Not in the BNF

Sir,

Clinicians are increasingly aware of drug side effects, largely relying on information provided by the *British National Formulary* (BNF). One evening a 67-year-old woman attended the accident and emergency department having had two episodes of quite severe chest pain during the day. These she related to longstanding heartburn. She had also coughed a little blood-streaked sputum. She appeared well and there were no abnormal signs despite her having ovarian cancer that had responded incompletely to standard therapy. Recently she had been given capecitabine, a chemotherapeutic agent.

An electrocardiogram showed flattening of ST segments in V5/6 but was otherwise unremarkable. Circulating troponin was borderline at 0.06. A chest radiograph was normal. Pending a lung scan the patient was admitted and started on heparin. Two hours later she suffered very severe chest pain followed by cardiac arrest from which she could not be resuscitated. Post-mortem examination showed no obvious cause of death. The heart weighed 270 g and the coronary arteries were fully patent.

Resort to literature in the hospital pharmacy showed that capecitabine (a pro-drug for 5-fluorouracil) may cause severe coronary artery spasm (Van Cutsem et al, 2002). Between 2001 and 2005 the Committee on Safety of Medicines received 144 reports regarding the adverse effects of capecitabine of which 28 were cardiotoxic (including four deaths). Cardiotoxicity is listed in the small print of the patient information leaflet but is not recorded in the BNF. We believe that for emergency care it would be helpful if all potentially life-threatening side effects of medications were listed in the BNF, however uncommon, and that they should be highlighted in patient information leaflets.

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Van Cutsem E, Hoff PM, Blum JL et al (2002) Incidence of cardiotoxicity with the oral fluoropyrimidine, capecitabine, is typical of that reported with 5-fluorouracil. *Ann Oncol* **13**(3): 484–5

Sir,

The BNF is a prescribing resource for use in a clinical setting. For the prescriber, it is primarily an aid for choosing drug treatment for a patient. As a pocket reference source the BNF is limited in the amount of information it can provide.

No single resource can provide all the answers about medicines. The BNF is not designed to provide the answer to whether a particular drug has caused a specific clinical disorder.

With regard to cancer chemotherapy, the BNF states: 'less detail is given on areas such as malignant disease since it is expected that those undertaking treatment will have specialist knowledge and access to specialist literature. The BNF should be interpreted in the light of professional knowledge and supplemented as necessary by specialised publications and by reference to the product literature.'

Graham Neale and Faria Qureshi's report makes distressing reading, but the case serves to illustrate that indiscriminate use of information resources could undermine clinical care – it is important for the clinician to understand the scope of an information resource and what questions it can and cannot answer authoritatively.

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Non-alcoholic fatty liver disease and diabetes: a 21st century epidemic

Sir,

Non-alcoholic fatty liver disease (NAFLD) is emerging as the most common cause of increased liver enzymes in the USA. Non-alcoholic steatohepatitis (NASH) represents the more severe end of the spectrum of NAFLD and is associated with progressive liver disease, fibrosis and cirrhosis.

The aetiology of NASH is unclear, but it is often associated with obesity, type 2 diabetes, and hyperlipidaemia and insulin resistance (Ahmed and Byrne, 2005).The prevalence of NAFLD in the USA may be as high as 30%. Furthermore, patients who have NAFLD appear to have a higher mortality than people in the general population. Diabetes is a risk factor for fibrosis progression and for overall and liver-related death among NAFLD patients (Ahmed and Byrne, 2005).

The prevalence of diabetes for all age groups worldwide is estimated to increase and the number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030 (Wild et al, 2004). Therefore, it is important to screen for diabetes once NALFD is diagnosed. It is likely that management of insulin resistance may reduce the progression of liver pathology and reduce complications, although evidence is lacking. Despite the risks, the only reliable tool for diagnosing NAFLD and monitoring its progress is liver biopsy (Ahmed, 2005). At present there is no reliable biochemical marker and the only treatment is a weight-reducing diet. It is likely that NAFLD-induced insulin resistance may be the harbinger of the metabolic syndrome.

The impact of NAFLD on the diabetes-related risks of cardiovascular disease may increase the burden not only on health-care systems but also on doctors. The human and economic costs of this epidemic are enormous. A concerted, global initiative is required to address the NAFLD–diabetes epidemic.

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