



WHO, L. Taylor

In Africa, where children are the main victims of malaria, delivery of antimalarial drugs through routine vaccination programmes is a promising new approach.

Intermittent drugs seen highly protective against malaria

Malaria drugs given intermittently at the same time as routine childhood vaccinations could cut malaria episodes by nearly two-thirds, according to a randomised, placebo controlled trial reported in the 12 May issue of *The Lancet*.

Dr David Schellenberg and colleagues from the Hospital Clinic in Barcelona, Spain, and the Ifakara Health Research and Development Centre, United Republic of Tanzania, randomly assigned either sulphadoxine-pyrimethamine, a commonly used antimalarial drug combination, or placebo to 701 infants living in a rural area of the United Republic of Tanzania. The treatment was given at 2, 3 and 9 months of age alongside routine vaccinations delivered through WHO's Expanded Programme on Immunization (EPI). All the children also received iron supplementation between 2 and 6 months of age.

The Ifakara area where the trial was conducted has a high rate of malaria transmission and malaria is especially severe in under-1-year-old children. The treatment, the study found, reduced the rate of clinical malaria by 59%, the rate of severe anaemia by 50%, the number of hospital admissions by 30%, and the rate of all febrile episodes by 13%. The treatment was well tolerated and no drug-attributable side-effects were observed.

Professor Pedro Alonso, head of epidemiology and international health at the Hospital Clinic Barcelona, and one of the study authors, told the *Bulletin*: "This drug costs less than 20 cents and our approach to using it makes use of existing contacts between the target population and health care workers. So this approach appears to be an extremely good buy."

One concern about using chemoprophylaxis is that drug resistance may develop. However, Alonso argues that because the treatment is directly observed there can be no under-dosing, with its associated increased risk of inducing resistance. "And the drug is only given in three doses, so it is unlikely to constitute a major contribution to the problem of resistance when you consider the large quantities of malaria drugs consumed in countries with high rates of malaria."

During a previous trial in the same area, full chemoprophylaxis between 2 and 12 months was associated with a large increase in the rate of malaria once treatment stopped, suggesting that the development of malaria-specific immunity had been delayed. However, no such rebound effect was seen in this study. "Because the children received only intermittent treatment they developed their own immunity to malaria just like those in the placebo group," says Alonso. "Once the treatment stops the children will

still go on to get malaria but they have been protected when they are most vulnerable."

Professor Brian Greenwood, head of the malaria centre at the London School of Hygiene and Tropical Medicine, comments: "This is a very important study. The difficulty in the past has been finding the right balance between protecting children from malaria at the most vulnerable time without impairing their natural immunity. This approach seems to have got it right."

Greenwood is currently participating with Ghanaian colleagues in a similar study in the north of Ghana, which is due to be completed in 18 months' time. "Hopefully our study, which has larger numbers, will provide independent confirmation about the value of intermittent drug treatment." ■

Jacqui Wise, London, UK

Drug-resistant HIV increasing, UK study finds

Over a quarter of people newly infected with HIV in the UK and not yet receiving treatment may be carrying mutant virus strains already resistant to antiretroviral drugs, according to a study reported in the 5 May issue of the *British Medical Journal*.

The study, which was conducted by the UK collaborative group on monitoring the transmission of HIV drug resistance, used genetic tests to measure viral drug resistance within 18 months of infection in 69 subjects who contracted the virus between 1994 and 2000. The researchers detected *primary* resistance to antiviral drugs — that is, in individuals not yet treated with drugs — in 14% of cases over the seven-year period. Of the 26 patients tested last year, seven, or 27%, had a resistant virus. A calculation of the risk of primary infection with drug-resistant virus suggested a steady increase since 1994, reaching a risk of about one in five by last year.

Corresponding author of the study Dr Deenan Pillay, with the UK's Public Health Laboratory Service and Birmingham University Medical School, notes that "the results are based on small numbers of patients and have therefore wide confidence intervals, so they should be taken as only indicative of what seems to be a disturbing trend". That trend, the researchers believe, is probably fuelled by the increasing use of antiretroviral drugs in the UK. Another contributing factor, they say, could be the

growing number of people engaging in unprotected sex among groups at high risk of HIV infection, which increases the likelihood of being infected by someone who has already been treated with antiretroviral drugs.

Commenting on the UK findings to the *Bulletin*, virologist and HIV-resistance expert Professor Mark Wainberg, director of the McGill University AIDS Centre in Montreal, Canada, said: "It is shocking. It's higher than anything I've seen until now, and if it's right, the UK would appear to be leading the world in regard to transmission of drug-resistant virus." Wainberg says that the figures are much greater than the 8–9% he reported from Canada last year. Reported figures from the US are between 15% and 20%.

If widespread access to treatment in the UK is a reason for high resistance rates, what are the implications for developing countries where the epidemic is most prevalent?

Dr Lynn Morris, head of the AIDS unit at South Africa's National Institute for Virology in Johannesburg, has conducted genetic analysis of HIV in more than 70 recently infected "drug-naïve" patients. "At this stage," she told the *Bulletin*, "we haven't found any resistant viruses."

Most patients in this part of the world, of course, still do not have access to antiretrovirals, so there is little pressure on the virus to mutate. But current efforts to lower the cost of these drugs and expand access to them in developing countries could increase the risk of resistance and its transmission. "The threat of resistance definitely doesn't mean that we shouldn't give drugs to developing countries," says Morris. "If we use that argument then we shouldn't be using TB drugs either. I think we need to make sure that people who get drugs are closely monitored and that they're on the right therapies."

WHO, in collaboration with the International AIDS Society and Italy's Istituto Superiore di Sanità, is planning a global HIV resistance monitoring network that, among other things, will keep track of trends in the prevalence of HIV drug resistance in parts of the world where antiretroviral therapy is being introduced. ■

Karen Birmingham, *London, UK*

Europe gets tough on smoking

In a move coherent with WHO's push for stringent legislation of tobacco products, the European Parliament, in a 15 May vote, approved of a package of far-reaching anti-smoking laws. The new rules — which now have to be adopted by the individual

European Union (EU) member states — will lower the maximum levels allowed for tar from 12 mg to 10 mg. Nicotine levels above 1 mg and carbon monoxide levels above 10 mg will be banned. The new rules will also require manufacturers to display giant health warnings on about a third of the surface of cigarette packets, up from less than 5% today.

Other measures of the EU directive, which will enter into force on 30 September 2002, include a ban on terms such as 'low tar,' 'ultra light' or 'mild.' Also, tobacco companies will have to compile a list of all ingredients in their products, together with their quantities and the reasons for their use. What's more, from the end of next year, EU member states will have the option to call for dissuasive colour photographs or other illustrations to be displayed on cigarette packs. Graphic pictures depicting the effects of smoking on the heart and lungs, on male sexual potency, or other smoking-related diseases are already in use on cigarette packs in Canada since the beginning of the year.

Passed by a large majority, the legislation received praise from all sides. Mr David Byrne, European Commissioner for Health and Consumer Protection, welcomed the new directive, saying that people needed to be made aware of the dangers of smoking. "Smoking is not cool — smoking kills," he said. In the EU alone, more than 500 000 deaths each year are due to tobacco consumption, according to WHO estimates. Worldwide, the annual toll is close to 4 million. Byrne's goal, he said, was to see "a reduction in the number of people smoking from one third of the European population to less than one fifth".

Dr Douglas Bettcher of WHO's Tobacco-Free Initiative called the new legislation "a very positive move. The EU is the first authority to ban such misleading descriptors as mild, low tar or light." For Bettcher the mandatory submission of comprehensive lists covering all ingredients in tobacco products is long overdue. "Tobacco can contain up to 60 carcinogens and as many as 4000 ingredients. Which other product of that sort do you know, for which the content does not have to be disclosed? Tobacco was — and still is — a regulatory no man's land. The EU legislation opens up a new pathway to reducing the harm caused by tobacco."

Some issues, such as the regulation of tobacco vending machines, fell by the wayside during ten weeks of a tedious "conciliation procedure" between Parliament, which called for stark health warnings on the machines, and the EU Council, which

refused such measures. Member of Parliament Jules Maaten, who saw the directive through the legislative process, said in a press release: "Despite the terrible health consequences, I believe that people have the right to smoke, but the tobacco manufacturers spend huge sums of money trying to make their products appear glamorous, and this image needs to be countered."

More EU tobacco restrictions are on the way. On 30 May 2001 the Commission proposed rules on tobacco advertising and sponsorship which would harmonize existing regulations in the various member states. The rules would outlaw tobacco ads in print media, radio and on the Internet. (TV advertising of tobacco has been prohibited since 1989.) This is the EU's second shot at trying to curb tobacco advertising; the first, dating from 1998, ended in defeat last October, when the European Court of Justice, following an appeal by tobacco companies and the German government, annulled the EU directive as there was no legal basis for prohibiting tobacco advertising which does not cross national frontiers.

The new anti-smoking laws could be linked to the WHO Framework Convention on Tobacco Control (FCTC), which is currently being negotiated by WHO's Member States. "We would hope that the FCTC is a road to tobacco control on a global level. The EU decision can provide some impetus for international action," Bettcher said. ■

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