

Serum concentrations (mg/L) of perhexiline and perhexiline metabolite

	Day 48	Day 75	Day 95
Perhexiline (therapeutic range, 0.15–0.60 mg/L)	0.37	0.82	0.27
Perhexiline metabolite	3.53	0.37	2.22
Ratio of perhexiline to perhexiline metabolite	0.10	2.22	0.12

celecoxib (a cytochrome P450 2D6 inhibitor) at a constant dose between Days 1 and 95, and meropenem (not a documented cytochrome P450 2D6 inhibitor) between Days 51 and 95. These patterns of administration suggest that neither of these drugs had a significant effect on perhexiline concentration. On the other hand, the laboratory evidence of a marked inhibition of perhexiline metabolism during treatment with citalopram suggests that caution is required when prescribing citalopram (or any other SSRI) for a patient taking perhexiline.²

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Cholestasis associated with the use of pravastatin sodium

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TO THE EDITOR: Hydroxymethylglutaryl coenzyme-A (HMG Co-A) reductase inhibitors (or statins) are widely prescribed, and any class-specific side effect has the potential to affect many thousands of patients. The statin drugs are well recognised as a cause of mild and usually transient hepatitis.¹⁻³ Cholestatic liver injury has been reported with simvastatin⁴

and atorvastatin,⁵ but pravastatin has only been implicated as a cause in one report.⁶

We report a 64-year-old woman who was twice treated with pravastatin sodium and who, on both occasions, demonstrated cholestasis, which, at its peak, was associated with minimal hepatocellular injury.

Our patient presented to the liver clinic of the John Hunter Hospital in 2001 for investigation of abnormal liver function test results. She was taking diltiazem, aspirin, irbesartan plus hydrochlorothiazide, and pravastatin as therapy for hypertension and hyperlipidaemia. She consumed less than 10 g alcohol per week. Liver function tests showed a predominant elevation of alkaline phosphatase and γ -glutamyltransferase, with a minimal rise in alanine and aspartate aminotransferases, a picture consistent with cholestasis rather than hepatocellular disease (see Box). She had started taking pravastatin in the three months preceding her referral, and commented that when she was taking the drug in the previous year she had also had abnormal liver test results. Her liver function test results in 1998 were normal.

Two ultrasound examinations of the liver, performed after five months of taking pravastatin in the first period and two months after beginning her second period of therapy, showed normal liver size and echogenicity, and no sign of obstructive liver disease. Tissue antibodies, viral studies for hepatitis viruses, α_1 -antitrypsin and iron studies were all either normal or negative. Renal function was normal throughout. She had no biochemical evidence of impaired hepatocellular function, and for this reason liver biopsy and endoscopic retrograde cholangiopancreatography were not undertaken.

In view of the association the patient made between previously ceasing therapy with the drug (because she felt unwell) and improving liver function, therapy (which was recommenced by the cardiologist for hyperlipidaemia) was again suspended and within two months liver test results improved markedly.

We believe that in the absence of other markers of liver disease and with improve-

ment of liver function on both occasions that therapy with pravastatin was suspended, it is likely that this patient has twice developed a cholestatic response to pravastatin.

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Paracetamol recall: a natural experiment influencing analgesic poisoning

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TO THE EDITOR: A potentially important, if somewhat crude, means of suicide prevention involves restricting the availability of commonly used methods. In 1967, for example, restrictions on barbiturate prescribing in Australia led to declines in its use for suicide and in overall suicides.¹ A crucial concern with this approach is that distressed individuals might use alternative, more lethal, methods. In Britain, there is just such a concern in relation to recent legislation restricting the availability of paracetamol.¹

Analysis of the natural experiment investigated by Balit and colleagues² does not, however, provide useful insights into the impact of paracetamol sales restrictions. Their most consistent finding was that, despite restricted availability for the period studied, paracetamol accounted for about

Patient's liver function test results during and after two periods of pravastatin therapy

Test	Normal range	Initial period					Second period*			
		Pravastatin			No pravastatin		Pravastatin		No pravastatin	
		Month 0	Month 4	Month 5	Month 6	Month 10	Month 0	Month 1	Month 2	Month 3
Bilirubin (μ mol/L)	< 20	7	13	5	7	10	11	11	7	9
Alkaline phosphatase (U/L)	< 115	230	362	220	213	242	291	347	186	171
γ -Glutamyltransferase (U/L)	< 25	259	625	353	231	195	297	463	167	126
Alanine aminotransferase (U/L)	< 40	26	85	31	25	28	25	49	16	18

*Commenced seven months after initial episode. Patient's results were normal two years before the initial period.