Development of Acid—Base Control

By

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(Received October 5, 1960)

The plasma CO_2 of the foetus is said to be in equilibrium with that of the mother, and work on the passage of lactic acid across the placenta goes to show that the overall acid—base regulation of the foetus is carried out through the maternal organism.

This is not to say that extensive acid—base readjustments may not go on within the foetus at some stages of gestation, and the contents of the large allantoic sac of the pig foetus at 46 days of age is a good example of this. The fluid in this sac has a pH of about 6, due largely to H of HCO_3, and contains 4 to 6 mEq NH_3/l. The volume of this fluid may be due largely to the activities of the kidney, but its composition is modified by the chorioallantoic membranes which contain a mechanism for the active extrusion of sodium [3, 9]. The human foetal kidney secretes an acid urine with a pH round about 6 and by the time of birth the kidneys of all mammals are normally able to maintain reasonably good acid—base stability in the internal environment of the animals they serve.

Adults seldom lower the pH of their urine below 4.8. 0.1 mEq of a strong acid would bring the pH of 1 litre of distilled water well below this but, owing to the phosphates and other buffer substances in the urine and to the ability of the kidney to convert some of the hydrogen ions in the tubular fluid into ammonium salts, the kidney of a healthy adult normally excretes up to 70 mEq of H ions per day. A little over half the total is usually buffered by the phosphates and the salts of weak organic acids and the remainder is neutralised by ammonia. When McCance and von Finck [7] first studied the corresponding mechanisms in newborn infants they found that healthy breast-fed infants excreted little or no phosphate. Consequently, their urine contained few buffer substances and ammonia played a correspondingly larger part in neutralising the H ions excreted by the kidney.

We have taken up this problem again in recent years. Fig. 1 shows the way in which the excretion of acid builds up in the early days of life. This is partly perhaps due to a rise in the glomerular filtration rate, but mainly to the increasing metabolic turnover of the developing infant.

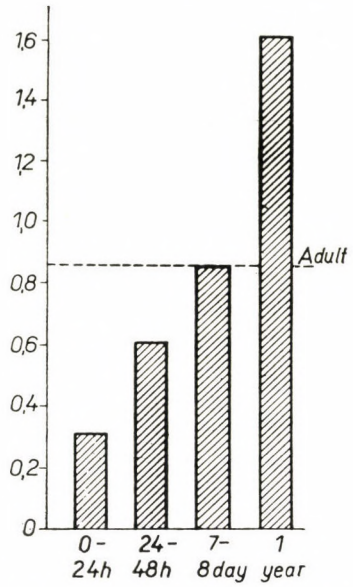

FIG. 1. Surplus anions (not combined with fixed base) m.Mol./kg./24 h.

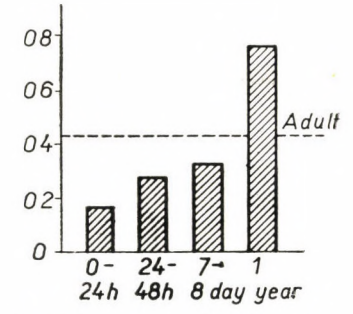

FIG. 2. Excretion of titratable acid m.Mol/kg./24 h

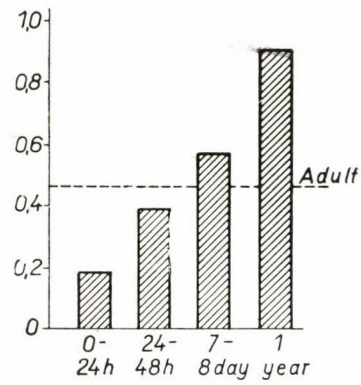

FIG. 3. Ammonia excreted m.Mol/kg./24 h.

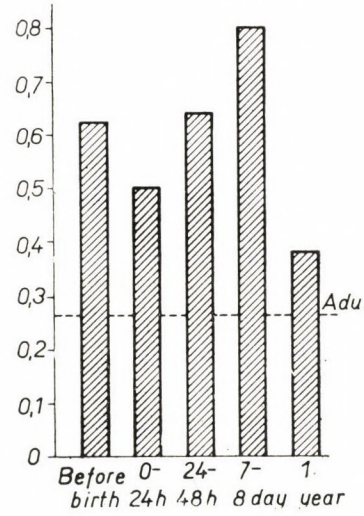

FIG. 4. Ammonia excreted m.Mol/24 h. G. F. R. ml./min.

Figs. 2 and 3 show how relatively little of the acid was buffered by phosphates at this age and how much of it was neutralised by ammonia, and Fig. 4 demonstrates this in another way [8, 10].

We have also studied the ability of the kidney of infants 7 days old to correct the effects of taking calcium or ammonium chlorides. Adults and infants were given 54 mEq of one or other drug per sq. m. of surface area. This lowered the plasma CO_2 at both ages by about the same amount so that the systemic effects may be assumed to have been similar. Fig. 5 shows the effect on the pH of the urine over the 8 hours after giving the drug. The response of the adult was characteristic — the pH fell rapidly

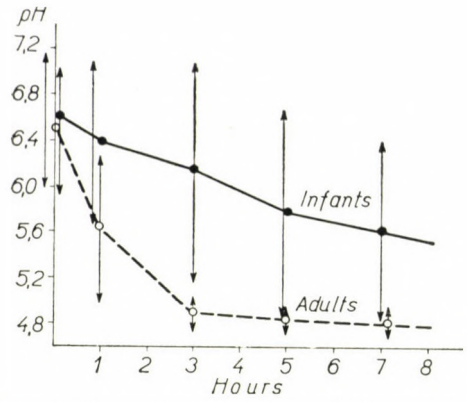

FIG. 5. The pH of the urine before and after giving 54 mEq/m² of NH_4Cl or $CaCl_2$ to adults and breast-fed infants 7 days old

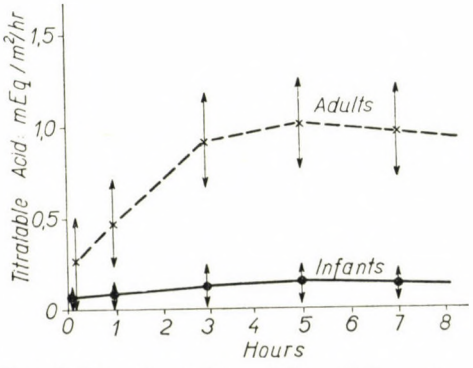

FIG. 6. The titratable acidity of the urine before and after giving 54 mEq/m² of NH_4Cl or Ca Cl_2 to adults and breast-fed infants 7 days old

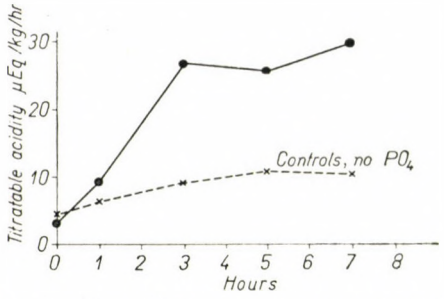

FIG. 7. The effect of pretreatment with neutral PO_4 (120 mg P/day) on the titratable acid excretion after giving 54 mEq/m² of NH_4 CI to breast-fed infants 7 days old

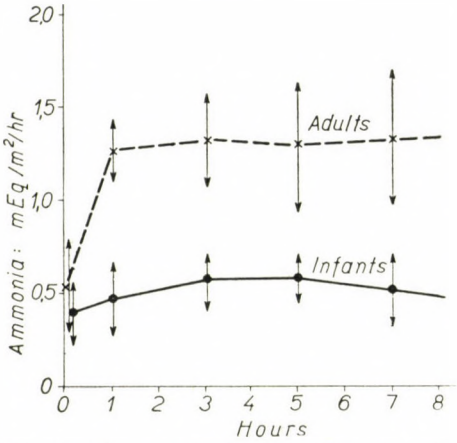

FIG. 8. The ammonia excretion in urine before and after giving 54 mEq/m² of NH_4Cl or CaCl to adults and breast-fed infants 7 days old

to the permissible limits and stayed there — but that of the infants was less effective. The average pH fell more slowly and had not reached 5 by the end of the test.

Fig. 6 shows the effect of the drugs on the excretion of titratable acid. The response of the infants was very small when compared with the healthy adults. This could have been foretold from the behaviour of the pH of the urine and the paucity of phosphates and other buffer substances in it. The response was considerably improved, as Fig. 7 shows, by administering 7 mEq of a mixture of sodium and potassium phosphates at pH 7.4 to the infants on the 5th, 6th and 7th days of their lives.

Fig. 8 shows the excretion of H ions as ammonium salts by infants and adults. The infants again make a poor showing on this basis of comparison, but per kg of body weight

these infants were excreting as much ammonia as the adults. This substantiates the findings set out in Figs. 3 and 4, and raises the whole question of what basis of comparison should be used for work of this nature. This is, however, too complex a subject to take up here.

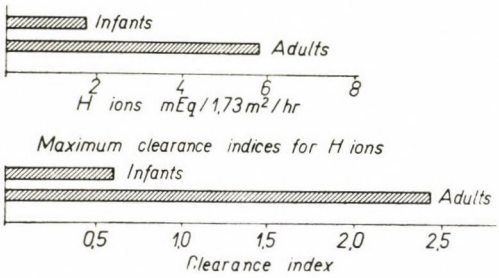

FIG. 9. Maximum rate of H ion excretion after the administration of phospate

Fig. 9 shows the maximum rate of H ion excretion (in all forms) attained by the infants and the adults after the administration of phosphates. It also shows the greatest H ion clearance indices obtained. This "index" was defined by ELKINTON, HUTH, WEBSTER and MCCANCE [4] as the rate of excretion of H+ ammonium ions in mEq [min] 1.73 sq. m. × the "total CO_2" in the plasma — also expressed in mEq. It probably demonstrates the real relationship of the newly born to the adult better than anything else because it takes into account the acid—base relationships in the corresponding sera.

Fig. 10 shows the percentage of the dose of acid which was excreted within 8 hours by the adults and the infants. Neutral phosphates had not been administered to the infants beforehand so that the results express the natural relationships. The infants excreted much less of the dose: they also excreted a much smaller percentage of the chloride ions. The value of this form of comparison is that it is largely independent of surface area or body weight and gives an almost independent assessment of the capacity of the newborn.

It would appear, therefore, that in correcting an internal acidosis the newly born human infant is hampered in several ways. (i) The ability to produce and excrete free H + ammonium ions in response to a similar internal stimulus is much less than that of an adult. (ii) The breast-fed

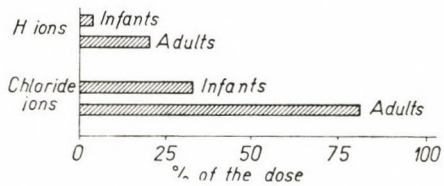

FIG. 10. Percentage of the potential H ions and chlorides in the NH_4Cl excreted in 8 hours

infant is handicapped in this to some extent at any rate by the fact that the urine contains no phosphates and hence no buffer substances. (iii) The ability to lower the pH of the urine is limited — this may be the result of (i) above, but a rapid fall in the pH of the urine should be facilitated by (ii).

The newborn baby is at one with most other newborn animals in being unable to correct an internal acidosis so readily as its adult counterpart. The puppy has been investigated more

completely than most others [1], but something the same holds for all. This is only another aspect of the generalisation which says that the renal capacity of the newly born is much less than that of the adult. Infants are vulnerable to acid forming foods and drugs [3, 5, 6], just as they are to water intoxication or too much sodium chloride, but on the whole the stability of the internal environment is well maintained. This is achieved, as in other respects, by a close integration of food, growth and renal function. Growth is not so important for regulating the maintenance of acid—base stability as it is for keeping down the concentration of urea and phosphorus in the plasma, but food is all-important. The food must supply everything necessary for growth, and at the same time provide the kidney with the minimum amount of work in the way of acid—base control. Breast milk probably does this better than anything else, but infants can maintain reasonable internal stability on cows' milk preparations which give rise to more sulphates and other acid products of metabolism than breast milk. It also, however, provides more neutral phosphate, with which the H ions in the urine can be buffered and so excreted in the free form, *i. e.* as titratable acid. Nevertheless the CO_2 and pH in the plasma of infants receiving cow's milk are lower on the whole than those found in breast-fed infants.

Dr. N. HATEMI has been responsible for a large part of the work reported in this communication.

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