Glucagon correlated with glucose ($r = 0.66$), lactate ($r = 0.36$), pyruvate ($r = 0.40$), and insulin ($r = 0.57$) but negatively with ketone bodies ($r = -0.46$) and triglycerides ($r = -0.62$). Cortisol correlated with glycerol ($r = 0.37$). Urine nitrogen excretion correlated with glucagon after operation ($r = 0.72$) more strongly than in controls ($r = 0.52$).

These findings show increased nitrogen excretion after moderate injury, associated with increased gluconeogenesis from amino acids. After injury, hormones appear to influence metabolism more strongly, while in fasting, relationships between metabolites appear important. After injury, even at low levels insulin inhibits lipid mobilization. Glucagon probably mainly affects the liver stimulating gluconeogenesis and ureagenesis. Cortisol appears to play a lesser role in moderate injury than we noted after severe injury, where it appeared to mediate the mobilization of peripheral protein and lipid stores (Batstone, Alberti, Hinks, Smythe, Laing, Ward, Ely & Bloom, 1976, Burns, 2, 204).

13. SUCCINIMIDE IN THE TREATMENT OF PRIMARY HYPEROXALURIA

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There is no universally satisfactory therapeutic agent for the control of urinary oxalate excretion in primary hyperoxaluria, although pharmacological doses of pyridoxine reduce the urinary oxalate excretion in some cases. Succinimide has been claimed to cause a significant reduction in urinary oxalate levels in patients with oxalate nephrolithiasis not due to primary hyperoxaluria (Thomas et al., 1971, Annales de Urologie, 5 U-145). We have carried out a trial of succinimide in three stone-forming children with type 1 primary hyperoxaluria who are not responsive to pyridoxine therapy.

Baseline urinary oxalate, glycollate and other organic acid levels were determined over 10 days during which no medication was given but a high urinary flow rate maintained. The patients were then given 160 mg/kg body weight succinimide orally per day. Urine was collected for a further 10 days before the patients were discharged on the same dose. Oxalic acid was determined by isotope dilution analysis and by gas/liquid chromatography, which also enabled glycollic and other organic acids to be measured.

During the first 10 days of the trial, there were no significant changes in oxalate or glycollate excretion. The following levels (mean mol/24 h anhydrous oxalic acid, with SD) were found:

*Patient 1 Pre-treatment:* 2.44, 0.54
*Succinimide:* 2.51, 0.77

*Patient 2 Pre-treatment:* 1.90, 0.29
*Succinimide:* 1.79, 0.21

*Patient 3 Pre-treatment:* 1.71, 0.30
*Succinimide:* 1.79, 0.24

The results of a longer term follow-up over 10 weeks on this regimen will be presented.

It appears that the proposed mechanism of Thomas et al. whereby succinimide acting, through succinate, as a substrate in the TCA cycle is able to stimulate the complete oxidation of glyoxylate to CO$_2$, rather than to oxalate is not significant in these patients. This investigation was approved by the Northwick Park Hospital Ethical Committee.

14. ORGANIC ACIDS IN HUMAN AMNIOTIC FLUID AND THE PREGNATAL DIAGNOSIS OF THE ORGANOIC ACIDURIAS

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Prenatal diagnosis of inborn errors of metabolism by direct chemical analysis of amniotic fluid for accumulating metabolites derived from the foetus offers the great advantage of rapidity over the more conventional determination of enzyme activities in cultured cells. Reliable diagnoses depend on comprehensive but specific methods and a detailed knowledge of the patterns and levels of metabolites normally present in the fluid.

We have examined amniotic fluid, obtained at 15–20 weeks gestation from 40 uncomplicated pregnancies with a normal outcome, for organic acids using quantitative and semi-quantitative extraction techniques, gas chromatography, and mass spectrometry. The major organic acids observed (µg/ml of fluid, mean ± SD) were: lactate (870 ± 122), pyruvic (7.6 ± 2.8), 2-hydroxybutyric (18.5 ± 5.7), 3-hydroxybutyric (9.9 ± 4.3), succinic (1.2 ± 0.4), fumaric + glyceric (3.1 ± 1.6), malic (3.1 ± 1), pyrogallulic (17.8 ± 7.2), erythrionic + threonic (1.9 ± 0.9), 2-oxoglututaric + 3-hydroxy-3-methylglutaric (2.8 ± 3.1), citric (74.4 ± 15.6), 4-hydroxyphenyl-lactic (0.9 ± 0.6) and palmitic (1.6 ± 0.3). Other acids observed included 3-hydroxyisovaleric (0.4 ± 0.2), acetoacetic (0.5 ± 0.3), 2-oxoacaproic (0.4 ± 0.2), 3-deoxyxerotonin (0.2 ± 0.1) and stearic (0.1 ± 0.1).

These results provide an aid to the prenatal diagnosis of the organic acidurias. The methods used permit the detection and quantification of all acidic metabolites potentially present in the fluid and will allow the diagnosis of known diseases for which the pregnancy is at risk and abnormal metabolites accumulate.

In such cases, where the nature of the accumulating metabolite(s) is known (for example in methylmalonic aciduria), the diagnosis is made more specific by use of selected ion monitoring with the mass spectrometer for characteristic ions. This approach should also permit the prenatal diagnosis of other organic acidurias that are expressed in the newborn infant at birth and allows the exploratory analysis of amniotic fluid for possible foetal inborn errors of metabolism in mothers with a history of unexplained early neonatal deaths or miscarriages. Wherever possible, confirmatory enzyme assays on cultured cells are advised, and mass spectrometric identification of accumulated metabolites is considered essential.

15. CORRECTION OF RENAL HYPERTENSION IN THE RAT BY LONG-TERM INFUSION OF ANGIOTENSIN INHIBITORS


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As in earlier studies in the rat intravenous injection of saralasin (180 µg/kg in this study) or converting enzyme inhibitor (1 mg/kg) produced a variable and usually small reduction of blood pressure in conscious rats with two-kidney hypertension of mean duration 42 days. However, prolonged infusion of saralasin (at 10 µg min$^{-1}$ kg$^{-1}$) or converting enzyme inhibitor (6.9 µg min$^{-1}$ kg$^{-1}$) gradually reduced blood pressure to normal in 15 of 16 rats. Control infusion of saralasin in normal animals or of glucose in normal and hypertensive animals did not reduce blood pressure. Plasma renin concentration correlated significantly with the early but not with the later fall of blood pressure ($r = +0.64, P < 0.02$ for the first). Plasma concentrations of renin and angiotensin II were closely related ($r = 0.91, P < 0.001$) except in rats receiving converting enzyme inhibitor, when angiotensin II was relatively reduced. The reduction of pressure was not associated with increased urinary sodium excretion.

16. EFFECT ON CONVERTING ENZYME INHIBITOR AND SARALASIN OF THE REFLEX CONTROL OF BLOOD PRESSURE

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