## Striking pay dirt in prime-number terrain

Against all odds, scientists using a special computer program to sift through gargantuan whole numbers in search of primes—numbers divisible only by themselves and 1—ventured into largely unexplored territory to bag a new record. Flushed out after 19 hours of calculation on a Cray-2 supercomputer at AEA Technology's Harwell Laboratory in Harwell, England, the largest prime number yet discovered has 227,832 digits, three times as many as the previous record holder (SN: 9/16/89, p.191).

"It was found by absolutely amazing luck," says computer scientist David Slowinski of Cray Research, Inc., in Chippewa Falls, Wis., who developed the software used in searching for so-called Mersenne primes.

Expressed in the form  $2^p - 1$ , where the exponent p is itself a prime number, Mersenne numbers hold a special place in the never-ending pursuit of larger and larger primes. These particular numbers have special characteristics that make it relatively easy to check whether a candidate is either a prime number or the result of multiplying together several smaller numbers.

With an exponent of 756,839, the new champion holds the distinction of being the 32nd and largest Mersenne prime ever found. However, because no one has yet checked all Mersenne numbers having smaller exponents, mathematicians can't be sure that no Mersenne primes lurk in the vast expanse between the record holder and the second-place Mersenne prime, which has an exponent of 216.091.

Indeed, the latest effort was entirely a shot in the dark. Checking for Mersenne primes provides a convenient test of how reliably a computer functions. When scientists at Harwell requested some numbers to try out while testing their machine, Slowinski provided a list of 100 candidates, selected arbitrarily from about 30,000 possibilities having exponents between 500,000 and 1 million. Incredibly, the Harwell scientists found a prime on their 85th try.

The discovery of such a large Mersenne prime by a hit-or-miss approach actually has little value for computational number theorists interested in the distribution of prime numbers and related mathematical issues. These mathematicians would prefer a more systematic attack that fills in all the gaps.

"It's more fun to go for the record," Slowinski admits. "We're interested in the big ones. We're more like boy scouts looking in the woods at night by flashlight than an organized sheriff's posse."

To fill in the gaps, several computer scientists have banded together to develop improved computer programs for identifying additional Mersenne primes.

Calling themselves the "Gang-of-Eight," these researchers have combined ideas from the fields of number theory and signal processing to create a remarkably efficient means of finding and verifying Mersenne primes.

"We've checked exponents from 524,287 down to 430,000 and found no primes," says Richard E. Crandall, chief scientist at NeXT Computer, Inc., in Redwood City, Calif., who participated in verifying the new record.

In an earlier effort, Walter N. Colquitt of the Houston Area Research Center in The Woodlands, Texas, used nearly 8,000 hours of computer time to go as high as 355,031 from his starting point at 216,092. In 1988, he and a colleague had discovered a previously overlooked Mersenne prime with an exponent between 100,000 and 130,000 (SN: 2/6/88, p.85).

"There's still a bit of a gap from about 370,000 up to 430,000, and there's an immense gap between 524,000 and 750,000," Crandall says. "Our program can be used to check up to 32 million, but it's a question of computer time. No one wants to give up the Cray time."

"The new record is going to be awful hard to beat," Colquitt adds. "The hardware has to get a lot faster."

Nonetheless, the search continues. "It's really an amusing sidelight or hobby when nothing else is going on," Slowinski confesses. "It's a shame how work interferes with the important things."

– I. Peterson

## Beta blockers, depression: Breaking the link

Beta blockers, a class of drugs frequently prescribed for high blood pressure, have been linked with depression in the past. But a new epidemiologic study may force doctors to reexamine the evidence linking beta blockers with the blues.

In general, physicians hail these drugs as a crucial weapon in the fight against hypertension, migraine headaches, certain forms of violent behavior and even stage fright. Yet during the 1980s, several scientific reports suggested beta blockers might cause clinical depression, a very serious disorder characterized by hopelessness and suicidal tendencies.

Now, Roselie A. Bright of the Food and Drug Administration in Rockville, Md., and Daniel E. Everitt of the Presbyterian Medical Center in Philadelphia offer evidence that may clear the shadow of depression from the beta blocker story.

Using Medicaid reimbursement claims filed in New Jersey from July 1980 to December 1983, the team identified 4,302 people who had at least one sign of serious depression, such as the use of antidepressant drugs or electroconvulsive shock therapy. The researchers then matched these individuals with 8,604 controls whose claim forms showed no signs of depression.

When the team went back and studied the claim forms for prescription drugs, they discovered an association between beta blockers and depression. Depressed individuals were 1.45 times more likely than controls to have taken beta blockers for at least a year before their mood disorder surfaced.

That seemed to lend credence to the earlier reports. But when the researchers added so-called confounding factors to their statistical analysis, the link between depression and beta blockers dissolved. The crucial factors were frequent use of prescription drugs, frequent trips to the doctor's office and repeated use of anti-

anxiety drugs called benzodiazepines, the team reports in the April 1 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION.

These data suggest that a statistical fluke might explain the seeming connection between beta blockers and depression. Everitt notes that a 1986 study he coauthored indicated an increased risk of depression among people taking beta blockers, but he now says that study didn't look hard enough at the confounding factors that can skew a statistical analysis.

Beta blockers don't appear to cause depression, at least in most people, he concludes. Rather, people who take beta blockers also appear more likely to get prescriptions filled for a variety of moodaltering drugs, including sedatives like the benzodiazepines, Everitt notes.

It is still possible that beta blockers cause depression in some cases, cautions psychiatrist Stuart C. Yudofsky of Baylor College of Medicine in Houston. Beta blockers are known to affect serotonin, a brain chemical that may be associated with depression, he says.

Everitt agrees. In the recent study, he and Bright looked for a link between long-term beta blocker use and depression. (The patients had taken beta blockers repeatedly during the year prior to their depressive episode.) However, he says, the study did not address the concern that some people may suffer depression right after taking a beta blocker drug. Until future research clears the question about short-term usage, Everitt advises physicians to consider switching patients to a different drug if they experience a first-time depressive episode shortly after starting treatment with beta blockers.

Yudofsky, who wrote an editorial accompanying the report, adds that most cases of depression among beta blocker users can be handled with traditional approaches such as antidepressants and psychotherapy. — K.A. Fackelmann

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