While such an immune-mediated metabolic impairment is therefore unlikely to be directly responsible for the development of the pathophysiology of Reye's syndrome, this does not preclude the possibility that aspirin itself or a metabolic product may play a more indirect role in the aetiology of this disease.

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Comparison of the effects of Fe^{2+} and Cu^{2+} on prostaglandin synthesis in rabbit kidney medulla slices

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The effects of Fe^{2+} and Cu^{2+} on the generation of medullary prostaglandins E_2 and $F_{2\alpha}$ have been compared. Fe^{2+} markedly promoted the lipid peroxidation of rabbit kidney medulla slices. The lipid peroxidation induced by Fe^{2+} inhibited both prostaglandin E_2 and prostaglandin $F_{2\alpha}$ formation to a similar extent. While Cu^{2+} produced only a small increase in lipid peroxidation, it had a powerful inhibitory effect on prostaglandin E_2 formation. Simultaneously, prostaglandin $F_{2\alpha}$ production was increased. In the presence of Cu^{2+} the net increased amount of prostaglandin $F_{2\alpha}$ was much smaller than the net decreased amount of prostaglandin E_2 (15–20%). These results suggest that Cu^{2+} has the potential to modulate prostaglandins E_2 and $F_{2\alpha}$ synthesis by affecting endoperoxide E_2 isomerase or endoperoxide reductase independent of its peroxidative action.

The ions of a number of transition metals are effective catalysts for the rapid peroxidation of unsaturated lipids. It has been reported that cupric copper (Cu^{2+}) is an active catalyst of lipid peroxidation, and acts as a strong pro-oxidant by catalysing the decomposition of hydroperoxides (Haase & Dunkley 1969). We have reported that Cu^{2+} stimulates the lipid peroxidation in rabbit renal cortical mitochondria (Fujimoto et al 1984). We have also shown that lipid peroxidation induced by ascorbic acid and Fe^{2+} inhibits medullary generation of prostaglandin E_2 (Fujimoto & Fujita 1982; Fujimoto et al 1983). The present study was undertaken to investigate the effect of Cu^{2+} on the biosynthesis of prostaglandins E_2 and $F_{2\alpha}$ in kidney medulla slices in comparison with that of Fe^{2+}.

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Materials and methods

Kidney medulla slices were prepared from male rabbits (2–2·5 kg) as described by Fujimoto & Fujita (1982). In all experiments the slices (0·4 g) were preincubated in 4·0 mL of 0·15 M KCl/0·02 M Tris-HCl buffer, pH 7·4, at 4 °C for 5 min. Following preincubation, the medium was discarded, the slices rinsed twice with the Tris-HCl buffer and incubated with the indicated concentrations of $FeSO_4$ or $CuSO_4$ at 37 °C for 30 min.

At the end of the incubation period, the slices were quickly removed from the medium, blotted lightly on filter paper, reweighed and homogenized in 5 mL of the Tris-HCl buffer. Aliquots, 5 mL, were mixed with 1·25 mL of 40% trichloroacetic acid and assayed for malondialdehyde by the thiobarbituric acid method (Tappel & Zalkin 1959), and it was expressed as thiobarbituric acid values (absorbance at 532 nm g^{-1} tissue).

We reported previously that the major prostaglandins produced in our incubation of medulla slices and recovered in the medium were prostaglandins E_2 and $F_{2\alpha}$ (Fujimoto et al 1983). Prostaglandins E_2 and $F_{2\alpha}$ in