crates, each 5 centimeters on a side.

All the interconnecting wires between chips on a wafer and between wafers would be made of the same superconductors used for conductors within the circuits on one chip. The choice of silicon as the primary structural material is based on the desire to make the computer from the same material as much as possible in order to minimize stresses and strains induced by the thermal cycling between room temperature and that of liquid helium. Since silicon's properties make it a good substrate material for each circuit, its use for the rest of the box seemed mandated as well.

Packing so many switches (about $10^8$) so tightly in a three-dimensional arrangement is not possible with silicon semiconductor electronics, yet such close packing is needed for proposed super-

# Rickettsiae: A New Vaccine for Rocky Mountain Spotted Fever

Rocky Mountain spotted fever (RMSF) is not one of the most widespread of diseases. Last year, the United States had 1115 cases, a record number; that is a mere pittance compared to more prevalent diseases, such as hepatitis and influenza, but nonetheless a sharp increase from the 774 cases reported in 1974. The majority of the victims are children, most of them in the so-called "tick-belt" states of Maryland, Virginia, North Carolina, South Carolina, and Georgia. As many as 10 percent of the victims of RMSF die, and in another 20 percent the kidneys, liver, and nervous system may be permanently damaged. The number of cases of RMSF may be markedly reduced, however, by use of a new vaccine that promises much better protection than has previously been available.

The disease, which is characterized by chills, headaches, high fever, and, at the outset, a rash on wrists and ankles, is caused by the tick-borne parasite *Rickettsia rickettsii*. Rickettsiae are small microorganisms that resemble viruses in that they can reproduce only in living cells of other organisms. The first vaccine against RMSF was prepared in 1924 by Roscoe R. Parker and R. R. Spencer of the United States Public Health Service, who crushed ticks in phenol and injected a suspension of the product. In 1938, Herald R. Cox, who was then also with the Public Health Service, developed a technique for growing rickettsiae in the yolk sacs of chicken eggs. The parasite could be harvested, killed with formaldehyde, and extracted with ether to yield a vaccine. A commercial product based on this technique was first marketed by Lederle Laboratories in 1948. A new study sponsored by the Food and Drug Administration and conducted in 1973 by Herbert L. DuPont, now at the University of Texas Medical School at Houston, Richard B. Hornick, and colleagues at the University of Maryland showed that neither the tick nor the egg vaccine conferred immunity in man, and the Lederle product was subsequently withdrawn from the market.

The new vaccine has been developed over the course of 8 years by Richard H. Kenyon and his associates at the U.S. Army Research Institute of Infectious Diseases at Ft. Detrick, Maryland. Their chief goals were to increase the number of rickettsiae obtained from cultures and to eliminate the egg yolk lipids and proteins that were a contaminant in the commercial vaccine. In most individuals given the vaccine, these contaminants often produce swelling and tenderness at the injection site and in people who are allergic to eggs can produce a much more severe reaction.

After screening several tissue culture systems to see which yielded the highest concentration of rickettsiae, they began growing the parasites in monolayer cultures of cells from duck embryos. The principal problem with this and all other culture systems is that rickettsiae are very sensitive to the penicillin and other antibiotics commonly used to prevent contamination of the cultures (the parasite is less sensitive to the antibiotics in man); contamination can thus be prevented only by scrupulous care in handling the cultures. After incubation, the parasite-infected cells are broken up by alternate freezing and thawing followed by sonication; the cellular debris is removed by centrifugation at low speed, and the rickettsiae, which remain in the supernatant are then killed with formaldehyde.

Kenyon found that substantial quantities of rickettsiae are present in the suspension, whereas a microscopic examination of the commercial vaccine revealed no intact parasites. He and his colleagues showed that injection of the suspension into guinea pigs induces formation of a high concentration of serum antibody to the parasite. They also found, however, that only limited quantities of pathogen-free duck embryo cells are available.

They thus replicated the work with chicken embryo cells and found that they obtained only slightly fewer rickettsiae. They then tested vaccines produced from both duck and chicken embryo cultures in rhesus monkeys and found that two doses of either vaccine, administered at 15- or 30-day intervals (the common procedure for killed-bacteria or killed-virus vaccines) provide complete protection against a subsequent challenge with the parasite.

They have since tested a dilute version of the chicken embryo vaccine in 16 human volunteers. They observed that a small quantity of antibody was induced, and that there were no apparent side effects. They are now planning to try the undiluted vaccine in ten more humans to see whether it confers protection. If that attempt is successful, Kenyon says, some further testing will be required, but the vaccine could be available for widespread use within 2 to 3 years if there is sufficient demand.

How large that demand might be is not clear. Before the Lederle vaccine was withdrawn from the market, the company sold about 25,000 doses per year. Use of that vaccine was somewhat limited, however, because of the local reactions to immunization and because of the relatively poor immunity it conferred. A better vaccine with fewer or no side effects might find a much larger market.

A major target might be children who live in the tick-belt states and who play in wooded areas. Another might be backpackers and hikers, who represent a growing segment of the population. The Army may also find it useful to immunize recruits because many of its training camps are located in tick-belt states. The population at risk thus seems large enough to support commercial production, despite the relatively small number of cases reported each year. No manufacturer has expressed interest in such production yet, but that would seem to be only a matter of time.

—THOMAS H. MAUGH II