Lisbon — More antimalarial drugs are in the developmental pipeline today than at any other time in history, Dr. Elizabeth A. Ashley reported at the 12th International Congress on Infectious Diseases. Two main factors can explain this welcome state of affairs. One is the impressive productivity of Chinese scientists in the People’s Republic in exploiting the potential of Artemesia annua, the plant also known as sweet wormwood or qing hao, from which artemisinin and related drugs are derived.

The other major factor has been the recent creation of public-private partnerships to aggressively support the drug development process, from compound identification through regulatory approval. In 2006 alone, the Medicines for Malaria Venture will take on 5-10 new drug-discovery projects. Other major players include the Drugs for Neglected Diseases Initiative and World Health Organization–sponsored programs.

Universities, foundations, pharmaceutical companies, and other institutions have pitched in. For example, the Walter Reed Army Institute of Research is expediting development of intravenous artesunate for severe malaria. Food and Drug Administration approval could come next year, said Dr. Ashley of the University of Oxford Tropical Medicine Program and the Shoklo Malaria Research Unit, Mae Sot, Thailand.

But the first new drugs for uncomplicated falciparum malaria to reach the market will be novel combinations of old drugs. WHO malaria treatment guidelines issued earlier this year declare artemisinin-combination therapies (ACTs) the new standard of care because strains resistant to chloroquine and sulfadoxine/pyrimethamine have become so common. The emphasis now is on developing affordable fixed-dose ACTs in a single pill having at least two unrelated mechanisms of action to prevent artemisinin resistance and boost adherence.

Only one fixed-dose ACT is available internationally. Artemether-lumefantrine (Coartem) is registered in 75 nations. Novartis markets it at a subsidized cost of $2.50 per course for adults. That’s still a lot of money in the poorest parts of the world, but “it’s easy to imagine that once other fixed combinations come into the market, prices will fall,” Dr. Ashley said.

Among the new combinations of old drugs that are likely to earn broad international approval within the next year or so are artesunate–pyronaridine, dihydroartemisinin-piperaquine, chloroquine–dapsone–artesunate, artesunate–malathion, and artesunate–amodiaquine, she said at the congress, which was sponsored by the International Society for Infectious Diseases.

“Ten or more antimalarial drugs are poised for approval in 3-5 years. Many are novel agents, some acting on new targets. They include cysteine protease inhibitors to cut hepatic trypanosomiasis drug–genation antifolates, synthetic peroxides, and farnesyltransferase inhibitors. Also in development are new synthetic artemisinin derivatives devoid of neurotoxicity in animals, unlike earlier derivatives.

In addition, tafenoquine is a long-acting 8-aminoquinoline now in clinical trials to replace 2 weeks of primaquine for nonfalciparum malaria. As with primaquine, it is contraindicated in patients with glucose-6-phosphate dehydrogenase deficiency.

Lisbon — Clinically moderate to severe hantavirus infections are invariably characterized by a distinctive pattern of serum lipid changes, reported Dr. Jan Clement at the 12th International Congress on Infectious Diseases.

The size of the lipid perturbations correlates with the severity of the underlying hantavirus infection. And because the lipid changes precede by several days, the deterioration in renal function and worsening thrombocytopenia that mark a serious hantavirus infection, the extent of the lipid abnormalities can be used as an early warning system regarding the viral illness to come, according to Dr. Clement of the Rega Institute for Medical Research at the University of Leuven, Belgium.

This is the first report linking serum lipid changes to the subsequent severity of hantavirus infection, he noted. Although the work was restricted to Belgian hantavirus patients, Dr. Clement has studied hantavirus infection in the 12th International Congress on Infectious Diseases.

There were significant correlations between the extent of hypercholesterolemia and low HDL and the degree of thrombocytopenia and renal impairment. For example, the two patients who developed hantavirus-induced adult respiratory distress syndrome require mechanical ventilation had the lowest values of these lipids recorded in the entire study: an average nadir of 53 mg/dL for total cholesterol and 5 mg/dL for HDL. In 38 patients with moderately severe hantavirus infection, defined by a peak serum creatinine in excess of 1.5 mg/dL, the mean nadir total cholesterol was 129 mg/dL. In contrast, total cholesterol bottomed out at a mean of 162 mg/dL in patients with a worse infection (a peak creatinine below 1.5 mg/dL).

The mechanism by which serum lipid changes serve as a predictor of the clinical severity of hantavirus infection is thought to be that the lipid levels provide an indirect measure of proinflammatory cytokine bioactivity, said Dr. Clement.

A certified activity. No registration fees required.

KEYNOTE ADDRESS BY David A. Snowdon, PhD

Lisbon — Before turning to the subject of how antihypertensive therapy can improve brain function in the elderly, Dr. David A. Snowdon, noted the importance of preventing dementia.

Dr. Snowdon is Dementia Congress Chair and Track II Chair – Psychiatry. He is also the Dementia Congress Chair. His Dementia Congress Chair role is to set the standards for the entire conference.

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