

## Cefotetan-induced life-threatening haemolysis

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**TO THE EDITOR:** A 32-year-old woman presented with fatigue and jaundice 12 days after an uncomplicated elective caesarean delivery. She had a haemoglobin level of 76 g/L (reference range [RR], 110–160 g/L), reticulocytosis ( $202 \times 10^9/L$ , 12.6%; RR,  $20\text{--}100 \times 10^9/L$ ) and hyperbilirubinaemia ( $139 \mu\text{mol/L}$ , 97% unconjugated; RR,  $<20 \mu\text{mol/L}$ ).

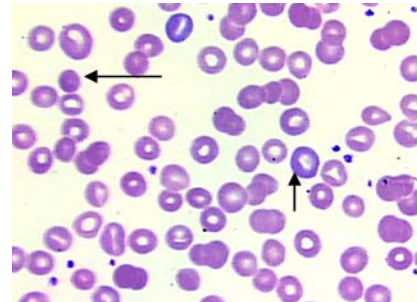
Within 24 hours, her haemoglobin level fell to 37 g/L, and a blood film showed spherocytes and polychromasia consistent with haemolysis (Box). A direct antiglobulin test was strongly positive for IgG and complement. The patient's obstetric case notes revealed administration of a single intravenous dose of cefotetan at the time of delivery. Donor red cells treated in vitro with this antibiotic reacted dramatically with the patient's serum, indicating the presence of antibody to the drug–red cell combination.

The patient was admitted to the intensive care unit and received 6 units of red cells over 24 hours, until the haemolysis resolved.

Cefotetan disodium is a broad-spectrum second-generation cephalosporin commonly used as prophylaxis in abdominal and pelvic surgery. It is given as a single intravenous dose at the start of the operation, and 50%–80% of the dose is excreted within 24 hours.<sup>1–3</sup> A positive direct antiglobulin test is seen in one in 250 patients treated with cefotetan, although this in itself does not always imply active haemolysis.

The true incidence of symptomatic haemolysis is difficult to determine for several reasons: the severity of haemolysis varies between patients, and, if mild, may go undiagnosed; the process is self-limiting; and, when the drug has been used perinatally, symptoms may not be distinguished from the fatigue and anaemia expected (and therefore accepted) by most new mothers. Furthermore, as in our case of caesarean delivery, the obstetrician is not always aware of drugs administered by the anaesthetist,

### Blood film in a woman with drug-induced haemolytic anaemia



Blood film taken on Day 1 of admission shows features of immune-mediated haemolysis, with polychromasia (vertical arrow) and spherocytosis (horizontal arrow). ◆

making the link between the antibiotic and haemolysis easy to miss.

The Adverse Drug Reactions Advisory Committee has 15 listings of haemolytic anaemia caused by cefotetan in Australia, which probably represents significant under-reporting. Indeed, the recognition of cefotetan-induced haemolysis prompted a US Food and Drug Administration review of its incidence in 2002, which revealed more than 85 reports worldwide, including 15 fatal cases.<sup>4</sup> Cephalosporins are the most common group of drugs to cause haemolytic anaemia (93% of all cases), with cefotetan alone accounting for 83%.<sup>5</sup> A patient with haemolytic anaemia induced by one cephalosporin carries a 10% risk of cross-reactivity with other cephalosporins and consequently should avoid further exposure if possible.

First-generation cephalosporins are less likely to cause significant haemolysis than second- and third-generation cephalosporins, yet are equally efficacious in surgical prophylaxis.<sup>1,3</sup> We therefore recommend the use of cefazolin as an alternative to cefotetan.

- 1 Shariatmadar S, Storry JR, Sausais L, Reid ME. Cefotetan-induced immune hemolytic anemia following prophylaxis for cesarean delivery. *Immunohematol* 2004; 20: 63-66.
- 2 Ehmann WC. Cephalosporin-induced hemolysis: a case report and review of the literature. *Am J Hematol* 1992; 40: 121-125.
- 3 Naylor CS, Steele L, Hsi R, et al. Cefotetan-induced hemolysis associated with antibiotic prophylaxis for cesarean delivery. *Am J Obstet Gynecol* 2000; 182: 1427-1428.
- 4 Viraraghavan R, Chakravarty AG, Soreth J. Cefotetan-induced haemolytic anaemia. A review of 85 cases. *Adverse Drug React Toxicol Rev* 2002; 21: 101-107.
- 5 Garratty G. Review: drug-induced immune hemolytic anaemia – the last decade. *Immunohematol* 2004; 20: 138-146. □

## Skin cancer medicine in primary care: towards an agenda for quality health outcomes

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**TO THE EDITOR:** The MJA is to be congratulated on promoting the debate related to the significant increase in the number of “skin clinics”.<sup>1</sup>

Standards are important in both the maintenance of the facilities and the formal training of the practitioners undertaking the assessment and care of patients. The four medical Colleges actively involved in treating skin conditions, who have their training programs accredited by the Australian Medical Council and their selection and assessment processes authorised by the Australian Competition and Consumer Commission, are the Royal Australian College of General Practitioners (RACGP), the Royal Australian and New Zealand College of Radiologists (Faculty of Radiation Oncology), the Royal Australasian College of Surgeons (RACS), and the Australasian College of Dermatologists.

The Colleges already have established standards for accreditation of facilities (eg, *Guidelines and standards for day surgery in Australia* <[http://www.surgeons.org/Content/NavigationMenu/FellowshipandStandards/AustraliaDaySurgeryCouncil/Guidelines\\_and\\_Stand.htm](http://www.surgeons.org/Content/NavigationMenu/FellowshipandStandards/AustraliaDaySurgeryCouncil/Guidelines_and_Stand.htm)>, or the RACGP *Standards for general practice* <<http://www.racgp.org.au/document.asp?id=17623>>) and have well established programs for training medical practitioners in the treatment of skin conditions. The Colleges base these programs on high standard “holistic” care that is not influenced by entrepreneurial medicine.

Our Colleges encourage the development of improved training programs at all times. It is important that we maximise the benefit of the structures and standards that currently exist. Our Colleges have already begun discussion about the ways we can build on our work to date. Our members, and the Australian public, expect specialist medical Colleges to take a lead in ensuring the quality of health care, and we will continue to do so.

- 1 Wilkinson D, Bourne P, Dixon A, Kitchener S. Skin cancer medicine in primary care: towards an agenda for quality health outcomes. *Med J Aust* 2006; 184: 11-12. □