13 - 6. Ethnopharmacology

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© SPMM Course 6. Ethnopharmacology Ethnicity is defined as a self-ascribed belongingness to a group with common geographical origins, race, language, religion, etc., which transcends kinship and neighbourhood. Ethnic categories retain a strong racial component. Race on the other hand is largely perceived by appearance and attributed to biological and genetic traits. Culture is a shared system of concepts or mental representations established by convention and reproduced by traditional transmission. Differences exist in the placebo response, compliance, doctor-patient relationship, social stress and health beliefs. The following are differences in the pharmacology of drugs administered. Absorption and availability Caucasians appear to have lower plasma levels of tricyclic antidepressants and attain plasma peaks later when compared with Asians (of Far Eastern ancestry as well as those from the Indian subcontinent). These differences have been attributed to a greater incidence of slow hydroxylation among Asians when compared with Caucasians Maximal haloperidol concentration in plasma after rapid tranquillisation is significantly high for Asians than Caucasians (Lin & Finder, Am J Psychiatry 140:490-491, 1983). Metabolism In the CYP system, variations in CYP2D6 are largely determined by genetic factors. (CYP2D6 metabolizes a number of antidepressants, antipsychotics, beta-adrenoceptor blockers, and antiarrhythmic drugs). The CYP2D6 variation is called debrisoquine/sparteine polymorphism: 4 groups exist –

1. Poor metabolizers: develop side effects quickly. Caucasians - the highest rate of poor metabolizers (nearly 7%). East Asians - lowest – 1%. These 7% Caucasians and 1% East Asians lack this enzyme, and so are poor metabolizers of risperidone and tricyclics
2. Intermediate metabolizers: higher in Asians (most Asians fall into this group – hence have more side effects though good drug efficacy)
3. Extensive metabolizers
4. Ultrarapid metabolizers: need high doses. 33% North Africans have multiple copies of CYP2D6, and so are ultra-rapid metabolizers. They require higher doses of risperidone. Only 5% Caucasians and 1% East Asians are ultra-rapid. 25% Indians may have this variant. CYP2C19 enzyme participates in the metabolism of omeprazole, propranolol and psychotropic drugs such as hexobarbital, diazepam, citalopram, imipramine, clomipramine, sertraline and amitriptyline. The incidence of poor metabolizers of CYP2C19 substrates is

© SPMM Course much higher in Asians (15–30%) than in Caucasians (3–6%). CYP2C19 polymorphism is mephenytoin related. Unlike CYP2D6, the variations in CYP3A4 often influenced by environmental (e.g. diet) factors. Nearly 40% Asians and around 60% South American Native Indians lack Aldehyde dehydrogenase enzyme in sufficient amounts to metabolise alcohol – this

serves as a natural deterrent in these communities. Pharmacodynamics The long form serotonin transporter polymorphism in Caucasians is associated with better SSRI response and tolerance while the opposite is true in South East Asians. Low COMT variant is seen in less than 20% of Asians and Africans, but nearly 50% of Caucasians show low variant. Adverse effects A well-known example from general medicine is that of Isoniazid – East Asians are most likely to be rapid acetylators and suffer from hepatotoxicity. But they have lesser peripheral neuropathy seen in slow acetylators. Chinese people had higher levels of extrapyramidal side-effects with haloperidol, and their blood levels were comparably high on equivalent dosages. On the administration of antipsychotics, Asian subjects were reported to produce greater serum prolactin levels than Caucasian subjects. This remains statistically significant after controlling for the difference in haloperidol concentrations, suggesting that the two groups differ in their dopamine receptor-mediated response. A summary of some relevant ethnic effects is given below. African Americans Asians Increased diagnosis of schizophrenia but decreased diagnosis of depression Have more side effects with lithium, tricyclics Higher tardive dyskinesia with antipsychotics. Better, rapid response to tricyclics and lorazepam, but poor response to fluoxetine. More depot medications received by African Americans. It is best to start at half of the standard dosage of all psychiatric medications Clozapine better effect in lower serum range, but higher incidence of agranulocytosis Taiwanese have lower required therapeutic level of lithium. Metabolise TCA slowly. Asians use herbal remedies more often than others.

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