picture is that the primordial gas coming out of the Big Bang somehow condensed into linear, or curved features before it collapsed into galaxies; the ones that he and Petrosian have found would thus represent the last remnants that have not yet collapsed.

There is some support for this scenario, says Lynds. The clusters where the arcs are seen are quite distant, about 5 billion light-years from Earth, which means that we are seeing them at a relatively young age. In cluster 2242-02 the arc does seem to have nodules along its length, as if it were beginning to break up into clumps about the size of small galaxies. And, he says, "The experience of people who study clusters is that they find more interesting alignments of galaxies than they would expect by chance. So it all hangs together in a vague sort of way."

Obviously, astronomers are going to need a lot more examples of the arcs before they can pin down any of these ideas. As Petrosian points out, "There is a limit to what we can learn from just three examples." Finding more may not be easy; if the arcs are primordial relics, then any other examples may well be further away. But then, a good many astronomers will certainly be trying.

And in the meantime, the original arcs are lost in the daytime sky until next autumn, when Lynds and Petrosian hope to observe them again. ■ M. MITCHELL WALDROP

Drug May Protect Brains of Heart Attack Victims

A controversial drug may reduce the damage to brain neurons that often occurs after the blood supply is interrupted

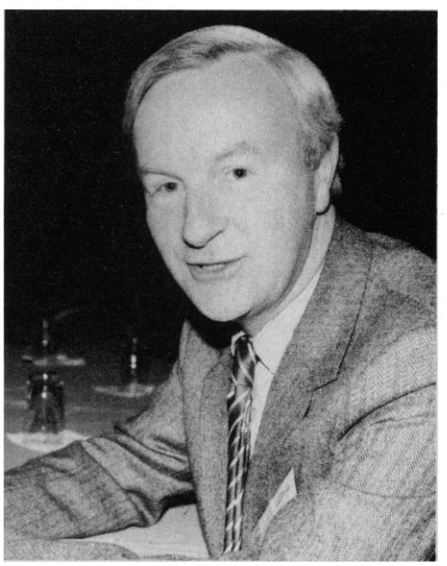
WHEN a heart attack or stroke deprives the brain of oxygen, nerve cell damage is often irreversible and virtually untreatable. This ischemic damage may be preventable, according to new results in experimental animals treated with a drug that was originally developed as an anticonvulsant. But some researchers challenge the basis for the drug's use and caution that it is still too early to know whether it will be effective in humans.

The potential for the drug, MK-801, to limit neuronal injury after ischemia depends on "the relatively new idea that excitatory neurotransmitters act as toxins and contribute to much of the brain damage," says Leslie Iversen of Merck Sharp & Dohme Research Laboratories in Harlow, England. He told participants at the recent American College of Neuropsychopharmacology meeting in Washington, D.C.,* that MK-801 penetrates the blood-brain barrier easily and blocks the effects of excitatory amino acids. These normally occurring transmitters, including glutamate and aspartate, are released at high, toxic levels when the brain is deprived of blood and oxygen.

The Merck researchers find, with gerbils and rats, that MK-801 protects neurons whether they give the drug before or after inducing ischemia to the animal's entire brain. As yet, they have no data suggesting whether MK-801 reduces neuronal injury when ischemia affects only a small area of the brain, a condition similar to brain damage from a stroke.

*The annual meeting of the American College of Neuropsychopharmacology was held from 8 to 12 December in Washington, D.C.

Two issues trigger controversy among other researchers who also study possible ways of limiting damage to neurons when blood flow to the brain is blocked. First, Fred Plum and William Pulsonelli of Cornell University Medical School note that the gerbil model used extensively by the Merck researchers is not representative of ischemic damage in other mammals because of the gerbil's propensity to develop prolonged seizures that may themselves produce and exacerbate brain damage. And because rodents are more susceptible to ischemic brain damage than primates, the Cornell researchers stress the importance of testing potential neuroprotective drugs in nonhuman primates before giving them to humans.



Leslie Iversen *says that the potential for MK-801 to limit neuronal injury after ischemia depends on "the relatively new idea that excitatory neurotransmitters act as toxins and contribute to much of the brain damage."*

A second area of controversy concerns the possible mechanisms of cell death in ischemia. Iversen points out that once the excitatory transmitter glutamate is released during ischemia, it probably triggers a feed-forward process: "The more excitation you have, the more glutamate release you have. Beyond a certain point nerve cells are no longer capable of surviving because they are being excited at the same time as they are being metabolically compromised."

According to Marcus Raichle of Washington University School of Medicine in St. Louis, however, brain damage in heart attack and stroke patients is a very complex process that cannot be explained solely on the basis of toxic levels of glutamate. Rather, ischemia produces "a terrible jungle of trouble," he says. It induces changes in oxygen levels, glucose metabolism, acidity, and calcium concentration, as well as the production of free radicals and other cellular substances that may be toxic. "But we can't throw up our hands and say that nothing can be done," he says. "We have to pick this thing apart, and excitatory amino acids may play an important role in the damage."

In the United States, MK-801 was tested initially as a potential anticonvulsant but the trials were suspended according to Marvin Jaffe of Merck Sharp & Dohme Research Laboratories in West Point, Pennsylvania. "We believe that MK-801, which was given orally to epilepsy patients, did not achieve adequate plasma levels," he says. "We are now entering into a series of studies to test the tolerance of healthy volunteers when the drug is injected systemically."

Iversen, Erik Wong, John Kemp, Tony Priestley, Antony Knight, Geoffrey Woodruff, and Ramy Gill, all of Merck, now find that MK-801 may salvage brain neurons from ischemia because the drug penetrates the brain in therapeutic quantities after a single injected dose, and it protects a large percentage (40% to 50%) of hippocampal neurons even 24 hours after ischemia occurs.

In these respects MK-801 offers benefits not seen with another glutamate blocker, 2-amino-7-phosphonoheptanoic acid (APH). Brian Meldrum of the Institute of Psychiatry in London and his colleagues have shown that APH also protects rat hippocampal neurons from ischemic damage, but only if it is injected directly into the brain before ischemia is induced—a distinct drawback if the drug were to be used clinically in humans.

One way the Merck researchers measure the therapeutic effects of MK-801 is by determining how many neurons the drug rescues from death. But according to Bruce Volpe, also of Cornell, "you need to do more than count the number of cells. Cell sparing is very important, but it is also critical to assess neuronal function." Volpe finds that of the 15 to 20% of heart attack victims who survive a subsequent 6 hours of coma, fewer than 10% can function well enough to return to their jobs. So a critical test for any protective drug would be to preserve neuronal function, particularly of the ischemia-sensitive hippocampal neurons that are essential for cognitive activities.

MK-801 "probably works on the sodium channel that is controlled by NMDA [*N*-methyl-D-aspartate] receptors," Iversen says, and its activity requires the presence of glutamate. "In the jargon of the trade, MK-801 is called an open channel blocker because it requires the ion channel [that is activated by glutamate] to be in the open position before it can act."

Because MK-801 is somewhat similar in its action to the psychostimulant phencyclidine (PCP), Iversen cautions that "we don't know how widely a compound like MK-801 can be used because of its similarities to PCP." He proposes that PCP may act by binding at two different receptor sites, one of which is the same class of NMDA receptors affected by MK-801. Jaffe indicates that it is still too early to tell whether injected doses of the drug cause PCP-like effects in the volunteers now being tested.

The Food and Drug Administration (FDA) approved MK-801 for initial clinical testing in the United States, and Merck is now conducting studies in volunteers for their tolerance to injected doses of the drug. According to Jaffe, if MK-801 shows no unexpected side effects at doses comparable to therapeutic levels in animals, then Merck will apply to the FDA to test it as a neuroprotective agent. ■ **DEBORAH M. BARNES**

ADDITIONAL READING

E. H. F. Wong *et al.*, "The anticonvulsant MK-801 is a potent *N*-methyl-D-aspartate antagonist," *Proc. Natl. Acad. Sci. U.S.A.* **83**, 7104 (1986).

R. P. Simon *et al.*, "Blockade of *N*-methyl-D-aspartate receptors may protect against ischemic damage in the brain," *Science* **226**, 850 (1984).

Values of Fundamental Constants Adjusted

Since many of the fundamental physical constants are related, when new measurements of improved accuracy accumulate, it is necessary to adjust the values of all to make them consistent

After a 5-year study, the Committee on Data for Science and Technology (CODATA) of the International Council of Scientific Unions has released its new recommended values of the fundamental physical constants.* As compared to those in the previous 1973 CODATA recommendations, the uncertainties in the new values are smaller by about a factor of 10, reflecting significantly improved accuracy in measurements, sometimes by altogether new techniques.

Although there are no earth-shaking changes in any of the constants, some of their values have changed by more than three times the uncertainties listed in the 1973 adjustment (see table). The statistical probability for this is only 1%, but statistics can be distorted by "bad data" in the literature that are not recognized. "Once you get rid of the bad data, everything hangs together well," says E. Richard Cohen of the Rockwell International Science Center in Thousand Oaks, California, who coauthored the CODATA report with Barry N. Taylor of the National Bureau of Standards (NBS) in Gaithersburg, Maryland. "No more big changes are expected in the future," adds Cohen.

Fundamental constants are different from international standards, such as the length of the meter and the duration of the second, and fall into several categories. Some are constants of proportionality in the equations of fundamental physical theories, such as Planck's constant (h), which relates the energy of a photon to its frequency, and the speed of light (c), which relates the energy of a body to its mass. Other constants, such as the mass (m_e) and charge (e) of the electron, characterize the elementary constituents of matter.

Still other constants are not fundamental in the usual sense, but nonetheless play a similar role. Some of these constants are conversion factors that relate the values of "as maintained" electrical standards to their-

Recommended values of selected fundamental constants from the 1986 least-squares adjustment.

Constant*	Recommended value†	Uncertainty (ppm)
α^{-1}	137.0359895 (61)	0.045
e	1.60217733 (49)	0.30
h	6.6260755 (40)	0.60
m_e	9.1093897 (54)	0.59
N_A	6.0221367 (36)	0.59
m_p/m_e	1836.152701 (37)	0.020
F	96485.309 (29)	0.30
$2e/h$	483597.67 (14)	0.30

*The constants are defined in the text except m_p, the mass of the proton. †The units for e are 10^{-19} C; for h, 10^{-34} J-sec; for m_e, 10^{-31} kg; for N_A, 10^{23} mol^{-1}; for F, C mol^{-1}; and for $2e/h$, Ghz/V. The digits in parentheses are the one-standard-deviation uncertainties in the last digits of the given value.

Système International (SI) definitions. For example, the value of the volt is maintained at various national standards laboratories, such as NBS, in terms of the frequency of the alternating current in a superconducting Josephson junction. The ratio of the "as maintained" volt determined in this way to the SI definition of the volt is a constant (K_V) that differs slightly from unity.

Despite the name fundamental, the constants are not independent. The fine-structure constant (α) that is a measure of the strength of the electromagnetic interaction in quantum electrodynamics is defined in terms of other fundamental constants and is proportional to ce^2/h. Similarly, the constant relating the "as maintained" volt to its defined value is proportional to h/e. Since these "composite" constants can be measured directly and are in every sense fundamental in their own right, it is a matter of taste which constants one regards as the composites.

More important, inconsistencies may arise between the directly measured value of a constant and the value or values inferred from the separate values of the various combinations of constants in terms of which it can be expressed. The procedure for ironing out inconsistencies, which was pioneered at the University of California at Berkeley in the late 1920s by Raymond Birge, is called a least-squares adjustment. The latest and most comprehensive adjustments have been those by Taylor, William Parker, and Don-

**The 1986 Adjustment of the Fundamental Physical Constants*, CODATA Bulletin 63 is available in North America from Pergamon Press Inc., Elmsford, NY, 10523 for $15 and elsewhere from Pergamon Press Ltd., Headington Hill Hall, Oxford OX3 0BW, United Kingdom.