

Rhabdomyolysis secondary to interaction of fusidic acid and simvastatin

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TO THE EDITOR: A 71-year-old man was admitted to hospital in 2002 with nausea, abdominal discomfort and myalgia. He was dehydrated and had mild right upper quadrant tenderness. No muscle tenderness was noted.

Five weeks previously, an infected right femoropopliteal gortex graft had been surgically removed. Methicillin-resistant *Staphylococcus aureus* was present on culture. Therapy with fusidic acid (250 mg three times daily) and rifampicin (600 mg daily) had been commenced, and the patient's condition improved. Fusidic acid therapy was continued because of unsatisfactory wound healing. On presentation he had been taking fusidic acid for 4 weeks. He had been taking simvastatin (40 mg nightly) for 8 years.

The patient had a history of generalised vascular disease and multiple

muscle pains and weakness, significantly impairing his mobility. The serum creatine kinase concentration was elevated at 66 710 U/L (normal range, 60–220 U/L), with a normal troponin I concentration. Myoglobinuria (567 200 ng/mL) was detected.

Simvastatin therapy was ceased, and there was prompt clinical improvement, with recovery of renal function and a gradual fall in the concentration of serum creatine kinase. On discharge 14 days after admission, his serum creatine kinase concentration was 1153 U/L and creatinine concentration was 0.12 mmol/L. Transaminase concentration readings fell rapidly in line with the creatine kinase concentration, suggesting they were of muscular rather than hepatic origin.

Three other cases of rhabdomyolysis have been reported as a result of interaction between an HMG CoA-reductase inhibitor and fusidic acid,¹⁻³ but there have been no previous reports from Australia.

Fusidic acid, like simvastatin, undergoes extensive first-pass metabolism in the liver (over 98%). Simvastatin is metabolised via the cytochrome P3A4 enzyme system. It is known that, if given concomitantly with inhibitors of this system (eg, macrolides and azole deriv-

Influenza outbreak related to air travel

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TO THE EDITOR: Modern air travel lends itself to aerosol transmission of viral infection. Infected individuals in modern aircraft represent a significant risk for other travellers during long journeys.

In September 1999, a person with an influenza-like illness joined other workers returning by aircraft to an isolated mine in north-western Australia. He was identified as unwell by a mine supervisor in the airport lounge but was allowed to board the BAe 146 aircraft (a 75-seat passenger jet aircraft). The flight lasted 3 hours 20 minutes. On landing in the evening, most workers were transported to their quarters in a 10-minute bus trip, but some, including the affected worker, travelled independently. They then went to their individual rooms.

The next day, the affected worker reported sick immediately on going to his work site and did not work for 4 days. The other workers undertook 12-

Aircraft seat allocations of index patient and affected passengers

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
G						F			F		I		F		F
F	M				M				M	M	F		F	F	
E					M						F				F
Aisle															
B										F	F	F			F
A			F								F				

I = index patient.

F = passenger developed influenza-like illness.

M = passenger developed mild upper respiratory tract illness.

hour shifts operating machinery or in offices, relatively isolated from other people. However, they may have mixed socially.

Over the next 3–4 days, 15 other workers presented with an acute influenza-like illness, with fever, cough, nasal congestion, anorexia and prostration. No serological tests were undertaken because of the remoteness of the mine.

All other workers on the flight were contacted by telephone 6 days after the flight. Five more were identified who had significant upper respiratory tract symptoms and were taking simple analgesics, but had continued to work. The airline reported that no staff from the aircraft had reported sick over the next week or so.

The seating positions of the affected workers on the aircraft, which was full, are shown in the Box. The index patient sat in seat 11G. Most of the other affected workers appeared to sit in a “plume” around him. The only affected workers who sat further away were the supervisor who assessed the index patient in the airport lounge (seat 3A) and a person who conducted a raffle during the flight and walked the length of the aircraft collecting money and ticket stubs (seat 1F). In aircraft such as the BAe 146, air is circulated and filtered, entering the passenger compartment through continuous vents just beneath the overhead lockers, circulating downwards and exiting from continuous vents under the seats. Air therefore tends to flow in two contrarotating circles, from ceiling to floor on either side of the aircraft. Infection could well have been transmitted by aerosol droplets to passengers behind the index patient, as

he coughed and sneezed throughout the flight. The immunisation status of the passengers was not recorded; most were aged 20–45 years.

This outbreak was relatively confined, as the passengers were in an isolated community, and those affected were managed in their rooms. However, the implications for the spread of airborne infection in passenger aircraft and into the wider community are obvious.

It must be stressed to the travelling public that people with this type of illness should not fly. Airport authorities at passenger check-ins should be encouraged to identify and formally assess potentially infected individuals, and should have the authority to take precautions against spread. □

Reducing inhaled corticosteroids in asthma is just the start

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TO THE EDITOR: Any doubts that many Australian doctors are prescribing inhaled fluticasone for asthma at inappropriately high doses are dispelled by the three reports in the 3 March issue of the *Journal*.^{1–3} Fluticasone has a flat dose–response curve for efficacy and a steep dose–response curve for adverse effects;¹ individuals with asthma are receiving high doses of inhaled fluticasone;² and there is a potential for the effects to be lethal.³

Each of these reports restricted its advice to negative recommendations about drug treatment (DON'T over-treat, BACK-titrate), but this is the right time to also promote positive recommendations about asthma management. All individuals with persistent asthma requiring daily therapy should have either skin testing or in-vitro testing to determine the presence of specific IgE antibodies to inhalant allergens.⁴ This might allow the option of allergen avoidance. In some studies, dust mite reduction was found to ameliorate asthma symptoms in sensitised individuals (National Health and Medical Research Council Level II evidence), although those findings are not sup-

ported by a meta-analysis. Repeated low-dose exposure to cat allergen in cat-allergic individuals with asthma leads to increased non-specific bronchial hyper-reactivity (Level II evidence).⁵ Allergen desensitisation in carefully selected cases with consultant supervision can lead to a significant reduction in medication requirement, and reduced specific bronchial hyperreactivity (Level I evidence).⁶ Treatment of concomitant rhinitis can itself lead to easier asthma control. A checklist of the “A,B,C...” of asthma triggers does not take long and often yields useful tertiary prevention strategies: Allergy (seasonality, dust, pets), Bronchial infection, Cold air/exercise, Drugs, Emotion/stress, Food and food additives, Gastro-oesophageal reflux, Hormones and pregnancy, Irritants including cigarette smoke, and the Job.

Inhaled anti-inflammatory treatment using cromolyns or corticosteroids, with or without consideration of oral montelukast, remains the cornerstone of asthma control when the disease is frequent or persistent. However, the search for allergic and other triggers by healthcare workers, individuals with asthma, and their carers can instil into the entire group a culture of prevention, which naturally leads to a brake on overtreatment. Such a culture is firmly entrenched in continental Europe and the United States. In Australia, there has been outstanding research into the epidemiology and immunology of asthma, but it's at the coalface where the individual with asthma gets advice. A diligent search for triggers, with appropriate management, should start at the first consultation, as the pen (or mouse) is poised to prescribe.

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