diseases. It is our belief that a committee should be established to monitor this issue that should include any countries from which Pilgrims and immigrants originate. The task of such committee should monitor, raise awareness and potentially initiate screening to minimize the transmission of communicable diseases.

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## Spontaneous recovery of propylthiouracil-induced fulminant hepatic failure in an 8-year old child

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Hepatotoxicity was first reported as a side effect of propylthiouracil for the treatment of hyperthyroidism in 1947.[1] Subsequently, several case studies have been reported.[2] Symptomatic propylthiouracil-induced hepatic injury is rare in thyrotoxic adults and less than 10 cases have been published in childhood.[3] The clinical course is usually benign once the drug is withdrawn, however, fatal cases have been encountered.[4,5]

We describe an 8-year-old girl with hyperthyroidism treated with PTU, developed fulminant hepatic failure and ended with spontaneous recovery. An 8-year-old girl presented with 3-week history of heat intolerance, tremor, restless sleep and weight loss. She was noted having diminished school performance due to poor concentration and progressive prominence of her eyes. On examination, her vital signs showed a heart rate of 120 beats/min and blood pressure of 140/89. She had tremor, exophthalmos, and palpable thyroid. The rest of the examination was unremarkable. Laboratory evaluation at presentation showed white blood cell 11.1, neutrophils 40%, lymphocyte 43%, alanine aminotransferase (ALT) 25 U/L (10-35), aspartate aminotransferase (AST) 32 U/L (10-45), alkaline phosphatase (ALK) 203 U/L [normal range (NR) 100-300], gamma glutamyltransferase (GGT) 10 IU/L (NR 7-23), total bilirubin 13 umol/L (NR 0-21), direct bilirubin 3 umol/L (NR 0-5), ammonia 23 umol/L (NR 0-55), prothrombin time (PT) 6 seconds (NR 11.9-14.3), prolonged thrombin time (PTT) 35 seconds (NR 34.7-42.2), free thyroxine (FT4) 91 pmol/L (NR 12-22), total triiodothyronine (TT3) 4.1 nmol/L (NR 1.3-3.1), thyroid stimulating hormone (TSH) 0.02 mU/L (NR 0.27-4.2). Antithyroperoxidase antibody was 189 (normal <12), thyroid stimulating immunoglobulin (TSI) was 150% (normal <120%). Thyroid scan showed diffuse homogenous uptake. She was diagnosed with Grave's disease and started on PTU 50 mg 3 times per day and propranolol 10 mg 3 times per day.

One month later, FT4 was 30 pmol/L, TT3 was 3.1 nmol/L, and TSH was 0.07 mU/L. 2 months later on the above-mentioned treatment, she presented with progressive yellowish discoloration of sclera, lethargy and fluctuation of her consciousness. Laboratory evaluations showed FT4 24 pmol/L, TT3 2.8 nmol/L, TSH 0.07 mU/L, WBC 8.4, neutrophils 26%, lymphocyte 40%, ALT 161 U/L, AST 144 U/L, ALK 233 U/L, GGT 143 IU/L, total bilirubin 645 umol/L, direct bilirubin 512 umol/L, ammonia 290 umol/L, PT 20.2 seconds and PTT 43.4 seconds. A PTU-induced hepatoxicity was suspected and PTU was stopped. Potassium iodide (SSKI) 300 mg 3 times a day was started, in addition to hydrocortisone 10 mg 3 times a day. Ultrasound liver showed hepatomegaly with increased echogenicity and normal hepatic blood vessels flow. Liver biopsy showed cholestatic hepatitis with acinar necrosis. Other causes of cholestatic jaundice were ruled out. Serological studies for hepatitis A, B, C, E viruses, cytomegalovirus and Epstein-Barr virus were negative. Metabolic work-up including serum ceruplasmin level, alpha-1-antitrypsin level, 24-hour urinary copper level and tandem mass spectrometry was unremarkable. Immunological studies indicating autoimmune hepatitis including antinuclear antibody, anti-smooth muscle antibody

and anti-mitochondrial antibody were negative. There was no clinical or biochemical evidence of interstitial nephritis, vasculitis, pulmonary interstitial fibrosis or skin involvement. Two weeks after starting SSKI, FT4 was 14 pmol/L, TT3 was 2.1 nmol/L, and TSH was 0.07 mU/L. Liver enzymes improved gradually to near normal levels over a 4-week period. ALT was 71 U/L, AST was 66 U/L, ALK was 102 U/L, GGT was 36 IU/L, total bilirubin was 43 umol/L, ammonia level was 60 umol/L, PT was 14 seconds and PTT was 37 seconds. The patient continued to be euthyroid and total thyroidectomy was performed followed by thyroxine replacement therapy. A PTU-associated hepatotoxicity is a rare and life-threatening complication of antithyroid drug treatment of hyperthyroidism. The estimated incidence of antithyroid drug-associated hepatotoxicity is less than 0.5%,[6] although the true incidence is unknown.[7] A PTU hepatotoxicity may occur at any age, but it predominates in females.[5] Its occurrence in childhood is extremely rare especially at young ages. We report here an 8-year-old girl with acute fulminant hepatic impairment who spontaneously recovered with supportive management. A PTU-induced hepatotoxicity usually develops within the first few months of PTU administration.[4] The mechanism of antithyroid drug hepatotoxicity is unknown, although positive lymphocyte sensitization studies in some patients who developed PTU hepatotoxicity suggest an immune reaction to PTU.[2] The presentation of PTU hepatotoxicity is clinically nonspecific. However, a search for other potential causes of hepatic dysfunction remains necessary. The clinical presentation may range from subclinical elevations of liver enzymes to severe cholestatic jaundice and encephalopathy.[5] Histologically, nonspecific hepatocellular necrosis is typically found on liver biopsy. Based on the severity of the disease process, the pathological findings may range from early signs of hepatocellular inflammation to submassive hepatic necrosis.[5] In our patient, liver biopsy showed severe hepatocellular necrosis with cholestasis. For unknown reason, PTU usually causes cytotoxic hepatitis while methimazole often causes cholestatic hepatitis.[8]

Kim et al[4] reviewed the medical records of 497 hyperthyroid adult patients treated with PTU. Six patients developed overt hepatitis and 5 patients had cholestatic jaundice. There were no statistical differences in age, gender, PTU dose, or T4 and T3 levels at initial diagnosis between patients with and without hepatic injury. Liver enzymes normalized in all patients between 16 and 145 days after the PTU withdrawal.[4] Our patient had a relatively short course with a smooth recovery 4 weeks after PTU discontinuation. Williams et al[5] reported 7 deaths secondary to PTU-induced hepatoxicity among 30 cases treated with PTU. Survivors were treated with radioactive iodine and one pediatric case had a liver transplant.[5] They concluded that prompt treatment of the underlying thyroid disease with radioactive iodine may diminish the chance of clinical deterioration from persistent hyperthyroidism and early recognition of the need for liver transplant may improve survival. In our patient, surgical thyroidectomy was preferred as our concern was regarding the oncogenic long-term effect of radioactive iodine and its possible adverse effect on the eye. On the other hand, the patient was on SSKI, which may interfere with radioactive iodine uptake. Upon recognition of hepatotoxicity, PTU should be discontinued. With supportive therapy, most patients should recover. However, death due to complications of liver failure occurred in 25% of the population reported herein.[5] Thus, early recognition of fulminant hepatic failure and intervention are extremely important. Several early prognostic factors are known to be associated with survival rates of less than 20% in fulminant hepatic failure.[9] These include patient age (<11 and >40 years old), duration of jaundice (>7 days) before the onset of encephalopathy, serum bilirubin concentration (>300 µmol/L), and prothrombin time (>50 s). Our patient had at least 3 of these prognostic factors; however she recovered smoothly after PTU discontinuation. The options for treatment of hyperthyroidism in such patients are limited. The PTU is contraindicated due to the unknown mechanism of hepatotoxicity and the reported recurrence of hepatic injury with PTU rechallenge. The majority of patients received definitive treatment with radioactive iodine, and this form of treatment was significantly associated with survival. The ideal treatment may be immediate radioactive iodine therapy when PTU hepatotoxicity is suspected. It was suggested that radioiodine treatment should be completed before the administration of iodine contrast for abdominal computed tomogram scans to evaluate the cause of hepatic dysfunction or iodide therapy for the thyrotoxic state.[6] Propranolol may be used to control the symptoms of hyperthyroidism until radioactive iodine has its full effect.[6] Alternatively, methimazole has been used successfully after hepatic enzyme levels normalize. Amiodarone was used in one patient followed by radioactive iodide.[10] Additional treatment modalities include plasmapheresis, dialysis and liver transplant.[5] Corticosteroids have been used in the management of PTU-hepatotoxicity,[3] although its benefit is doubtful.[3] Hydrocortisone was used in our patient in which was tapered gradually post-operatively. The use of potassium iodide alone after recognition of hepatotoxicity was tried long time ago.[11] The maximal suppression of thyroid hormone levels by potassium iodide is usually produced within 7–14 days and last from 1 to more than 50 days. As iodide can also provide substrate for thyroid hormone synthesis, it is usually used in combination with antithyroid drugs. In our patient, potassium iodide was successfully used alone and produced adequate suppression of thyroid hormones.

In conclusion, fulminant hepatic damage induced by PTU is rare during childhood. Close clinical and biochemical follow-up is necessary to early predict this complication.

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## **Rimonabant as potential treatment for the neglected epidemic of diabetes in the Middle East and Arabian Peninsula.** *Implication for prevention*

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The clustering of insulin resistance, dysglycemia, dyslipidemia, hypertension and central obesity represent the major features of metabolic syndrome. These clusters of factors may share common etiology and each of which is a risk factor for cardiovascular disease. The metabolic syndrome appears to affect between 10 and 25% of adult populations worldwide. Several studies have described the association between metabolic syndrome, diabetes and cardiovascular disease. The prevalence of diabetes for all age groups worldwide was estimated to be 2.8% in 2000 and 4.4% in 2030. The total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030.[1] The number of people with diabetes is increasing in the Middle East and Arabian Peninsula due to population growth, aging, urbanization, and increasing prevalence of obesity and physical inactivity. Quantifying the prevalence of diabetes and the number of people affected by diabetes, now and in the future, is important to allow rational planning and allocation of resources. In the Arab world, which comprises 22 countries and has a total population of almost more than 300 million, high prevalence of diabetes has been reported from many countries.

The estimated prevalence of diabetes has increased in the Arab countries from 2-3% in 1980 to a current prevalence of approximately 20%.[2] In Saudi subjects, the age group of 30-70 years followed for 5 years period between 1995 and 2000. A total of 17,232 Saudi subjects were selected in the study and 16,917 participated (98.2% response rate). Four thousand and four subjects out of 16,917 were diagnosed to have diabetes. This study concluded that the overall prevalence of diabetes in the Kingdom of Saudi Arabia is 23.7%. The prevalence in males was 26.2% while 21.5% in females. Diabetes was more prevalent among Saudis living in urban areas (25.5%) compared to rural Saudis (19.5%). The important conclusion from this study is that 27.9% were unaware of having diabetes.[2] In the light of the observed increase in prevalence of obesity in many countries of the Arab world and Middle East, the number of cases of diabetes currently or in following decades may be considerably higher than expected. Therefore, management of obesity is crucial in order to reduce the epidemic of diabetes. Orlistat, anti-obesity medication was shown to reduce diabetes by 37%.[3] Recent exciting new data suggests that inhibition of endocannabinoid system might be beneficial in the treatment of the metabolic syndrome. The discovery of endocannabinoid system dates back almost 4000 years, when the therapeutic and psychotropic actions of the plant Cannabis sativa were first documented. The endocannabinoid system contributes to the physiological regulation of energy balance, food intake, lipid and glucose metabolism through both central and peripheral effects. Many different regulatory actions