1 Lyell A. The staphylococcal scalded skin syndrome in historical perspective: emergence of dermopathic strains of Staphylococcus aureus and discovery of the epidermolytic toxin. A review of events up to 1970. *J Am Acad Dermatol* 1983;9;:285-94.
2 Melish ME, Glasgow LA. The staphylococcal scalded skin syndrome. Development of an experimental model. *N Engl J Med* 1970;282:1114-9.
3 Dowsett EG, Petts DN, Baker SL, *et al*. Analysis of an outbreak of staphylococcal scalded skin syndrome: strategies for typing 'non-typable' strains. *J Hosp Infect* 1984;5:391-7.
4 Blanc MF, Janier M. Staphylococcies exfoliantes (SSSS) de l'adulte. *Ann Dermatol Venereol* 1986;113:833-43.
5 Amon RB, Dimond RL. Toxic epidermal necrolysis: rapid differentiation between staphylococcal induced disease and drug induced disease. *Arch Dermatol* 1975;111:1433-7.

*(Accepted 24 April 1987)*

**Western Infirmary, Glasgow G11 6NT**
R O'KEEFE, MB, CHB, research registrar
J H DAGG, MD, FRCP, consultant physician
RONA M MACKIE, FRCP, FRCPATH, professor of dermatology

Correspondence to: Professor MacKie.

# Cross hepatotoxicity between non-steroidal anti-inflammatory drugs

Non-steroidal anti-inflammatory drugs such as ibuprofen, flurbiprofen, ketoprofen, naproxen, and fenoprofen are generally considered to be well tolerated and effective. Benoxaprofen, which is structurally related to these drugs, was withdrawn from use because of severe and potentially lethal hepatotoxicity and other side effects. Less severe and apparently less frequent hepatic impairment has been reported with ibuprofen, naproxen, and fenoprofen.[1] We report a case of cross hepatotoxicity between two derivatives of propionic acid, naproxen and fenoprofen.

## Case report

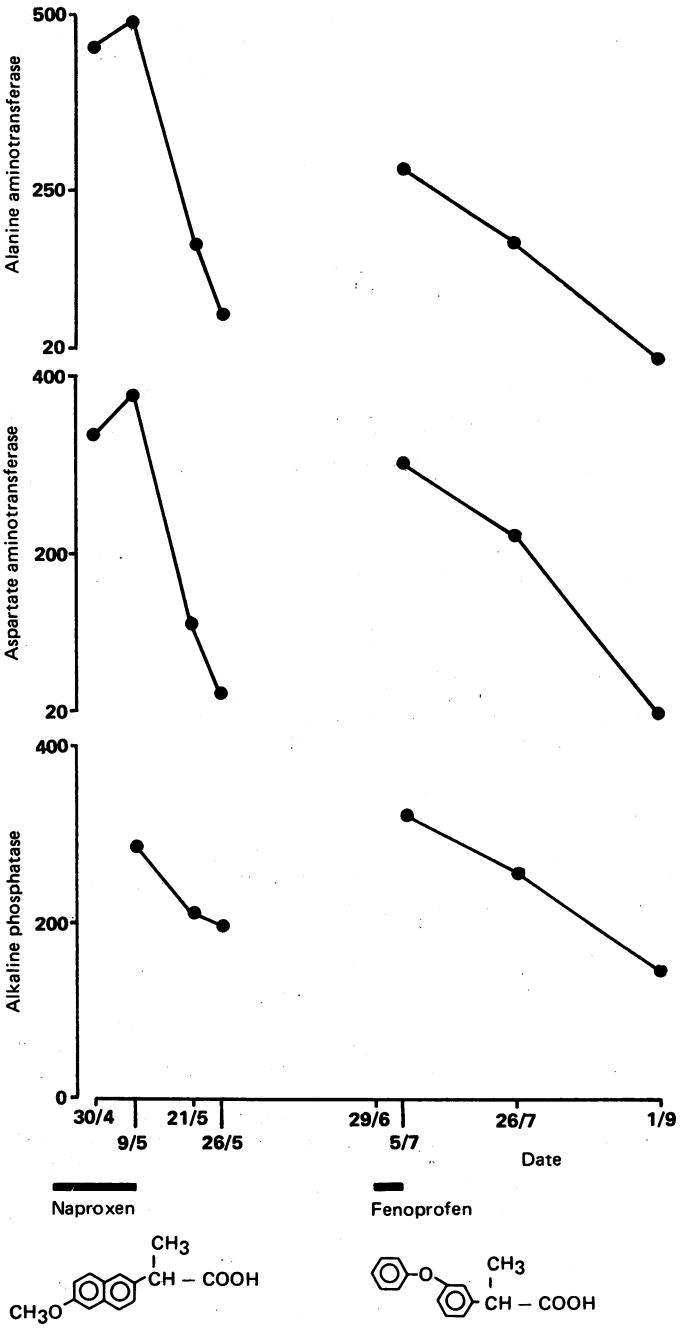
A non-alcoholic woman of 67 was admitted to hospital on 9 May 1986 for acute icteric hepatitis. Except for an episode of unexplained jaundice six years earlier she had no history of liver disease and had not received any blood transfusions. From 21 April 1986 she was given naproxen by mouth 500 mg daily for pain in the hip related to arthrosis. On 30 April she complained of nausea, abdominal pain, and malaise; on 3 May she became jaundiced. On admission her body temperature was normal. The liver measured 10 cm on the midclavicular line and was not tender. The drug was discontinued. The results of tests were: white cell count $5{\cdot}5\times10^9$ /l, eosinophils $3{\cdot}8\times10^8$ /l, total serum bilirubin 78 μmol/ l, serum alanine aminotransferase 450 IU/l (normal <20), serum aspartate aminotransferase 330 IU/l (normal <20), serum alkaline phosphatase 280 IU/l (normal <170), and serum γ-glutamyl-transferase 349 IU/l (normal <18). Hepatitis B surface antigen was absent but hepatitis B surface and core antibodies (IgG) were detected in serum, anti-hepatitis A virus IgM was absent, and antitissue antibodies were not detected. Ultrasonography of the liver and biliary tract yielded normal results, as did endoscopic retrograde cholangiography. Histological examination of a liver specimen showed fibrosis and infiltration of the portal tracts with inflammatory cells and a moderate hepatocellular necrosis. In a few days the clinical symptoms disappeared and the results of liver function tests improved (figure).

From 29 June another non-steroidal anti-inflammatory drug, fenoprofen 300 mg daily, was given to the patient for her joint pain. On 3 July she complained again of nausea, malaise, and severe abdominal pain. Abnormalities in the results of liver function tests rapidly recurred. Clinical examination showed nothing abnormal except for a body temperature of 38·5°C. After withdrawal of the drug abdominal pain disappeared promptly and the results of liver function tests progressively returned to normal values (figure).

## Comment

In this patient the following arguments suggest that the drugs derived from propionic acid were the cause of the hepatic injury: (*a*) the recent institution of treatment before the appearance of clinical and biological symptoms, (*b*) the quick improvement after discontinuing both drugs, (*c*) the striking similarity between the reactions associated with two chemically related drugs, and (*d*) the absence of other explanations. In addition, several cases of hepatitis induced by naproxen have been reported with similar clinical and biological patterns.[2] Hepatic injury due to naproxen is rarely associated with manifestations of hypersensitivity in contrast to hepatitis related to ibuprofen. Hepatitis associated with fenoprofen seems very rare and is mainly characterised by cholestasis with mild hepatocellular necrosis.[3]

Our case report suggests a cross hepatotoxicity between two propionic acid derivatives. Comparison of the chemical structures of the two drugs (figure) shows that the propionic acid chain is probably responsible for the toxic effect of both drugs on the liver. Reports of cross hepatotoxicity between two chemically related drugs are rare. Recent reports of such a cross hepatotoxicity concern antidepressants: mianserin and nomifensine,[4] and amineptine and clomipramine.[5]




Time course of activities (IU/l) of serum alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase in relation to administration of naproxen and fenoprofen.

In practice patients whose hepatitis has been induced by non-steroidal anti-inflammatory drugs derived from propionic acid should not be given non-steroidal anti-inflammatory drugs of the same chemical class. Such administration is not always followed by hepatic injury, however, as shown by a patient who suffered from hepatitis induced by fenoprofen and later took naproxen with no problems.[3]

1 Abadia R, Jammet P, Christoforov B, Cremer GA. Hépatotoxicité des médicaments couramment utilisés en rhumatologie. *Ann Med Interne (Paris)* 1985;136:590-600.
2 Victorino RM, Baptista A, Silveira JC, De Moura MC. Jaundice associated with naproxen. *Postgrad Med J* 1980;56:368-70.
3 Stennett DJ, Simonson W, Hall AC. Fenoprofen-induced hepatotoxicity. *Am J Hosp Pharm* 1978;35:901.

4 Zarski JP, Aubert H, Rachail M. Toxicité hépatique des nouveaux antidépresseurs. A propos d'une observation. *Gastroentérol Clin Biol* 1983;7:220-1.
5 Larrey D, Rueff B, Pessayre D, *et al.* Cross hepatotoxicity between tricyclic antidepressants. *Gut* 1986;27:726-7.

*(Accepted 24 April 1987)*

**Service d'Hépato-Gastroentérologie and Unité de Pharmacologie Clinique, Centre Hospitalier Universitaire, 80030 Amiens Cedex, France.**
M ANDREJAK, MD, professor of medicine
T DAVION, MD, intern
J L GINESTON, MD, hospital practitioner
J P CAPRON, MD, professor of medicine

Correspondence to: Dr Capron.

# Management of blisters in minor burns

The best way to manage blisters in minor burns is controversial. Recommended procedures include deroofing,[1 2] aspiration,[3] and leaving blisters intact.[4] The choice of treatment is usually based on clinical impression and experience. We investigated the effects of these three treatments on bacterial colonisation of the blister fluid or surface of the burn and on wound pain in patients with minor burns.

## Methods and results

Altogether 202 patients attending two accident departments for treatment of minor burns were included in the investigation. The extent of injury averaged 1% of body surface area; all burns except one were partial thickness and healed with conservative treatment. Only thermal burns of the arms and legs that could be treated with paraffin gauze dressings were included; most were of mixed depth. All residual sprays and ointments used in first aid were removed by washing with sterile saline. The patients were asked to attend the next weekday burns clinic and were seen thereafter two or three times a week for dressings.

During the first part of the study blisters were left intact for up to 10 days to determine the risk of colonisation or infection of blister fluid; fluid was aspirated through a single puncture hole. In the second part blister fluid was aspirated through a single puncture hole at the first follow up visit and the blister dressed. The lumen of the blister was swabbed once during the next 12 days. Throughout the investigation exposed tissue burns were swabbed once up to 12 days after injury. Sampling times were comparable in aspirated and exposed burns. The sample of fluid (intact burns) and swab (aspirated and exposed burns) were analysed according to standard bacteriological methods. Some of the blisters which were aspirated in the second part of the study were actively deroofed. Patients whose blisters were aspirated or deroofed were asked at least one day later whether the pain in the burnt area had increased, decreased, or remained unchanged after treatment. Differences were assessed by $\chi^2$ tests.

*Effect of different treatments on bacterial colonisation*

| | Blister treatment | | |
|---|---|---|---|
| | Intact (n=110) | Aspirated (n=104) | Exposed (n=102) |
| No (%) colonised any bacterium | 15 (14) | 73 (70) | 78 (76) |
| No (%) colonised with *Staph aureus* | 2 (2) | 19 (18) | 45 (44) |

The table records the incidence of colonisation in the three study groups. The overall incidence of colonisation with micro-organisms was much lower in the intact blisters than in either the aspirated blisters or the exposed tissue burns ($p \ll 0{\cdot}05$). The incidence of infection with the potential pathogen *Staphylococcus aureus* was significantly lower in both the intact and aspirated blisters compared with the exposed burns ($p \ll 0{\cdot}05$). Furthermore, aspiration and deroofing had a different effect on the patients' perception of wound pain. None of the 37 patients whose blisters were deroofed experienced a reduction in pain (in 16 pain increased and in 21 it was unchanged), but aspiration reduced pain in 27 out of 73 patients (15 increased, 36 unchanged). This difference was significant ($p < 0{\cdot}05$).

## Comment

Our results show that an intact blister roof prevents colonisation of minor burns by bacteria, especially *Staph aureus*. This conclusion supports the findings of Cope, who observed infected fluid in only one intact blister in 26 patients (*Streptococcus pyogenes*). The importance of colonisation of small burn wounds in terms of morbidity and healing is unknown, but colonisation should be minimised. Infection is a severe problem with major burn injuries, and the portal of entry of the organisms is probably the burn wound.

Our results suggest that in minor burns blisters should be left intact whenever possible and not be deroofed if they rupture spontaneously. Deroofing is likely to lead to more pain and an exposed surface is associated with a higher incidence of colonisation with *Staph aureus*. Obviously these findings should not dictate an inflexible policy toward treatment. Many blisters will spontaneously rupture and deroof. If blisters are to be drained because of their size or site aspiration is preferable to deroofing, which is warranted only when infection is clinically evident.

1 Hummel RP. Initial wound management. In: Hummel RP, ed. *Clinical burn therapy*. Boston: John Wright, 1982. 87-110.
2 Muir IFK, Barclay TL. Local treatment of the burn wound. In: Muir IFK, Barclay TL, eds. *Burns and their treatment*. London: Lloyd-Luke, 1974: 68-9.
3 Bruck M. The management of small burns. In: Artz CP, Moncrief JA, Pruitt BA, eds. *Burns—a team approach*. Philadelphia: W B Saunders, 1979: 165-8.
4 Lewis SR, Lynch JB, Blocker TG, *et al.* Evaluation of topical burn therapy over the past 20 years. In: Matter P, Barclay TL, Konickova Z, eds. *Transactions of the 3rd international congress on research in burns*. Berne: Hans Huber, 1971: 108-11.
5 Cope O. The treatment of surface burns. *Ann Surg* 1943; 117: 885-93.

*(Accepted 24 April 1987)*

**St Richard's Hospital, Chichester PO19 4SE and Charing Cross Hospital, London W6 8RF**
ANDREW H SWAIN, PHD, FRCS, senior registrar, accident and emergency medicine

**Charing Cross Hospital, London W6 8RF**
BERGE S AZADIAN, BSC, MRCPATH, consultant clinical microbiologist
CHARLES J WAKELEY, BSC, MB, senior house officer, accident and emergency medicine

**Odstock Hospital, Salisbury SP5 3LE**
PETER G SHAKESPEARE, BSC, PHD, director, Laing laboratory

Correspondence to: Mr A H Swain, Accident and Emergency Department, Worcester Royal Infirmary, Worcester WR1 3AS.

# Cervical cytology screening: a comparison of two call systems

A study was undertaken to investigate two methods of call up as part of the pilot scheme for the Nottingham cervical cytology programme, in which the health authority and the family practitioner committee are collaborating. There is a consensus that such programmes should closely involve general practitioners and that encouragement from them achieves high rates of response.[1 2] This study was designed to discover whether a letter of invitation from the general practitioner to women with no record of having had a cervical smear test would be more effective if it contained a definite date and time for a smear test than if it just invited the woman to contact the surgery and make her own arrangements.

## Patients, methods, and results

Five general practices, which did not have an established programme, agreed to participate in the project. They comprised four two doctor and one four doctor partnerships and represented a reasonable geographical spread within the authority from inner city to suburban. Women aged 45-65 were identified from the register of the family practitioner committee. There were 2264 women in the five practices. Notes were available for 2174, and of these 906 (42%) had no record of having had a cervical smear. The general practitioners were asked to exclude any women they did not wish to call for a smear; 68 were excluded, most because of hysterectomy but some because of other medical conditions.

Fifty women from each practice were randomly selected to take part in the study with 25 in each study group. This size of sample was chosen so that the project could be completed in a reasonable time without creating an excessive demand for smears in the practices in the short term. The first group was sent a letter inviting the patient to contact the surgery to make arrangements for a smear test (letter only group). The second group was sent one that included an appointment for a smear and asked the patient to make alternative arrangements with the surgery if it was inconvenient or if she wished to cancel for other reasons (appointment group). Both groups were asked to respond within three weeks of receiving the letter. Non-respondents in both groups were sent up to two reminders; they were similar to the first letter except that the alternative of attending a health authority clinic was mentioned.

Before the letters were sent three women left their practices, and of the 247 letters sent seven were returned as "address unknown." This reduced the number in the letter only group to 122 and that in the appointment group to 118. Responses to the two methods of call are shown in the table.