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Shortfall in front-line antimalarial drug likely in 2005

In Nov 2004, the WHO announced a shortage of artemether and lumefantrine, the artemisinin-based therapy used officially to treat malaria in 40 countries. Novartis (Basel, Switzerland), which manufactures the drug, has secured sufficient artemisinin derivatives for 30 million treatment courses in 2005, but over half of that will be produced in the last 3 months of the year, after the high transmission season in many malarious areas. The lack of raw materials is expected to continue during the first 9 months of 2005. This has caused a serious shortfall as from Nov 2004 that is likely to last until March this year, with further problems possible over the summer.

"The impact will be severe in areas with high-level parasite resistance to multiple antimalarial drugs, particularly southeast Asia, and southern and eastern Africa, where chloroquine and sulfadoxine-pyrimethamine are increasingly ineffective", comments Joel Berman (Fogarty International Center, National Institutes of Health, Bethesda, MA, USA). Other countries

may not be so badly affected. Sanjeev Krishna (Department of Cellular and Molecular Medicine, St George's Hospital Medical School, London, UK) points out that, in Uganda, it has been shown that a combination of amodiaquine and sulfadoxine-pyrimethamine is an adequate and cheaper treatment for malaria, compared with amodiaquine and artesunate. "Countries considering switching to artemether-lumefantrine as a first-line treatment may have to consider such alternatives as an interim measure", he comments.

The current crisis stems from the lack of natural product. Most of the natural *Artemisia annua* plant is grown in China and commercial growth of the plant outside of Asia could help. Walther Wernsdorfer (Institute of Specific Prophylaxis and Tropical Medicine, Medical University of Vienna, Austria) thinks that if an initiative to grow plants in eastern Europe were started without delay, "it would not be too late for producing a large enough crop by the summer of 2005". Krishna says there should be plenty of opportunity to increase growth of

Artemisia in countries such as Tanzania and India, but obtaining an adequate yield of artemisinin can be a problem. "Harvesting and extraction facilities also need to be managed in parallel with encouragement to grow plants. It may be a year or two before supply can meet demand", he warns.

Hope also lies with Jay Keasling's group (University of California, Berkeley, CA, USA). The Gates Foundation announced in December that they were providing a \$43 million grant to aid research there to produce an active artemisinin derivative using genetic engineering, with microbes as factories. "This sum should go a fair way to cover the R&D cost of the project but it is important to remember that artemether is only one component of the formulated drug, and accounts only for 20% of its total cost", says Wernsdorfer. "Getting more readily available artemisinin is a move forward, but cheaper artemisinin is only part of the picture", he concludes.

Kath Senior

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Artemisia annua in a growth chamber

Andy Crump, TDR, WHO/SPL

First US SARS trial launches

Researchers at the US National Institute of Allergy and Infectious Diseases (NIAID) have launched a trial to test the safety of a preventive vaccine against severe acute respiratory syndrome (SARS). The DNA vaccine, which encodes the spike glycoprotein of the SARS coronavirus, induces both a neutralising antibody response and "very good T-cell immunity", says Gary Nabel, director of the NIAID Vaccine Research Center in Bethesda, MD. Ten healthy volunteers will receive the vaccine, and researchers will do periodic follow-up examinations over 6 months.

The vaccine's mechanism of action is different from that of the inactivated virus vaccine that is being

tested in China, Nabel told *TLID*. "That vaccine really only induces antibody responses. We think it's wise to have additional mechanisms of protection available, should the virus break through the neutralising antibody response." The two approaches could also be complementary, he notes. "One of the things we are now testing in animals is the ability of the DNA to prime an immune response generating both the cellular and humoral response, then boosting it with inactivated virus. This gives us another way to modulate immune function."

NIAID pushed ahead with the vaccine after Gabel and colleagues showed that it reduced viral replica-

tion by more than six orders of magnitude in the lungs of infected mice (*Nature* 2004; **428**: 561-64). Moreover, "the technology could be developed quickly, because we've been using it for AIDS and Ebola vaccine, so we had everything in place to move forward rapidly", says Gabel. And, he adds, "it's a safer vaccine to make and administer compared with the inactivated virus vaccine, because the workers who grow the wild-type viruses are exposed. They've done it safely so far, but the more we can avoid working with the virus, particularly in large supply, the better off we'll be from a public health perspective".

Marilynn Larkin