problems, particular socio-economic conditions, birth rate, and levels of literacy, nutrition and mortality. This means that any essential drug list must vary from one country to another — with an appropriate list, perhaps 80 - 90% of diseases can be controlled reasonably effectively but there must be room for the introduction of the most modern and advanced preparations if the need exists.

The industry, however, needs collaboration at a national level and, as the spokesman remarked, it is regrettable that a health ministry is often given a low priority in developing countries, thereby preventing the recruitment of the few available competent administrators. Health budgets in many developing countries are much lower than, for example, military budgets.

In the conclusions of the workshop, the point was again made that, although the drug industry has not been blameless nor have governments, the doctors must accept the main responsibility for any unbalanced drug usage on the following grounds: doctors have controlled the use of modern drugs from the time of their appearance and have advised on the control of the drug trade and the use of modern drugs by less educated health staff and the population; doctors have trained and supervised all categories of health staff who use the drugs; and finally, doctors in poor countries have tended to follow the pattern of drug usage in rich countries, an attitude which has permeated through to the lower echelons of health staff.

In concluding, Erik Holst called for more discussions between members of various health professions on the one hand and the pharmaceutical industry on the other. 'Even failure should be debated if we are to deal seriously with the promotion of health in other countries.'


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**Paracetamol-induced acute renal failure in the absence of severe liver damage**

Acute renal failure following paracetamol overdosage in association with fulminant hepatic failure or massive hepatic necrosis has been well described.1-3 This complication has been reported in about 10% of severely poisoned patients.3 Less commonly, renal failure may occur in the absence of hepatic failure but in association with abnormal liver function test results.3-4 Impairment of renal function has been recorded in rare instances in the absence of any clinical or biochemical evidence of liver damage.3 Characteristically, liver damage is apparent 2 - 4 days after ingestion of paracetamol whereas renal failure becomes evident 1 week after ingestion. However, back pain, proteinuria and haematuria occur within 36 - 48 hours and are reported invariably to herald renal failure.4 It may be mild and transient, or severe enough to necessitate dialysis. In moderately severe cases not requiring dialysis, serum urea and creatinine concentrations increase progressively for 7 - 10 days before gradual recovery of renal function.5

Paracetamol overdosage is thought to cause renal tubular necrosis in the same way that it damages the liver, through covalent binding of a highly reactive metabolite normally trapped by conjugation with reduced glutathione.5 Hypotension or volume depletion can contribute to the renal damage. Sulphhydryl compounds such as N-acetylcysteine may prevent renal as well as hepatic damage if given within about 10 hours of paracetamol overdosage.5

We have recently treated a 16-year-old girl who ingested 8 - 10 g paracetamol (16 - 20 Beserol tablets: paracetamol 500 mg, chlormezanone 100 mg per tablet). Although she was seen by her doctor, blood levels of paracetamol were not measured and no specific treatment was given. During the following 2 days she vomited on a number of occasions and complained of severe loin pain. Decreased urine output was noted on the 3rd day after drug ingestion. She was admitted to hospital on the 4th day, when the only clinical abnormalities were a temperature of 37.4°C, mildly decreased hydration with a blood pressure of 105/70 mmHg, and marked bilateral loin tenderness. There was no hepatomegaly or liver tenderness. The urine contained 1+ blood and polygonal tubular cells on microscopy. The urine urea level was 119 mmol/l and the sodium level 37 mmol/l. Urine culture was negative. The serum urea level was 13.3 mmol/l (normal 1.7 - 6.7 mmol/l) and the creatinine level was 374 μmol/l (normal 75 - 115 μmol/l). Liver function tests revealed only mild abnormality with a total bilirubin value of 19 μmol/l (normal 1 - 17 μmol/l), aspartate transaminase 32 IU/I (normal 0 - 12 IU/I) and γ-glutamyl transferase 63 IU/I (normal 6 - 28 IU/I). Ultrasonography of the abdomen revealed enlarged kidneys with no evidence of hydronephrosis. With attention to adequate hydration, renal function returned to normal 9 days after ingestion of the paracetamol.

Chlormezanone is not known to be nephrotoxic but it is an enzyme inducer and might have contributed to the increased formation of toxic paracetamol metabolites. Although dehydration may have contributed to the renal impairment the features were compatible with a toxic, paracetamol-induced, acute tubular necrosis. The low urinary urea and the high urinary sodium levels favour acute tubular damage rather than pre-renal failure. The swollen kidneys are also consistent with oedema secondary to renal damage. Renal capsular swelling was thought to account for the loin pain.

Although the renal failure was mild and did not require dialysis, it might have been prevented by early administration.
Modified chymopapain administration

The FDA Drug Bulletin for August 1984 notes that the recommended procedures for administering chymopapain for disc lesions have been modified after reports of serious neurological events associated with the drug. Both the American manufacturers of chymopapain have sent out letters to relevant health professionals about the adverse effects and the new recommendations.

Chymopapain was approved in 1982 by the FDA for intradiscal injection to treat patients with herniated intervertebral discs not responding to conservative therapy. The number of serious neurological adverse events has not been great in comparison with the number of patients involved. It is estimated by one manufacturer that 72 000 patients have been treated with chymopapain and only 30 have experienced a serious adverse reaction, including paraplegia or paraparesis, cerebral haemorrhage or transverse myelitis. Another manufacturer has reported 16 cases among 50 000 patients worldwide. Patients receiving injections in two or more disc spaces appear to be at increased risk.

It is now recommended that the procedure for administering chymopapain be modified as follows: discography should be carried out at least 3 - 4 days before the chymopapain injection and not as part of the procedure. Secondly, an injection of saline or water into the nucleus pulposus should precede chymopapain injection and this should take place in conjunction with high-quality X-ray views of the disc. If there is any question about satisfactory placement of the needle, the procedure should be abandoned. The injection should also be limited to one disc unless there are definite indications that more than one disc is involved. Since most of the serious neurological complications have occurred when general anaesthesia was used, local anaesthesia is recommended whenever possible. Lastly, the manufacturers stress the need for special training in chemonucleolysis before undertaking the procedure.

Becloamethasone and eczema

Atopic eczema in its more severe manifestations can be a nightmarish condition to manage in children. Steroid drugs such as prednisolone can be very effective when given systemically, but have the disadvantages of serious side-effects and difficulty in weaning patients off them, so that clinicians are reluctant to use them. Since it had been noted that high-dose beclomethasone dipropionate given by inhalation to children with asthma had also improved their eczema, a trial was designed in which children with atopic eczema were given beclomethasone dipropionate orally and nasally (Heddie et al., Br Med J 1984; 289: 651-654). Beclomethasone is systematically absorbed and rapidly metabolized in the liver to inactive metabolites. Although it has been used extensively in the prophylaxis of asthma, it has given rise to few local or systemic adverse effects.

Twenty-seven children with moderate or severe atopic eczema were treated in this trial, which was double-blind and placebo-controlled with cross-over. All the criteria studied, measured clinically and assessed parentally, improved on this treatment, and no adverse side-effects were noted. The reason for giving combined nasal and oral beclomethasone was that it seemed more effective than either oral or nasal beclomethasone alone.

Dexamethasone as an anti-emetic

One of the major side-effects of cancer chemotherapy is the nausea and vomiting which it may produce. Not infrequently, cytotoxic 'cocktails' have to be discontinued or modified because of this distressing effect, and can easily lead patients to believe that the cure of the disease may well be worse than simply putting up with it. The commonly used anti-emetics have only been moderately successful, and more effective drugs are constantly being sought. One of these appears to be dexamethasone, which was compared with prochlorperazine in 42 patients undergoing chemotherapy for cancer (Markman et al., N Engl J Med 1984; 311: 549). The drug was well tolerated; 25 patients taking dexamethasone experienced no nausea compared with 14 taking prochlorperazine, and 29 patients did not vomit compared with 18 receiving prochlorperazine. Somnolence was noted in both groups, but was less evident in those patients on dexamethasone (12%) than in those on prochlorperazine (60%).

Dexamethasone appears to be a safe and effective anti-emetic in these patients.