

# ACUTE HEPATITIS ASSOCIATED WITH BLACK COHOSH AND OTHER HERBAL REMEDIES

The use of herbal remedies is increasing across the world. General practitioners, in particular, need to be aware that many of their patients are taking these over-the-counter preparations, and often will not report their use.

An article in the *Medical Journal of Australia* reports on 6 patients who presented with severe hepatitis after taking herbal remedies. One woman used only black cohosh (*Cimicifuga racemosa*) for 1 week, while the other 5 were taking various combinations of herbs for 6 - 18 weeks before their symptoms started. Only 4 told their GP that they were taking herbal products before they were referred to specialist care. The first patient was taking the herbal remedy to relieve menopausal symptoms, another patient took the remedies as a liver tonic, and yet another to lose weight. The remaining patients took the remedies in the belief that they would promote general health. None of the patients took more than the recommended dose, although this varied between the different products.

Only 2 of the patients were taking other medication. One was taking temazepam and the other low-dose aspirin. One patient also suffered from Huntington's chorea and another was diagnosed with ovarian adenocarcinoma shortly after presenting with hepatitis. She had no evidence of metastatic spread to the liver.

All the patients developed jaundice and a predominantly hepatocellular liver enzyme abnormality — serum alanine aminotransferase level was >1 000 U/l in each case. There were also moderate elevations of the cholestatic enzymes. Three patients developed pruritis. The INR was raised in 2 patients. Peripheral blood eosinophilia was not present in any of the patients.

No cause for the liver disease other than the herbal remedies was found. Serology for hepatitis A, hepatitis B and hepatitis C was negative in all cases. The antinuclear antibody was positive in 2 of the patients, and smooth-muscle antibody and antimitochondrial antibody titres were negative for all patients tested. All the patients had normal

imaging of the liver by upper abdominal ultrasound or CT examination.

Percutaneous liver biopsy was performed in 5 of the patients with severe hepatitis. One patient required a liver transplant and the liver removed at transplant was available for study. All the biopsies were typical of acute hepatitis, consistent with severe viral hepatitis. These changes are typically found in severe immunological reactions and are not the changes of direct toxic injury.

Three patients with persistent jaundice and severe pruritis were treated with oral prednisone, resulting in immediate improvement of symptoms.

It is useful to look at what each patient was taking. All herbal remedies carry a risk of adverse reactions as there are many factors that contribute to the potential toxicity of herbs. These include misidentification, variability in the time and place of collecting the plant, use of the wrong part of the plant, incorrect storage, contamination during preparation and inconsistency in nomenclature and labelling of the final product. There are also adulterants, such as corticosteroids, added to some products. Remedies may also have multiple ingredients that make it difficult to determine the causative agent and possible mechanism of injury. Demonstrating hepatotoxicity often comes down to showing that the illness started soon after taking the preparation and improved when it was stopped.

In the cases illustrated here, the hepatitis resolved after stopping the preparation in all but one woman, who required urgent liver transplantation. She was taking black cohosh, which is widely used in Europe for its supposed beneficial effects on menopausal symptoms. It contains a mixture of alkaloids, tannins and terpenoids, and had not (at the time of the report) been reported to be hepatotoxic.

Valerian and mixtures of skullcap and valerian have been associated with hepatitis, and 2 patients were using this combination, while another used skullcap without valerian.

Black cohosh was also in the mixture taken by 1 of these patients. The fifth patient was taking a combination of herbs that included chaparral. This is known to cause subacute hepatitis, but no deaths have been reported. The sixth patient was taking a preparation containing a mixture of herbs advertised as a fat metaboliser and a fluid retention remedy. Greater celandine (*Chelidonium majus*) has been associated with acute hepatitis characterised by marked cholestasis. Buchus leaf contains pulegone, a volatile oil, which is also found in pennyroyal oil. Pulegone has been reported as being hepatotoxic.

As the authors point out, the true incidence of hepatic damage caused by herbal medications is not known. The incidence of hepatotoxicity from Chinese herbal remedies had been estimated at between 0.2% and 1%. It is not only medical practitioners who need to be aware of the risks of herbal remedies. The public, who all too often assume that these preparations can do no harm, need education about the potential risks.

In South Africa most herbal substances are marketed without proof of efficacy or safety under the label of dietary supplements. However, due to the increasing number of complementary medicines being sold in South Africa, the Complementary Medicines Working Group of the MCC recommended a call-up of these medicinal products. The MCC determined that from 22 February 2002 all preparations or mixtures of substances that fall under the definition of a medicine are subject to a call-up process that was instituted as a primary step towards registration of these products as medicines. Hopefully this process will increase the safety of the herbal preparations that are proliferating in our pharmacies, and help with the process of consumer education.

Whiting PW, *et al. MJA* 2002; **177**: 440-443.

**Bridget Farham**

## SINGLE SUTURE

### COSTING INADEQUATE WATER AND SANITATION

Children living in homes without sewage or water connections and which use small water containers have 54% more episodes of diarrhoea than those with these connections and which use large containers. Even with adequate water connections, children in Peru living in houses that lack decent sewage connections had a 1.8 cm growth deficit compared with their more fortunate peers. These statistics are bad enough, but it also appears that early childhood diarrhoea and stunting are associated with long-term decrements in cognitive development and school performance. A useful field measure is HAZ-2 — the height-for-age Z score at 2 years. This has repeatedly been shown to be a readily measurable indicator of early childhood diarrhoea and a marker of inadequate water and sanitation which leads to developmental impairment. A priority of the WHO Millennium Declaration is to decrease the number of people without adequate water and sanitation by half by 2015. HAZ-2 scores offer a useful means of evaluating projects with this aim in mind.

Checkly W, *et al. Lancet* 2004; **363**: 112-118.

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