and a second endoscopy four weeks after receiving naproxen, etodolac, indomethacin, or azapropazone showed that 20 patients (25%) had gastric antral erosions. Duodenal erosions were found in only 1 patient (1%) who also had gastric erosions. In a separate study on 81 rheumatic patients with iron deficiency anaemia, 30 (37%) had gastric ulcer or erosions whereas only 3 (4%) had duodenal ulcers or erosions.

The aim of prescribing misoprostol with an NSAID, however, has to be defined, especially because about a quarter of symptom-free individuals receiving NSAIDs also have gastroduodenal erosions or ulcer. The importance of these lesions lies in the associated morbidity (dyspepsia) and life-threatening complications such as haemorrhage and perforation. Graham's data show no significant difference in the relief of pain between misoprostol or placebo. As Graham points out, there is no evidence that the reduction in the frequency of ulcer is associated with reduction of life-threatening complications. In addition, duodenal ulcers contribute equally towards these complications in patients receiving NSAIDs[1] and Graham's study cannot demonstrate any prophylactic effect of misoprostol on duodenal ulcers. We accept his suggestion that a specially designed study will be required to demonstrate an effect of misoprostol on duodenal ulcer formation. His argument, however, that "the evidence suggests that misoprostol should prevent both gastric and duodenal ulcer induced by NSAIDs" is unfounded.

Thus the rationale for combination therapy based on the available data is insufficient and stronger evidence is needed. In addition the group that might benefit from such therapy needs to be identified.

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1. Somerville K, Faulkner G, Langman M. Non-steroidal anti-inflammatory drugs and bleeding peptic ulcer. *Lancet* 1986; i: 462–64.

PARACETAMOL AND PEPTIC ULCER

SIR,—Professor Piper and Dr McIntosh (Nov 19, p 1192) suggest that their data, published after our report, demonstrate that there is no association between previous paracetamol use and newly diagnosed peptic ulcer. The 95% confidence intervals that they report for the association are 0·6–2·9 for weekly use and 0·5–2·6 for daily use. The lower limit would correspond to a negative association, and the upper limit to a positive association much larger than the one we reported. We submit that Piper and McIntosh do not have sufficient data to establish the negative that they claim.

An inference to be drawn from our work is that individuals with undiagnosed peptic ulcer may occasionally be treated for pain thought to be arthritic. If the pain of an incipient ulcer may be mistaken for low-back pain, then even in a well-controlled observational study the reported association between non-steroidal anti-inflammatory drugs and ulcers will be inflated.

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LABORATORY CONFIRMATION OF CORTINARIUS POISONING

SIR,—Cortinarius poisoning is characterised by acute nephritis, which can prove fatal. The symptoms can take a long time to appear. The two *Cortinarius* spp most often responsible are *C orellanus* and *C speciosissimus*.[1] The main toxin is orellanine, which is decarboxylised under ultraviolet light to give a stable, non-toxic molecule called orelline. However, there are intermediaries that may bind covalently with glutathione and proteins to cause renal disturbance.[2] These species were thought edible until 1957,[3] and poisoning is still reported in several European countries (including the UK[4]). We have confirmed *C orellanus* poisoning in a young woman by assaying orellanine in plasma and renal biopsy specimens.

A 31-year-old psychiatric patient ingested two fruit bodies of *C orellanus*. She was admitted to hospital as soon as symptoms appeared, 9 days later, with acute renal damage (creatinine 1100 μmol/l). Haemodialysis and plasmapheresis plus haemoperfusion led to partial recovery of renal function. Other treatments included frusemide, diltiazem, dopamine, and vitamin C and aminoacid mixtures. There was no fever or liver abnormality. Biopsy on day 4 revealed tubular necrosis and interstitial fibrosis. On day 13 the patient returned home with satisfactory renal function. 4 months after she ingested the toxic fungus her plasma creatinine was 240 μmol/l and 6 months later biopsy revealed tubular recovery but with worsening interstitial fibrosis.

Biological fluids were passed through an 'Amberlite XAD' column.[5] Plasma samples (0·5–1·2 ml) were loaded directly; urine and haemodialysis fluids were concentrated first. Tissue was homogenised with 1 ml methanol/water, centrifuged, and then passed through the resin. Orellanine was detected by fluorimetry on cellulose chromatograms after thin-layer chromatography and photodecomposition.[2] We used two-dimensional chromatography.

We did not detect any orellanine or orelline in urine despite the assay sensitivity (10 ng). Orellanine and its photodecomposition metabolites were detected in the first plasma sample; the concentration of orellanine was 6 mg/l (0·02 mmol/l). Plasma taken after the first haemodialysis was free from detectable orellanine and orelline, as were the haemodialysed fluids. In renal tissue extracts the orellanine level was 7 μg in 25 μl (first biopsy) and 24 μg in 8 μl (second). In the second sample orelline was the major metabolite.

These assay data show that the toxin remained in the blood for at least 10 days; that haemodialysis cleared circulating toxin but not toxin bound to renal cells; that the release of orellanine and its metabolites from renal cells was very slow; and that orelline predominated, with lower concentrations of orellanine and partly decxidised metabolites. These findings support the view[2] that cortinarius toxicity is caused by metabolites derived from the photochemical rearrangement of orellanine. Our analytical procedure permits the precise diagnosis of orellanine poisoning.

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1. Rapior S, Andary C, Privat G. Chemotaxonomic study of orellanine in species of *Cortinarius* and *Dermocybe*. *Mycologia* 1988; 80: 741–47.
2. Andary C, Rapior S, Fruchier A, Privat G. Cortinaires de la section *Orellani*: photodecomposition et hypothèse de la photosynthèse de l'orellanine. *Cryptogamie Mycol* 1986; 7: 189–200.
3. Grzymala S. Massenvergiftung durch den Orangefuchsigen Hautkopf (*Cortinarius orellanus*). *Zeitschr Pilzkunde* 1957; 23: 139–42.
4. Short AIK, Watling R, MacDonald MK, Robson JS. Poisoning by *Cortinarius speciosissimus*. *Lancet* 1980; ii: 942–44.
5. Rapior S, Andary C, Mousain D. *Cortinarius* section *Orellani*: isolation and culture of *Cortinarius orellanus*. *Trans Br Mycol Soc* 1987; 89: 41–44.

^{99m}Tc-HMPAO WASHOUT IN PROGNOSIS OF STROKE

SIR,—The outcome of a major cerebrovascular event is difficult to establish and usually depends on the type, extent, and localisation of the lesion. Established clinical scores[1–3] are poor predictors and a simple early test would be most useful. Regional cerebral blood flow (rCBF) and cerebral blood volume (CBV) measurements with positron emission tomography (PET)[4] and single-photon emission tomography (SPET)[5] have been used to demonstrate neurovascular mechanisms during the course of cerebrovascular lesions. After a "stroke" collaterals develop with an increase in CBV, vascular