ROBERT SMITH, The University of Ottawa

Explicitly accounting for antiretroviral drug uptake in theoretical HIV models predicts long-term failure of protease-only therapy

Mathematical models of HIV therapy have traditionally amalgamated the action of antiretroviral drugs, trading the complexity of the situation in favour of simpler—and hence mathematically tractable—models. However, the effects of ignoring such dynamics remain underexamined. In this paper, the traditional method of dosing (where the dose is modelled implicitly as a proportional inhibition of viral infection and production) is compared to a model that accounts for drug dynamics via explicit compartments. Four limiting cases are examined: frequent dosing of both major classes of drugs, absence of either drug, frequent dosing of one drug alone, or frequent dosing of the other drug alone. When drugs are absent, both models predict that the virus will dominate and the uninfected T cell counts will be low. When reverse transcriptase inhibitors are given frequently, both models predict that the virus will be theoretically eliminated and the uninfected T cell counts will be high; this is true regardless of whether the reverse transcriptase inhibitors act alone or in conjunction with protease inhibitors. However, if protease inhibitors alone are given frequently, then the implicit model predicts that the virus will be eliminated and the uninfected T cell counts will be high, whereas the (more realistic) explicit model predicts that the reverse situation may occur. In the latter case, critically, protease-only regimens may ultimately result in the death of the patient. It follows that the impact of drug regimens consisting only of protease inhibitors must be urgently re-examined, if such outcomes have been based on overly simplistic modelling.