From the forests of Africa to the front lines of the war on terror, there’s a common need: Vaccines that work quickly and effectively, don’t need refrigeration or special handling, can be mass-produced quickly, don’t require a needle or multiple doses, and don’t cause side effects.

Whether it’s anthrax, hepatitis, influenza or bird flu, the need for better ways to create immunity among large numbers of people remains the same. But many current vaccines fall far short on many counts, and no vaccines exist against many dangerous microbes.

This year, hopeful data emerged for a new vaccine strategy developed by Allergy & Clinical Immunology faculty in conjunction with the Michigan Nanotechnology Institute for Medicine and Biological Sciences. The team is led by Allergy chief and MNIMBS director James R. Baker, Jr, MD and Allergy faculty Anna Bielinska, PhD, Alexander Chepurnov, PhD, Dr. Sci. and Michele Jaffe, MD, MPH.

The needle-free vaccine is based on a nanoemulsion: a suspension of nano-scale soybean oil droplets in water and alcohol. It looks like creamy white hand lotion. But the 200- to 300-nanometer oil droplets have the ability to break open and kill microbes, without harming human cells.

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Nanoemulsion particles lyse virus and incorporate viral antigens into their structure. The particles are then rapidly taken up by antigen-presenting dendritic cells to enhance presentation to helper T-cells.
When blended with microbes, or certain microbe proteins, and applied to the inside of the noses of laboratory animals, the nanoemulsion mixture becomes a vaccine. It penetrates the mucous membrane of the nose, and exposes specialized immune-system cells, called dendritic cells, to the microbe’s characteristic proteins. This triggers the formation of antibodies that prepare the body to fight off the actual organism in later encounters.

The University applied for a patent on this “mucosal vaccine” in the spring of 2000, and data on its effectiveness as an anthrax vaccine in animals were presented at the Department of Internal Medicine’s annual scientific meeting and several national infectious disease meetings.

So far, it appears to possess many of the qualities needed in an ideal vaccine, though more testing is needed before it can be tried in humans.

For the anthrax experiments, the vaccine was prepared using a recombinant protein from the bacterium Bacillus anthracis. When guinea pigs were vaccinated in their noses and then injected six months later with anthrax spores, all of them survived—while none of the unvaccinated comparison animals did. When the researchers challenged vaccinated animals by placing anthrax spores directly in their noses, 70 percent of the animals survived.

Vaccinated animals had raised specific antibodies and released other immune-system components called cytokines—characteristic of a kind of cellular immunity called a TH1 response. They didn’t show much sign of another type of response, called TH2, which may trigger the post-vaccination symptoms of fever and worse that can be seen with certain conventional vaccines.

Besides being effective after only one or two applications in the nose, the vaccine holds several other promising properties. For one, the nanoemulsion didn’t cause any structural changes in the surface protein antigens (epitopes) that trigger the formation of antibodies—something that often happens in conventional vaccines and can lessen their power to create immunity. Also, the nanoemulsion vaccine doesn’t need refrigeration, because its inherent antimicrobial properties keep any contaminating bacteria and fungi from growing.

In addition to the successful anthrax trial in guinea pigs, which was funded by the National Institutes of Health’s Great Lakes Regional Center of Excellence for Biodefense and Emerging Infectious Diseases Research, the U-M team is trying the approach in other diseases.
Trials of the vaccinia virus, which causes cowpox in cows and is a stand-in for the human smallpox virus, have gone well in mice. Soon, the approach will be tried in non-human primates. Previous studies using influenza viruses combined with nanoemulsion and delivered as a spray after exposure to the virus were also successful in animals.

Meanwhile, a hepatitis B trial in animals has yielded good initial results. This research is being funded by a $6.3 million grant from the Bill & Melinda Gates Foundation that MNIMBS received in 2005 as part of the Grand Challenges in Global Health Initiative.

The developing world especially needs a better vaccine against hepatitis B, which causes chronic liver disease and can lead to liver failure or cancer. The virus is widespread in Asia, South America, eastern Europe and Africa, with as many as 10 percent of Asian adults carrying a chronic infection. Liver cancer brought on by hepatitis B infection is the third leading cause of death for Asian men.

More than a billion people have been vaccinated against hepatitis B since the first vaccine was introduced in 1982, and it has been effective for many of those who have been able to receive it. But the existing vaccine has many shortcomings—including the need for three injections into the muscle, and the fact that it needs to be kept cold to assure its stability.

This year, the U-M team began to see promising results from animal trials of nanoemulsion combined with the current hepatitis B vaccine proteins. In 2008, the Gates Foundation funding will help fund a Phase I human trial.

The scientists are preparing their results for publication. A University of Michigan spinoff company, NanoBio Corporation, has licensed several previous patents issued to U-M for nanoemulsion technology, and is seeking business partners to move forward with vaccines against anthrax, influenza and other diseases. This year, NanoBio secured $30 million in venture capital funding to continue its development of nanoemulsion products.

It may still be a while before nanoemulsion mucosal vaccines are ready to be used in the millions of people who need better protection against disease. But this year brought the kind of rapid progress that’s needed to get to that point. The faculty and clinic team spent much of 2006 planning the move, which includes renovations to 7,800 square feet of space at a cost of $1.4 million. It will give U-M a location for its flagship Allergy Clinic that is convenient for patients and can offer more space for education, clinical research and community services. The division’s administrative offices and the extract lab where immunotherapy extracts are prepared will also move to the new location, and the walls will be decorated with art donated by Mrs. Ann Preuss, whose late husband Dr. Lawrence Preuss completed an allergy fellowship at U-M. The Division will maintain clinical activity at the Reichert Health Building, Briarwood Health Associates and Livonia Center for Specialty Care.

The Food Allergy Center, directed by Marc McMorris, MD (above), will be one of the region’s leading resources for patients and families. It serves adults and children who have allergies to everything from peanuts and milk to wheat and strawberries, and reaches out to schools, churches and daycare centers to educate others about the needs of food-allergic patients. The new facility will provide space for multi-disciplinary care, education, research and community programs.

With food allergies and all other allergic conditions such as atopic dermatitis rising in incidence nationwide, the need for this new space is more pressing than ever.