EDITORIAL

ADVERSE DRUG REACTIONS

Two articles in this issue of the journal by Nderitu *et al.* and Malele *et al.* prompted me to write this editorial. Both articles focus on adverse drug reactions (ADRs) among HIV/AIDS patients in Kenyan and Tanzanian hospitals. A recent literature search on the internet (Google) using the phrase "adverse drug reactions" returned 5,570,000 results in 0.25 seconds. A pharmacological profile or description of any drug would be incomplete if it did not include information on any ADRs associated with its clinical use. In most textbooks of pharmacology, this topic is given wide coverage.

The phrase "adverse drug reactions" is used to denote harmful or undesirable effects associated with the legitimate use of the drug when administered at the recommended normal dosage. ADRs may be observed following a single dose or prolonged use. Many ADRs go unreported since many patients are unable to differentiate them from the disease condition being treated. For example in malaria and typhoid, nausea and vomiting is common and patients are unlikely to differentiate these from nausea and vomiting associated with drugs used in treatment.

The use of any drug is based on benefit/risk ratio. For drugs used to treat minor ailments such as headache, stomachache, flatulence, etc., any significant form of ADR would be considered unacceptable and patients may prefer to put up with the condition rather than the ADR. The same cannot be said for drugs used to treat cancer, HIV/AIDS, hypertension, epilepsy, etc. At what point then are ADRs judged to be acceptable? In any given situation, the clinicians will choose from the drug or combination of drugs based on several considerations and not just ADRs. Efficacy and duration of treatment are important determinants. Multidrug therapy is often the rule rather than the exception in chronic diseases such as cancer, hypertension and diabetes. At times it may be possible to substitute one drug in the combination to minimize the ADR. A typical example is the substitution of nevirapine in the antiretroviral (ARV) combination therapy which is the subject of the article by Malele *et al.* in this issue of the journal.

Adverse drug reactions are classified based on various criteria. For example, ADRs which are dose-dependent and predictable and which form the highest percentage of ADRs are placed in one class. Those ADRs which are genetically determined are also placed in one class. For example, people deficient in glucose-6-phosphate dehydrogenase (G6PD) are intolerant to primaquine (an 8-aminoquinoline derivative) as is evidenced by hydrolysis of red blood cells (RBCs), leading to haemolytic anaemia. Peripheral neuropathy observed in some patients after administration of isoniazid is yet another example of genetically linked ADRs. Yet another category are the ADRs which are not dose-dependent, unpredictable and defy rational explanation which are classified together under the term 'idiosyncracy'. In the 1960s, a condition known as subacute myelo-optic neuropathy (SMON) was observed among Japanese patients who had been treated for "travellers' diarrhoea" with clioquinol, a halogenated 8-aminoquinoline. This idiosyncratic ADR is rarely encountered outside Japan and no rational explanation has ever been advanced.

A new specialty in pharmacy known as pharmacovigilance now focuses on ADRs. The School of Pharmacy at the University of Nairobi introduced a master's degree programme in Pharmacovigilance/Pharmacoepidemiology in the year 2012 and this programme is one of the most popular postgraduate courses at the School, second only to Clinical Pharmacy. It would be reasonable to teach a pharmacovigilance course in the medical school undergraduate curriculum, as a distinct topic, in recognition of its importance. ADRs can range from mild (nausea, dizziness) to more serious life

threatening conditions and even fatal ones and at times necessitate hospitalization. Symptoms may manifest in a number of ways including the following: miscarriage, birth defects, gastrointestinal bleeding, deafness, erectile dysfunction and loss of libido, amenorrhoea, alopecia, insomnia, dry mouth, nausea, vomiting, nightmares, peripheral neuropathy, seizures, rashes, fever, weight gain and spontaneous tendon damage.

The liver and kidney are important organs in metabolism and excretion of drugs, respectively. Any disorder which affects these two organs will compromise their function. For example, hepatotoxicity leading to decreased drug metabolism will result in accumulation of drugs simulating an overdose, hence ADR. Decreased renal excretion of some drugs will also lead to accumulation, and in the case of aminoglycosides, this is often manifested as deafness. The age of the patient is an important determinant in ADR. Examples include the "gray baby syndrome" in neonates following administration of chloramphenical. Co-morbidity, common in HIV/AIDS, is also a contributory factor in ADR. For example treatment of tuberculosis (TB) with rifampicin in HIV/AIDS patients on highly active antiretroviral therapy (HAART) leads to drug interaction at the level of drug metabolism and is manifested as ADR.

In the paper by Nderitu *et al.*, the authors have made an important observation, i.e., ADRs interfere with adherence to ARV therapy, and in some case lead to mortality. The same observation has been made by Malele *et al.* Poor patient compliance often leads to treatment failure especially where the drugs have to be administered for a long duration. In the case of TB, the World Health Organization (WHO) recommended directly observed therapy (DOT) where the patient is required to take drugs daily in the presence of a health worker or another responsible person. This simple intervention measure improved the outcome of TB therapy significantly.

In 2011, the Agency for Healthcare Research Quality (AHRQ) showed that sedatives and hypnotics were a leading cause of ADRs seen in the hospital setting in the USA. A similar study in African countries is likely to yield different results because sedatives and hypnotics are not as widely used in Africa as they are in the developed countries.

Prof. Charles K. Maitai,

Editor-in-Chief.