Medicinal mishap
Flecainide and neutropenia

Case
A 73-year-old woman was admitted to hospital for investigation following a short episode of slurred speech which was diagnosed as a transient ischaemic attack. She had a history of paroxysmal atrial fibrillation, transient ischaemic attacks, essential hypertension, duodenal ulcer, chronic hepatitis B infection and acoustic neuroma.

Her drug history found that she had been switched from metoprolol to flecainide 50 mg twice a day for control of her atrial fibrillation three months previously. The only other drug she had been taking was omeprazole 20 mg twice a day for two years.

An incidental finding on admission was a white blood cell count of 2.5 x 10⁹/L, with a neutrophil count of 0.61 x 10⁹/L. Reactive lymphocytes were present. The remaining white cell differential was within normal ranges. Haemoglobin was normal, with a slightly raised mean cell volume. Platelet count was reduced at 127 x 10⁹/L.

Liver function tests were mildly abnormal, consistent with chronic hepatitis B infection. Renal function was normal for age and testing for autoimmune and rheumatoid disorders, HIV and haematological malignancy was negative. C-reactive protein was 15 mg/L and erythrocyte sedimentation rate was 19 mm/hour.

On day two of admission, the neutrophil count dropped to 0.28 x 10⁹/L. Flecainide was ceased on the same day. Five days after stopping flecainide, the neutrophil count had risen to 1.59 x 10⁹/L. Omeprazole was continued throughout and metoprolol reinstated for rate control of her atrial fibrillation.

Comment
Flecainide is a class 1c antiarrhythmic drug indicated for use in supraventricular arrhythmias in patients without structural heart disease. It is not recommended for use in chronic atrial fibrillation.

Agranulocytosis is a rare but serious complication of antiarrhythmic drugs. It has previously been associated with procainamide, quinidine and flecainide. The mechanism by which agranulocytosis develops with flecainide is not clearly understood, however a putative mechanism involves the development of flecainide-specific IgG antibodies.1,2

This is the first case of flecainide-induced neutropenia reported to the Therapeutic Goods Administration in which no other drugs were suspected to have contributed.3 There have been 32 cases reported to the Food and Drug Administration in the USA, with three-quarters of cases occurring within six months of starting flecainide.4

In this case the neutropenia could not be attributed to any other drug, concurrent disease or infection. Additionally, there was a plausible time relationship between starting flecainide and developing a neutropenia which resolved after the drug was stopped.

Conclusion
There was a probable causal association between flecainide and neutropenia. This is a rare adverse reaction associated with some antiarrhythmic drugs and this may be the first such report in Australia.

REFERENCES