nal [to the scientific community] that we attach great value and importance to research that does not have to be justified on the basis of its relevance to some application." At the same time, he wants scientists to know that the Administration is not planning to write them a blank check. "When you get into big bucks," he says, "curiosity-driven research has to meet additional criteria," such as serving other national goals, if it hopes to be funded. "That's the issue with the Superconducting Super Collider and the space station."

Gibbons says the new system will clarify what the government spends on basic research, even if it is to be called by other names. The figure of $14 billion contained in the president's 1994 budget request "is probably in the ballpark," he says, adding, "but I'm not sure that the way it's being spent is optimal. Have we ever looked at that figure? Should it be be five times bigger or three times smaller? Before you can answer those questions, you need to have confidence in the numbers. And right now I don't."

Once the Administration has confidence in the numbers, the next step—linking expenditures to national needs—will require tighter management of the budget. That's where the National Science and Technology Council comes in. Clinton this month approved the formation of the panel proposed in Gore's report and gave it authority to see that the Administration's R&D priorities are mirrored in the budgets of individual agencies.

The new council will oversee science policy in the same way the National Security Council and the National Economic Council coordinate those sectors. Gibbons says the council will "have great powers of persuasion" as individual agencies begin to develop an R&D budget each year and that it will operate "in parallel" with preliminary discussions between each agency and OMB. The goal, says Gibbons, is to reach "agreement on major areas" of R&D spending before each agency submits its budget to the White House. This would represent a big change from the traditional way of doing things, in which the departments and agencies make their own individual pitches to OMB.

Gibbons says he hopes the council will be up and running by January, in time to begin reviewing what will eventually become the president's 1996 budget request to Congress. Its membership is expected to include Cabinet secretaries and agency heads, with Clinton as its chairman and Gore as its vice chairman. Much of the actual work will be carried out by officials at the various science agencies, he says, and the president would attend meetings "as needed."

One result of the new accounting methods and administrative structures will be more central control over the R&D enterprise. Asked whether this arrangement is a move toward establishing a Department of Science and Technology, Gibbons grins. "Heavens, no," he says. "This is in lieu of one. It's a virtual department."

–Jeffrey Mervis

AUTOIMMUNE DISEASES

Treating Arthritis With Tolerance

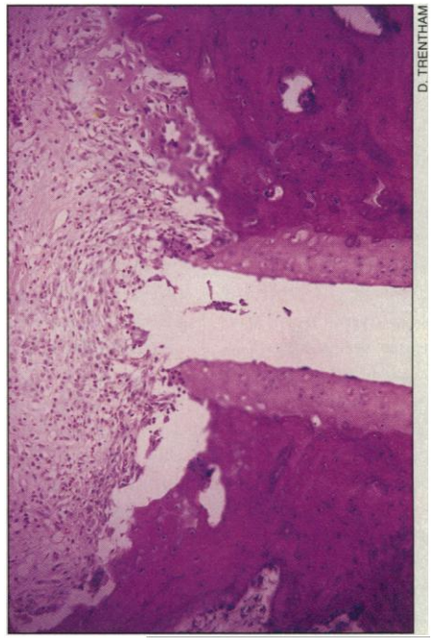
Autoimmune diseases are biological betrayals: the body's own immune system, which is supposed to protect it against infection, instead turns traitor for unknown reasons, attacking apparently normal tissues. These acts of treason can take many forms. One of the more common is rheumatoid arthritis (RA), in which the joints become painful and swollen under immune system assault. RA symptoms can be relieved somewhat by suppressing the assault with steroid drugs or drugs that block cell proliferation. But these treatments carry the risk of serious side effects such as accelerated bone loss, cataracts, and liver damage.

Now an apparently less toxic RA treatment may be on the horizon. On page 1727, Harvard rheumatologist David Trentham and his colleagues report they have significantly reduced RA patients' symptoms by feeding them type II collagen, a protein common in joint cartilage and a possible target of the autoimmune attack in RA. The Harvard group's approach, called oral tolerization, takes advantage of a trick used by the body to prevent immune reactions to the foods we eat: Foreign proteins that enter the body through the digestive system suppress immune responses to those proteins instead of triggering them. Oral tolerization attempts to reduce autoimmune attacks by feeding the patients proteins—collagen, in this case—that are found at the site of autoimmune disease and that may have triggered the autoimmunity in the first place.

When the approach was first tried in humans, patients suffering from multiple sclerosis were fed preparations of the brain substance myelin (*Science*, 26 February 1993, p. 1263) and showed some improvement, although the results were not statistically significant. But the RA results are more dramatic, and the study has been met with cautious enthusiasm by researchers who study autoimmunity. "It's reason for optimism that we're on the right track," says Howard Dickler, chief of the immunology branch at the National Institute of Allergy and Infectious Diseases. The caution, however, is prompted by a shortcut in the study design that may have exaggerated the results, and most researchers urge skepticism until larger studies confirm the findings.

In addition to Trentham, the team that conducted the RA study included Howard Weiner and David Hafler, the Harvard immunologists who directed the multiple sclerosis trial. Sixty RA patients participated in the trial, which was sponsored by Auto-Immune, a Lexington, Massachusetts, biotech company founded in 1988 to commercialize oral tolerization based on the results of animal studies conducted by Weiner. After stopping other arthritis treatments, half of the patients took daily liquid doses of chicken collagen for 3 months while the other half received placebos. Neither the patients nor their physicians knew which treatment the patients received.

The patients were examined periodically and when the study was completed, those who had taken collagen had a 25% to 30% reduction in observed swelling and pain in their joints, while the condition of patients in the placebo group had worsened slightly. Four of the patients receiving collagen had improved so much that their disease seemed to be in remission.



D. TRENTHAM

Arthritic attack. This rat joint shows damage to bone *(dark red)* and cartilage *(pink)* possibly caused by immune cells assaulting collagen protein in the cartilage.

Just how oral collagen produces such results is something of a mystery. Weiner found that feeding collagen to rats triggers the production of suppressor T cells. These cells travel to the joints, where collagen is found, and there prevent other types of T cells from mounting an attack and causing inflammation. But

whether this mechanism is acting in humans has not yet been determined.

Despite that uncertainty, scientists familiar with the RA study are encouraged because it has expanded the applications of oral tolerization, fueling hopes that it may be useful in the treatment of other autoimmune diseases, whose targets range from the thyroid gland to the neuromuscular junction. "Any of these T cell mediated diseases might be targets for this kind of therapy," says Ohio State University immunologist Caroline Whitacre, who is also studying oral tolerization. And the treatment seems to have virtually no side effects, a welcome improvement over present RA treatments.

Nevertheless, most researchers contacted by *Science* say they will remain skeptical until they see whether larger studies also produce encouraging results. "It's certainly very promising," says clinical immunologist Noel Rose of Johns Hopkins University. But, he adds, "these diseases are notoriously remitting and exacerbating. You need fairly long-term studies on large numbers of people to get truly reliable results."

A more specific concern relates to Trentham's study design. Joel Kremer, head of rheumatology at Albany Medical College, was one of several immunologists who reviewed the study for AutoImmune, and he says the reviewing team noted that the study lacked an initial drug-free period. Such "washout periods" allow the effects of previous medications to wear off. During the washout time, the symptoms of patients with active disease should flare up, establishing a baseline for testing collagen's effects.

Without the washout, "there are two possible interpretations," says Kremer. "One is that this drug really does something because it can stop [post medication] flares, which are the most serious forms of the disease that we see." Or the disease could have been in remission, in which case the collagen had little to suppress.

Trentham acknowledges that the study had a bit of a "quick and dirty" character to it, because he was "still seeking a yes or no answer as to whether there was anything there or not." With a qualified "yes" from this study, he and AutoImmune are designing a larger, multicenter trial that would include a washout period and 6 months of treatment with a range of collagen doses. Recruitment for the trial will begin early next year, with results anticipated sometime in 1995.

Before those next results are in, the researchers caution RA sufferers against popping over-the-counter collagen pills. If the findings hold up, dosage is likely to be crucial, and there's little chance that such supplements could provide the right amount of type II collagen. Pill-poppers would only add frustration to their stiffness and pain.

–Marcia Barinaga

MICROELECTRONICS

Is the Third Time a Charm for A Superconducting Computer?

Ten years ago yesterday (on 23 September 1983), dreams of creating ultrafast computers from superconducting materials seemed to die when IBM announced the end of its highly publicized $100 million program of research and development on Josephson junctions. These devices—nothing more than two layers of superconductor separated by a thin insulating barrier—had seemed highly promising as the basis for a new generation of computers. But 20 years of research led IBM to conclude that, fast as they might be, they would never manage to stay far enough ahead of silicon technology to make a large investment pay. Eight years later, in 1991, an equally grandiose Japanese effort sponsored by the Ministry of International Trade and Industry came to a barren end.

Yet in spite of these two failures, the dream of challenging silicon with superconducting circuits remains alive in an effort Konstantin Likharev of the State University of New York at Stony Brook calls "the third major attempt—and probably the last"—to harness Josephson technology in computer circuits. Likharev and his collaborators have already built a variety of devices based on the technology, which they plan to test next summer. Parallel projects are under way at other institutions including the University of Rochester and the National Institute of Standards and Technology.

All these efforts combine Josephson junctions with a new kind of logic, invented by Likharev and his colleagues, that promises to overcome the drawbacks of earlier strategies. Instead of using voltage differences to represent the 0s and 1s of data—the downfall of the earlier effort because it limited the switching speed—Likharev's scheme relies on single quantum units of magnetism. IBM physicist Mark Ketchen calls the strategy, known as rapid single flux quantum logic (RSFQ), the best bet yet to "see what really is the potential of superconducting technology for high-speed digital computation."

If this third try succeeds, it could open the way to computers or communications circuits that live up to the original hopes for Josephson junctions. Already, simple RSFQ circuits made of the low-temperature superconductor niobium are running at speeds of 50 billion cycles a second, 1000 times faster than the fastest personal computers and 100 times faster than the fastest silicon devices. "If we improve the technology," says Likharev, an avowed optimist, "which is relatively easy to do, we hope to achieve speeds of around 300 billion operations a second." And because the devices are superconducting, the energy consumed is infinitesimal. "We're spending 10^{-19} joules per operation," says Likharev, "which is something like a million times less than the usual silicon memory cell in your computer would require."

Plenty of people think such optimism is cockeyed. They point out that no one has yet standardized the production technology enough to make large-scale computer memories. Furthermore, high-temperature superconductors, which would be much preferable to the low-temperature materials Likharev and his colleagues exploit, are so balky that researchers struggle to fashion even simple circuits and logic devices.

To Likharev and his co-workers, those drawbacks pale in the face of the technology's promise. Any logic element—an ordinary transistor, for example—has to switch between two states, corresponding to the binary digits 0 and 1, in response to an external signal. Because Josephson junctions are superconducting, that signal can be minuscule —less than a millivolt, compared to a volt for a silicon transistor—and a smaller signal means faster switching.

Quick change artists. Both the IBM and Japanese efforts to exploit this responsiveness were based on the Josephson junction's ability to switch between superconducting and non-superconducting states. Ordinarily, pairs of electrons "tunnel" across the gap without resistance, in a superconducting current. But if too large a current surges into the junction, its superconductivity breaks down, and the gap becomes a barrier. That creates resistance to the flow of current, resulting in a voltage difference across the gap. In the IBM and Japanese schemes, these two states —the low voltage tunneling state and the high voltage resistive state—represented 0 and 1, and a junction could be switched between them with a pulse of current.

A critical limitation in this scheme, says IBM's Ketchen, is that the junctions don't always reset themselves to 0 when the incoming current abates. Once the Josephson junction is in the voltage state, it lingers there even after the incoming current drops all the way to zero. The faster the circuits are run, the larger the problem becomes; at a billion cycles per second, which is the minimum speed needed to compete with silicon, the junctions don't reset themselves fast enough to keep up. "That phenomenon," says Ketchen, a veteran of the IBM program,