The ratio of RNA-P: total protein, on the other hand, shows an increase in both the homogenate and 'soluble' fraction; this results from the lowering in the total protein value used in this calculation as a consequence of the removal of milk protein.

SUMMARY

1. The distribution of total protein and ribonucleic acid phosphorus in five fractions of the rat mammary gland have been determined at three stages of the lactation cycle: on the twentieth day of pregnancy and on the third and eighteenth days of lactation.

2. At the end of pregnancy, ribonucleic acid phosphorus is largely localized in the 'soluble' fraction of the mammary gland. Lactation produces a redistribution of total ribonucleic acid phosphorus such that the majority of it is found in the smaller particulate fractions of the tissue suspension.

3. Lactation produces a relative increase in the amount of protein associated with the smaller particulate fractions at the expense of the 'large-particle' fraction. All these fractions, however, show an increase in total amount from late pregnancy to late lactation.

4. The ratio of ribonucleic acid phosphorus to total protein is low in all fractions in late pregnancy but has risen to a high value in the 'small-particle' fraction by the end of lactation.

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The Excretion of Urea, Ammonia and Purine End-products by the Newborn Animal

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It is usually taught that mammals other than primates, and insects except the Diptera, excrete 80–100 % of the uric acid they form only after oxidizing it to allantoin. In dogs in particular, apart from the Dalmatian coach-hound, it would seem that the amount of uric acid in the urine is normally minute, and that, even after injecting the acid, 98 % of it enters the urine as allantoin (Best & Taylor, 1955; Evans, 1956). The uric acid excreted by the Dalmatian coach-hound, once thought to be due to a purine metabolism resembling that of primates, is now attributed to there being no mechanism in the renal tubules for reabsorbing uric acid (Friedman & Byers, 1948; Miller, Danzig & Talbott, 1951). Yet Madsen, Earle, Heemstra & Miller (1944) reported finding uric acid infarcts in the kidneys of newborn piglets suffering from a disease which they described as 'acute uremia'. Morrill (1952*a*, *b*) found accumulations of uric acid crystals in the kidneys of piglets which appear to have had a similar if not identical disease.

In another connexion it was noticed in this Department that in newborn puppies urea might form less than 30 % of the total N excreted. The turnover of protein in the body has not been so well explored in the newborn period as in adult life, and the information which can be obtained about cellular metabolism from a study of the excretion of the end-products of nitrogenous metabolism in the urine made it seem desirable to examine the excretion of the important end-products, uric acid and allantoin, and also that of urea and ammonia by newborn mammals. Human infants, piglets and puppies were chosen for the investigation.

MATERIAL AND METHODS

Urine formed before birth and passed at the time of birth or very shortly afterwards has been collected from eight full-term babies, five piglets and three puppies. Collections over the whole of the first 48 hr. of life have been made on seven babies, and on the seventh day on six of them. These babies were treated in the normal way and put to the breast every 4 hr. from the second day of life onwards. They obtained 8–15 ml. of colostrum at first, 20–30 ml. by the end of the second day and 300–500 ml. of milk on the seventh day. None had any cow's-milk supplements. A total of eighteen piglets from four litters have been put into metabolism cages as soon as they were born and all their urine was collected for 40 hr. Four of these piglets, one from each litter, were given sow's milk, four an equal volume of water, and four nothing. The liquid was given by stomach tube every 2 hr. as described by McCance & Widdowson (1956). In addition, a fourth piglet from each of three of the litters was given the same quantity of a solution of sodium chloride in water (0·5, 0·7 or 0·9%). A fifth pig from each of these three litters was given salted sow's milk made up so that the concentration of sodium chloride in the water of the milk was 0·5, 0·7 or 0·9%. Puppies, one from each of four litters, have also been fed by stomach tube every 2 hr. Dog's milk was used for the first and sow's milk for the other three. Urine was collected from the puppies as described by McCance & Widdowson (1955). The experiments on the puppies lasted for 24 hr. Collections of urine (24 hr.) from two men and four women, and isolated specimens from three adult pigs and nine dogs, have also been analysed.

All urines were collected under toluene and stored in a refrigerator at 4°. Total nitrogen was determined by the micro-Kjeldahl technique with copper selenite as catalyst, and urea by Lee & Widdowson's (1937) method. Ammonia was estimated either by distilling in a micro-Kjeldahl apparatus at pH 8, with phenol red as indicator, or, where the samples were small, in a Conway unit (Conway, 1950). Results obtained for the same urine by the two methods were found to agree very closely. Uric acid was determined as recommended by King (1946) and allantoin by the method described by Young & Conway (1942). It was found that uric acid gave the same colour reaction as allantoin by this method, 1·0 mg. of uric acid being equivalent to about 0·06 mg. of allantoin. The uric acid content of the urine of newborn infants and adults was sufficient to account for the small amounts of colour which were produced by the allantoin reagents. The values given for allantoin in the urine of adult and newborn pigs have been corrected for the colour due to uric acid.

RESULTS

Table 1 shows the average concentration of nitrogen in the urines of man, the pig and the dog at several stages of development, and the percentage of the total nitrogen excreted as urea. As has been found by others (Folin, 1905*a*; Cathcart, 1907; Barlow & McCance, 1948), urea accounted for 80–90% of the total nitrogen in the urine of healthy adult men and dogs. It was always below 80% in pigs. In all three species the figure was lower in the newborn period than in the adult, and in the puppy it was only 20–30% just before and in the 12 hr. after birth. The newborn puppies' urine contained 10–25% of protein nitrogen, but even when the results are expressed on a protein-free basis urea still accounted for only about 30% of the nitrogen in the urine passed at birth and during the first 12 hr. afterwards. The proportion of urea increased rapidly, and during the second 12 hr. of the 24 it comprised 65% of the total nitrogen, or 71% on a protein-free basis.

The newborn of all three species excreted a higher proportion of their nitrogen as ammonia than did the corresponding adults (Table 2), and the ammonia coefficient was always highest in the urine formed in the uterus and passed at birth.

The figures for uric acid and allantoin are shown in Table 3. The results on adult men and dogs confirm those of earlier workers; newborn piglets and puppies, like human babies (Barlow & McCance, 1948), excreted more of the total nitrogen as uric acid than did the adults, but in all three species the excretion of uric acid was more variable than that of urea or ammonia. The proportion of the total nitrogen present as uric acid in the

Table 1. *Percentage of the total nitrogen excreted as urea by newborn babies, piglets and puppies compared with adults of the same species*

Standard deviations of the percentages have been given where the numbers were 6 or more. Figures in parentheses denote number of observations.

	Man		Pig		Dog	
Nature of urine	Total N (mg./100 ml.)	Total N as urea (%)	Total N (mg./100 ml.)	Total N as urea (%)	Total N (mg./100 ml.)	Total N as urea (%)
Formed *in utero* and passed at birth	80 (8)	72±4·8	196 (5)	64	308 (3)	23
First 24 hr. after birth	562 (7)	70±5·7	175 (4)	58	545* (3)	28
					886† (3)	65
Second 24 hr. after birth	733 (7)	76±4·6	154 (4)	72	—	—
Seventh day	132 (6)	82±3·5	—	—	—	—
Adult	660 (6)	85±3·7	804 (3)	76	1560 (9)	88±5·1

* 1st 12 hr. † 2nd 12 hr.

Table 2. *Excretion of ammonia by newborn babies, piglets and puppies compared with adults of the same species*

Results for ammonia nitrogen are expressed as percentage of total nitrogen. Standard deviations have been given where the numbers were 6 or more.

Nature of urine	Man	Pig	Dog
Formed *in utero* and passed at birth	10·2 ± 1·55	10·4	15·0
First 24 hr. after birth	7·6 ± 0·40	8·0	14·9*
			8·6†
Second 24 hr. after birth	7·4 ± 0·56	6·2	—
Seventh day	6·7 ± 0·87	—	—
Adult	3·5 ± 0·48	1·9	2·5 ± 0·82

* 1st 12 hr. † 2nd 12 hr.

Table 3. *Excretion of uric acid and allantoin by newborn babies, piglets and puppies compared with adults of the same species*

Results are expressed as percentage of total nitrogen. Standard deviations have been given where the numbers were 6 or more.

	Man		Pig		Dog	
Nature of urine	Uric acid	Allantoin	Uric acid	Allantoin	Uric acid	Allantoin
Formed *in utero* and passed at birth	9·9 ± 3·35	0	2·7	1·5	2·7	27·2
First 24 hr. after birth	9·0 ± 3·57	0	1·1	1·4	1·6*	13·5
					0·6†	4·6
Second 24 hr. after birth	8·3 ± 2·92	0	1·1	1·5	—	—
Seventh day	3·8 ± 1·45	0	—	—	—	—
Adult	2·2 ± 0·81	0	0·7	2·8	0·4 ± 0·07	3·6 ± 0·88

* 1st 12 hr. † 2nd 12 hr.

Table 4. *Effect of food and of sodium chloride on the percentage of nitrogen excreted as urea by piglets in the first 24 hr. of life*

	Percentage of total N excreted as urea			
	Litter 1	Litter 2	Litter 3	Average
Fed on milk	60·3	53·8	59·3	57·8
Given water only	68·8	58·7	67·5	65·0
Fed on milk + NaCl*	55·6	44·2	40·3	46·7
Given water + NaCl*	63·5	53·4	51·1	56·0

* Litter 1 had 0·5 %, litter 2 had 0·7 % and litter 3 had 0·9 % of NaCl.

puppies' urine fell rapidly, so that during the second 12 hr. after birth the figure was little higher than it was in the adult. Although King's (1946) method is not specific for uric acid, it is unlikely that the differences between the newborn and the adult could have been accounted for by interfering substances such as polyphenols or methylxanthines, e.g. caffeine.

The urine formed by puppies in the uterus contained 27 % of its nitrogen in the form of allantoin. Again the proportion fell rapidly, so that the urine passed during the second 12 hr. of life resembled adult urine in the relative proportions of the total nitrogen present as uric acid and allantoin.

DISCUSSION

The percentage of the total nitrogen excreted as urea seems generally to be lower in the newborn than in the adult of the same species. This is not due to starvation or to a low-protein diet (Folin, 1905*b*). It may in some species be due partly to the excretion of much nitrogen in the form of protein, but a more important reason is that the balance between anabolism and catabolism is so strongly weighted on the side of anabolism. Tissue proteins are little broken down, and since so much of the protein in the food is used for purposes of growth the formation of urea is small; hence its concentration in the plasma, and consequently the percentage of the urea nitrogen in the urine, remains low. The administration of sodium chloride to piglets has been shown to decrease catabolism of protein (McCance & Widdowson, 1957), and Table 4 shows that it also decreases the percentage of the total nitrogen excreted as urea. McCance & Finck (1947) reported that the ammonia coefficient of the urine of newborn infants was on the whole higher than that of the urine passed by adults. The present results confirm this and extend the observation to other species. The high coefficient is not the result of the pH of the urine being very low, for the pH of the urines passed by human infants at birth (average 6·3) was almost the same as that of the urines passed by the adults (average 6·0). Nor is the high coefficient the result of the kidney at this age being able to form ammonia with great facility, for the evidence which has been collected indicates that glutaminase activity is not so great in the newborn as it is in the adult (Cort & McCance, 1954; Hines & McCance, 1954). The relatively great excretion of ammonia in the new-

Table 5. *Concentration of uric acid in the urine of babies and of piglets fed with milk and receiving nothing*

Results are expressed as mg. of uric acid/100 ml. of urine.

		Piglets		
	Human babies	Receiving milk	Receiving water	Receiving nothing
First 24 hr. after birth	151	5·3	7·3	56·0
Second 24 hr. after birth	185	4·6	6·7	87·0

born period may be partly due to the fact that the titratable acidity is so low (McCance & Finck, 1947) that nearly all the acid to be eliminated by the kidney must be combined with ammonia or fixed base. The main reason for the high coefficient is, however, the small amount of nitrogen, and particularly of urea, in the urine. The total excretion of ammonia/kilogram of body weight or/square metre of surface area is lower in the newborn than at older ages (Widdowson & McCance, 1958). The uric acid infarcts which have been found in the kidneys of ailing newborn piglets are easily explained. They are due to the relatively large amounts of uric acid excreted by these animals in the newborn period, coupled with a small volume of urine which is the outcome of the dehydration from which the animals suffer when they get too little milk. Table 5 shows the concentration of uric acid in the urine of piglets which were given sow's milk by stomach tube, and of other piglets which received the same volume of water, or nothing at all, for the first two days of life. The urine of the starved and dehydrated piglets contained 8–20 times as high a concentration of uric acid as that of the other animals. The urine of normal healthy babies contains an even higher percentage.

Since puppies also excrete a higher proportion of their end-products of purine metabolism as uric acid than do adult dogs, this would seem to be characteristic of the newborn, at least of some species, and to be a sign of incomplete chemical or physiological development—chemical if it is due to the necessary uricase activity's still being undeveloped, physiological if it is due to a very low renal threshold for uric acid. The present investigation does not enable one to distinguish between these two alternatives.

SUMMARY

1. The excretion of urea, ammonia, uric acid and allantoin by newborn babies, pigs and puppies has been studied, and the results have been compared with values for adults of the same species.

2. The percentage of the total nitrogen excreted as urea was lower in the newborn than in the adult of the same species. This has been attributed to the turnover of amino acids being directed towards anabolism at this age.

3. The newborn baby, pig and puppy excreted a higher proportion of their nitrogen as ammonia than did the adults. The reasons for this are discussed.

4. Newborn pigs and puppies excreted more of their purine end-products as uric acid than did the corresponding adults. In the urine formed by puppies in the uterus allantoin contributed a higher percentage of the total nitrogen than did urea. The percentage contributed by allantoin declined rapidly after birth.

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