

# Cross Cultural Newsletter

## “Ethnicity & Response to Psychotropic medication: Practical implications”

29<sup>th</sup> October 2014



**Diwali** also known as *Divali*, *Deepavali* and the "festival of lights", is an ancient [Hindu festival](#) celebrated in autumn every year. On the same night that Hindus celebrate **Diwali**, [Jains](#) celebrate a festival of lights to mark the attainment of *moksha* by [Mahavira](#) and [Sikhs](#) celebrate [Bandi Chhor Divas](#).

Dear Members,

Once again, this is to report on a very successful meeting. Despite the change in our regular meeting dates from Tuesday to Wednesday, 30-40 of our members attended. Our speaker was **Dr Aram Kim**, Senior Registrar for Maternal Mental Health, WDHB. Although it is a highly complicated subject, **Dr Kim** was able to simplify such as to make it both easily digestible and appealing to our members.

Apart from cultural and psychological factors, biological and ethnicity based sensitivity is an important factor affecting the cross-cultural application of psychotropic medication. This evening's talk comprised of the following sections: **historical** background of development in ethno-psycho-pharmacology; factors causing variation (**pharmacokinetics, pharmacodynamics and other factors**); Practical applications including ethnicity based recommendations and final summary and conclusions.

**Dr Kim** first portrayed **the evolution of concepts** from the old belief that medication response is universal to the current understanding that variations are indeed present and that awareness of such would help to build therapeutic alliance in medication treatment. **Dr Kim** then clarified a number of easily misused terms including the difference between **ethnicity** (biological /genetically based variation); **race** (a physical manifestation of similarities and differences—not necessarily only genetic) and **cultural** (psychosocial / behavioural variations). Although all can affect a patient's compliance to medication, **Dr Kim's** talk was mainly confined to the ethnic variations. However, in passing, he also mentioned how psychosocial behavioural practices could influence the genetic variations. Study of the ethnic variations among Asian is important in the New Zealand context in view of the rising Asian populations.

**Dr Kim** then went on to describe **the three main areas** affecting variation : **pharmacokinetics** ( Kinetics in short), **pharmacodynamics** ( referred to as dynamics hereunder), and **other social cultural factors**. **Pharmacokinetics** is the process by which medication is absorbed, distributed, metabolised and excreted; whereas **pharmacodynamics** is the response of the body to the medication. **Pharmacogenetics** is genetic variation affecting both how drugs are absorbed, metabolised (kinetics) and respond to medication (dynamics). After clarifying these terms, **Dr Kim** then described in detail the two key corner stones underlying variation: **kinetics and dynamics**.

Gene variations affect the **kinetics mainly through the distribution and rate of metabolism**. In terms of distribution, genetic variation affects the structure and quantity of certain **glycoproteins** which bind the medication and thus influence the levels of unbound drugs in the plasma and ultimately the availability of the medication to the target organs. Apart from distribution, which is also affected by the amount of body fat, the most significant gene influence on kinetics is the **rate of metabolism which is carried out by a host of enzymes**. In psychiatry, the **cytochrome P450 groups** are the major ones involved. Of these, four subgroups are important. But the key one is **CYP2D6**. Genetics affect the functionality of these enzymes varying from those that has no function, through those less efficient, to normal ones, and not least to hyper-functioning ones. The consequence is the rate of metabolism is affected. According to the rate of metabolism, people could be classified as poor metabolisers, intermediate metabolisers, efficient metabolisers, and ultra-metabolisers. The clinical implication is that those poor metabolisers and intermediate metabolisers would have a higher level of the medication and thus also side effects to the same dose of

medication that the other two groups. **In this regard, up to 50-70% of Asians are intermediate metabolisers.** The clinical implications are that they **may require lower than normal dose** of the medication and be sensitive to side effects. This is especially so when there is a narrow therapeutic window which could be easily overshoot eg nortriptyline or risperidone. To add onto the complexity, **a number of other factors** eg other medications, dietary substances could affect the efficiencies of these enzymes by either enhancing their functioning (inducers) or compromising them (inhibitors). An examples is with risperidone for which SSRIs and thioridazine are all inhibitors of the respective cytochromes, increasing the level of the drug by reducing its metabolism; whilst dexamethasone is an inducer enhancing metabolism thus reducing the level. **Dr Kim** quoted a number of examples of such interactions between medications, and dietary substances. Of the latter group, alcohol and smoking are notorious agents as inducers (eg in the case of clozapine) or inhibitors. In the face of such complexities, science has come to the help. **Diagnostic chips** (Amplichip) have been around for a number of years to identify those poor and intermediate enhancers. However, they are not easily available and still costly to perform. More importantly, they are mainly adjusted for some ethnicities and may not be useful in other ethnicities such as Polynesians.



National Day decorations - Beihai Park – Oct 2014

Having presented such a complicated biogenetic subject on cytochromes, **Dr Kim** then turned his attention to **dynamics**. **In this, genes are known to affect receptor sensitivities and transporter efficiency in affecting receptor functioning.** He gave an example of the serotonin transporter gene link to responses to SSRI in depressive patients. In some ethnicities such as the Han Chinese, the long Allele variant is responsible for good response, whilst among Korean and Japanese, the reverse is true. Another major gene influence is through the **COMT activity** affecting response to the anti-parkinsonian agent Levodopa. **High percentages of Asians are poor responders due to the variation in COMT activity.** Because of heighten receptor sensitivities, certain medication such as lithium or Risperdal need only lower therapeutic serum levels to work. (eg Lithium at .5-6 meqv/l)

Other **environmental and dietary and psycho-socio-cultural factors** affect both the kinetics and dynamics of medication. Cooking methods for food such as **grilling; consumption of coffee, tea and cigarette smoking all influence the response to medication.** In general, **caffeine enhances and tea inhibits.** **Clozapine** is affected by smoking. As to psycho-socio-cultural factors, illness concept, perception and acceptance of treatment strategies, and trust in the therapist all influence compliance and effectiveness (some no doubt through the placebo effect). On the other hand, concomitant use of indigenous treatment can cause interactions that can either be positive (augmenting) and negative (side effects).

Finally, **Dr Kim** provided the audience with **ethnicity-based suggestions. In general, for Asians, a lower dose of haloperidol, clozapine, risperidone, TCA, benzodiazepines and lithium is required. With clozapine and Risperdal, Asians are more sensitive to side effects such as agranulocytosis with clozapine and EPS and hyperprolactinaemia with risperidone.**

**Dr Kim's final words** which I find very useful are **"Be careful and avoid over-generalisations, individual differences exist within an ethnic group"**. Similarly, the age old motto of **"Start low, go slow"** still remains useful. The meeting closed at 830. The DVD is now available for ordering. Thank you once again for your enthusiastic support.

I look forward to seeing you at our next meeting on Thursday, 27<sup>th</sup> November  
S Wong  
For Cross Culture Interest Group

For a more accurate rendition of the presentation, **please request the DVD** from Diane Evans at [dianee@adhb.govt.nz](mailto:dianee@adhb.govt.nz)  
(please send \$2 stamps to help cover costs)

For ADHB staff, previous newsletters and flyers can be viewed on the Intranet – click on this link  
[http://adhb.intranet/Mental Health/Resources/CrossCulture.htm](http://adhb.intranet/Mental_Health/Resources/CrossCulture.htm)