reusable forceps, and also that they were more cost effective.

The use of disposable biopsy forceps eliminates the risk of infection and of pyrogen or endotoxin reactions that may arise if organic debris remains on reusable biopsy forceps after sterilization.

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Proton Pump Inhibitors and Gastric Acid Secretion

TO THE EDITOR: Proton pump inhibitors (PPIs) are the most potent inhibitors of gastric acid secretion in use for the treatment of various acid-related disorders. However, because of their unique pharmacology (1), these agents are most effective after oral administration when the parietal cell is stimulated to secrete acid in response to a meal. Accordingly, PPIs should optimally be administered before or with a meal. This regimen is required despite a prolonged duration of action because the plasma half-life of PPIs is quite short (~2–3 h), and the use of single-dose oral PPIs in fasting individuals does not reliably provide adequate acid suppression. They should also not be used in conjunction with histamine-2 receptor antagonists, somatostatin analogues, prostaglandins, or other antisecretory agents until the antisecretory effects of the latter drugs have abated (1, 2).

Pantoprazole recently was approved by the United States Food and Drug Administration as the only PPI for use as an *i.v.* formulation in the United States. Omeprazole and, to some extent, lansoprazole are used in other countries in this manner. It is expected that pantoprazole will have at least equivalent efficacy, even if the precise therapeutic role of *i.v.* PPIs has not been firmly established. A recent report by Lau *et al.* (3) on patients with upper GI hemorrhage due to ulcers for whom endoscopic therapy was initially employed to achieve hemostasis demonstrated that *i.v.* omeprazole was effective in decreasing recurrent bleeding and hence the need for surgical intervention. In this study, omeprazole was administered as an 80-mg bolus followed by *i.v.* infusion at a rate of 8 mg/h. Whether PPIs administered in a similar manner will be effective in preventing GI hemorrhage associated with stress-related erosive syndrome (SRES) has not yet been determined. Two recent studies in mechanically ventilated patients suggested that an omeprazole-suspended bicarbonate solution not only may prevent clinically significant SRES-induced hemorrhage, but is also safe and cost-effective (4, 5). However, the study designs employed in these trials were limited in scope, including nonrandomization and open labeling, and patient numbers were small. Omeprazole and lansoprazole are acid-labile prodrugs that have been formulated as granules with an enteric coating designed to dissolve at pH 5.5. Thus, with the bicarbonate suspension, the protective enteric coating is dissolved. Although the drug is purportedly protected from the acidic environment in the gastric lumen by the bicarbonate, many other factors may influence acid exposure, including the amount of bicarbonate as well as the pH and volume of the solution used to flush the suspension through a nasogastric tube. It is therefore possible that the PPI released from the granules undergoes acid-catalyzed conversion to the reactive species, a thiophilic sulfenamide, with inactivation of the drug before arrival at its intended target site (6, 7). PPIs are prodrugs that, after systemic absorption, are targeted to the highly acidic milieu of the secretory canaliculus of secreting parietal cells (1, 8). It is in this structure that they are normally activated to form the sulfenamide. Targeting and, hence, local activation after oral dosing are best achieved postprandially, when most parietal cells are active. Because individuals at risk for the development of SRES are generally fasting, these drugs would likely be less effective in providing prolonged acid suppression unless administered in a manner that maintains a plasma level exceeding that generally achieved by oral dosing (1).

Although *i.v.* pantoprazole is currently approved by the Food and Drugs Administration only for those individuals with GERD who are unable to tolerate oral PPIs, it is quite likely that it will prove beneficial and thus will be used widely for other indications, including the prevention of

recurrent hemorrhage due to ulcers and stress prophylaxis. However, appropriate studies should be conducted to determine the effectiveness of various *i.v.* pantoprazole regimens in different clinical scenarios. Until the completion of these studies, however, based on the pharmacokinetic properties of PPIs and the above omeprazole study (3), if the decision is made to prescribe *i.v.* pantoprazole to prevent recurrent hemorrhage associated with peptic ulcer, we recommend that a loading dose of 80 mg be followed by a continuous *i.v.* infusion of 8 mg/h. The cost associated with *i.v.* administration is significant, and the regimen should thus be changed to 40 mg *p.o.* before breakfast as soon as it is deemed safe for the individual to consume food.

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Liver Cirrhosis in Erythropoietic Protoporphyria: Improvement of Liver Function With Ursodeoxycholic Acid

TO THE EDITOR: Erythropoietic protoporphyria (EPP) is an inherited disorder of heme synthesis caused by deficiency of the mitochondrial enzyme ferrochelatase. Chronic liver disease is the most severe and rapidly progressive complication of EPP, requiring liver transplantation in some patients. The pathogenesis of liver damage in EPP is not clear. Data from mouse models suggested that EPP causes an abnormal bile composition, which was found to be cytotoxic (1). In humans, cholestasis results from intracellular and canalicular precipitation of protoporphyrin (2).

We report on a 74-yr-old female patient with a history of photosensitivity beginning in early adolescence. Jaundice and abnormal liver function parameters were first observed 10 yr before admission. EPP was diagnosed by a 1000-fold increase of protoporphyrin in erythrocytes, when she was referred to our hospital primarily because of jaundice, weight loss, and decreased liver function of unknown origin. Chronic viral, autoimmune, toxic, or other metabolic diseases were excluded. Family history for photosensitivity or liver disease was negative. On admission she had a more than 15-fold elevation of total and direct bilirubin, a 7-fold elevation of γ-glutamyltransferase, and a 2- to 3-fold elevation of ALP and transaminases. Laboratory tests for hemolysis were negative. Liver function was impaired, as indicated by decreased PT (56%), cholinesterase activity (1.4 kU/L), and serum albumin (27 g/L). Ultrasound showed liver cirrhosis with a moderate amount of ascites requiring diuretic treatment, and a moderate enlargement of the spleen. Liver biopsy confirmed the EPP-related liver cirrhosis. Liver transplantation was critically discussed.

Because of pathophysiological considerations that liver damage in EPP is related to cholestasis, we started an experimental treatment with ursodeoxycholic acid (UDCA) (18 mg/kg body weight), which was reduced to 10 mg/kg body weight and 5 mg/kg body weight after 3 and 6 months of treatment, respectively. After 2 wk of treatment we observed a marked reduction of cholestasis parameters, with a further improvement to normal values within the following 6 months (Fig. 1). During the same period of time PT, cholinesterase activity, and serum albumin improved to normal values. Diuretic treatment was discontinued without reoccurence of ascites. The Child-Pugh score was initially 10 (Child C) and normalized within 6 months of treatment to 5 points (Child A). Photosensitivity markedly improved. Re-evaluation of the patient 1 yr after onset of UDCA