

The proband's older sister delivered two babies at term and breast-fed both of them; this suggests that *TRHR* is not essential for female fertility and lactation. Therefore, we conclude that TRH action is not required for breast and pituitary development in humans, nor is it required for expression of the thyrotropin-beta gene (*TSH β*) or the prolactin gene (*PRL*).

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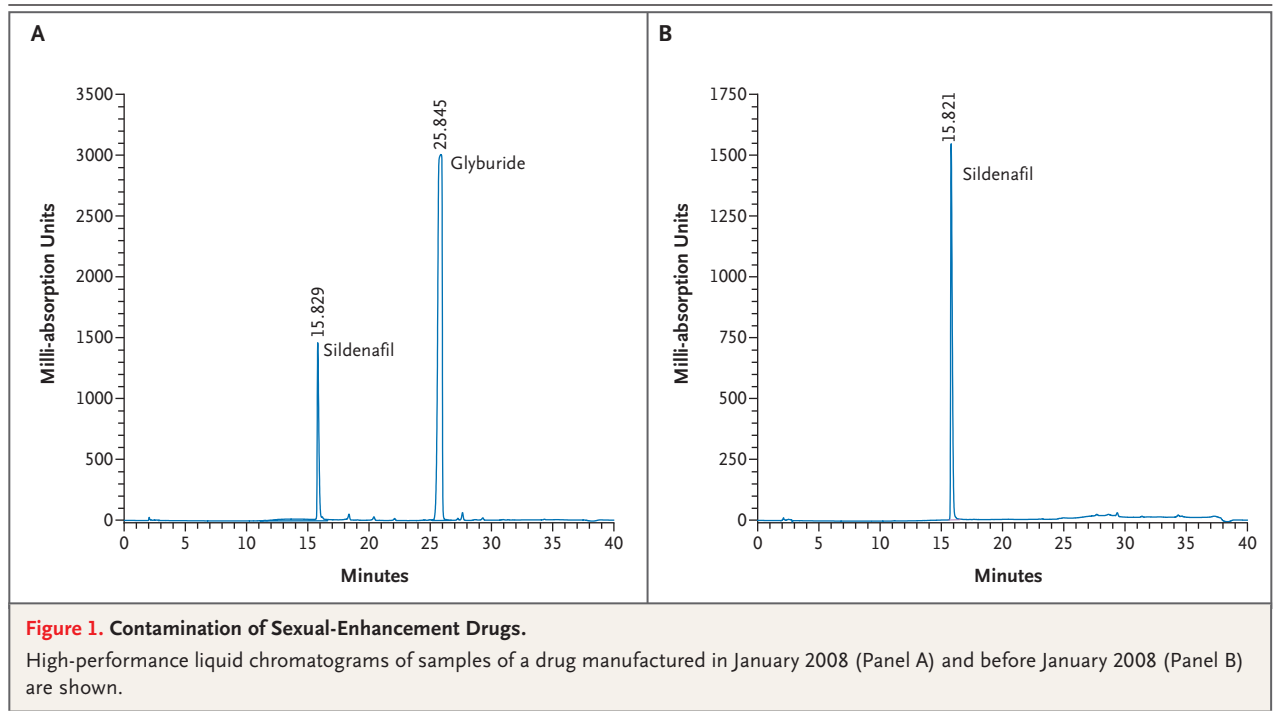
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An Unusual Outbreak of Hypoglycemia

TO THE EDITOR: The off-label use of drugs for the enhancement of sexual performance in persons without erectile dysfunction is a phenomenon that is increasingly recognized.¹ These drugs are available in illegal forms, including counterfeit versions of brand-name drugs for the treatment of erectile dysfunction and purported herbal remedies containing synthetic phosphodiesterase type 5 inhibitors.² We describe an outbreak of severe hypoglycemia in Singapore; this outbreak was associated with contamination of illegal sexual-enhancement drugs with glyburide.

Between January 1 and May 26, 2008, a total of 150 nondiabetic patients with severe hypoglycemia were admitted to the five public hospitals in Singapore. All the patients except one were men, and they ranged in age from 19 to 97 years (median, 51). Seven patients remained comatose as a result of prolonged neuroglycopenia, and four subsequently died.

Glyburide was detected in blood or urine samples obtained from 127 of these patients (85%). On specific questioning, 45 patients (30%) admitted ingesting illegal sexual-enhancement drugs before the onset of hypoglycemia. Drug samples obtained from these patients and from drugs seized in police raids were analyzed by means of high-performance liquid chromatography. Four preparations were contaminated with glyburide in amounts ranging from 13 to 100 mg per tablet (Fig. 1A). These drugs included a counterfeit of Cialis (tadalafil) and three herbal preparations for the purported treatment of erectile dysfunction (Power 1 Walnut, Santi Bovine Penis Erecting Capsule, and Zhong Hua Niu Bian).³ All four products also contained sildenafil in amounts ranging from 0.5 to 110.0 mg per tablet. Santi Bovine Penis Erecting Capsule and Zhong Hua Niu Bian also contained trace amounts of tadalafil and sibutramine.



Batches of Power 1 Walnut and Santi Bovine material manufactured before January 2008 were tested and contained only sildenafil, suggesting that the contamination was recent (Fig. 1B). Between January and June 2008, similar cases of hypoglycemia were reported in the press in Hong Kong; these reports implicated other brands of illegal sexual-enhancement drugs.^{4,5} We speculate that simultaneous contamination of several brands of drugs is consistent with a common manufacturing source. The drug packaging contained names of fictitious overseas factories, so it is not known whether there was deliberate or accidental contamination.

It would appear that more effective collaboration between national and international drug-regulatory bodies and enforcement agencies will be required to address clandestine manufacturing processes, the cross-border movement of drugs, and the subsequent spread of these adulterated medications through online sources.

We believe that physicians should be cognizant of this phenomenon when evaluating patients with severe unexplained hypoglycemia, particularly if a clustering of cases is noted. Furthermore, consumers should be informed of the risks associated with these illegally produced drugs.

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