

TAMING MALARIA

MALARIA is one of the biggest killers ever — estimated by medical historians to have killed more people than all wars and other diseases combined. It continues to rack up victims, taking nearly a million lives a year, while half the world's population lives under its menace.

Man is fighting back — world leaders at the United Nations announced last September a program to end malaria deaths by 2015 — but the Plasmodium parasite that causes the disease is a tricky enemy. The conventional warfare, vaccines — that defeated smallpox and that nearly wiped out other diseases, like polio — aren't as easily adapted to malaria. Most other diseases are caused by viruses or bacteria, which are simple organisms. The malaria parasite — there are four kinds — is much bigger and more complex. Plasmodium falciparum is one of the most common, and the deadliest. Plasmodium vivax, which is the other most common, Plasmodium ovale and Plasmodium malariae all can turn up infections long after a person is initially bitten by a mosquito.

Many viruses have a handful of genes and synthesize only a few proteins; malaria parasites have 5,300 genes and synthesize thousands of proteins, says Peter Agre, director of the Johns Hopkins Malaria Research Institute in Baltimore, Maryland. Normally the body recognizes an invasion by viruses, bacteria or parasites and produces antibodies to counterattack. The malaria parasite changes its proteins throughout its life cycle, making it even harder for the body — and researchers — to fight.

"There is no licensed vaccine against any parasites that infect humans," says Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases at the National Institutes of Health in Bethesda, Maryland. A malaria vaccine would be a major scientific first.

Usually when people manage to recover from a serious disease they have lifelong immunity. Vaccines leverage this phenomenon, by provoking the body into reacting to a form of the virus or bacteria without a person actually having to be sick. A malaria attack, however, doesn't make people completely immune, though adults tend to suffer less than children. Those under five make up 90% of malaria deaths.

"The nature of the immune response against a parasite like malaria is more complex than against a typical childhood virus like measles, mumps or rubella," Dr. Fauci says. "When we're trying to protect with a vaccine, it's much more difficult with malaria."

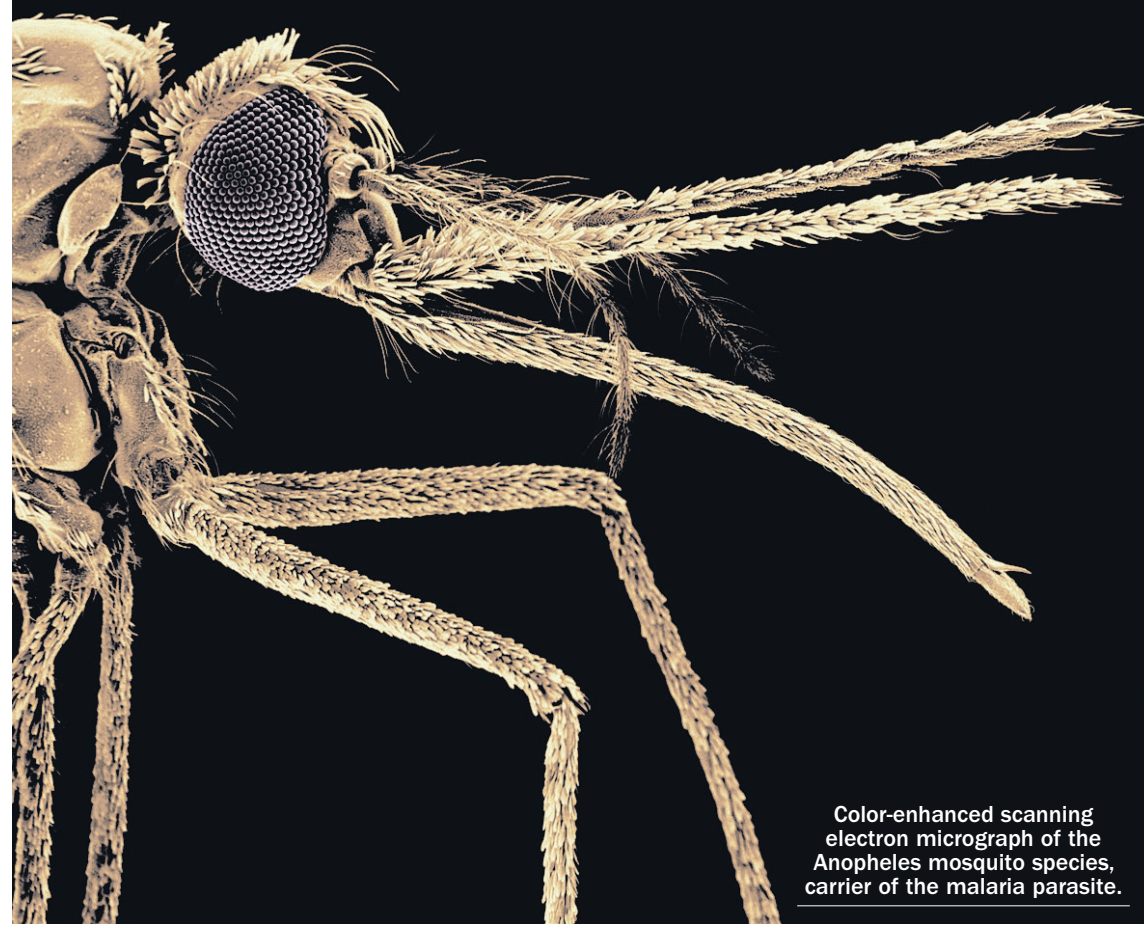
The vaccine candidate closest to approval, called RTS,S, is being developed by GlaxoSmithKline PLC of the U.K. since 1987. It is soon to begin Phase III clinical trials in Africa, with results expected in 2011. Depending on the results it can then seek license approval in Europe and the U.S., which will allow it to sell the vaccine in Africa. RTS,S takes aim against Plasmodium falciparum.

Malaria is transmitted when an infected mosquito bites a human. The parasite quickly heads for the person's liver to start reproducing. In some relapsing forms of malaria, some of the offspring lie dormant there, striking much later. After

Vaccine researchers zero in on a complex foe

Success would give a shot in the arm to the global campaign to stop deaths caused by the persistent parasite by 2015; one candidate moves closer to approval with others under study

By Catherine Bolgar



Color-enhanced scanning electron micrograph of the Anopheles mosquito species, carrier of the malaria parasite.

Stages of malaria

- 1** Infected mosquito bites person, transmitting parasite
- 2** Parasite heads to person's liver and starts reproducing
- 3** Parasites move into blood stream, infecting red blood cells
- 4** Infected red blood cells burst, releasing new progeny parasites, causing illness
- 5** Another mosquito bites infected person and acquires parasite

several days in the liver, progeny parasites head into the blood stream, infecting red blood cells, and setting up a new reproductive cycle. Infected red blood cells subsequently burst, releasing new progeny parasites that in turn infect other red cells — that's the point when people are sick. Eventually, another mosquito bites and drinks up the parasite along with the blood, passing malaria on to the next person bitten.

RTS,S takes aim at the parasite at the liver stage, keeping a person from becoming very sick, or sometimes from getting sick at all. RTS,S is an important advance, but unfortunately it wouldn't stop malaria the way the Salk vaccine stopped polio, says Dr. Agre.

There are two reasons for this. The efficacy (the proportion of people vaccinated who do not go on to get the disease) in individuals inoculated with RTS,S is under 50%, whereas the Salk vaccine provided more than 90% protection against some strains of polio. And people

who survived polio didn't infect others, but those who survive malaria retain the parasite and are still infectious to themselves and others.

It's too new to know how long efficacy might last. Even if a vaccine isn't 100% effective, the key to controlling malaria is "how many new people does an infected person infect," says Brian Greenwood, professor of tropical medicine at the London School of Hygiene and Tropical Medicine. "If we can stop it infecting more than one other person by vaccination, eventually it will die out."

An ideal vaccine would be very safe (i.e. not make people sick just by getting the vaccine), at least 95% effective, and not too sensitive to heat, he says. RTS,S must be kept cold, which presents a logistical problem, because the hardest-hit countries are in Africa.

Some two dozen other vaccine candidates are under study or at various stages of development. None is as far along as RTS,S. Some, like

expensive, averaging around \$1 billion (€754 million). Malaria's complexity raises the potential cost of a vaccine, although nobody knows by exactly how much. Public and philanthropic funding is offsetting some of the expense of fundamental research. The Global Fund to Fight AIDS, Malaria and Tuberculosis, founded by the Group of Eight leading industrialized nations in 2002, is the biggest donor, approving \$2.7 billion of five-year malaria grants in 2008, though that money also goes to other means of fighting malaria, such as insecticide-treated bed nets and medicines. The European Malaria Vaccine Initiative collected over €3 million in 2008 from the Netherlands, Ireland, Sweden and Denmark. The U.S. President's Malaria Initiative, launched in 2005, received \$300 million in funding, again for a variety of malaria measures. The Bill and Melinda Gates Foundation, which raised the ante in the malaria fight by aiming for eradication, gave \$287 million to the PATH (Program for Appropriate Technology in Health) Malaria Vaccine Initiative, based in Seattle, Washington. And New York-based Malaria No More, founded in 2006, joined its partners in the malaria community to invest \$1.9 million in 2007 in technical assistance which helped raise the success rate for proposals to the Global Fund.

Though malaria is particularly challenging to fight in the medical lab, it was vanquished in the U.S. and Europe through simpler means: spraying, screens and nets, and medi-

"The nature of the immune response against a parasite like malaria is more complex than against a virus like measles, mumps or rubella."

cines (along with the benefit of cold winters to knock down the mosquitoes). "The complexity of malaria is relatively low compared to other issues," says Scott Case, CEO of Malaria No More, speaking from New York, though he's probably better known as co-founder of online travel company Priceline.com. "But the impact is high because it's hundreds of millions of people who suffer."

Ending malaria would help pull much of the world out of poverty. Africa loses 1.5 to two percentage points of GDP annually through deaths, lost productivity to illness and medical expenses — African families spend as much as 25% of their income on treating malaria. An investment of approximately \$2 billion a year to fight malaria in Africa would help unlock more than \$12 billion in lost annual GDP. A healthy Africa is critical on economic and national security levels, Mr. Case says.

The push to end global malaria deaths is important in other ways, as well. Malaria has been knocked down before, only to resurge with a vengeance. It wasn't eradicated from the U.S. until the 1940s. But that doesn't necessarily mean malaria is gone forever. The Anopheles mosquito, which carries malaria, still lives in the U.S.

Vaccine development also is

April 25 is World Malaria Day.

MONEY & INVESTING

Swedbank cuts in Baltics after slipping to a loss

By ANNA MOLIN

STOCKHOLM—After swinging to a loss in the first quarter, Swedbank AB set out plans to scale down operations in the Baltic states and Ukraine as it expects big loan losses in those markets.

The Swedish bank said it will reduce the number of employees and branches in the Baltics, targeting cost savings of about 15%. It will also make "significant cuts" in Ukraine, where the sharp depreciation of the hrynia prompted it to write off the remainder of its goodwill, a total of 1.3 billion Swedish kronor (\$154 million), in the first quarter.

"We are now seeing a downturn of historical dimensions, visibility is low and therefore a firm resolve to act is correct to manage our destiny," new Chief Executive Michael Wolf said on Thursday. Swedbank "needs to address some areas of change," he added.

However, Mr. Wolf stressed that Swedbank has no plans to leave the Baltics, where it is the largest bank and has around 17% of total group lending.

In the three months ended March 31, the Swedbank swung to a net loss of 3.36 billion kronor from a net profit of 2.9 billion kronor a year earlier.

Net interest income rose 11% to 5.8 billion kronor thanks to widening lending margins. That wasn't

enough to absorb a charge of 6.85 billion kronor for loan losses and provisions, up from 288 million kronor a year earlier.

In the Baltics alone, loan-loss provisions skyrocketed to 4.24 billion kronor from 173 million kronor a year earlier, while Swedbank's share of impaired loans jumped to 4.9% from 2.3% at the end of the year. The bank said it couldn't rule out future goodwill impairments on its Baltic units.

The bank's core Tier 1 ratio, a measure of capital adequacy, dipped to 9.4% from 9.7% at year-end, indicating the weakening Baltic economies have put further pressure on its capitalization.

Mr. Wolf said that following a recent 12.4 billion kronor rights issue, Swedbank is adequately capitalized to meet current challenges. However, he declined to give a long-term forecast, since "no one can predict how the macroeconomic situation will develop going forward."

The bank has begun selling savings branches in Sweden, set up bad-bank units in the Baltics to deal with problem loans and dipped into the Swedish government's guarantee program to fund itself.

New Chief Financial Officer Erkki Raasuke said the bank has raised 227 billion kronor through the guarantee thus far and could issue almost as much before hitting the 450 billion kronor guarantee limit.

EU to register credit raters

New requirement ramps up supervision of S&P and Moody's

A WSJ News Roundup

STRASBOURG, France—Credit-rating companies will for the first time have to register and be supervised to operate in the European Union under a law adopted by the European Parliament on Thursday.

The Parliament voted 569-47 in favor, overcoming the last major stumbling block for a deal EU governments reached last week that could bolster confidence in financial markets.

This introduces a legally binding registration system and a supervisory regime for credit-rating com-

panies, which have taken some of the blame for the financial crisis because they assigned favorable ratings to debt that later turned out to be far riskier.

Under the new rules, rating firms would be liable for their opinions and could face EU sanctions if found guilty of professional misconduct. That cost them their licenses to rate debt in the 27-nation bloc.

The rules also demand credit-rating companies disclose some information to financial supervisors to prove that they understand the risks of the debt they examine.

A group of financial-market regulators from each of the EU nations, the Committee of European Securities Regulators, will oversee registration for the first year. Each rating company will be monitored more closely by a "college of super-

visors" with members from each country where it operates.

In the longer term, the commission will propose a new regulator to monitor ratings, which would fund itself by charging clients—either the bank that issues the debt or the potential investor who wants to buy it.

The requirements would mean big changes for the \$5 billion-a-year industry dominated by New York-based Standard & Poor's, a business segment of publisher McGraw-Hill Cos., and Moody's Corp. Most investments require two ratings, and these two companies mop up the bulk of the market.

The companies have been widely criticized for failing to give investors adequate warning of the risks in subprime-mortgage securities.

Russia cuts interest rates as unemployment rises

By LIDIA KELLY

MOSCOW—Russia's central bank said it will cut its lending rates and increase reserve requirements in a move showing cautious confidence in the ruble's stability and slowing inflation amid the economic gloom.

The country's first rate cut in nearly two years—by a half-percentage point—comes a day after Prime Minister Vladimir Putin demanded cheaper domestic borrowing and follows weeks of pressure from banks

and companies struggling with debt repayments.

However, it also comes on a day when the Economy Ministry called the International Monetary Fund's most recent forecast of 6% contraction in Russian gross domestic product "realistic enough," suggesting the country's recession is deepening.

The central bank's decision will bring its refinancing rate, used as a baseline indicator for interbank lending, to an annualized 12.5%. The rate for overnight repurchasing agreements, the main source of

short-term liquidity provided by the central bank, will slide to 9.5%.

At the same time, the central bank said it will raise minimum reserve requirements on retail deposits to 1% as of May, and will follow with monthly increases of 0.5 percentage point until August.

Separately, the ranks of Russia's jobless swelled by 400,000 in March and are likely to keep growing, according to new estimates from Russia's government statistics agency. The data for March put the unemployment rate at 10%, the highest in eight years.

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*Lipper - Offshore Universe. Performances, Ranking & Quartile are calculated with A Share, data as of March 31, 2009. The prospectus of this fund approved by the CSSF can be obtained upon request at the head office of SGAM, 170 place Henri Regnaud, 92078 Paris, La Defense. Capital is not guaranteed and a decline in equity markets can cause loss in value.

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