alurnin supplementation (figure 1). Hepatic expression of TLR4 and associated pathways: Cirrhotic NAR animals had greater hepatic TLR4 expression which was reduced by alurnin administration. Hepatic TLR4 gene array confirmed the activation of TLR4 dependent pathways in the cirrhotic NAR animals, which was abrogated by alurnin infusion.

Conclusion NAR animals have significantly greater liver injury, increased sensitivity to LPS and mortality which is prevented by alurnin administration. Our data show for the first time that the mechanism of the protective effect of alurnin is consequent upon restoration of gut junctional proteins and reduction of hepatic TLR4 expression.

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**THE POTENT UREASE INHIBITOR FLUROFAMIDE EFFECTIVELY SUPPRESSES AMMONIA PRODUCTION BY THE COLONIC MICROFLORA**

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Abstract: Ureolysis by colonic microorganisms gives rise to a significant fraction of the portal vein ammonia load; colonic urease inhibition would therefore be a logical approach to reducing systemic ammonia in patients with hepatic encephalopathy. This was trialled in the 1960’s in a small number of patients, using the urease inhibitor acetohydroxamic acid (AHA); disappointing clinical results led to the approach being abandoned. However, AHA is not a particularly potent inhibitor of urease; more potent inhibitors have since been developed, one of which is flurofamide. It is possible flurofamide might be more effective in this context, but no relevant work has been reported; we have conducted an initial laboratory study into the effects of flurofamide on ammonia production by the colonic microflora, in particular the flora of the right colon.

**Methods** Patients attending for routine colonoscopy who did not have inflammatory bowel disease or change of bowel habit were approached to take part. At colonoscopy, 50 mls sterile water was introduced into the right colon, and aspirated back into a polyp trap. These washings were transported to the laboratory for processing within 2 – 4 hours; a mechanical cell count was performed, and the samples were incubated for 22 hours in urea-containing culture medium with various concentrations of flurofamide, under both aerobic and anaerobic conditions. Following incubation, ammonia and urea levels in the medium were measured.

**Results** As expected, colonic washings produced ammonia when cultured in urea containing medium, although ammonia production did not correlate directly with the number of organisms in the inoculum. Lower concentrations of flurofamide had variable effects on ammonia production, but higher concentrations reduced levels to an average of less than 5% of the ammonia generated in the absence of flurofamide (figure 1). Results from aerobic and anaerobic cultures were very similar; there was no evidence for flurofamide toxicity. Urea levels were difficult to interpret due to assay variability and the high baseline level of urea.