd and 4th days of life and fell during the three days on which 4.3% dextrose in 0.18% saline was given by mouth. There was a negative balance of 3.82 mEq on the 3rd and 4th days and positive balance of 9.57 mEq during the three days saline was given, followed by a total negative balance of 7.27 mEq from the 8th to 14th days inclusive. There was an over-all negative balance of sodium of 1.52 mEq during the 3rd to the 14th day.

In *Case 2* there were considerable losses of sodium in the stools from the 5th to 8th days. The losses in the urine did not exceed 1.0 mEq except on the 10th and 11th days following the intravenous infusion of 33 mEq of sodium as sodium lactate on the 9th and 10th days. The small loss on the 9th day when the intake was 20.74 mEq is very striking. The sodium balance was negative only on the 11th day. There were large losses by suction from the 3rd to 8th days and in the faeces on the 15th and 16th days.

Blood Chemistry (Table 1). In *Case 1* on admission the serum sodium concentration was low, but rose within 24 hours to 155 mEq/litre in the absence of any intake and fell two days later and remained within the normal limits thereafter. The serum potassium concentration was high on the 7th day, but otherwise was well maintained. The chloride concentration was generally raised and bicarbonate was at first low. The urea concentration was raised

TABLE 3
DAILY POTASSIUM: NITROGEN RETENTION RATIO IN CASES 1 AND 2 (mEq/g.)

		Day of Life																			
		3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	
Case 1	...	6.8	4.8	3.4	3.2	2.3	2.1	2.2	3.5		7.8	4.6	2.4	4.2	3.9	2.7	2.2	4.7	2.4	3.1	
Case 2	...		3.3	2.5	1.5	3.7	1.4	0.9	2.7	2.9	3.9	1.9	1.9	2.2	1.3						

on admission and did not fall for several days, but there did not seem to be much relation between urine volume, total nitrogen excretion, and the blood urea concentration.

In *Case 2* on admission, the serum chemistry was within the normal range. Sodium concentration declined slowly until sodium lactate was given on the 9th day. This was probably due as much to dilution by the infusion of 0.18% saline as to the loss of sodium in aspirated fluid. Very little sodium was lost in the urine except on the 10th and 11th days following the lactate infusion. Bicarbonate was raised from the 10th day in association with a low chloride concentration. Blood urea rose after the second operation.

Potassium : Nitrogen Ratios. The ratios between potassium and nitrogen balances are shown in Table 3. In *Case 1* at first, during the period of negative balances, the ratio was high, probably because of intracellular dehydration and a higher rate of loss of potassium in the urine. On the 12th day, the high ratio was due to the greater retention of potassium when the balances of both potassium and nitrogen had become positive following the starting of milk feeds. In *Case 2*, the ratio exceeded 3.0 on three days and was below 2.0 on six days. This, perhaps, indicates as well as the actual balances, the small losses of potassium both in the urine and by gastric aspiration.

Changes in Body Weight. In *Case 1* during the initial three-day period of starvation, the weight fell by 8.75%, which resembles that of a baby, from our earlier series of normals, who lost 9.75% in the first three days (birth weight 3.87 kg.), but who received 31 ml. milk per day (less than 0.1% body weight) on the first two days and only 15 ml. on the third day (Wilkinson, Stevens, and Hughes, 1962). In *Case 1*, the oral administration of a solution containing 0.18% sodium chloride and 4.3% dextrose and of a 5% solution of dextrose was associated with a temporary increase in weight followed by a slow fall as the water and sodium were excreted; reference to Fig. 1 shows that the weight of this baby did not begin to rise again until the 12th day when the equivalent of most of the sodium administered on the 5th to 7th days had been excreted.

In *Case 2* there was a much slower fall in weight associated with the intravenous administration of 0.18% sodium chloride in 4.3% dextrose and sodium lactate solution. In spite of this, by the 15th day of life, weight loss amounted to 21% of the body weight on admission.

Discussion

These two babies showed remarkable capacity to tolerate starvation in very different circumstances. In *Case 1*, during the first four days of life, starvation was complete. During the next six days, the total caloric intake never exceeded 40 per day (26 calories per kg.) and was usually less than 30 per day (20 calories per kg.), the water intake varied from 65 to 225 ml. per day, and the sodium intake also fluctuated up to 6.3 mEq per day. Even from the 11th to the 16th days, the milk intake provided less than the recommended requirement of 120 calories per kg. per day (Levine, 1956), and his progress might have been even more rapid if milk feeds had been larger. For 16 days the caloric intake of *Case 2* was confined to small quantities of glucose in the fluids administered by infusion or by mouth and reached a total of more than 50 calories per day (22 calories per kg.) only on the 16th day of life; on only three earlier days did the total calories reach 20 per day (7 calories per kg.). Gamble (1947) showed that the consumption of 100 g. glucose per day by an otherwise starving adult who was allowed free access to water reduced the consumption of body protein by about one half and prevented ketosis. It is not known how much glucose or its equivalent is needed to produce a similar effect on the newborn baby, but in *Case 1* reduction in the urinary output of nitrogen was associated with the consumption of 10 g. glucose (25 calories per kg.) on the 6th day and 6.5 g. (16 calories per kg.) on the 7th day. McCance and Strangeways (1954) found that tissue katabolism was less marked in newborn infants than in adults subjected to comparable degrees of starvation and the ratio of potassium to nitrogen in the urine was twice as great. In both our cases there was a good deal of variation in the urinary potassium : nitrogen ratio; in *Case 1* it was 6.8 at first and then fell to less than 3, but in *Case 2* it was never above 3.7 and in general was lower than in *Case 1*. When expressed per kg. body weight per 24 hours the urinary outputs of both potassium and nitrogen were rather lower than they would have been in adults.

In *Case 1* the oral administration of sodium and water between the 5th and 7th days seemed to produce

improvement in the appearance and clinical state of the baby, and survival following the earlier losses of gastro-intestinal fluid by vomiting may have depended in part on this provision. Nevertheless, the equivalent of nearly all this sodium was excreted in the urine by the 15th day of life and only then did sodium balance become positive, even though the balances of potassium and nitrogen had already been positive for four days since the oral intake of milk had been started. In this baby, who was premature, there was little if any relation between the volume of the urine and its content of sodium. During the first two days of the study, the sodium output in the urine was large, but declined when dilute (0.18%) saline was administered by mouth; there was also a reduction in the serum sodium concentration and it seems possible that both the reduction in sodium excretion and the fall in serum sodium concentration were due to the administration of water in excess of sodium.

It should be noted that in *Case 2* there was almost no change in the rate of water intake at the time of the administration of the sodium whereas in *Case 1* although the sodium load was rather less in terms of body weight (8 mEq/kg. compared with 11 mEq/kg.) the water load was much larger (308 ml./kg. compared with 77 ml./kg.). In *Case 2*, though the urinary output of sodium was increased, most of the added sodium was retained. Though this baby suffered from fibrocystic disease it is unlikely that at this stage this would much affect the sodium balance.

The behaviour of these two babies is similar to that of puppies given water instead of milk (McCance and Widdowson, 1958) or infants or piglets to whose milk supply salt has been added (McCance and Widdowson, 1957). This poor excretory capacity for additional loads of water or sodium chloride is not surprising when it is remembered that a baby who is fed human breast milk absorbs about 80% and retains about 65% of the materials in the milk; the excretory capacity of the kidneys seems to be related to this normal need to excrete the equivalent of only about 15% of the intake.

Changes in body weight must be interpreted with great care. In *Case 1* the rapid loss on the 4th to 6th days was due to vomiting as well as starvation but the continued loss from the 8th to 12th days due to the excretion of sodium and water was offset by retention of some of the materials in the milk which was being consumed. In *Case 2* loss of weight was not much affected by the continuous intravenous infusions. A rise or the maintenance of weight which is due to the administration of fluid by intravenous infusion is not of the same significance as when it is the result of the consumption, digestion, and absorption of milk.

During the 12 days of metabolic study of *Case 2* only about 360 calories were provided as dextrose. The total basal requirements for the whole of this period, i.e. 42 calories per kg. per 24 hours (Benedict and Talbot, 1915) were about 1,600 calories of which 1,200 would have had to be derived from the infant's own tissues. The requirements for full activity, i.e. 92 calories per kg. per 24 hours (Smith, 1959) would amount to about 3,600 over 12 days for this child of which about 3,200 would have to be endogenous. In these 12 days this baby lost 600 g. in weight equal to 20% of his birth weight. The negative nitrogen balance of 4.663 g. is equivalent to 29 g. protein ($N \times 6.25$) or 140 g. of wet muscle out of the total weight loss of 600 g. This baby was born at term and was not oedematous and the remaining 460 g. of weight lost might be either fluid, glycogen, or fat. The volumes of fluids administered by intravenous infusion were about equal to the expected insensible water loss and the small volumes of urine which were passed, which precludes a disproportionate loss of body water. Even the provision of the basal energy requirements would involve the complete oxidation of 157 g. fat and it is likely that the incomplete oxidation that occurs in starvation would result in the destruction of a larger quantity than this. Based on the figures of Widdowson and Spray (1951) the total body protein and fat of this baby at birth were 360 g. and 480 g. respectively so that it seems likely that only 8% (29 g.) of the protein but perhaps more than 30% of the fat was consumed during these 12 days of starvation.

The main purpose of this report is to draw attention to the severe degree of partial or complete starvation which not uncommonly may be inflicted on newborn babies, and to their tolerance of it for a prolonged time. Clearly the sooner such patients are fed the better. In some circumstances this may require the use of a jejunostomy rather than parenteral methods if the requirements for growth as well as daily maintenance are to be fully satisfied.

We are indebted to the nursing staff of The Hospital for Sick Children without whose help in the collection of the specimens these studies would have been impossible. During the course of this investigation one of us (L.H.S.) held a Nuffield Fellowship and another (A.W.W.) was in receipt of a personal grant from the Medical Research Council.

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