Food, Growth and Homoeostasis in the First Week of Life

By

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From the time an animal is conceived until it dies the volume and composition of its body fluids must be maintained within well-defined limits and, whatever mechanisms are responsible before birth, the moment the animal is born its own organs must take over full responsibility. We know that the kidneys of the newborn animal or baby are functionally "immature". Young babies, particularly premature babies, have low urea clearances and glomerular filtration rates, and this is true whether they are compared with adults on the basis of surface area or of body weight (Table 1). This has in fact been one of the main reasons for condemning the infant kidney as inefficient. But so long as urea excretion keeps up with protein catabolism so that the concentration of urea in the blood does not rise the kidney must be doing all that is required of it.

Table 1
Urea and Inulin Clearances of Newborn Babies and Adults
(ml per min)

	per 1.73 sq. in.	per 70 kg
Inulin clearance		
Infant	17	42
Adult.	75	75
Urea clearance		
Infant	34	82
Adult.	120	120

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Table 2 shows some results we have obtained for the nitrogen intakes and excretions of babies in the first week of life [5]. On the first and second days they had no food and catabolised some of their own tissue protein to provide part of the energy they required. Their kidneys did not excrete all the end products of protein catabolism, and the level of urea in the body fluids rose. By the time they were one week old, the breast-fed babies were taking in 400 mg nitrogen per kg body-weight per day. They absorbed about 80 per cent of this, and they retained over 50 per cent for purposes of growth.They excreted in in the urine an amount of nitrogen equivalent to only 25 per cent of the intake, and by this time their renal function had matured sufficiently far for them to do this, and the level of

TABLE 2

Nitrogen Balances of Babies in the First Week of Life

	Day 1	Day 2	Days 6—8	
			Breast milk	Cow's milk formula
N intake mg/kg/24h	0	0	397	598
N in urine ,, ...	40	70	117	221
N in faeces ,, ...	—	—	67	73
N „balance" ,, ...	−40	−70	+213	+340
Blood urea mg/100 ml	22.4	37.2	17.5	37.9

TABLE 3

Nitrogen Balances of Newborn Piglets and Puppies which were "Fed" and "Not Fed"

	Piglets given: —		Puppies given: —	
	Milk	Water	Milk	Water
N intake mg/kg/24h	3500	0	2500	0
N output ,, ...	350	250	246	194
N „balance" ,, ...	+3150	−250	+2254	−194
Blood urea mg/100 ml	30.4	35.7	86.2	38.7

TABLE 4

Potas, um Balances of Babies in the First Week of Life
(mEq/kg/24 hr)

	Day 1	Day 2	Days 6—8	
			Breast milk	Cow's milk formula
K intake	0	0	2.28	4.56
K in urine	0.35	0.41	0.70	1.94
K in faeces	—	—	0.38	0.58
K „balance"	−0.35	−0.41	+1.20	+2.04

urea in the blood had fallen again to a low level. In spite of this, if the urea clearances of these week-old breast-fed babies are calculated they appear very low by adult standards, as babies' clearances always do, but this in itself is no indication that their kidneys are inefficient. When we consider that by the seventh day the full-term breast-fed baby is dealing with twice as much protein per kilogram body-weight as an adult who is having 100 g of protein

TABLE 5

Effect of Giving KCl and Water or KCl and Milk to Newborn Piglets

	Water	K Water	Milk	K Milk
K intake (mEq/kg/24hr)	0	26	8.0	27
K excreted (mEq/kg/24hr)	3.9	23.1	1.6	16.5
K „balance" (mEq/kg/24hr)	−3.9	+2.9	+6.4	+10.5
Serum K (mEq/l)	4.3	9.3	4.3	5.9
Signs of toxicity	None	Paralysed	None	None
Change in body weight (mg/kg birth weight)	−111	−104	+109	+103

a day, and his blood urea is falling, we realise the vital importance of the stabilising effect of growth at this time of life. The babies having cow's milk preparations had a higher nitrogen intake than the breast-fed babies; Table 2 shows that they retained a little more; they excreted twice as much nitrogen in the urine, but the concentration of urea in their body fluids was higher. Mother's milk is just right for the integration of growth and renal function in each species, and it is no stranger that cow's milk should more than saturate a baby's growth requirements for nitrogen than that human milk should not support the growth requirements of fast-growing newborn rats.

The human infant grows very slowly compared with many mammals. The piglet and puppy grow much more rapidly, for they both double their birth weight in the first week, whereas the human baby takes 6 months to do so. Table 3 shows the nitrogen balances of piglets and puppies which were fed with sow's or dog's milk by stomach tube for the first one or two days of their lives [2, 3]. The nitrogen intakes per kg of body weight were 6—9 times as high as those of breast-fed babies, but these animals were perfectly well able to deal with all this nitrogen, for they used 90 per cent of it for purposes of growth, and this left only 10 per cent or so to be excreted by the kidney as urea. Piglets and puppies that received nothing but water, and were therefore not able to grow, excreted nearly as much nitrogen in their urine as their fed littermates: and this nitrogen came from the catabolism of their own tissue protein. It is true that the blood urea of the fed piglets rose from the newborn level of 20 to 30 mg/100 ml, but this rise of 10 mg/100 ml accounts for only 25 of the 3150 mg of nitrogen that were retained. The blood urea of the puppies rose more, but even here the rise to 86 mg/100 ml accounts for only 300 mg of the 2200 mg retained. All the rest was used for purposes of growth, and growth far outweighed the importance of the kidney in maintaining nitrogen homoeostasis in these fast growing animals.

Table 4 shows the intakes, excretions and retentions of potassium by the babies whose nitrogen balances are shown in Table 2. The balances were negative on the first and second days when the babies had no food, but by the 6th—8th day they were positive both on breast milk and cow's milk. The intake of potassium from the cow's milk formula was almost twice as high, as it was from breast milk, and the retentions were also almost twice as high. This high retention of potassium from cow's milk has been observed previously by Clement Smith and others, particularly in premature babies and, knowing that it has so far remained a puzzle as to where bottle-fed babies store the extra potassium they retain, we have taken up this problem in piglets. We have given newborn piglets sow's milk, or sow's milk plus added potassium chloride, or water only, or water plus potassium chloride by stomach tube for the first two days of life, and have followed the excretions of potassium and the body composition at the end [4]. Table 5 shows the effect of these treatments on the serum potassium and on the excretions and retentions. The animal having water only, and therefore no potassium by mouth, excreted more potassium than the piglet having sow's milk providing 8 mEq of potassium per kg per 24 hours. The piglet having water was not able to grow, but the one having milk was growing rapidly. When extra potassium was added the animal that was fed incorporated into its body tissue or excreted the extra load of potassium without any great rise in serum potassium and without any clinical symptoms. The one having potassium chloride in water could not grow. It became paralysed, in spite of the fact that it retained very much less potassium, less even than the piglet having sow's milk alone, and this again emphasises the importance of growth as a homoeostatic mechanism. Table 6 shows

TABLE 6

Effect of KCl on the Composition of Piglet Muscle

	K mEq/kg	mEq K/gN
At birth	73	4.7
40 hr old given:		
Water	75	4.9
Water + KCl	92	6.3
Milk	69	4.7
Milk + KCl	74	5.1

the composition of the skeletal muscle of these piglets. If we reckon the skeletal muscle accounts for about 25 per cent of the weight of the newborn piglet, then a rise of 17 mEq K per kg of muscle is equivalent to 4.2 mEq per kg of body weight, which accounts for a large part of the potassium retained by the piglet given KCL in water. The K/N ratio in the muscle of both the fed and unfed animals having additional potassium was mate-

TABLE 7

Effect of Food and Growth on Phosphorus Homoeostasis in Newborn Infants

	1st Day	2nd Day	7th Day	
			Breast milk	Cow's milk formula
P intake (mg/kg/24hr)	0	0	20	100
P in urine (mg/kg/24hr)	0.2	4.2	0.4	40
Serum P (mg/100 ml)	6.1 (at birth)	7.9	6.8	9.0

rially altered, but what the changes were at cell level is quite unknown.

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Table 7 shows the effect of food and growth on phosphorus homoeostasis in newborn babies [6]. The level of phosphorus in the serum of the baby at birth is well known to be higher than that of its mother. The average value we found in this series of babies was 6.1 mg per 100 ml, while their mothers had an average value of 3.9 mg per 100 ml. The average concentration rose in the first two days of life, then fell again if the babies were breast-fed and rose still further if they were having a cow's milk formula. There is nothing new in this — it has been shown many times before, but the pattern of urinary excretion is perhaps not so well known. The excretion was very low on the first day, but it was significantly higher on the second day when the serum level was rising. This was a manifestation of starvation and tissue breakdown. By the seventh day the average intake of phosphorus by the breast-fed infants had risen to 20 mg/kg/day, but in spite of this the excretion of phosphorus in the urine had fallen to 0.4 mg/kg. The babies fed on a cow's milk formula had intakes of 100 mg/kg and they excreted 40 mg which is much more than the babies getting breast milk or than any of the babies in the first 48 hours. The capacity of the babies to incorporate phosphorus into their growing tissues was evidently more than saturated and the excess was excreted in the urine. The bones and soft tissues both take up phosphorus, and since the urine of the

TABLE 8

Intake and Urinary Excretion of Phosphorus by Starving and Well-fed Piglets (mg per kg per 24 hr)

Experiment	Water only		Fed cow's milk	
	Intake	Urine	Intake	Urine
1	0	15.2	352	0.6
2	0	7.3	420	1.8
3	0	11.0	370	1.7
4	0	6.9	435	2.6
Mean	0	10.1	394	1.7

breast-fed babies contained so little phosphorus it makes one wonder whether their capacity to incorporate phosphorus into their growing tissues was fully met.

Table 8 shows the intakes and urinary excretions of phosphorus by newborn piglets fed on sow's milk or water for the first two days after birth [6]. In spite of the large amounts of phosphorus ingested with the milk, the animals given milk excreted much less phosphorus than those given water. The effects of food and starvation, therefore, are just the same in the piglet as in the human baby, and again it is seen how nicely the amount of phosphorus in mother's milk has been adjusted by nature to satisfy the growth requirements of her young. The intakes and retentions of phosphorus by the piglets were 20 times higher per kg than those of the babies, and this is no doubt related to their more rapid growth.

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We have recently been studying the absorptions, excretions and retentions of strontium, calcium and magnesium by breast-fed and bottle-fed babies one week old. Table 9 shows the calcium and magnesium balances [5]. All the babies retained calcium and magnesium and the babies having the cow's milk preparation, which contained more of these elements than breast milk, retained more. This is a well-known fact, but what has not been appreciated hitherto is that, in spite of the higher intakes and absorptions on cow's milk, the urinary excretion is lower. We think the reason is that the small amount of phosphorus in breast milk is limiting the deposition of calcium and magnesium in bone. The ratio of phosphorus to calcium is higher in cow's milk than is breast milk. The extra phosphorus enables the bottle-fed babies to utilise more of the calcium and magnesium in cow's milk, so that less of these two metals is excreted in the urine. We put this theory to the test by giving breast-fed babies a solution of neutral sodium and potassium phosphates. The urinary excretion of calcium and magnesium fell to levels quite as low as they were in babies receiving cow's milk.

Table 10 shows the average results we have obtained for strontium [7]. The strontium intake was far higher on cow's milk preparations than on

TABLE 9

Intake, Urinary Excretion and Retention of Calcium and Magnesium by Breast-fed and Bottle-fed Babies (mg per kg per 24 hr)

Type of food	Calcium			Magnesium		
	intake	excretion in urine	retention	intake	excretion in urine	retention
Breast milk	36	5	15	3.5	0.6	1.6
Cow's milk preparation	135	2	79	10.5	0.3	6.7

TABLE 10

Intake, Excretion, Absorption and Retention of Strontium by Breast-fed and Bottle-fed Babies (μg per kg per 24 hr)

Type of food	Intake	Excretion			Absorption	Retention
		urine	faeces	total		
Breast milk	8	14	14	28	−6	−20
Special cow's milk preparation	36	2	24	26	+12	+10
Commercial cow's milk preparation	72	2	19	21	+53	+51

breast-milk; we used two different cow's milk preparations, one of which contained twice as much strontium as the other. In spite of this the breast-fed babies excreted much more strontium in their urine, just as they did more calcium and magnesium, and probably for the same reason, for additional phosphate reduced their excretion of strontium to a very low level.

Both urine and faeces of the breast-fed babies contained more strontium than the food. These babies were therefore excreting the strontium that was in their bodies at birth, and if we reckon that the bones of a newborn baby contain 5 mg of strontium, then supposing the excretion continued at the observed rate, in about 3 months the breast-fed baby would have had no strontium left inside it.

All the babies receiving the cow's milk preparations retained strontium and the amount retained depended upon the amount in the milk. If the retention had continued at this rate, then those having the commercial cow's milk preparation would have doubled the amount of strontium in their bodies in about one month.

Our investigations have been limited to the metabolism of stable strontium. If the ratio between stable and radioactive strontium is the same in the food as in the body, then the radioactive component will behave in the same way as the stable element as regards its absorption and excretion, so these results give some indication as to what may be happening to strontium^{90}. The baby of today already has some strontium^{90} in its bones at birth. During the first months of life the source of strontium^{90} for the breast-fed baby is its mother's milk: and the negative balance for stable strontium makes it unlikely that any strontium^{90} will be retained so long as the baby is fully breast-fed. Infants receiving cow's milk preparations containing more strontium^{90} than breast milk, probably retain a portion of the strontium^{90} along with the stable element. They are therefore likely to have more strontium^{90} in their bodies than breast-fed babies, first because more is ingested, and second because a higher proportion of the intake is retained.

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