

was found to be an independent risk factor, suggesting that the association between hyperhomocysteinaemia and coronary artery disease was probably the result of a higher prevalence of smokers in the hyperhomocysteinaemic group in their population or an interaction between the two risk factors. Although the authors did not postulate the mechanism of cigarette smoking in causing hyperhomocysteinaemia, cessation of smoking should be included in the treatment plan for hyperhomocysteinaemia.

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Treatment of 'warfarin intolerance'

Sir,

Hypersensitivity to food substances may cause symptoms pertaining to the central nervous system (headaches, hyperactivity, 'mental fuzziness', etc) or musculoskeletal system (body aches and pains, arthralgia, etc),^{1,2} mimicking other pathological conditions such as migraine, psychiatric illnesses, chronic fatigue syndrome, rheumatism, etc. A variety of food substances, including maize protein and lactose, are used in the formulations of drugs as bulking agents. Hence, hypersensitivity to these food components may cause 'drug intolerance' that may clinically present as nonspecific neurological, musculoskeletal or gastrointestinal disorders. Maize protein is used as a bulking agent in several widely used drugs, including warfarin, prednisolone, atenolol, isosorbide dinitrate, ibuprofen and piroxicam. Therefore, symptoms due to maize allergy may be incorrectly attributed to the drug and may even result in the withdrawal of the drug from clinical use in these cases.

Sodium cromoglycate has been used to treat various food allergies^{3–5} with beneficial effects in some patients. We report a case of 'warfarin intolerance' in a patient with apparent maize protein allergy successfully treated with sodium cromoglycate.

A 59-year-old man, presented to the Anticoagulant Clinic in November 1995, having commenced warfarin for atrial fibrillation. He had a history of ischaemic heart disease requiring surgical treatment with a coronary

artery bypass graft earlier in the year. Since starting anticoagulant therapy he had experienced generalised muscular aches and joint pains. He had apparently suffered from a 45-year history of allergy to maize-containing foods which provoked symptoms identical to his current complaints. However, no precipitating antibodies to maize were detected on counter-current electrophoresis (dilutions of maize from 1:4 to 1:8000 were run against patient's undiluted serum). Total serum IgE was 134 ku/l. Test for specific IgE (Elisa technique) to maize was negative but that for specific IgG (Pharmacia Cap technique) to maize gave a borderline result. In view of the troublesome nature of his symptoms, warfarin was discontinued and he was commenced on enoxaparin 20 mg subcutaneously once a day. His symptoms resolved within a few days. A week later, warfarin was re-introduced with concurrent oral sodium cromoglycate (200 mg bid) treatment. The patient has remained asymptomatic over a follow-up period of six months and is currently on maintenance dose warfarin and sodium cromoglycate.

Since food substances are widely used in drug formulations, hypersensitivity to a food substance may develop 'drug intolerance' and may preclude the use of the drug. Clinicians should be aware of such possibilities and the true nature of the 'intolerance/adverse reaction' should be investigated and treated appropriately. Furthermore, the response of this patient to sodium cromoglycate clearly indicates that such 'intolerance' may be amenable to simple treatment enabling the continued use of the drug.

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Presentation of *Plasmodium vivax* malaria

Sir,

Malaria can present in unusual forms. *Plasmodium falciparum* malaria has been known to be associated with urticarial reaction,^{1,2} but *P. vivax* malaria presenting with urticaria is a rare association.^{3,4} We report here a case where *P. vivax* presented as recurrent anaphylaxis leading to syncope.

A 44-year-old man presented to the emergency room with complaints of generalised itching and flushing, and mild puffiness of the

face for which he had been to see his general practitioner. While waiting for this medication, he felt dizzy and collapsed. Being recumbent, he regained consciousness and was prescribed antihistamines. He gave a history of feeling feverish a day before. The patient was observed for 24 hours and then discharged. The blood smear was negative for malarial parasite. Two days later, he again presented to clinic with fever up to 103°F and chills. This time his blood smear was positive for *P. vivax* so he was treated with chloroquine.

One year later, he again presented to the emergency room with generalised itching and flushing of one-hour duration, and while entering the emergency room, fainted. On examination, his pulse was 52 beats/min regular, blood pressure 60/40 mmHg, and temperature 36.6°C. He was treated with antihistamines and hydrocortisone. He was fine after 24 hours and was discharged. Three days later, he again presented with fever and chills, generalised erythematous rash and itching. His temperature was 38.4°C, pulse 74 beats/min and blood pressure 100/50 mmHg. His blood smear was positive for *P. vivax* and he was again treated with chloroquine. Later, he was put on weekly chloroquine prophylaxis for a year and has not had any recurrence.

The repeated episodes of anaphylaxis and urticarial rash indicate that these were related to malaria infection. Orthostatic hypotension has been reported as a prominent clinical feature of malaria⁵ and has been attributed to a combination of relative bradycardia and peripheral vasodilatation. This to our knowledge is the first case of vivax malaria presenting as urticarial flushing leading to syncope, which on one occasion even preceded the development of fever. The exact mechanism of anaphylactic reaction in malaria is not clear; a detailed study is needed to identify the immune mechanism involved.

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