impaired liver function related to hepatic metastases. The doses were related to body surface area, and, because the patient was grossly overweight, the dose of chemo therapy may also have been too low.

We consider that these profound metabolic abnormalities were probably caused by the cytotoxic chemotherapeutic agents, perhaps by inducing renal tubular damage. The case was unusual in that although the patient received continuous calcium, vitamin D, and magnesium replacement until the time of her death, satisfactory control was never achieved. As far as we know this has not been reported previously in association with mitozantron.


Small bowel perforation associated with an excessive dose of slow release diclofenac sodium

Mr R Harkin and others (Queen Elizabeth Hospital, Birmingham B15 2TH) write: Intestinal perforation associated with the ingestion of indomethacin is a well recognized complication of this drug, and is said to occur at high risk of death. There have been seven deaths among the 18 cases reported to the Committee on Safety of Medicines (CSM) between 1982 and 1986. It has also been suggested that long acting preparation of indomethacin, was withdrawn because of a number of reported perforations, although the relationship to the local toxicity with the formulation and drug delivery system. The risk of perforation is also present with other non-steroidal anti-inflammatory drugs thought to have a lower incidence of effects.

A 70 year old man was referred with a 24 hour history of pain in the left ileac fossa. He had a fever and was vomiting. Twenty seven years previously he had had a laminectomy for a prolapsed intervertebral disc. He had subsequent osteoporotic fractures and had been taking a combination of dipipanone hydrochloride and cyclazocine hydrochloride (Ticodan) twice daily for two weeks. Two weeks before admission he had been prescribed the recommended dose of diclofenac sodium, 100 mg daily, in a sustained release preparation (Voltarol Retard). During the week before admission he had increased the dose to 100 mg four times daily.

An initial diagnosis of acute diverticulitis was made, and was confirmed when the patient was taken to theatre and laparotomy was performed. The patient died of hypovolaemic shock. He had a temperature of 38°C and a heart rate of 100, although his blood pressure was normal. A small abscess cavity was also noted in the ileac fossa, probably from the terminal ileum. A biopsy from the edge of a perforation showed no specific features. The perforations had healed initially and had remained confined within a small abscess cavity beside the sigmoid colon in the left ileac fossa, thus accounting for his localised signs at presentation. The abscess had ruptured subsequently and was found to be filled with necrotic material and with cat gut, and he made an uneventful recovery. Blood cultures and faecal samples were negative for bacteria.

To our knowledge this is the first reported case of small bowel perforation associated with the ingestion of slow release diclofenac sodium (a phenylalkanone derivative). Non-steroidal anti-inflammatory drugs, including indomethacin and fenamic acid derivatives, given orally or parenterally to rats cause small bowel perforation in a high percentage of cases. The two holes were over-sewn with cat gut, and he made an uneventful recovery. Blood cultures and faecal samples were negative for bacteria.

Our patient was suffering from pain that had been difficult to control over a long time, and he had increased his dose of diclofenac sodium to four times the recommended dose. The perforation could have been caused by high local drug concentrations, a factor that might have been exacerbated by taking the combination of dipipanone hydrochloride and
cyclozine hydrochloride, which could have slowed his intestinal transit rate. Systemic toxicity is an alterna-
tive possibility. In view of the animal studies small bowel and urinary tract perforation was as unex-
epected especially in association with the high dose of dico-
fenac sodium that this man was taking.

Mesalazine enemas are often prescribed for pain that is unremitting and difficult to
trol, but their therapeutic window is small. With high dose slow release preparations it is easy to
reach harmful concentrations by taking relatively few	tablets. Patients taking slow release preparations of non-steroidal anti-inflammatory drugs should be
warned specifically of the dangers of increasing this
dose beyond that recommended. The risk of localised
toxicity may be increased when non-steroidal anti-
flammatory preparations are taken in conjunction with
opioids or their derivatives, which decrease intestinal motility.

2 Langman MJ, Morgan L, Woolard A. Use of anti-inflammatory enemas with small or large bowel perfora-

Unilateral deafness as a complication of the mumps, measles, and rubella vaccination

Des J Næs-Nielsen and B Walter (Audiological Department, Aalborg Hospital, DK-9000 Aalborg, Denmark) write: A 7 year old girl, who had been foun deal her leaving by pure tone audiome-
try two years earlier, received a mumps, measles, and rubella vaccination without any immediate com-
plications. Eleven days later she had a slight fever which, in addition to an enlarged lymph node, was she was deaf in her left ear. She had no dizziness, headaches, or earaches.

One month after the vaccination an ear, nose, and throat specialist found that she had a profound hearing impairment in her left ear by pure tone audiometry.

The audiometric examination showed that the impair-
ments apart from the hearing loss. Pure tone audi-
ometry showed anacusis in her left ear. In her right ear the hearing level was 0 dB, with normal speech discrimina-
tron. An enlarged vestibular and stapedial reflexes could be elicited from either ear. Ipsilateral stapedius reflexes were present in the right ear. Tympanometry was normal in both ears. Examination findings of the ears, nose, and throat were otherwise normal. Caloric testing showed no response in either ear to warm water and only one half equal response to cold water. Posturographic nystagmus was normal.

Eleven weeks after the mumps, measles, and rubella vaccination IgG antibodies to the mumps virus were found. Immunoglobulins M and A could not be found. The girl had never had symptoms of mumps. Her hearing impairment has not changed during the past 11 months, and she still has no other complications.

Mumps is usually a benign disease, but it is an important cause of unilateral hearing impairment in children. With the development of the combination mumps, measles, and rubella vaccination vaccination should become more widespread, so reducing the amount of unilateral hearing loss in children. Adverse reactions to combination mumps, measles, and rubella vaccinations are mainly in the form of fever. There are few serious complications, and most are reversible.

The Department of Health in Denmark knows of no other case of hearing impairment after mumps, measles, and rubella vaccination. Only two cases of unilateral deafness have been reported before as a result of mumps vaccination in Denmark.

In our patient it seems reasonable to believe that the unilateral anacusis was caused by the mumps component of the vaccine since no symptoms of mumps, and measles, and rubella vaccine. This seems to be a rare complication, but it is important to be aware of this possibility during the first years of the vaccination programme, as it is only in older children that we will be able to discover this side effect. When nearly all children over 3 years of age have been vaccinated the discovery of unilateral deafness will be delayed and the relation to the vaccine will be difficult to prove.


Myocardial microthrombi in systemic lupus erythematosus

Professor Priscilla Kincade-Smith (Department of Medicine, Royal Alexandra Hospital, Houston, TX 77030, USA) writes: The case reported by Dr J H Brown and others (28 May, p 1505) is similar to a series of 12 cases of microangiopathic haemolytic anaemia (May 28, p 1297). In all our cases the clinical characteristics of this lupus syndrome closely resembled that of the case European group. Eight of the 10 women in whom the test was performed had a positive test for anti-
phospholipid (anticoagulant) antibodies. These patients had thrombotic tendencies in arteries, veins, and glomerular capillaries as seen in biopsy specimens. These findings are typical of thrombotic microangiopathy.

The patient in this European group were successful, and pregnancy precipitated the acute thrombotic microangiopathy in most of our patients. One, however, had a previous episode of com-
plete occlusion of a femoral artery and may have been on an oral contraceptive agent. This prompts the question whether the 22 year old patient described by the cecetologists, and two required a laparotomy for pelvic
disease. Unnecessary laparotomy was thus avoid-
ed in 29 of the 39 patients (74%), an important saving in a country where surgical resources are scarce. When the appendix could not be seen at laparoscopy an appendectomy was carried out. When the appendix was normal and no other cause of the patient's problems could be found the patient was either observed in hospital or had an immediate appendectomy. We have not found that laparoscopy is safe in men with suspected appendicitis in the North Solonians as most of them present with signs of late appendicitis (a mass or peritonitis). Laparoscopy is unnecessary and hazardous in such patients.


Which patients should undergo laparoscopy?

Dr Hamish Mc Foster (Hunter Oncology Centre, Waratagh, New South Wales 2298, Australia) writes: I agree with Mr S Patterson-Brown and others that a laparoscopy should be performed on all women who have a negative appendectomy and who present with a clinical diagnosis of acute appendicitis (14 May, p 1363). The clinical diagnosis of acute appendicitis in women is difficult, especially in those of childbearing age. Accuracy rates can be as low as about a half. In the North Solonians province of Papua New Guinea laparoscopy has been used before operation in virtually all women with suspected appendicitis in an attempt to reduce the rate of unnecessary exploration and appendectomy. Over three years 39 women with suspected appendicitis had laparoscopy and were observed or received antibiotics for pelvic inflammatory disease. Eight had appendi-
cectomies, and two required a laparotomy for pelvic disease. Unnecessary laparotomy was thus avoid-
ed in 29 of the 39 patients (74%), an important saving in a country where surgical resources are scarce. When the appendix could not be seen at laparoscopy an appendectomy was carried out. When the appendix was normal and no other cause of the patient's problems could be found the patient was either observed in hospital or had an immediate appendectomy. We have not found that laparoscopy is safe in men with suspected appendicitis in the North Solonians as most of them present with signs of late appendicitis (a mass or peritonitis). Laparoscopy is unnecessary and hazardous in such patients.

Undergraduate medical education

Professor R M Harden (Centre for Medical Educa-
tion, University of Dundee, Dundee DD 1 951, Scotland) writes: A course运作 called DDI (De-
velopment of diagnostic and interventional skills) in British (9 July, p 136) is misleading. His estimate of five educationalists working full time on medical educational problems in British medical schools is low. In this unit alone we have eight staff working full time in this subject. Dr Jolly's information about the lack of training programmes in medical education is also incorrect. In the North Solonians, in one week courses in medical education, which have so far attracted more than 600 medical teachers from the Francophone world, have been given. In addition we have an instance learning diploma course in medical education.

This was designed to meet the needs identified by Professor Peter Richards for “clinical teachers who understand the complexity of medicine to think outside the patterns of medical education for the future” (7 May, p 1279). The first two doctors have now completed the course successfully and 50 are enrolled currently.