

January, 2004, administration of measles vaccine was recommended between 12 and 24 months of age, instead of between 12 and 15 months when children have the greatest risk of contracting measles. There is no established system to check vaccination status on entry to the school systems.

Strong political and social desire has to be inspired, and vigorous educational campaigns for policy makers and the general public are required. If there are clear strategies and prioritisation on vaccine policies, and a strong will to combat the disease, measles in Japan can be controlled. The great success of near elimination of measles on the American continents is strong encouragement.<sup>5</sup> It is time for the Japanese government to regain leadership on this issue.

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## First-line and second-line antiretroviral therapy

The results of the 2NN study (April 17, p 1253)<sup>1</sup> confirm that nevirapine combined with stavudine and lamivudine is a

valid option for a first-line antiretroviral therapy. This information is crucial for all clinicians working in developing countries, since this combination is not only the cheapest but also the only fixed-dose combination to date that has been prequalified by WHO.<sup>2</sup> Fixed-dose combinations reduce the pill burden, increasing ease of use, minimising the risk of drug resistance, and facilitating drug supply.<sup>3</sup>

In his accompanying Commentary,<sup>4</sup> Andrew Carr supports the importance of this fixed-dose combination. Two additional advantages of nevirapine over efavirenz for the developing world not noted in the Commentary are that it can be used in pregnant women and in children younger than age 3 years. Carr's claim that efavirenz co-formulations are available is unfortunately ahead of its time: technical difficulties mean that such efavirenz-containing combinations are unlikely to be produced for at least 2 years; intellectual property constraints could delay this even further. Currently, only two co-formulations based on non-nucleoside reverse-transcriptase inhibitors are available in developing countries, and both contain nevirapine.

There might be concern over increased toxicity associated with use of nevirapine-based regimens, particularly in countries with no or little laboratory monitoring capacity. However, Médecins Sans Frontières (MSF) has been using nevirapine-based first-line regimens since mid-2001, mainly as a fixed-dose triple combination of stavudine, lamivudine, and nevirapine. Of more than 5000 patients currently treated with nevirapine by MSF, fewer than 2% have had to stop due to hepatotoxicity.<sup>5</sup> The median CD4 count in this cohort at baseline was 67 per  $\mu\text{L}$  (IQR 19–139), which could explain the relatively low prevalence of hepatic injury in this very immunosuppressed group.

Our experience is that this nevirapine-based first-line regimen is safe, affordable, and convenient to use. Our major concern is to find a second-line regimen, since there are no fixed-dose combinations for second-line treatment to date. Furthermore, because second-line drugs are mostly monopoly

products, the prices are much higher than first-line fixed-dose combinations.

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In his Commentary on the 2NN study, Andrew Carr<sup>1</sup> recommends that nevirapine and protease inhibitors should not be co-administered with rifampicin, and that the efavirenz dose should be adjusted to 800 mg/day when given with rifampicin. This advice goes along with recommendations in the recent past, which were based on pharmacokinetic data showing that rifampicin interferes with concentrations of nevirapine and protease inhibitors when they are co-administered.

However, two recent studies, albeit small, showed a favourable HIV clinical and virological response in patients who received concurrent nevirapine and rifampicin.<sup>2,3</sup> On the basis of these data, updated recommendations leave open the option of possible co-administration of these two drugs, with close clinical and virological monitoring.<sup>4,5</sup> Optional is an increase in nevirapine dose (such as 300 mg twice daily),<sup>4</sup> probably in patients who weigh 60 kg or more. As for efavirenz, the co-administered dose could be reduced to the standard 600 mg/day if 800 mg/day is intolerable.<sup>4</sup>