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 that urea in the human infant 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.2 The discrepancy between the hypothesis of urea in the gut but also from excretion of urea in the skin. A significant proportion of N released from hydrolysis of urea in the gut is also known to be recycled into urea or excreted as ammonia in the breath. In healthy adults, a normal protein intake about 20% of synthesised urea is not excreted in urine, and an insignificant amount of urea N is incorporated into protein.3 Whether such a salvage of N occurs in newborns is not known. Data on breast fed infants, both pre-term and full term, have shown that most of the urea ingested is not bioavailable—that is, it is not hydrolysed in the gut.4 Several pre-term newborns show that the rate of urea synthesis measured by isotope tracers ranges between 3 mg and 6 mg N/kg/hour, which is similar to the rate of urinary urea N 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.7 However, the rate of urinary urea N excretion was similar to that reported by others. Thus the discrepancy between synthesis and excretion was astro-nomical (80%). Interestingly, the recycled N was not visible as a concentration of urea in the plasma. Several concerns can be raised regarding the validity of measurements in their study—the 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 metabolism in the newborn’. It may be important only when protein intake is marginal or only in certain animal species.

**SATHIS C KALHAN**
Department of Pediatrics, Case Western Reserve University School of Medicine, Cleveland, Ohio 44106, USA


**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 circumstance; whether it is important in infancy; and the nature of the importance. We have formally addressed the methodological criticisms raised.1 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 ontogenetic timing of events 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.3 The degree to which the three phases for urea kinetics can be identified: (i) shortly after birth before the microflora are properly established, little or no salvage; (ii) up to 6 weeks of age, with an established flora, salvage is very high in response to the intense metabolic demand; and (iii) after 6 to 8 weeks of age, when salvage is moderate. For each phase there are clear differences in nitrogen metabolism, as identified by 

**EMLA and informed consent in neonates**

**Editor,—**We were very interested in the account of the use of EMLA cream in 21 neonates,1 following an earlier trial in seven babies.2 There seem to be few direct reports of the safe use of EMLA in newborns, though Koren suggested that EMLA is in widespread and unlicensed use in North America for circumcisions.3 We were interested in what other investigators have found regarding the use of EMLA. The use of EMLA is not recommended for babies under 1 year of age in the United Kingdom, but the use of EMLA in infants older than 1 month has recently been approved in the USA.4

Neonates may be at increased risk of methaemoglobinaemia, due to their thin skin, low concentrations of methaemoglobin reduce (z) in their blood, slow metabolism of lignocaine and prilocaine. Lignocaine is more readily oxidised to methaemoglobin than is adult haemoglobin.

We obtained ethical committee approval for a randomised, double blind trial of EMLA cream in newborn babies. Parents were warned verbally and in writing of the risks of methaemoglobinaemia and advised about our methods of ensuring safe use. Fully informed verbal and written consent was obtained. Exclusion criteria were clinically apparent anaemia, oxygen treatment, cyanotic congenital heart disease, weight of less than 1500 g or a baby taking antileukaemic drugs.

We restricted the dose of EMLA or placebo to 0·1 ml/kg/bodyweight applied once only to an area of skin measuring 2×1 cm for exactly one hour. Each baby was watched closely for 12 hours for evidence of any rash, change or desaturation, if necessary using a pulse oximeter or other monitors. Blood tests for methaemoglobin, lignocaine, prilocaine and methaemoglobin reductase concentrations


**Fresh frozen plasma and neonatal sepsis**

**Editor,—**Acunas and colleagues conclude that fresh frozen plasma (FFP) is less effective than intravenous immunoglobulin as an adjunctive treatment for neonatal sepsis.1 They also highlight the possible risk of viral transmission with its use. FFP may also contain viable donor lymphocytes, exposing the recipient to potential graft-versus-host disease.2 Therefore, FFP may be prevented by irradiation of blood products,3 FFP is not routinely irradiated on most neonatal units and therefore TA-GvHD may be a place potential disadvantage of the use of FFP in newborns.

**DAVID BURGNER**
Newborn Emergency Transport Service, Royal Alexandra Hospital for Children, Camperdown, Sydney, NSW 2050, Australia

Urea and its bioavailability in newborns.

S C Kalhan

Arch Dis Child Fetal Neonatal Ed 1994 71: F233
doi: 10.1136/fn.71.3.F233