



Electrocardiograph trace falls to zero (arrow) indicating moment of death by a criterion likely to be replaced.

Death and suspended animation

While doctors seek definitions of the end of life, their laboratory colleagues make the task harder

Mimicking death

It has been suspected for the past few years that oxygen is not the physiological tyrant that scientists once thought it was.

The idea is still pretty popular, even among scientists, that whatever tissues lack, the one thing they cannot last long without is oxygen. It is axiomatic, for instance, that after three minutes of halted blood circulation, the brain dies for lack of oxygen.

That this axiom may not be true is rather forcefully demonstrated by experiments performed by a group under Lt. Col. Gerald Klebanoff, chief of experimental surgery of the Aerospace Medical Laboratory at Lackland Air Force Base in San Antonio, Tex.

Col. Klebanoff has succeeded in putting 26 dogs in a true state of suspended animation, in which they required neither oxygen nor nutrients.

Faced with Col. Klebanoff's results and other low temperature results, many scientists at the Society for Cryobiology meeting in Washington early this month concluded that it is time to discard the oxygen barrier. It has been already suggested that the problem of circulation stoppage to the brain is not lack of oxygen. Rather, the brain is unable to get circulation going again.

The brain is well supplied with capillaries. Brain researchers now are turning to the idea that as soon as circulation to the brain stops, the network of capillaries becomes choked with masses of blood platelets, tiny disks that aid in blood clotting.

After the clotting occurs, if circulation starts up again there are sectors of the network through which blood can-

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Defining death

Transplant surgery has brought with it efforts in many parts of the world to define the symptoms of death. And while the controversy roils, current research seems to make the definition even more difficult.

It is a problem with which the doctors must live, even if there are some who deny they have any need to wrestle with it.

During a meeting of 13 heart transplant surgeons in Capetown, South Africa, last month, for instance, there was no heated controversy among them on the question of determination of death.

It was, reports Dr. Denton Cooley of Houston, Tex., who has performed eight transplants so far, "probably because all of us had answered this question for ourselves a long time ago." This means essentially that the donor should have no electrical brain waves. When the brain dies, the person dies. But the problem remains, when is the brain finally dead?

When the members of the World Medical Association, representatives of some 700,000 physicians, met in Australia this month, they sidestepped the problem—deliberately.

According to Sir Leonard Mallen, president of the association, "With scientific advances and new methods of resuscitation always coming up, it would be silly of us to give a definition which could be outmoded within half an hour."

The delegates did adopt a code that calls for two physicians unconnected with a transplant team to determine the donor's death—whatever that is.

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not pass. The closed sectors die. The longer circulation is down, the more of the brain is damaged, to the point of death. This would explain the progressive brain damage that occurs when circulation is interrupted.

Tissues can be protected either by getting rid of the clot-prone blood before circulation is stopped, or by reducing or eliminating the tissues' need for oxygen by cooling them.

Both methods in tandem obviously would produce the best results; and this is what Col. Klebanoff does. He has kept dogs in suspension for 80 minutes, then revived them again, with 75 percent success.

Among implications of such work must now be included interplanetary and interstellar travel under hibernation, and suspension to wait for the "Brave New World." Col. Klebanoff himself expects research one day to go in that direction. For the moment, however, the process is limited in concept to a few hours or days at most.

Col. Klebanoff sees some immediate benefits of the technique, however, as well as possible human application within two or three years. The first fruit is likely to fall in the biochemists' labs.

One of the difficulties faced by biochemists is the extreme and unscientific variability of their living subjects. If you want to study the effect of a drug on a dog's kidney, for instance, you either have to inject the drug into the whole dog with kidney in place, or remove the organ and treat it.

The first way puts the whole dog between stimulus and response, so that effects observed might be direct or they might be fourth-hand. The second way deprives the kidney of its working environment and may affect the result. Various ways around this dilemma are practiced, but what is really needed is an animal, like Col. Klebanoff's dogs, with all the switches turned off.

Then the undisturbed kidney could be turned on again, leaving the rest of the dog out of action. Monitoring the operation of the organ would provide a baseline against which experimental tinkering could be measured.

In a very few years, Col. Klebanoff thinks, refrigerated, bloodless perfusion will be tried on humans in surgery.

Anesthesia would be unneeded and its risks avoided. The surgeon would not have to race the clock in the knowledge that his stop-gap measures to support full metabolism work only so long. The surgical field would be bloodless and the tissues given an easily handled plastic consistency.

In a pinch suspended animation might be used to hold a dying patient over

until supportive measures could be arranged or transplant organs obtained.

The technique throws something of a wrinkle into current discussions about the definition of death. Various august bodies around the world have attempted this definition, though some physicians feel the attempt is mistaken.

Though a flat brainwave is generally coming to be accepted as the sign of death, Col. Klebanoff's dogs did survive flat brainwaves. He provides the answers, a bit circularly, by saying that, first, his dogs are cooled and need no oxygen, second, that they will not suffer brain clots because they lack blood, and third, the acid test, that they are revivable.

Col. Klebanoff says his dogs are drained of blood while an electrolyte cooled to between 0 and 5 degrees C. is pumped in to replace it.

The blood count is taken down by this method to between 0 and 2 percent of normal in about 14 minutes. Within 20 minutes the core temperature of the dog reaches 5 to 10 degrees C., about the temperature of meat in a fairly cold refrigerator. The perfusion fluid is kept circulating slowly with gentle pressure.

At this point the dog exhibits no vital signs whatsoever. There are no brain waves, reflexes, heart or respiratory activity.

Anyone not knowing what is going on would have to conclude that the animal is dead. By every known clinical test it is, though Col. Klebanoff believes some slight brain activity might be detected by an electroencephalograph more sensitive than any he's been able to apply.

The majority of the dogs which do not survive, he says, die not from brain damage but heart damage. The pressure of the perfusion pump strains the heart, vulnerable in its cooled state, and it fails on rewarming.

The survivors all show some heart damage on the electrocardiogram. However, the abnormal traces disappear after about a month of recuperation. In other respects the revived dogs seem to behave as 40-pound mongrels should.

Preliminary work along these lines has been going on for half a dozen years. Blood in animals has been successfully replaced with an artificial oxygen carrier. And a Japanese team replaced the blood in the brains of cats with electrolyte, isolated the brains and froze them (SN: 11/5/66, p. 368). Upon thawing, the brains showed evidence of electrical activity.

Russian researchers demonstrated almost two years ago (SN: 12/24/66, p. 536) that the brain can survive lethally low atmospheric concentrations of oxygen, provided it is cooled.

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During the Capetown meeting the surgeons agreed that neurological examination and electroencephalograph tracings should show no signs of cerebral activity if death were to be declared. But "we did not define the length of time this should be so," Dr. Cooley declares.

"In most heart transplants performed to date, this period exceeded two hours," he says. "In two of my donors, there was a flattened EEG for four days prior to transplantation."

The old criterion of a stopped heart and breathing as a sign of death depends on what caused the stoppage.

Dr. Roger L. Black, assistant director of the National Institutes of Health's clinical center, says heart and lung stoppage might be proof of death in a cancer patient, but not in a drowning victim. Mouth-to-mouth resuscitation can get the heart and lungs going in many cases.

At the NIH center, definition of death is left to the individual physicians with individual patients.

"The dialogues on this issue are most welcome, however," Dr. Black says. "Physicians across the country and the world have been confronted with problems that further discussion could help solve."

And dialogues there have certainly been. The American Medical Association's House of Delegates at the June 1968 convention in San Francisco approved ethical guidelines for organ transplantation; which included a paragraph on donor death.

The AMA would require an independent corroboration of death to be determined by the clinical judgment of the physician using "all available currently accepted scientific tests."

And a 13-member committee of the Harvard Medical School issued clinical guidelines for finding brain death, or irreversible coma. They suggest, in the August 5 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION: lack of brain waves; lack of response to any stimulus; no reflexes; no movement, or breathing, for at least an hour. Both clinical and machine tests should be repeated after 24 hours.

"At present," says the committee, "the law of the U.S. in all 50 states and in the Federal courts treats the question of human death as a question of fact to be decided in every case. When any doubt exists the courts seek medical expert testimony concerning the time of death of the particular individual involved. However, the law makes the assumption that the medical criteria for determining death are settled and not a doubt among physicians."