

## ***HIV RESISTANCE TO ANTIRETROVIRAL THERAPY***

Treatment failure often (though not always) occurs because a patient's strain of HIV has developed resistance to one or more of his/her antiretroviral medications. The manner by which HIV develops resistance to ARVs is similar to the way in which bacteria or mycobacteria (e.g. TB) develop resistance to antibiotics: insufficiently potent drug therapy selects for mutant strains that are resistant to the medications administered to the patient. These mutant strains then replace the wild-type strain due to their selective replication advantage in the face of drug pressure, leading to treatment failure. Resistance to antiretroviral medications most commonly develops in the setting of suboptimal adherence, but can occur even in patients who maintain very high levels of adherence to their medications. For example, a patient with poorly controlled diarrhoea may not fully absorb his or her medications, leading to sub-therapeutic drug levels in the blood, which could lead to the development of resistance.

Cross-resistance between ARVs within drug classes is common; for example, a strain of HIV that is resistant to NVP is very likely to be highly resistant to EFV as well and *vice versa*. Cross-resistance is not as common within the NRTI and PI classes, but can occur. Considerations of potential cross-resistance must therefore be incorporated into the design of second-line and salvage treatment regimens.

Laboratory assays have been developed to estimate the patterns of resistance that have developed in a given patient's strain of HIV. Though imperfect, these assays have demonstrated clinical efficacy in aiding the design of second-line treatment regimens following treatment failure. Unfortunately, these assays are very expensive and not widely available in the Caribbean. However, where available, a resistance assay can provide valuable information for patients experiencing treatment failure.

Even in the absence of resistance testing, knowledge of the patterns of resistance and cross-resistance that commonly develop in patients failing specific regimens allows for reasonably accurate empiric decision-making in designing a second-line regimen. For example, patients failing an NNRTI-based initial treatment regimen commonly develop one or more mutations that confer high-level resistance to all available NNRTI medications. Hence, a second-line regimen for these patients should be PI-based rather than NNRTI-based. These concepts are discussed more fully below and are summarised in *Table 9*. A more detailed discussion of antiretroviral resistance and resistance assays can be found in *Appendix F*.