create a shock wave that would momentarily double the pressure at the cavity wall, springing the walls briefly outward about 2 cm. The Pacer scientists intend to study how the shock will affect the cavity wall, and how the steam will affect other minerals, particularly anhydrite seams that occur in salt domes.

The Pacer cavity would be filled with 1 million tons of water which the thermonuclear explosions would vaporize into high-temperature steam at about 200 times atmospheric pressure. The steam would continually circulate through surface facilities, which would draw out heat to power turbine generators and filter out the fine particles of newly bred fissionable material carried up by the steam. New detonations would maintain the cavity temperature at about 500°C. At this high temperature, the tendency of the salt cavity walls to deform, or "creep," must be seriously considered to determine whether the cavity would slowly collapse. The Los Alamos scientists hope to be able to certify, with rigorous computer codes, that the cavity will remain stable for periods exceeding 20 years. They will also check calculations that show that the hot cavity only rises, like a bubble, extremely slowly through the salt formation.

Emphasis on Breeding

The power that can be produced with a Pacer system depends on the number of thermonuclear devices that are fired each year. About 700 devices with a 50-kiloton yield would be sufficient to produce 2000 megawatts of electricity for a year. But five times that power could ultimately be produced from breeding in the same system. After looking at the potentialities for 2 years, "We're placing our emphasis on the system as a breeder," says Robert G. Shreffler at Los Alamos, "and in that mode the heat is a secondary consideration."

The thermonuclear device for Pacer will use pure deuterium fuel which produces plentiful fast neutrons that are ideal for breeding. Uranium-233 and plutonium-239 could be bred equally easily. But the scientists working on Pacer are concentrating on uranium-233 because they believe that shipping it to "burner" reactors around the country would be much less risky than shipping plutonium because uranium-233 could be diluted with natural uranium, and potential saboteurs would hardly have the sophisticated isotope separation equipment needed to enrich it again. Uranium-233 would be bred from thorium, which would be either placed on the outside of the thermonuclear device or incorporated into it, because the neutrons would only travel a few meters before they were slowed down by the dense steam. Uranium-233 bred by rapid neutron bursts would be free of the gamma ray contamination, from uranium-232, that would occur if it were slowly bred in a reactor.

Besides the material intentionally bred in the Pacer cavity, there would be radioactive fission fragments and tritium from the thermonuclear reaction. Considerable effort is being made in the design of the Pacer device to make it as clean as possible, but tritium is an inevitable product of the fusion reaction. Approximately 7 kilograms of tritium would be produced each year, most of which would go into the steam in the form of tritiated water (HTO).

The economic feasibility of the project is quite sensitive to the cost of the thermonuclear devices, and the program's critics think that cost will prove to be the plan's downfall, even if it proves technically feasible. The most authoritative estimate of the expense of thermonuclear devices, published by the AEC during the heyday of Plowshare, puts the cost of a 50-kiloton device at $420,000. The goal of the Pacer program is to reduce this figure, through careful engineering, exhaustive testing, and mass production, by a factor of 10. According to a Livermore scientist familiar with the Plowshare program, "the lower end of this range seems terribly optimistic."

A further impediment to great cost savings would be the need to use devices with a lower yield than 50 kilotons, either to employ smaller cavities or to reduce the effect on the environment. To a first approximation, large and small thermonuclear devices apparently cost about the same. But Shreffler thinks that a cost reduction by a factor of 10 is well within the range of feasibility and that a cost of several hundred thousand dollars would "still be in the ballpark" for a breeder system. Several tests of the Pacer device are planned during the 1976–1978 study period at the Nevada proving site.

Provided that the 3-year study of the Pacer concept does not prove it unfeasible, scientists at Los Alamos and RDA plan to field test the idea in a small salt cavity with approximately 200 explosions of low-yield (0.1-kiloton) devices. The cavity for these tests could be in a less ideal salt formation, perhaps in a salt mine where the ease of access to the room would expedite experiments. No test site has been selected yet, nor have Pacer officials even completed criteria by which it would be chosen.

The administrators at ERDA are now considering the pros and cons of Pacer. According to one scientist involved in the Pacer program, "We think this is a program for a peaceful nuclear explosion with universal applications and the only one that makes sense. What we are asking is to give the idea a chance."

—WILLIAM D. METZ

Hepatitis B: A New Vaccine Ready for Human Testing

The search for hepatitis viruses has accelerated rapidly in the last few years, and several different groups of investigators have observed two viruses that are thought, but have not been proved, to cause the two forms of hepatitis. Unfortunately, no one has been able to grow either of the viruses in culture, which is normally one of the most important steps in the production of a vaccine. Last month, however, two investigators told a National Academy of Sciences symposium on hepatitis that they had independently employed a novel, but not unprecedented, approach that sidesteps that requirement. They have isolated viral antigens from human carriers of hepatitis and used them to prepare a vaccine that has proved successful in chimpanzees and that should be tested in humans in the near future.

One group that prepared the vaccine was headed by Robert H. Purcell of

the National Institute of Allergy and Infectious Diseases (NIAID) and John L. Gerin of the NIAID–Atomic Energy Commission Molecular Anatomy Laboratory in Rockville, Maryland. The second group was composed of Maurice R. Hilleman, Eugene B. Buynak, Robert R. Roehm, Alfred A. Tytell, Alexander U. Bertland, and George P. Lampson of the Merck Institute for Therapeutic Research in West Point, Pennsylvania.

The new vaccine is for hepatitis B, a debilitating disease characterized by inflammation of the liver, fever, weakness, loss of appetite, malaise, headache, and muscle pain. It is most frequently transmitted by infusion of blood from infected individuals, but recent evidence indicates that it is also transmitted by intimate association with infected individuals. It is generally considered the more dangerous form of hepatitis, particularly since many of those exposed to it are already ill. About 7500 cases of hepatitis B are reported in the United States each year, and some investigators say that there may be several times as many unreported cases.

The foundation for the present work on the vaccines was laid by Baruch S. Blumberg and Irving Millman of the Institute for Cancer Research in Philadelphia. In 1964, Blumberg observed a foreign substance, initially called Australia antigen, in the blood of an Australian aborigine. Four years later, Alfred M. Prince of the New York (City) Blood Center observed a similar substance, now called hepatitis B surface antigen (HB_sAg), in the blood of patients with hepatitis B. The two substances were subsequently shown to be identical and to be part of the coat of the suspected hepatitis B virus.

HB_sAg is a viruslike particle about 22 nanometers in diameter. It was once thought to be the causative agent of hepatitis B, but that theory was discarded when it was shown that the antigen contains no nucleic acids. The best evidence now available indicates that the nucleic acid core of the presumed hepatitis virus replicates in the nucleus of liver cells (where it causes tissue damage) and migrates to the cytoplasm, where it is sheathed in the HB_sAg coat. For reasons that are not well understood, the cytoplasmic messenger RNA directs the production of very large amounts of excess protein coat.

Blumberg and Millman thus suggested that this excess antigen could be separated from the blood, purified, and used as a vaccine. They even patented the idea, but they had no facilities to test the concept. Furthermore, there was then considerable resistance to the theory that the antigen was specifically linked to hepatitis B, and most investigators agreed that the first step toward production of a vaccine should be firm identification of the causative virus.

Soon thereafter, Saul Krugman of the New York University Medical Center demonstrated that the vaccine concept was feasible. He obtained blood serum from individuals who were chronic carriers of HB_sAg, diluted it with water, and heated it to 98°C for 1 minute to inactivate any viruses that might be present. He then injected the material into children who were scheduled to be admitted to the Willowbrook State Institution in New York within a short time. The injections were shown to protect about 70 percent of the children when they later were exposed to hepatitis, which was endemic at the institution. The work was halted, however, when Willowbrook stopped accepting new children. Krugman's experiments were not definitive, furthermore, in that they did not prove that the antigen was responsible for the effect. Since hepatitis virus was present in the blood of the carrier, it could have served to immunize the recipients of the vaccine, even though it was inactivated by the heat treatment.

Similar Procedures

Spurred by the results of Krugman and others, the NIAID and Merck groups independently isolated the antigen and used it to prepare a vaccine. The procedures they used were quite similar. Both started with plasma from chronic carriers of the hepatitis antigen. Purcell and Gerin used plasma containing only one of the four major subtypes of the antigen; the Merck group's plasma contained two subtypes in a ratio of 9 : 1. Both groups separated the antigen from viral particles in the blood by centrifugation.

Purcell and Gerin then purified the antigen by further centrifugation, whereas the Merck group used undisclosed chemical procedures. And finally, both groups treated the purified antigen with formalin to inactivate any remaining virus particles. Many tests showed that the two vaccines do not produce hepatitis in laboratory animals and do not contain infectious viruses, but that they do stimulate the production of antibodies to HB_sAg in guinea pigs. The Merck vaccine was further shown to be free of blood proteins and blood group substances.

Purcell and Gerin's biological testing appears to have proceeded further. They gave two of six chimpanzees a vaccine prepared from HB_sAg subtype *ayw* and each of the other four one of the following: a vaccine of the same subtype, but which had not been exposed to formalin; the blood serum from which that vaccine was made; a vaccine made from subtype *adr*; and the solution used as the diluent for the vaccines. A seventh chimpanzee served as a control. The materials were given in two doses, a month apart. All four of the animals given the vaccines developed antibodies to HB_sAg. None of them developed hepatitis, but the one animal given the untreated serum did.

Six months later, all seven animals were given an infectious dose of hepatitis B virus subtype *ayw*. None of the three animals given the *ayw* vaccine developed any evidence of hepatitis. The animal given the *adr* vaccine became infected but did not develop any signs of the disease, suggesting that the severity of the infection was blunted by vaccination with the different subtype. The Merck group observed a similar formation of antibodies in chimpanzees given three doses over an 8-week period. Their experiments with a challenge dose of the live virus, however, are still in progress.

The next step, provided Food and Drug Administration approval is obtained, will be limited testing in humans to ensure that the vaccine is safe. That will be followed by more extensive testing to demonstrate that it works. This process will probably take at least 5 years. Merck already has some 200,000 doses of the vaccine available for such tests.

Once the vaccine is found safe and effective, it should find many uses. One group for which protection will be useful are individuals who process blood or who work in blood banks and hospitals. Doctors and dentists would also benefit from such protection. Another large group that would benefit by vaccination includes individuals who live in close quarters, such as those in institutions and military installations. It would be useful also for individuals who at some time might be likely to require a blood transfusion. Other beneficiaries, although it might be hard to identify them as a group, are drug abusers, who often contract hepatitis by using unsanitary injection paraphernalia.—THOMAS H. MAUGH II