News

New light on malaria parasite life cycle fuels hope for prevention and treatment

Discoveries made independently by two US research teams reveal insights into key stages of the malaria parasite's life cycle and could, according to experts, spur development of a vaccine and new drugs against the disease.

One discovery, reported in the 5 January issue of *Science* by Ana Rodríguez and her colleagues at the Departments of Medical and Molecular Parasitology, and of Pathology at the New York University School of Medicine, relates to the early or infective form of the malaria parasite that is injected into a person by mosquitoes. At this so-called sporozoite stage, the parasite moves quickly to the liver. The researchers have shown that, contrary to current wisdom, sporozoites do not develop in the first liver cell they enter, but rather wander about, puncturing four or five different cells, until they find a "suitable" cell to settle in for a few days.

What's more, the researchers showed, sporozoites don't need the little sacs, or membrane vacuoles, that most bacteria and parasites use to protect themselves during entry into a cell until they settle down to develop: they can also "choose" to penetrate cells directly.

After the sporozoite elects its final liver cell to squat in, the research team observed, it spends a few days replicating into thousands of so-called merozoites, that eventually burst out of the liver cell to invade blood cells. It is the repeated invasion and rupture of blood cells by merozoites that causes the cyclical fever typical of malaria.

Malaria researcher Stephen Hoffman of the US Naval Medical Research Institute in Rockville, Maryland, says this research represents "a very elegant expansion of our understanding of the liver stage of the parasite's life cycle".

Dr Rodríguez and her colleagues believe that the "sporozoite migration" through several liver cells that they have witnessed may be essential for the parasite to proceed to the merozoite stage of its life cycle.

Other members of the team, including malaria research pioneers Ruth and Victor Nussenzweig, first saw this migrating behaviour in a video microscopy film they had made in 1989, but were unsure how to interpret it. Dr Rodríguez joined the team last year and she and a colleague, Maria Mota, conducted a series of painstaking lab experiments that confirmed the validity of the finding. They observed, too, that in most instances the sporozoite's hit-and-run behaviour lethally damaged only a minority of liver cells. Most cells survived. They also demonstrated that this behaviour is seen not only with species of the malaria parasite that infect animals, as the video showed, but also with *Plasmodium falciparum*, the most deadly species that infects humans.

In a comment to the *Bulletin*, Dr Hoffman said: "The liver is the ideal target for drugs and vaccines to prevent malaria ... because the liver stage is the longest single stage in the parasite's life cycle. The parasite takes at least five and a half days to develop from entry into the liver into the stages that are released into the blood. And during those five and a half days the patient is not ill. So it's a tremendously important window to attack the parasite. But it is extremely difficult to study the liver stages, so I really welcome the Rodríguez discovery."

In a remarkable month for malaria research, another US research team, headed by Daniel E. Goldberg, Professor of Medicine and Molecular Microbiology in the Howard Hughes Medical Institute at the Washington University School of Medicine, St Louis, reported another discovery related to the malaria parasite's life cycle.

In the 2 January issue of the *Proceedings of the National Academy of Sciences*, the St Louis team described work showing that when merozoites break out of red blood cells they do so in little sacs, or "parasitophorous vacuolar membrane-enclosed merozoite structures" (PEMS). Once the PEMS are outside the red blood cell, the researchers showed, the merozoites can be trapped within the PEMS by treating the PEMS with a chemical called E64, a so-called "protease inhibitor". E64 appears to block the merozoites' mechanism for escaping the PEMS, so preventing the invasion of new red blood cells. Similar enzyme inhibitors are used as part of the triple therapy against AIDS.

If this laboratory finding can be confirmed, it could, Dr Goldberg believes, offer a new route for developing drugs to prevent full-blown malaria disease. ■

Robert Walgate, *London*

Film actors' flaunting of tobacco brands rises despite ban

Endorsement of tobacco brands by actors appearing in US-made feature films has increased significantly since 1990, when the American film industry adopted voluntary guidelines on paid tobacco brand endorsements, according to a US study published in the 6 January issue of *The Lancet*.

The US film industry adopted the guidelines just as the US Congress was holding hearings to examine partnerships between the tobacco and the film industries. The guidelines ban tobacco companies from making payments to film-makers and actors in exchange for featuring tobacco products in films.

But the ban has done little to reduce tobacco brand appearances, says James Sargent, a Professor of Pediatric and Adolescent Medicine at the Dartmouth-Hitchcock Medical Center in Lebanon, New Hampshire, and lead author of the *Lancet* paper. Dr Sargent's research team scrutinized the top 25 US box office films from 1988 to 1997, a total of 250 films. They split the films into two groups, those made before the guidelines took effect and those made afterwards. The researchers then measured the number and type of tobacco brand appearances found in each film.

The overall prevalence of brand appearances — found in more than a quarter of the films, with tobacco use appearing in more than four-fifths — didn't change after the ban took effect, but there was a dramatic increase in the proportion of films showing actors using specific tobacco brands: from 1% of films before to 11% after the ban. Four US cigarette brands accounted for 80% of the brand appearances (see pie-chart).

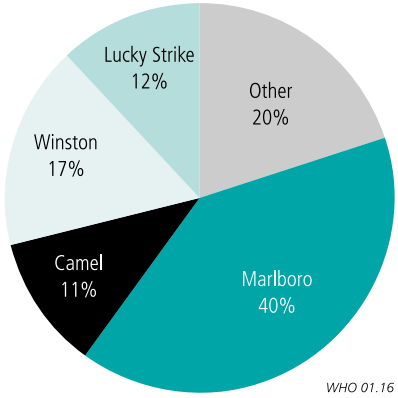
"Actor endorsement is just the kind of thing companies are willing to pay lots of money for," Sargent says. As evidence he points to other product placement deals. Producers of a 1997 James Bond film, *Tomorrow Never Dies*, received nearly US$ 98 million from corporations in return for featuring their brands of such goods as beer, spirits, car, and mobile phones.

Julia Roberts prepares for a smoke in *My Best Friend's Wedding*

Marlboro man billboard features in *Volcano* as backdrop to film credits

Photographs, courtesy J.D. Sargent

Tobacco brands depicted in films



courtesy *The Lancet*

Meanwhile, Walt Disney studios charged companies US$ 60 000 to have an actor use their product in the film *Mr Destiny*.

Tobacco companies deny that they are paying to have their products featured in films, saying that such deals fall under their voluntary ban. "We don't pay for product placement in movies. We don't even provide products to movie producers," says Daniel Martz, spokesperson for Philip Morris International, maker of Marlboro cigarettes. Though Sargent says there is not any direct evidence that tobacco companies are paying for product placements, he believes the film industry must take responsibility for the message it is sending when it shows tobacco products in films. US films are marketed to a global audience, and that means they are reaching the same foreign markets that tobacco companies are targeting most now that they face a rapidly declining US market. "Movies are a big social influence. When actors endorse brands, whether they are paid or not, they are marketing a tobacco product to an international audience, and they need to take responsibility for that", Dr Sargent commented to the *Bulletin*. Questioned by the *Bulletin* as to how film actors view the issue, Greg Krizman, National Director of Communications for the US Screen Actors Guild, would only say, "We're very sensitive to it". ■

Christie Aschwanden, *Nederland, Colorado, USA*

Salt lowers blood pressure even in non-hypertensive people

Eating a salt-poor, vegetable-rich diet for one month can substantially lower blood pressure in people with above-optimal blood pressure levels, in addition to those who are frankly hypertensive, according to findings of a US study published in the 4 January issue of *The New England Journal of Medicine* by Frank Sacks and fellow members of the DASH (Dietary Approaches to Stop Hypertension) Sodium Collaborative Research Group. The study, which was supported by the National Heart, Lung, and Blood Institute (NHLBI), part of the US National Institutes of Health, involved 412 people with systolic blood pressure levels between 120 mm Hg and 159 mm Hg. Participants were randomly assigned to eat either a typical US diet alone or the vegetable-rich, low-fat, low-carbohydrate, so-called DASH diet alone, at three different levels of daily sodium intake — 3300 mg (average for US), 2400 mg (recommended maximum) and 1500 mg — for each diet. After 30 days, the group on the DASH diet at the lowest sodium intake showed the greatest drop in blood pressure — 7.5 mm Hg and 11.5 mm Hg, for the hypertensive and non-hypertensive participants, respectively, below the final blood pressure levels of those who had eaten the typical US diet. Whichever diet was eaten, the magnitude of the mean drop in blood pressure was inversely related to daily salt intake. The study findings, commented NHLBI Director Claude Lenfant, "lay to rest the long-standing controversy over whether sodium reduction lowers blood pressure in people who do not have hypertension". ■

John Maurice, *Bulletin*

In Brief

Gates gives US$ 15.1 million for new drugs against African sleeping sickness and leishmaniasis

An international consortium of experts on drug development and delivery is to receive a US$ 15.1 million grant from the Bill and Melinda Gates Foundation to work on new drugs against two tropical parasitic diseases, African sleeping sickness (trypanosomiasis) and leishmaniasis. An estimated 300 000 to 500 000 Africans are infected with African sleeping sickness and about 60 million are at risk. Leishmaniasis is a disease that in its cutaneous form can be as disfiguring and disabling as leprosy and in its visceral form can be fatal if untreated. It infects an estimated 12 million people in 88 countries, and about 350 million people are at risk. Drugs exist for both diseases but are either not effective enough or are too expensive for wide use in the poor countries where these diseases are prevalent or have serious side-effects. The international consortium comprises scientists from the University of North Carolina at Chapel Hill in the US, the London School of Hygiene and Tropical Medicine in the UK, the Swiss Tropical Institute, the Kenya Trypanosomiasis Research Institute, and Immtech International Inc., a US biopharmaceutical firm. ■

Diary

Gates offers US$ 1 million prize for best health contribution

The Bill and Melinda Gates Foundation has established a US$ 1 million prize to be awarded annually to an organization that has made an exceptional contribution to the improvement of health throughout the world. Nominations must be received on or before 28 February 2001 by the Global Health Council, a US-based non-profit health organization, which will choose the winner. "Any organization from any country in the world that has substantively improved the health and the lives of people in need may be nominated," the Council has announced. The prize will be awarded on 31 May during the Council's annual international conference in Washington, DC. *Enquiries to: Laurel Mackin, Global Health Council (tel.: +1 202 833 5900; email: gatesaward@globalhealth.org; website:www.globalhealth.org/awards/gates_info.php3).* ■