An observation on the ethnic uniqueness of the debrisoquine and sparteine antimodes: a study in the Ngawbé Guaymí Amerindians of Panamá

Recently it has been suggested that ethnic specificities might characterize the antimodes of isoniazid acetylation in two Amerindian tribes (Inaba & Arias, 1987), and the debrisoquine oxidation in Nigerians and Ghanaians (Iyun *et al.*, 1986).

We, therefore, wish to report preliminary estimates of debrisoquine and sparteine antimodes of Ngawbé Guaymí Amerindians of Panamá and the frequency of poor metabolizers for both drugs.

Sparteine sulphate 50 mg and debrisoquine hemi-sulphate 10 mg were coadministered to the same 84 Ngawbé Guaymí subjects (68 males, 16 females; ages 12 to 53 years). All the details of the sparteine study have recently been published elsewhere (Arias *et al.*, 1988a). The clinical and analytical protocols employed in the debrisoquine study have also been reported (Jorge *et al.*, 1989). The study was approved by the Ethics Committee of the University of Panamá.

Figure 1 presents the frequency distribution histograms of the $\log_{10}$ metabolic ratios of debrisoquine and sparteine in the same 84 Ngawbé Guaymí subjects.

The data show that the region of location of the antimodes of debrisoquine and sparteine can be placed between 0.65–0.85 units of the logarithm of the metabolic ratios: the midpoint class interval of the region of lowest distribution density, i.e. equidistant from the internal, adjacent limits of the two modes.

This range-value contrasts with the ones proposed for Caucasians: 1.08 (DB); 1.3 (SP). These antimodes of the Ngawbé Guaymí result in 5.9% (5/84) poor metabolizers for debrisoquine and sparteine. The same subjects were poor metabolizers for both drugs. In contrast, no poor metabolizers have been found in the Cuna Indians, the only other Amerindian group which has been studied. In this group, 210 subjects were studied with sparteine, and 89 with debrisoquine (Arias *et al.*, 1988b; Jorge *et al.*, 1989).

The antimodes for both drugs in the Ngawbé

Figure 1 Frequency distribution histograms of the $\log_{10}$ metabolic ratios (a) of debrisoquine (debrisoquine/4-hydroxy-debrisoquine), and (b) of sparteine (sparteine/dehydrosparteines). Results obtained in 84 Ngawbé Guaymí Amerindians. The antimode for both drugs appears to lie within the same range: 0.65–0.85 units of $\log_{10}$ metabolic ratio. Antimodes for Caucasians are 1.3 for sparteine and 1.08 for debrisoquine (referenced in the text).

Guaymí subjects were closer in value to each other than those reported for Caucasians or for any other ethnic group. We are currently undertaking a study of a greater number of subjects, with the intention of applying more theoretical approaches (Jackson *et al.*, 1988a,b) to obtain

more precise estimates of the antimodes of this population.

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TOMÁS D. ARIAS & LUCÍA F. JORGE
The World Health Organization Collaborating Centre, Instituto Especializado de Análisis, and Facultad de Farmacia, Universidad de Panamá, Panamá, República de Panamá.

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Nabilone as effective therapy for intractable nausea and vomiting in AIDS

Nabilone is a synthetic cannabinoid (Ward & Holmes, 1985) with powerful anti-emetic properties. In the U.K. at the present time the only licensed indication for its usage is in the control of nausea and vomiting resulting from the administration of cytotoxic chemotherapeutic agents used in the treatment of neoplastic disease (ABPI, 1989).

A 52 year old bisexual HIV-seropositive man who had developed a cryptosporidial infection of his gastrointestinal tract was recently treated in the Infectious Diseases unit. He had originally been diagnosed as having the acquired immune deficiency syndrome (AIDS) in April 1988, following a bout of *Pneumocystis carinii* pneumonia. The cryptosporidial infection led to the development of intractable nausea and vomiting which in turn severely compromised the patient's ability to maintain a satisfactory

enteral nutritional input. Furthermore it proved impossible to treat his underlying cryptosporidiosis (no reliable anti-cryptosporidial drug has as yet been discovered) as well as to control his gastrointestinal symptoms with conventional agents such as prochlorperazine, cyclizine, domperidone and high-dose intravenous infusions of metoclopramide. In view of the severe distress sustained by the patient, he was commenced on oral nabilone 1 mg twice daily; the therapeutic response was remarkably successful, resulting in complete cessation of the patient's nausea and vomiting, which made the patient feel more comfortable generally. The patient was maintained on nabilone for 4 days, the only side effect being a degree of drowsiness which the patient found acceptable prior to the terminal stages of his illness. He ultimately died of a probable septicaemia.