

# AIDS BRIEFS

## TREATMENT SIMPLIFICATION IN HIV-POSITIVE CHILDREN

HIV-positive children with a detectable viral load in spite of taking potent antiretroviral therapy may safely simplify their treatment, according to a study published recently in the *Journal of Acquired Immune Deficiency Syndrome*. This simplification does not appear to result in disease progression or a further increase in viral load. Treatment in this study was simplified by stopping therapy with a protease inhibitor, while carrying on with the nucleoside reverse transcriptase inhibitor (NRTI) and although this led to a drop in CD4 percentage, this was not clinically significant in any of the children.

It has been observed that children with a detectable viral load who discontinued their protease inhibitor, but who continued to take NRTIs, remain clinically stable. The authors of this paper conducted a retrospective study of all children in whom treatment simplification had been used. Treatment simplification is the term used for discontinuation of one class of drugs in a multi-class antiretroviral combination, when there are either side-effects or ongoing viral replication.

They examined 26 children who were followed for at least 6 months after discontinuing their protease inhibitor. Data were also available for 21 children after a year and for 11 children 2 years after treatment was simplified. At the start of the study, the median age of the children was 7 years and the median viral load 10 000 copies/ml. The most commonly used nucleoside combinations were 3TC with AZT, or 3TC with d4T. Resistance testing of 16 children at baseline showed that 14 had extensive dual or triple-class resistance.

All children completed 24 weeks of follow up and none experienced any HIV disease progression. Viral load did not change significantly but there was a statistically significant fall in CD4 percentage, but not to the extent that the children became at risk of an AIDS-defining illness. This was the case for those 21 children who were still being followed up at week 48. Only 11 children were still taking a simplified regimen at week 96, and the results were similar to those at weeks 24 and 48.

The study showed that partial treatment interruption, or treatment simplification, was not associated with clinical disease progression in these 26 children. However, further prospective studies are needed before clinical recommendations can be made.

Abadi J *et al.* *J Acquir Immune Defic Syndr* 2006; **41**: 289-303.

## BREAKING TRIOMUNE TABLETS FOR PAEDIATRIC DOSING

Triomune tablets, a fixed dose of stavudine, lamivudine and nevirapine, is one of the cheapest regimens available in sub-Saharan Africa and is commonly prescribed to adults. It is also used for paediatric treatment by halving and quartering tablets, but it is unclear whether the doses of the drugs obtained in this way are correct. A paper presented at an HIV pharmacology workshop in Lisbon recently, suggests that dividing adult Triomune for use by children may result in under-dosing.

The study was carried out jointly by the Radboud and Nijmegen universities in the Netherlands and two hospitals in Malawi and Zambia, in conjunction with the British Medical Research Council (MRC). The aim of the study was to investigate whether Triomune tablets that are routinely divided for use by children provide the same active ingredients, particularly for children who are malnourished.

Researchers carried out a retrospective study of 127 HIV-positive children, 71 in Malawi and 56 in Zambia, between the ages of 3 months and 16 years, treated with Triomune. They were assessed for steady-state concentrations of nevirapine. The Malawian children were more malnourished and had longer post-dosing sampling times than the Zambian children. The median nevirapine concentrations were 4.8 in Malawian children, compared with 7.0 in Zambian children. Only those children receiving doses comparable with the adult dose were actually receiving the target nevirapine concentrations of 300 mg/m<sup>2</sup>/day. Of the children, 2% were on sub-therapeutic levels, while those who received a quarter to a half tablet were more likely to be under-dosed. Those prescribed 200 mg and less than 350 mg were also under-dosed. Lower prescribed dose, lower height-for-age and younger age were all independently associated with lower levels of nevirapine. BMI-for-age was a stronger predictor of this in Malawian children, indicating higher levels of wasting in this population.

Researchers do not recommend the use of quarter tablets or of dividing Triomune in young children to avoid the possibility of under-dosing. Nevirapine levels may be reduced in children with stunted growth, while levels were increased in children with wasting.

L'homme R *et al.* Paper presented at HIV Pharmacology Workshop, Lisbon, Abstract 2, 2006.

## EARLY WEANING NEEDS NUTRITIONAL SUPPORT

A study from Côte d'Ivoire has found that encouraging HIV-positive mothers to stop exclusive breastfeeding altogether at 6 months increases the risk of stunted growth in their children unless the mothers can introduce sufficient food to replace the nutritional value of breastmilk. This means that mother and child health programmes that promote exclusive breastfeeding as a way of reducing the risk of HIV transmission need to provide information on nutrition at the time of weaning as well.

Researchers carrying out the DITRAME Plus study in Côte d'Ivoire set out to find out whether children who were weaned early, following the current recommendations to wean at 6 months, were poorly nourished or growing poorly. They questioned 260 HIV-positive mothers every week until their children were 9 months old, about what food the child had received in the previous day and in the previous week. After the child was 9 months old, they interviewed the mothers every quarter. Infants were classified as exclusively breastfed, predominantly breastfed, mixed fed or formula fed.

The mothers were taught how to breastfeed correctly and had group sessions on the benefits of exclusive breastfeeding, how to start weaning and what food to introduce at weaning.

At 4 months, 39% of the infants were receiving mixed feeding, 30% were predominantly breastfed, 8% were exclu-

sively breastfed and the remaining 23% had already been weaned. By 6 months, virtually all the children had stopped breastfeeding.

Fluids other than breastmilk were introduced into the diet very soon after birth, mainly with tap water.

Researchers found that children who were poorly fed at weaning at 6 months had a lower height for age at 12 and 18 months and a lower weight for age at 9, 12 and 18 months. This finding was not altered when HIV-positive children were excluded from the analysis. Children who were poorly fed at 6 months had a 50% higher risk of stunted growth at any time between 7 and 18 months. The authors concluded that the critical period around the weaning process appeared to be a predictor of a child's future nutritional status.

These results were found in women who received intensive counselling on nutrition and breastmilk substitutes from the beginning of the weaning process until 9 months. In addition, these women were then followed up regularly and asked about their child's nutrition. There is a suggestion that these outcomes are the best possible, and may be worse in other situations.

The conclusion is that there needs to be intensive nutritional support for women who are weaning their children earlier than the local norm in areas where food resources are poor.

Becquet R *et al.* *Pediatrics* 2006; **117**: 701-710.

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## SINGLE SUTURE

### FRUIT AND BOWEL CANCER

Conventional wisdom would have it that consuming large quantities of fruit and vegetables protects against bowel cancer. But it would seem that it is only fruit that is protective. A study published in *Cancer Research* used data from more than 34 000 women who had undergone colonoscopy or sigmoidoscopy during follow-up between 1980 and 1998, as part of a study of the incidence of adenomas of the distal colon and rectum in the Nurses Health Study. Their consumption of fruit and vegetables was assessed in 1980, 1984, 1986, 1990 and 1994. A total of 1 720 cases of adenoma were diagnosed between 1980 and 1998 and it was frequent consumption of fruit that was inversely related to the risk of polyps, rather than vegetable consumption. Women who reported eating more than 5 servings of fruit per day had less risk of developing colorectal adenomas than women who ate less fruit. The same relationship was not found for vegetables, although there was a relationship between eating legumes and a lower risk of polyps.

Michels KB, *et al.* *Cancer Res* 2006; **66**: 3942.