To the Editor: Fatal fulminant hepatic failure (FHF) associated with thalidomide (Thalomid, Celgene Corp, Warren, NJ) therapy has not been reported previously, to our knowledge. We describe a case in which a woman receiving thalidomide therapy for multiple myeloma experienced fatal FHF.

Report of a Case. A 64-year-old woman with stage IIIA multiple myeloma was found to have disease progression 8 months after autologous peripheral blood hematopoietic stem cell transplantation. She received a combination of doxorubicin, vincristine, and dexamethasone as first-line chemotherapy before transplantation. Her medical history included chronic carrier state for hepatitis B (hepatitis B surface antigen positive, hepatitis B e antigen negative, hepatitis B e antibody [HBeAb] positive, and normal liver function). She was treated with single-agent thalidomide (100 mg/d). Her other medications included metoprolol and aspirin. At initiation of treatment, liver function test results and the international normalized ratio (INR) were normal (albumin level, 3.7 g/dL; INR, 1.1).

Twelve days after initiating therapy, the patient experienced confusion, abdominal pain, and jaundice. Physical examination revealed altered mental status, scleral icterus, jaundice, asterixis, and anasarca. Laboratory investigations showed elevated transaminase (aspartate aminotransferase, 490 U/L; alanine aminotransferase, 410 U/L) and bilirubin (total, 16.7 mg/dL; direct, 10.2 mg/dL) levels. The alkaline phosphatase concentration was normal (101 U/L). Hepatic synthetic function was markedly impaired (albumin level, 1.2 g/dL; INR, 4.1). Ultrasonography of the liver and computed tomography of the abdomen showed moderate hepatomegaly with no biliary ductal dilatation. The patient was admitted to the hospital and thalidomide treatment continued.

On the second hospital day, the patient experienced oliguric renal failure (creatinine level, 2.6 mg/dL; serum urea nitrogen concentration, 18 mg/dL) that was unresponsive to intravascular volume expansion and necessitated hemodialysis. The clinical picture of normal findings on renal ultrasonography, greater urinary osmolality than serum osmolality, urinary sodium level less than 10 mEq/specimen, and no evidence of sepsis was consistent with hepatorenal syndrome.

Serologic studies for hepatitis A, hepatitis C, and hepatitis delta antigen yielded negative results. Hepatitis C RNA, cytomegalovirus, herpesvirus, and Epstein-Barr virus DNA were undetectable on polymerase chain reaction. Testing for primary biliary cirrhosis and autoimmune hepatitis (antinuclear antibody, antimitochondrial antibodies, antismooth muscle antibodies, and anti-liver kidney microsomal antibodies) produced unremarkable findings. The serologic results for hepatitis B virus (hepatitis B surface antigen positive, hepatitis B surface antibody negative, IgM antibody to hepatitis B core antigen negative, hepatitis B e antigen negative, and HBeAb positive) and undetectable hepatitis B DNA on polymerase chain reaction (performed at the Mayo Clinic in Rochester, Minn) were identical to her baseline pattern (chronic carrier state). The positive HBeAb, negative IgM antibody to hepatitis B core antigen, and undetectable DNA levels were not consistent with the pattern seen in hepatitis B reactivation and replication. Thalidomide was discontinued, and transient improvement in transaminase levels (aspartate aminotransferase, 226 U/L; alanine aminotransferase, 235 U/L) ensued (peak values before discontinuation were 510 U/L and 598 U/L, respectively). Despite these efforts, the patient died of worsening coagulopathy, acidosis, and renal failure on the 14th hospital day.

Discussion. Thalidomide is approved by the US Food and Drug Administration for the treatment of multiple myeloma and erythema nodosum leprosum. Rare cases of transient hepatitis associated with thalidomide have been reported, but thalidomide-induced fatal FHF with encephalopathy and hepatorenal syndrome has not been described previously. The lack of any obvious cause of the patient’s hepatic failure despite exhaustive investigations and the temporal relationship of hepatic dysfunction with the initiation of thalidomide therapy indicate severe drug-induced hepatic injury. According to the adverse drug reaction probability scale of Naranjo et al, our case has a score of 6, indicating a probable association between thalidomide and FHF. Thalidomide does not undergo major hepatic metabolism, and the mechanism by which it potentially causes hepatic injury is not precisely known. It may involve interference with the hepatic metabolism of NAD-adenoribosylation.

In patients with hepatic injury of unclear etiology, thalidomide should be recognized as a possible cause, and strong consideration should be given to withholding this medication to avoid catastrophic results.

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1. Celgene Corp. Thalomid (thalidomide) [product information]. Summit, NJ: Celgene Corp.

Home Blood Glucose Testing

To the Editor: In his excellent review on the use and benefits of home blood glucose monitoring, Dailey1 failed to mention one of the main reasons why more people do not perform this valuable assessment—the cost of test strips. In the United Kingdom, the manufacturers of blood glucose meters provide the devices free of charge to primary and secondary care medical centers for distribution to patients. However, the cost of the test strips more than pays for this apparent (but ultimately false) altruism.

To assess the cost of test strips, one needs to know the average number of test strips performed per patient per year. Dailey’s review mentions the costs of test strips for patients who use home blood glucose testing, but does not provide an estimate of the average number of test strips performed per patient. To calculate the cost of test strips, one must know the average number of test strips performed per patient per year. Without this information, it is impossible to accurately assess the cost of test strips.

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While it is hard to justify rationing test strips for patients with type 1 diabetes, those with type 2 disease are at the mercy of insurance companies and governments that are continuously engaged in reducing health care budgets. Limiting test strips has been perceived as a way to control spending. Currently, 20 different types of strips are available in the United Kingdom. The cost of 50 test strips varies between £13.64 ($26.68, 20.38 Euros) and £16.26 ($31.81, 24.29 Euros).3

Thus, although mounting evidence suggests that home blood glucose monitoring is an extremely useful adjunct to hemoglobin A1c measurement, until the cost of test strips decreases, there will always be a financial obstruction to physicians to get patients to test more frequently.

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Tobacco on Campus, 1804 and Today

To the Editor: Dr Carl E. Lundstrom’s compelling review of Philip Cash’s biography of Dr Benjamin Waterhouse1 highlights Waterhouse’s pioneering contributions to vaccination in the United States, which led to his being known as “the Jenner of America.” Far less recognized is Waterhouse’s outspoken stance against tobacco. Indeed, his address to the students of Harvard Medical School in 18042 may well represent the earliest antitobacco lecture at an American university. Warning of the consequences of smoking on the lungs and the adverse effects of chewing tobacco on the digestive system, he pleaded with the students to “quit then this pernicious habit....Take all your cigars and tobacco, and in some calm evening carry them on to the common, and there sacrifice them to health, cleanliness, and decorum.”

How tragic and incredible it is that, in the face of millions of deaths attributable to tobacco in the ensuing 2 centuries and an ongoing prevalence of cigarette smoking among college students (currently >25%), most universities and faculty pension funds still invest in tobacco stocks,4 more than 30 universities welcome job recruiters for cigarette manufacturers,5,6 and a tobacco company remains the principal sponsor of the college rodeo championships.7 In February 2007, Philip Morris of the United States, the nation’s largest cigarette manufacturer, donated $25 million to the University of Virginia for research on addiction and youth smoking, $20 million of which will go to the School of Medicine.

One hopeful sign is that 43 campuses across the United States, primarily community colleges and commuter schools, are now smoke free.

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2. Waterhouse B. [Caution to young persons concerning health, in a public lecture delivered at the close of the medical course, in the chapel at Cambridge Nov 20, 1804; containing the general doctrine of chronic diseases; shewing the evil tendency of the use of tobacco upon young persons: more especially the pernicious effects of smoking cigars; with observations on the use of ardent spirits in general]. Cambridge, Mass: University Press; 1805 [available through the University of Alabama Center for the Study of Tobacco and Society, Tuscaloosa].

CORRECTION

Incorrect e-mail address: In the article by Hall & Hall entitled “A Profile of Pedophilia: Definition, Characteristics of Offenders, Recidivism, Treatment Outcomes, and Forensic Issues,” published in the April 2007 issue of Mayo Clinic Proceedings (Mayo Clin Proc. 2007;82:457-471), an incorrect e-mail address appeared in the footnote on the title page. The correct e-mail address is dr.rcwhall@att.net.
Learn about the potential side effects of thalidomide. Includes common and rare side effects information for consumers and healthcare professionals.  


Extras - acute fatty liver of pregnancy, HELLP, toxins, ischaemic necrosis, vascular, metabolic, autoimmune, Wilsonâ€™s disease, Budd-Chiari, post hepatic surgery, idiopathic. Sepsis. HEPATIC ENCEPHALOPATHY. sleep disturbance. asterixis. hyperreflexic. can be hemiplegic.