

## Letters to the Editor

### Disseminated intravascular coagulation caused by the insecticide Propoxur

Sir,  
Haematological side effects due to exposure to insecticides are well known.<sup>1,2</sup> Laboratory studies have shown that these insecticides and their derivatives can be mutagenic and haematotoxic.<sup>3</sup> Exposure to Lindane and DDT have been associated with aplastic anaemia,<sup>4</sup> Chlorane with refractory megaloblastic anaemia,<sup>5</sup> and Propoxur combined with DDVP with acute leukaemia.<sup>6</sup> Hyper- and hypocoagulability after exposure to Sarin, Parathion and Mevinphos have been observed.<sup>7,8</sup> There is no published record of coagulation disorders caused by Propoxur. Recently we saw a 24 year old female after suicidal ingestion of approximately 120 ml of the household insecticide Propoxur (1% 2-isoproxyphenylmethyl carbamate). Immediately after taking it she repeatedly vomited, became confused and lapsed into coma. On examination, she had bradycardia, pin point pupils, frothing from the mouth and twitching of her facial muscles. No improvement was observed after repeated intravenous injections of atropine. Within 4 hours of admission, she developed gross haematuria, bleeding from nose and mouth, large confluent ecchymotic lesions over whole body, bleeding from intravenous sites and hypotension. Lumbar puncture revealed slightly raised proteins and many red blood cells. Haemoglobin was 7.9 g/dl. Total leucocyte count was  $12.5 \times 10^9/l$  with neutrophils 78%, lymphocytes 20% and eosinophils 2%. Platelet count was  $40 \times 10^9/l$ . Prothrombin time (one stage) was more than 120 seconds (against a control of 12 seconds). Partial thromboplastin time with kaolin and thrombin time were more than 120 seconds each (against normal of 36 seconds and 13 seconds respectively). Serum fibrinogen level was 80 mg/dl and levels of fibrin degradation products were  $40 \mu\text{g/ml}$  (normal less than  $10 \mu\text{g/ml}$ ).

Blood transfusion and dopamine infusion were started, but the patient expired shortly afterwards. Post-mortem samples from liver, lungs, kidneys and heart showed alveolar oedema in the lungs, but histology of the other organs was unremarkable.

In a study of 1300 cases of anticholinesterase exposure coagulation abnormalities were not clinically significant, mild haematuria (2 cases), thrombophlebitis (1 case) and possibly coronary thrombosis (2 cases) being the only manifestations.<sup>3</sup> This may not be entirely true and fatal bleeding may result due to consumptive coagulopathy.

Anoop Misra,  
Sanjeev Kapoor,  
O.P. Malhotra,  
R.R. Singh

Department of Internal Medicine  
All India Institute of Medical Sciences  
New Delhi-110029, India

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### Clonazepam-induced Tourette syndrome in a subject with hyperplexia

Sir,  
Hyperplexia (HPX), or abnormal startle response, refers to a condition in which stimulus (somatosensory, auditory, or visual) results in an exaggerated jumping response. The pathophysiological mechanisms of this disorder are not understood. Fariello *et al.*<sup>1</sup> suggested that interruption of descending thalamic pathways with resultant disinhibition of more caudal brainstem nuclei is important in the production of abnormal startle behaviour. Andermann *et al.*<sup>2</sup> implied the existence of serotonergic abnormalities since startle-induced epileptic seizures have been successfully treated with clonazepam, a serotonin agonist. We report a patient in whom clonazepam produced Tourette-like symptoms in a patient with HPX.

This 37 year old man developed an exaggerated startle reaction at age 21 years. A shout or any other unexpected stimulus caused him to jump, to flex his upper limbs abruptly, to emit an involuntarily shout, and occasionally to fall to the ground. These startle reactions were absent during sleep. The patient's father had suffered similar symptoms since childhood. Two years before presentation, the patient accepted treatment and was given sodium valproate, which proved therapeutic, but had to be discontinued owing to marked and excessive sedative effects. Four months before presentation, clonazepam was prescribed (average dosage 8 mg/day). This produced marked amelioration of the patients' HPX. Two months later, however, the patient was seen again, for routine evaluation and disclosed frequent eye-blinking, grimacing, episodic neck flexion, arm arching and shoulder shrugging

that could be suppressed voluntarily for a short period. Furthermore, his speech had become strained and low volumed, at times disappearing altogether. The dosage of clonazepam was gradually reduced to 2 mg/day over the following 2 weeks. This resulted in the exacerbation of the HPX. The Tourette-like symptoms gradually diminished over the next month and his speech became more clear and loud.

Serotonergic mechanisms have been implicated in the pathogenesis of Tourette syndrome. Singer *et al.*<sup>3</sup> and Crosley<sup>4</sup> have postulated that serotonin deficiency underlies the major symptoms of this illness. In fact, cyproheptadine (a serotonin antagonist) has been reported to exacerbate Tourette syndrome.<sup>4</sup> In view of this, it is surprising that our patient developed this syndrome following administration of a serotonin agonist which would be expected if anything to ameliorate such a condition. However, it is significant that the syndrome only appeared approximately 2 months after therapy with clonazepam had been initiated. This may indicate that the agent produced subsensitivity of postsynaptic serotonin receptors during this period resulting in the presentation of a paradoxical Tourette syndrome.

M.A. Gillman  
R. Sandyk  
*South African Research Institute  
Suite 9 Highlands House,  
(NBS Centre)  
173 Louis Botha Avenue,  
Orange Grove 2192,  
Johannesburg, South Africa*

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#### Hypercalcaemia due to sarcoidosis

Sir,

Dr Gibbs and Dr Peacock<sup>1</sup> maintain that hypercalcaemic sarcoidosis results from a raised serum 1,25 dihydroxy vitamin D. They do not say, however, why it occurs in the first place. It is likely that the increased vitamin D level is secondary to the apparent disappearance of the parathyroid hormone in these cases. Immunoglobulins secreted by granulomas in the parathyroid glands appear to block the actions of the hormone, unless hydrocortisone is given as well. The hypercalcaemia is then corrected in most cases, and the vitamin D3 falls to normal, also. The abnormality persists, however, in exceptional cases, probably because there is then tertiary hyperparathyroidism or a parathyroid adenoma present.<sup>2,3</sup> Thirty six cases of this rare syndrome have been reported.

Gerald A. MacGregor  
*Percy Place  
31 Epsom Road  
Guildford  
Surrey GU1 3LA, UK*

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