Urea and its bioavailability in newborns

EDITOR.—Jackson suggests that colonic salvage of urea N—that is, its return to the body N pool and contributing to the effective supply of N—is an important component in the handling of urea N in the newborn.1 Although of interest for nitrogen economy during growth, pregnancy, low protein intake or during hibernation in bears, such a hypothesis does not appear to be a valid one in the newborn child, is not based on compelling evidence.

The estimates of urea N salvage are based on incomplete excretion in urine of the total urea synthesised in the body. The discrepancy between the high rates of urea N derived in studies of normal full-term newborns that show the rate of urea synthesis measured by isotopic tracers ranges between 3 and 6 mg N/kg/hour in six neonates after major abdominal surgery.2 However, the rate of urea N excretion is similar to that reported by others. Thus the discrepancy between synthesis and excretion was astrologically (80%). Interestingly, the recycled N was derived from dietary urea nitrogen. Several concerns can be raised regarding the validity of measurements in their study—route of tracer administration, the catabolic state of the infant, the accuracy of urine collection, etc. All question the conclusion regarding the salvage of urea N in these infants.

Thus published data on newborn babies do not support the concept that 'urea production and salvage appear to be normal features of urea Synthesis in early infancy'. It may be important only when protein intake is marginal or only in certain animal species.

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Dr Jackson comments:
Dr Kalhan's comments revisit a longstanding controversy which simply underlines the need for good data in a difficult area of investigation. There are three points of importance: whether salvage of urea-nitrogen has functional importance under any circumstances; whether it is important in infancy; and the nature of the importance. We have formally addressed the methodological criticisms raised. Based on an extensive series of investigations we know for adults that normally 25% of daily urea-nitrogen production is salvaged.2 In infants and children the major factors which influence the rate of salvage are the content and rate of metabolism determined in part by energy intake, the absolute protein intake relative to the magnitude of the metabolic demand for protein, and the presence of a functional colonic microflora.

The data on which the three phases for urea kinetics can be identified are: (i) shortly after birth when the microflora are properly established, the age of urea N is greater than the time of excretion measured in a number of balance studies;5 6 In contrast, Wheeler et al observed very high rates of urea N synthesis (about 17-3 mmol N/kg/day or 20 mg N/kg/hour) in six neonates after major abdominal surgery. However, the rate of excretion of urea N excretion was similar to that reported by others. Thus the discrepancy between synthesis and excretion was astrologically (80%). Interestingly, the recycled N was derived from dietary urea nitrogen. Several concerns can be raised regarding the validity of measurements in their study—route of tracer administration, the catabolic state of the infant, the accuracy of urine collection, etc. All question the conclusion regarding the salvage of urea N in these infants.

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Lipid peroxidation as a measure of oxygen free radical damage in the very low birthweight infant

EDITOR—We read with interest the paper by Inder et al on lipid peroxidation as a measure of oxygen free radical damage in preterm infants. They showed a rise in malondialdehyde detected by the thiobarbituric acid (TBA) test over the first week which was significantly greater in those infants developing chronic lung disease. We have also used the TBA test to detect lipid peroxidation in 132 very preterm infants during the first seven days after birth. Concentrations rose from a median of 2.13 μmol/l (1.63–2.77 range) on day 1 to 3.27 μmol/l (2.49–4.48) on day 7 in those not developing chronic lung disease and from 2.07 μmol/l (1.16–2.98) to 3.77 μmol/l (2.6–4.21) in the 40 infants who developed chronic lung disease. No significant difference was observed. It is of interest that our values for the TBA test were about 30 times lower than those of Inder et al, in keeping with other published values for the test. We used a fluorimetric method, but the HPLC technique used by Inder et al generally gives lower values than the fluorimetric method. Until these differences are explained, we cannot accept the authors' findings as evidence for lipid peroxidation in very preterm infants.

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Dr McIntosh comments:
In our studies using EMLA cream we were attempting to reduce pain and distress (apparently unsuccessfully) in newborn infants receiving heel pricks. The parents were informed that EMLA cream had not been used other than in our own study on neonates, but that it was commonly used and with no problem in older children. We knew about the possibility of methaemoglobinemia but at the time of starting the study there was only one report of this problem in a child who was also receiving a sulphonamide, so we did not believe that we ought to inform the parents of this specific but theoretical hazard.

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were available, and intravenous methylene blue, the antidote, was to hand.

Our trial was abandoned after 22 infants had been entered. Obtaining fully informed consent was usually difficult due to mothers' fears of methaemoglobinemia and lack of reports of the safety of EMLA in neonates, so recruitment was too slow to complete the trial within a reasonable length of time. Randomisation had resulted in five babies given EMLA and 17 placebo.

No baby who received EMLA became blue, desaturated, or developed symptoms, so five neonates were treated safely with EMLA on our fairly stringent regimen. We would be interested to know how the Edinburgh team coped with explaining and countering the possible hazards of methaemoglobinemia which do not seem well researched in neonates. Knowledge of the safe use of EMLA in their 28 neonates as well as our precautions in five babies, and Koren's suggestions of unofficial safe use should greatly facilitate obtaining informed consent in future trials.

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EMLA and informed consent in neonates.

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