MORE ABOUT . . . COMMON INFECTIONS — LOCAL AND SYSTEMIC

ADHERENCE TO ANTIRETROVIRAL THERAPY

CATHERINE ORRELL, *MB ChB, MSc, DCH*
Desmond Tutu HIV Foundation, Division of Medicine, University of Cape Town

WHAT IS ADHERENCE?

Adherence to antiretroviral therapy (ART) means how correctly a person is managing to take his/her medication. The term 'adherence' is preferable to 'compliance', as compliance implies that some prompting is necessary to ensure that the medication is taken, whereas adherence is voluntarily driven by the individual. Adherence means taking the correct dose of medication at the right times, every day, for as long as ART is required.

WHY IS ADHERENCE IMPORTANT?

A number of studies have proved adherence to be crucial to the sustained virological and clinical benefit of ART.[1,2] The more doses taken correctly, the more likely it is that virological suppression will be achieved and therefore maintained. To achieve an 80% chance of complete viral suppression, more than 95% of doses need to be taken; for a twice daily regimen this means missing less than one dose every second week. There is a rapid decline in virological benefit as adherence drops. Someone taking 70% of his/her doses has only a 6% chance of achieving viral suppression at 1 year.

It is not easy for anyone to maintain such high levels of adherence. Many South Africans struggle to complete 6 months of tuberculosis therapy, taken just once a day, 5 days a week, despite a national programme of directly observed therapy (DOT). ART demands twice daily medication, every day, including weekends, for life. No clinic system has the capacity to take responsibility for monitoring every dose taken. Responsibility for successful, long-term viral suppression must lie with the individual on therapy.

From lessons learned from the Cape Town Aids cohort (CTAC) and the Hannan Crusaid Treatment Centre (HCTC) in Gugulethu, Cape Town, we know that South Africans can adhere to ART.[3,4] What is the key? Engendering a responsible attitude to therapy is crucial. Thorough pre-treatment education is vital in order to develop a full understanding of HIV disease and the benefits of ART. HIV-positive people commencing therapy need to do so with realistic expectations in terms of expected health benefits, possible side-effects and daily tablet burden.

At the HCTC everyone commencing therapy must attend a number of pre-treatment education sessions covering the following:

- the basics of HIV (lifecycle of the virus, staging of disease and opportunistic infections, nature of a CD4 cell)
- principles of ART (why and how ART works, reasons for adherence, what happens to the viral load and CD4 count when on ART)
- details of specific medications, tablet number and dosing instructions
- expectations of the clinic team of a patient on therapy.

This information is broken into modules and presented in a weekly group session led by the counselling team. All the information is covered in a 3-week cycle. There is rarely a need to rush the commencement of ART. Patients with particularly low CD4 counts are more likely to achieve and maintain the benefits of ART with better adherence, and should not be pushed through the education process too rapidly.

PREDICTING ADHERENCE

Unfortunately there are no absolute predictors of adherence. Nursing staff are more likely to be correct in their assessment of a patient's likely adherence than doctors, who do no better than random. It is known that people with an ongoing alcohol problem, or those who are acutely depressed, will struggle with adherence, so these issues must be thoroughly addressed before starting ART. At the HCTC the major reason for non-adherence noted to date is alcoholism.

MONITORING ADHERENCE

No measurement of adherence is completely accurate. Clinic-based counting of tablet returns gives a reasonable estimate in the majority of cases, and can be done quickly at every visit. The HCTC counselling team performs a surprise tablet count at every patient's home once in every 4 months. This

seems to provide a better account of adherence, as patients are unable to prepare their returns in advance, but is labour intensive. Another well-used method for assessing adherence is the completion of questionnaires by patients, thus recording their dosing over the previous 4 days, perhaps best used in a trial situation when there is ample time and impartial staff available.

SUPPORTING ADHERENCE

The discovery of a non-adherent patient should not come as a surprise. Asking a patient to achieve 95% adherence at all times is no small matter. Life factors — deaths, new relationships, financial stresses, and even side-effects — can result in a decrease in adherence.

Patients should not feel that they are being judged for doing a bad job, but rather that adherence is monitored to allow the health care team to advise them and to offer them added support. This support may take the form of a daily dosing diary, a pill box that can be filled daily or weekly, and/or the involvement of a family member in the treatment process. Patients should be encouraged to join an educative support group, preferably with others also on ART.

WHAT ABOUT DOT?

DOT should not be the first solution to non-adherence. Most patients will respond to education and the support outlined above. Those who fail a first regimen, despite full adherence support and re-education, may respond to DOT. Our present primary care service could not provide this support for a twice daily, every day regimen. To observe all doses, a family member may need to be recruited. The patient needs to understand that second line therapy is the last chance they have for long-term viral control.

EXPANDING ACCESS

As ART access increases, staff time becomes an increasingly stretched resource. Counsellors should play a key role in ensuring that patients are well informed before receiving treatment. The HCTC employs a team of counsellors who are all HIV positive, the majority of whom are on ART.

Starting a patient on ART should be an intensive process, but one that should bring the satisfaction of treatment success.

References available on request.

PREVENTING ANTIMALARIAL RESISTANCE WITH ARTEMISININ-BASED COMBINATION THERAPY

KAREN I BARNES, *MB ChB*
Senior Lecturer, *Division of Pharmacology, University of Cape Town*

Malaria morbidity and mortality is rising, principally as a result of increasing antimalarial resistance.[1] Resistance means that there is a shift to the right in the dose-response (concentration-effect) relationship. *Plasmodium falciparum* has developed clinically significant resistance to all classes of antimalarial drugs, with the possible exception of artemisinin derivatives.[2]

Resistance is thought to arise from spontaneous chromosomal point mutations or gene duplications, which are independent of the drug selection pressure. Once formed, these more resistant parasites have a survival advantage in the presence of antimalarial drugs. This is determined by the intrinsic frequency with which these point mutations occur and the degree of resistance conferred by the change.

Several factors encourage the spread of resistance. These include:

- The proportion of transmissible malaria infections exposed to subtherapeutic concentrations of an antimalarial.
- The drug concentration profile (a long elimination phase favours resistance), the pattern of drug use and the level of immunity in the community.

Antimalarial resistance results in prolonged illness, hospitalisation and death as well as a vicious circle of an increase in treatment failure, leading to increased gametocyte carriage and thus increased malaria transmission, particularly of resistant parasites, further increasing drug pressure and antimalarial drug resistance.

In the 1960s resistance to chloroquine developed almost simultaneously in South-East Asia and South America, and has spread remorselessly so that

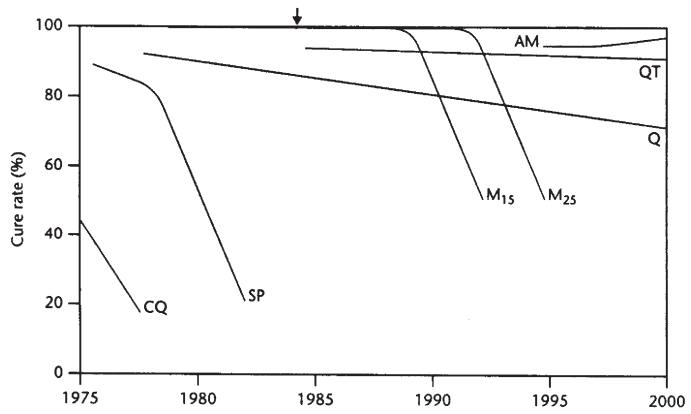

Fig. 1. Antimalarial drug efficacy on the north-western border of Thailand.[7] The decline of antimalarial efficacy of chloroquine (CQ), sulfadoxine-pyrimethamine (SP), mefloquine 15 mg/kg then 25 mg/kg (M15, M25), and quinine (Q) is contrasted with the very slow decline in the efficacy of quinine-tetracycline (QT) and the sustained efficacy of artesunate plus mefloquine (AM).