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NEW INDICES

OF

PERINATAL GROWTH

By

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PREFACE

To the best of the author's knowledge, this thesis contains no material previously published or written by another person, except where due reference is made in the text. It contains no material which has been submitted or accepted for the award of any other degree or diploma in any University.

(A. Hocking)

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SUMMARY

This thesis describes two new indices of perinatal morbidity relating to intrauterine growth retardation, namely neonatal water metabolism and protein metabolism.

Water metabolism was studied by determining body water turnover rates of 106 newborn infants, using the non-radioactive isotope of water, deuterium oxide (D_2O). The rate at which D_2O is excreted from the body can be expressed as a rate constant of water turnover. Water turnover rates of the infants were correlated with independent obstetric and paediatric assessments of the newborn infants. The neonates were classified by strict clinical criteria into three main groups, fully grown ("normal"), borderline (exhibiting some features of growth retardation) and clearly intrauterine growth retarded. There were highly significant differences between the water turnover rates of each of these groups, the medians of the rate constants ($x10^4$) being 73.3, 85.9 and 100.2 (h^{-1}) respectively. This test is also quantitative, in that infants who were more clinically growth retarded displayed higher water turnover rates.

Body water turnover rates are simple to perform by this method of isotope dilution and the collection of neonatal urine samples is convenient, using a paper towel placed inside the infant's nappy. However, 4-8 urine samples are necessary for this test to be performed.

A test requiring only a single urine sample would be ideal and, for this reason, the measurement of 3-methylhistidine was considered. Urinary excretion of 3-methylhistidine has been shown to be an index of myofibrillar protein breakdown and 3-methylhistidine/creatinine ratios give a measure of protein turnover. Measurement of this amino acid has never before been undertaken in relation to intrauterine growth retardation in neonatal urine or amniotic fluid samples.

3-methylhistidine/creatinine ratios have been measured in amniotic fluid of foetuses ranging from 16-21 weeks and 27-42 weeks gestation. The ratio is high in amniotic fluid in early gestation (approximately 60 nmol/μmol),

decreasing at term to a level of approximately 10 nmol/µmol. The first neonatal urine ratio correlates well with the corresponding term amniotic fluid ratio. A rapid rise in the 3-methylhistidine/creatinine ratio occurs postnatally, reaching a plateau at around two days.

In a sample of eight normal and seven intrauterine growth retarded infants, the ratio in the first neonatal urine sample was consistently lower in the normal than in the growth retarded group. There is a possibility that the 3-methylhistidine/creatinine ratio may be used as an indicator of growth retardation.

The measurement of water turnover rates is a simple quantitative test for growth retardation and, although it is not certain whether 3-methylhistidine/creatinine ratios yield a quantitative result, it may potentially be used antenatally, as well as neonatally. Both tests are advantageous, in that they are independent of the gestational age of the infant, birth weight, behaviour and appearance.

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ABBREVIATIONS

Abbreviations used in the text are as follows;

IUGR	=	intrauterine growth retardation
ln	=	natural logarithm
3MH	=	3-methylhistidine
Cr	=	creatinine
D_2O	=	deuterium oxide
ppm	=	parts per million