Parasite vaccine hunt follows new roads

It has been more than 190 years since the discharge from cowpox pustules was used to protect humans from smallpox in a new process called vaccination. Since then, the science of developing protective drugs has evolved into a highly technical field with some amazing successes, particularly against bacteria. Parasitic diseases, however, traditionally have proven more resistant, despite their worldwide prevalence. But with some new tricks in hand, scientists now are closing in on the debilitating parasites that cause malaria and other diseases.

To date, there is no commercially available vaccine against a parasite. But through biotechnology, the development of such a vaccine may be only a matter of time spent in laboratories here and abroad. "Antiparasite vaccines have been a longtime objective, but now there's a slightly harder push," says David Sacks of the National Institute of Allergy and Infectious Diseases. "With some parasites, [vaccine production] is about to be feasible." Sacks, who discussed his research at this month's Recombinant DNA/Hybridoma Congresses in San Francisco, is one of a growing number of scientists who are using specific components of a parasite to induce immune responses.

For example, French researchers have produced a vaccine that partially protects rats and hamsters against parasites called schistosomes. As many as 300 million people may be infected with the parasites, which live in snails and enter the body in infected water. Those infected show a wide range of symptoms, often serious.

According to a report in the March 12 NATURE, the vaccine was made by isolating a protein from the surface of *Schistosoma mansoni*, and then – using now-common genetic engineering techniques – enticing *Escherichia coli* bacteria to produce the protein in abundant amounts. The authors say vaccination of animals with this recombinant protein "induces a strongly cytotoxic [parasite-killing] antibody response," comparable to that seen after immunization with the "native" protein.

Because parasites have a complicated life cycle – often encompassing several hosts and multiple growth stages – there may be more than one way to develop vaccines against a particular organism. This is true in the search for a vaccine against malaria, which threatens hundreds of millions of people living in areas where the malaria parasite is found.

In Sweden, researchers are looking for an agent to disarm the so-called merozoite stage of the malaria-causing *Plasmodium falciparum*, using techniques they describe in the March PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES (Vol.84, No.5). The merozoite is the parasite's form that invades the host's red blood cells, bringing about fever and chills.

The Swedish scientists previously had identified a substance deposited in red blood cell membranes during invasion. In the present study, they used *E. coli* to make large amounts of a segment of this substance; antibodies made in rabbits against this "synthetic" compound stopped merozoite invasion of red blood cells *in vitro*.

At the National Institutes of Health (NIH), a different stage of *P. falciparum*, called the sporozoite, is a target of malaria vaccine development. (Sporozoites are injected into a host by mosquitoes and then travel to liver cells, where they replicate into merozoites.) A sporozoite-blocking vaccine developed by the U.S. Army is currently in early clinical trials using military volunteers; test results are expected in June. That vaccine contains a section of a protein found on the surface of *P. falciparum*, which is expected to produce an antimalaria immune response in those vaccinated. However, NIH experiments indicate that some fine-tuning may be necessary if the Army vaccine is to be broadly effective.

Experiments in mice at NIH suggested that not all those vaccinated with the new vaccine will mount a protective immune response, apparently because the vaccine used too narrow a segment of the surface protein. Although it is yet undetermined whether there will be problems with the Army vaccine, NIH scientists are looking for additional sites on the surface protein that recognize a subgroup of blood lymphocytes called T cells, as described in the Feb. 27 SCIENCE.

According to Jay A. Berzofsky, one of several NIH workers involved in the project, a T-cell recognition site newly discovered by the group apparently primes T cells to an earlier and higher immune response when later challenged with *P. falciparum* than does the segment used in the Army's vaccine. Berzofsky told SCIENCE NEWS that emphasis is being placed on T-cell sites because there is some evidence that protection against malaria depends not only on antibody production, but also on separate cellular immunity.

Surface properties of parasites also interest Sacks. He is concentrating on immune responses against sugars found on the surfaces of the parasite causing Chagas disease, a primary cause of heart disease in areas where the parasite is endemic. In addition, he is investigating the surfaces of the leishmania group of parasites, which cause ulceration of mucous membranes in animals and people and are carried by sand flies.

Using antibodies against antibodies – called anti-idiotypic antibodies (SN: 4/12/86, p.231) – Sacks says he has elicited "superlative immunity" against leishmania in mice. The use of such antibodies is an "easy approach" and an alternative to injecting actual parasite components, he says. Such availability, along with other advantages, such as the elimination of possible infection from injecting whole parasites, explains the current technical tinkering with bits and pieces of parasites being done in vaccine development. *– D.D. Edwards*

High blood pressure: Drugless treatment?

Used by nearly 15 million people in the United States, drugs to lower high blood pressure are a common factor in maintaining health. But, concerned over possible adverse effects, a number of researchers are exploring drugless methods to treat the disorder, which is known to increase the risk of heart disease. Two such studies, one of actual remission of hypertension and the other of its control through diet, are reported in the March 20 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION.

To determine whether hypertensive people can in some cases safely discontinue using blood pressure drugs, Andrew L. Dannenberg of the National Heart, Lung, and Blood Institute and William B. Kannel of Boston University School of Medicine analyzed data already accumulated in the Framingham (Mass.) Heart Study. (The extensive study has followed the cardiovascular health of its subjects for 32 years.) Dannenberg and Kannel found that, although most people must continue antihypertensive drug use throughout their lives, a small group of individuals may have a long period of remission without medication. Therefore, they conclude, "guidelines for medical care of hypertensive persons will need to be updated."

Another alternative may be that of control through nutrition. Researchers in Chicago and Minneapolis report the final results of a four-year study on the effects of overweight, excess salt and alcohol on blood pressure. They found that 39 percent of mild hypertensives who lost at least 10 pounds, decreased their sodium intake by 36 percent and drank no more than two alcohol drinks per day maintained normal blood pressure without drugs, compared with only 5 percent of those who discontinued drug therapy but did not adjust their diet. However, initial blood pressure levels also affect the outcome.

– D.D. Edwards