AIDS briefs

Carraguard unfortunately shows no anti-HIV effect

A recent study, published in the *Lancet*, shows that the topical vaginal gel Carraguard does not prevent the transmission of HIV.

This is a disappointing result, given the urgency of finding female-initiated HIV prevention methods. Skoler-Karpoff and others undertook a randomised, placebo-controlled, double-blind trial in 3 South African sites in sexually active, HIV-negative women aged 16 years and older. A total of 6 202 participants, who were randomly assigned by a block randomisation scheme to Carraguard (*N*=3 103) or placebo (methylcellulose (*N*=3 099)), were instructed to use one applicator of gel plus a condom during each vaginal sex act. Participants were followed up for up to 2 years. Visits every 3 months included testing for HIV presence and pregnancy, pelvic examinations, risk-reduction counselling, and treatment for curable sexually transmitted infections and symptomatic vaginal infections. The primary outcome was time to HIV seroconversion. Analysis was in the efficacy population (a subset of the intention-to-treat population, excluding participants for whom efficacy could not be assessed).

For the primary outcome (time to HIV seroconversion) the authors analysed 3 011 women in the Carraguard group and 2 994 in the placebo group. HIV incidence was 3.3 per 100 woman-years (95% confidence interval (CI) 2.8 - 3.9) in the Carraguard group (134 events) and 3.8 per 100 woman-years (95% CI 3.2 - 4.4) in the placebo group (151 events), with no significant difference in the distribution of time to seroconversion (p=0.30). The covariate-adjusted hazard ratio was 0.87 (95% CI 0.69 - 1.09). Rates of self-reported gel use (96.2% Carraguard, 95.9% placebo) and condom use (64.1% in both groups) at last sex acts were similar in both groups. On the basis of applicator testing, however, gel was estimated to have been used in only 42.1% of sex acts (on average) (41.1% Carraguard, 43.1% placebo). A total of 1 420 (23%) women in the intention-to-treat population had adverse events (713 Carraguard, 707 placebo), and 95 (2%) women had adverse events that were related to gel use (48 Carraguard, 47 placebo). Serious adverse events occurred in 72 (2%) women in the Carraguard group and 78 (3%) in the placebo group, only one of which was considered possibly related to gel use (placebo group).

Skoler-Karpoff S, *et al. Lancet* 2008; 372: 1977-1987.

Children starting antiretrovirals in sub-Saharan Africa have a low risk of death

An international team of investigators have found that there is a low risk of death in children in sub-Saharan Africa who start antiretroviral therapy, according to a study published in the *Journal of Acquired Immune Deficiency Syndromes*.

The risk of death was 7%; three-quarters of these deaths occurred in the first 6 months after the start of therapy. However, there was a high risk of children being lost to follow-up, generally caused by severe ill health.

Investigators from the Kids' Antiretroviral Treatment in Lower-Income Countries (KIDS-ART-LINC) Collaboration, a network of paediatric HIV treatment programmes in sub-Saharan Africa, set out to determine the 2-year risk of death or loss to follow-up for children aged under 15 who started HIV treatment. They recruited 2 405 children from 16 clinics; most were boys and the median age was 5 years.

Two-thirds of children started antiretroviral therapy with a combination that included a non-nucleoside reverse transcriptase inibitor (NNRTI), with the remaining one-third taking a protease inhibitor-containing regimen.

The median duration of follow-up was 20 months, and during this time 153 deaths were recorded. Given the severe immunodeficiency and poor health of many of the children at baseline, it is not surprising that over half (57%) of these deaths occurred during the first 3 months after the initiation of treatment. A further 17% of deaths occurred in the next 3 months, with 16% being recorded in the next 6 months. Only 9% of deaths were recorded in the second year of antiretroviral treatment.

A total of 187 children were lost to follow-up, with 42% being lost during the second year of treatment.

Overall, the probability of death was estimated to be 5% at 6 months, 6% at 12 months and 7% at 24 months. The probabilities of being lost to follow-up were 3% at 6 months, 5% at 12 months and 10% at 24 months.

Severe immunodeficiency, severe anaemia and very poor health were all associated with an increased risk of death. Only poor health was associated with an increased risk of being lost to follow-up.

There was no association between the risk of death and age when HIV treatment was started, or type of HIV regimen used. However, the authors emphasise that the risk of loss to follow-up was higher and that 60% of losses occurred during the first year.

The KIDS-ART-LINC Collaboration. *J Acquir Immune Defic Syndr* 2008; 49: 523-531.

Widespread resistance to antiretrovirals among children in the Central African Republic

A study published recently in the *Journal of Acquired Immune Deficiency Syndromes* shows that children who have started antiretroviral treatment in the Central African Republic are infected with a wide variety of subtypes, do not adhere well to treatment and seldom have an undetectable viral load. Resistance to antiretroviral drugs is also widespread.

The common form of treatment in this region is with the combination pill containing d4T/3TC/nevirapine. Investigators from the Central African Republic and France recruited 52 children who were receiving antiretroviral treatment. The median age was 8 years. Researchers determined the HIV subtype,

adherence to treatment, and presence of drug resistance.

The most commonly used antiretroviral regimen was d4T/3TC/nevirapine, with 46% of children receiving this in a co-formulation and a further 19% as separate pills. Adherence was rated as 'poor' (below 60%) in 57% of children, with only 14% having 'very good' adherence (above 90%).

HIV subtype was measured in 26 children. The most commonly found were CRF11_cpx (38%), AE (15%), and AG (12%).

Before HIV treatment was started, median CD4 cell percentage was very low, being just 6%, median CD4 cell count at this time being 128 cells/mm^3. After 6 months of treatment, median CD4 cell percentage had increased to 15%, with median CD4 cell count being 420 cells/mm^3.

After 6 months of treatment, only 25% of children had a viral load below 50 copies/ml, all these children having adherence above 90%. Median viral load in the remaining children was approximately 2 000 copies/ml.

A total of 26 children had resistance tests. Only 23% had HIV that was fully sensitive to anti-HIV drugs, the remaining 77% having HIV that was resistant to at least 1 anti-HIV drug. Overall, 5 (19%) had resistance to 1 drug in their treatment, 4 (54%) to 2 drugs and 1 (4%) to all 3 drugs.

Gody J-C, *et al. J Acquir Immune Defic Syndr* 2008; 49: 566-569.

BRIDGET FARHAM

Single Suture

Hopelessness strongly associated with the metabolic syndrome

A Swedish study has found that feelings of hopelessness and an inability to change lifestyle are associated with the presence of the metabolic syndrome in men. Recent studies have also found that lack of hope is linked to cardiovascular morbidity and mortality.

This study looked at the relationship between hopelessness and the metabolic syndrome in a population of 1 743 non-diabetic men aged between 42 and 60 years at baseline. Hopelessness was measured by expectations of the future and of reaching goals. The study found that hopelessness was strongly associated with the metabolic syndrome in these middle-aged men, independent of other depressive symptoms and traditional cardiovascular risk factors. These findings suggest that hopelessness is very closely related to the metabolic syndrome. Therefore lifestyle management of the metabolic syndrome should also take into account patients' expectations more thoroughly than previously thought; an inability to expect to reach goals could have major influences on the ability to change lifestyle.

Valtonen M, *et al. Scand J Public Health* 2008; 36: 795-802.

Single Suture

Relatives of cancer sufferers more likely to recover from colon cancer

If colon cancer runs in your family, you are more likely to recover from the disease yourself. This is according to Jennifer Chan from the Dana-Faber Cancer Institute in Boston and her team. She and her colleagues tracked around 1 000 people with colon cancer at the same stage, who had chemotherapy between 1999 and 2001. In 30% of those with parents or siblings who had had colon or rectal cancer, the disease came back. The recurrence rate for patients without a close family history was 40%. The effect was greater among those who had more relatives with cancer.

The team suggests that the genes that enhance chemotherapy may be inherited with those that make cancer more likely. If the team can identify these genes, the same proteins may be used to improve the effects of chemotherapy for everyone with cancer.

New Scientist, 7 June 2008.