tion of these gp 120 vaccines has been tested in more than 1,200 human volunteers. Both this first generation and the present form of the vaccine produced no significant side effects and stimulated antibody production in 99.5% of humans. However, generating antibodies against HIV may not be enough to ensure protection from infection; cell-mediated immunity may be essential.

Although no one can predict for certain how effectively gp 120 vaccines will protect healthy individuals from contracting HIV, few scientists have high hopes. "No scientist that I know in the vaccine field has any expectation at all that the vaccine is going to be effective, and I can list ten or 15 names at the drop of a hat," Desrosiers says.

But even if clinical testing proves the vaccines are effective in only a small number of individuals, the efficacy trials will be worth the effort, Esparza counters. "If the vaccine is 30% or 40% effective, with this information we may be able to identify what immunological parameters correlate with protection." In order to proceed, we need proof of concept, Kallings adds.

The next type of vaccine to progress to clinical efficacy trials most likely will be a live vector vaccine that places portions of HIV in a harmless virus, such as canarypox. However, Berkley cautions, "It will be at least 2000 before the canarypox virus vaccine moves forward, and there is some question whether

A clinical trial to test high-risk individuals just got under way in Thailand. While steeped in controversy, many believe this trial is critical to furthuring knowledge of the role of HIV vaccines. Unicef/Jeremy Horner

South

of disease that are prevalent in the developed world. Eventually, the vaccines trickle down to developing countries. "I would much rather see developing countries make their own vaccines. That gives them intellectual property rights," Berkley says.

Critical to mobilising policymakers in these countries will be the work of community groups. As with many past treatment battles, most researchers acknowledge that for vaccine research to advance full throttle, community activists must step forward to apply pressure.

Developing a vaccine for HIV "may be a solvable problem or it may not," Berkley sums up, "but we ought to give it our best shot."

or not it will progress to trials even then."

Next in line are naked or purified DNA vaccines, which transport pieces of HIV DNA to harmless bacterial DNA. The DNA vaccines are attractive because they can be adapted to different HIV strains, explains Esparza. But there is no specific timetable for taking DNA vaccines from phase I safety trials to clinical efficacy testing, Berkley asserts.

Other forms of HIV vaccine are still further away from actual testing in humans, including the ones that are considered to be the most promising and the most controversial – live attenuated vaccines. Vaccines that inject live but weakened forms of primate HIV have been most effective in protecting monkeys and chimpanzees from subsequent infection. They are created by deleting one or more of the virus' nine genes from its genome. "Most scientists in the field agree that live attenuated HIV vaccines have far outperformed other vaccine approaches in terms of efficacy in animals," Desrosiers says.

According to Ruth Ruprecht, these vaccines are dangerous due to their residual potential for causing AIDS. It was thought that live attenuated vaccines would cause a short-term viral surge but then provide long-term protection against subsequent challenge with HIV. In experiments on both adults and newborn monkeys, however, Ruprecht, an associate professor at Harvard Medical School, has found that a live attenuated vaccine made from the primate version of HIV – simian immune deficiency virus (SIV) – causes AIDS in animals. Of the eight newborn monkeys who received the SIV vaccine, five are dead of AIDS, one has full-blown AIDS, and two have signs of early HIV disease. "We see the same spectrum of disease that we see with the wild type virus,» she summarises.

> We see the same spectrum of disease that we see with the wild type virus

In order to assure that live attenuated vaccines could be made safe enough for use in humans, Desrosiers has been trying to define a wide range of attenuation. "We've shown we can achieve virtually any level of attenuation simply by varying the number and the location of deletion mutations in SIV," he explains. He's also discovered, however, that the more attenuated the vaccine becomes, the less effective it is. "For the development of a live attenuated vaccine to be practical, one has to strike an appropriate balance." He concludes that "the prospects for a [live attenuated] vaccine that works are pretty bleak."

However, most researchers would agree the jury is still out on which vaccine avenue to pursue and for how long. It's clear that prevention efforts on all fronts must continue until we have one or more definitive prevention measures accessible to all people at risk for HIV.

Vaccine Sessions

Tuesday: C27 Vaccines in Human Trials

Thursday: A41 Vaccine Trials in Humans

Thursday: A45 Vaccines: Animal Models