Alcor Foundation
7895 East Acoma Drive
Scottsdale, AZ 85260-6916

Phone 480-905-1906
Fax 480-922-9027
Information 877-GO-ALCOR
email info@alcor.org
web http://www.alcor.org

The Biology of Cryonics

A Quick Summary for Medical Professionals

by Charles Platt, for Alcor Foundation, November 2002;
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1. Fundamental Purpose

We believe that intelligence, memories, and personality are determined primarily by the structure and chemistry of the human brain. Our aim is to preserve the brain so faithfully that its unique identity will also be preserved, so that future science may be able to revive the individual. We realize that this is highly speculative, but we feel that human life is sufficiently precious to justify our attempt, even though the outcome is unknown.

2. The Nature of Life and Death

Neurons depend on a steady supply of oxygen and glucose delivered by the blood stream. At normal body temperature, after about ten minutes of cardiac arrest, most neurons have consumed their last reserves of fuel and a complex process of ischemic injury has begun. While this process is not fully understood, we know that the outcome of cardiopulmonary support (CPS) tends to be poor if it is attempted on patients who have endured more than six to eight minutes of zero blood flow at normal body temperature.

This picture changes dramatically when a patient experiences hypothermia (lowered body temperature) after cardiac arrest. Resuscitation medicine has successfully revived patients after more than two hours without any vital signs, in cases where the patients have fallen into ice-cold water or snow. From the Arrhenius equation, which was derived more than a century ago, we understand that all chemical reactions occur more slowly at lower temperatures; and harmful chemical reactions on a cellular level are no exception to this rule.

Resuscitation medicine also has determined that medications such as antioxidants and calcium channel blockers may help to inhibit postischemic injury.

3. Initial Procedures

We begin our attempt to protect and preserve the brain by using medications, CPS, and external cooling immediately after cardiac arrest. From our perspective, so long as the integrity of the brain is protected, the patient retains some chance of renewed life in the future.

Ideally, within minutes after legal death has been pronounced, we immerse the patient in a portable ice bath, inject medications to minimize blood coagulation and postischemic injury, provide oxygen, and use mechanical CPS to induce circulation. This process of cooling coupled with metabolic support continues without interruption as we move the patient to a suitable location (often a mortuary) where we raise the femoral vessels, cannulate them, and wash out the blood with a preservation solution similar to formulations that are used routinely to preserve organs donated for transplantation.

4. What We Need

To perform our initial procedures, ideally we hope that legal death will be pronounced quickly. We prefer that the patient will have an IV installed, enabling us to administer drugs such as heparin and streptokinase to reduce the risk of blood clotting. We will attempt to intubate a patient to maximize the effective delivery of oxygen. Because the patient has been pronounced, the steps we take are not classified as medical procedures and are not subject to medical regulations.

If hospital policy or other circumstances make it impossible for us to perform our procedures postmortem, we will move the patient offsite as rapidly as possible. At a minimum, we hope to inject heparin and administer some CPS to circulate the heparin throughout the body.

5. What Can Go Wrong

Our procedures will be less effective if we cannot reach a patient promptly. Blood clots will obstruct our access to the circulatory system, and may result in catastrophic brain damage. A prolonged period of cardiac arrest at normothermic temperature will also cause brain damage. The precise length of this interval, and the reversibility of ischemic injury, are controversial; but obviously we have a better chance if we can intervene promptly. Time is of the essence.

If a patient is atherosclerotic, fragile blood vessels will be difficult to cannulate and may rupture during perfusion. If a patient suffers from respiratory conditions such as pneumonia, the lungs may be unable to oxygenate the blood. We cope with these problems as best we can.

Our worst-case scenario is accidental death, which may entail an autopsy. In such

Our members choose the “neuro option” for various reasons. First, we may be able to provide more effective and complete cryoprotection if our efforts are focused solely on the brain. Second, our long-term maintenance costs are much lower. Third, the patient will be easier to relocate if this is ever necessary. Alcor has successfully moved all of its whole-body patients from our previous location in California to our current facility in Arizona, but this was a difficult and delicate operation. By contrast, a neuropatient can be transported in a small LR-40 Dewar in a minivan.

At the present time Alcor can apply vitrification techniques to whole-body cases as well as neuropatients. Under good conditions the brain is expected to vitrify in both types of patients. Other tissues in whole-body patients are expected to undergo vitrification or limited freezing depending on the tissue type. Alcor treats the entire body of whole-body patients with advanced cryoprotectants to inhibit ice formation.

12. Informed Consent

We caution all of our members and applicants that the results of human cryopreservation are impossible to predict. All members have been fully informed about the possibilities of irreversible damage that may prevent resuscitation by any future technology, and they have signed documents affirming that they are taking a gamble where the odds are unknown.

We do everything we can to eliminate any chance that we are offering false hope to people who are afraid of death. We will not accept members unless they or their agents are competent to make medical or legal decisions. We are cautious about accepting last-minute cases where a patient’s rationality is in doubt.

On the other hand, when we are sure that a person has given informed consent for our procedures, we will defend our right to provide those procedures. In some cases, family members have objected to cryonics, and have sued to take possession of of cryopreserved patients in our care. We have resisted such challenges vigorously, because we believe that all people have an absolute right to choose the way in which they are treated after legal death, so long as their choice does not violate the law or harm other people.

13. Additional Information

Cryonics raises many questions that may not be covered in this brief document. If you would like to learn more about our procedures or the principles on which we have based them, we will be happy to respond. As a tax-exempt organization, part of our purpose is to disseminate information. We also maintain a library of informative publications and can provide references to relevant papers by cryobiologists.

10. Damage Repair

Many cryonics patients were preserved before vitrification was possible. Their brains were protected only by a glycerol solution, which could not prevent significant injury. Some people suggest that we may be wasting our resources by preserving people who have been subjected to such damage.

This is not necessarily true. Nobel laureate Richard Feynman predicted in 1959 that mechanical devices could be miniaturized down to the molecular level. He pointed out that there is no physical law to prevent us from moving individual atoms, which could be assembled to create “molecular machines.”

Feynman’s prediction has been validated by the scanning-tunneling electron microscope. Scientists at IBM have demonstrated that this device can use an ultrafine probe to manipulate individual atoms.

Computer scientist Eric Drexler suggested that this principle could be applied in an entirely new area of science which Drexler named “molecular nanotechnology,” meaning that it would work on the scale of a nanometer—one billionth of a meter. Drexler proved theoretically that a molecular machine the size of a bacterium could contain onboard computing power equivalent to a modest-sized microprocessor chip. The machine could make copies of itself, or could be programmed to perform tasks in the same way that industrial robots are programmed today. He suggested that billions of molecular machines could invade a cryopatient and perform repairs on individual cells. Thus, nanotechnology offers some hope of repairing ice damage.

This is highly speculative, and we do not expect sophisticated nanotechnology in the near future. Still, our cryopatients are in no hurry. At the temperature of liquid nitrogen, they remain unchanged as the years pass.

Our goal is to refine the process of cryopreservation to the point where it causes so little damage, a person can be resuscitated without any need for repairs via technology that has not been developed yet. In the meantime, we provide the best protection we can, because this is the only alternative to permanent death.

11. Preserving Only the Brain

We are confident that tissue regeneration will be perfected to the point where a new human body can be regrown around a brain. This technology will be a natural progression from imminent technologies that will enable spinal regeneration, limb regeneration, and organ regeneration following severe trauma. Since many Alcor members feel confident that future science will be capable of growing a new body, they choose to preserve only the brain. In practice this means that we preserve the entire head of each “neuropatient,” since the skull provides optimal protection for the brain. The remainder of the patient is usually cremated.

a case the waiting period can last for days, and the autopsy usually entails dissection of the brain. When the patient is finally released into our possession, we will still attempt cryopreservation if the patient’s signup documents directed us to make this attempt under any circumstances. We have an ethical and legal obligation to follow our members’ wishes, even in situations where future resuscitation seems vanishingly plausible.

6. Subsequent Procedures

After blood washout and perfusion with organ preservation solution, the patient is moved as quickly as possible to our operating room. If legal death has occurred in a remote location, the patient is covered with bags of ice, placed in a standard mortuary shipping container, and transported to Alcor by scheduled airline or chartered jet.

Our task now is to protect the patient from freezing damage. Normally, as the temperature falls below 0 degrees Celsius, ice grows between cells causing cellular dehydration and mechanical injury. Ideally we prevent this damage by perfusing the patient with a “vitrification solution” similar to solutions that have been used experimentally for ice-free preservation of transplantable organs. The solution is circulated at increasing concentration, and decreasing temperature, through the vascular system for four to five hours. It replaces more than half of the water around and inside cells with chemicals that prevent ice formation, even at an extremely low temperature. When the process is complete, we cool the patient to -196 degrees Celsius, which is the temperature of liquid nitrogen. For all practical purposes, biological processes cease.

7. Long-Term Cryopreservation

Liquid nitrogen is cheaply available in bulk in many urban areas. We receive deliveries from a local supplier and pipe it into “Dewars” that function like oversize Thermos bottles. Each Dewar is vacuum-insulated and large enough to hold four whole-body cryopatients. Since the liquid is delivered at –196 degrees, we do not need refrigeration equipment. Gradually some heat penetrates the Dewars and causes some of the liquid nitrogen to vaporize, but when the level falls, we receive another delivery to replace the boiloff. Our storage facility is unaffected by power outages, and our reserves of liquid nitrogen can last for up to a month between deliveries.

While Alcor cannot guarantee the survival of its cryopatients or itself as a corporate entity, we are a nonprofit, tax-exempt organization under section 501(c)3 of the tax code. Our bylaws were designed to protect us from hostile acquisition or asset-stripping, and all of our patients are prepaid, usually via life insurance policies. After we cover the costs of cryopreservation, the remainder of each patient’s funding is placed in a trust that generates interest to pay for liquid nitrogen for the indefinite future.

8. The Legal Basis for Cryonics

The Uniform Anatomical Gift Act (UAGA), which has been adopted by all 50 states, provides a mechanism by which medical or research organizations may take possession of organs that are donated for transplant or research. Our members have executed a document affirming their desire to donate all of their organs—their entire body—to Alcor. Thus, Alcor is entitled to take possession of the patient under the Uniform Anatomical Gift Act. We will be glad to provide a copy of any member's UAGA document to any medical organization or professional who will respect our member's wishes for confidentiality.

Burial and cremation of human remains are controlled by state laws, but human cryopreservation is not subject to these statutes, since it is a relatively new process. Naturally Alcor must comply with legal requirements such as pronouncement of death by a medically qualified person, and must execute standard documents that enable transportation of a deceased person across state or county lines. We are affiliated with a mortician who insures that correct procedures are followed.

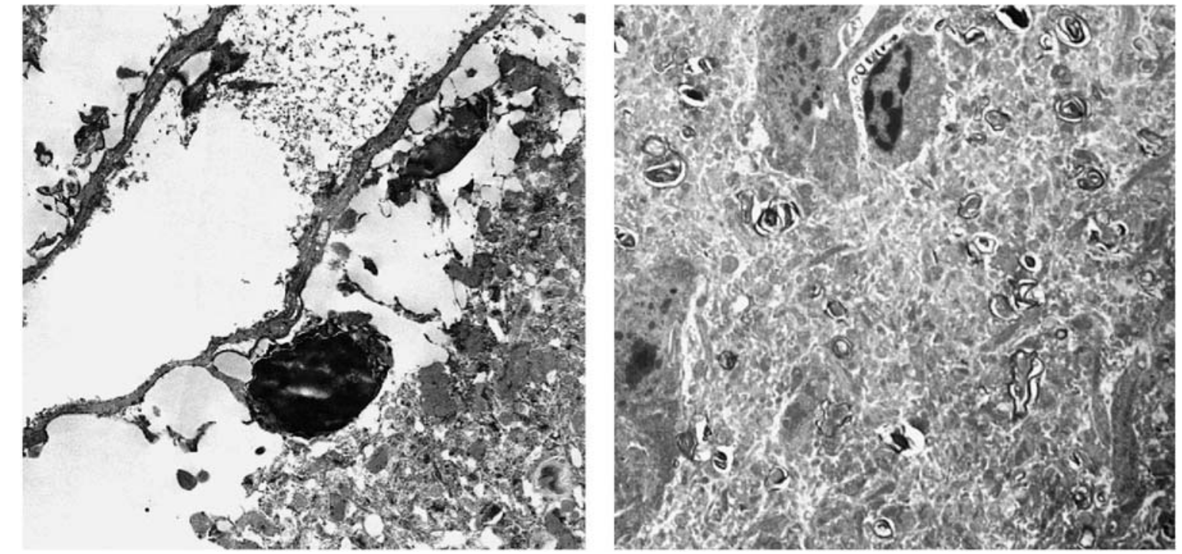
Some people have suggested that we could optimize brain preservation if our members could choose their time of death. This is often true, especially in cases involving cerebral tumors. However, assisted suicide remains illegal in almost every state, and would provide grounds for an autopsy. In any case, our primary motivation is to maximize human life, not curtail it. For obvious ethical and legal reasons Alcor cannot be involved in any treatment of a patient before legal death is pronounced, and cannot attempt to influence the pronouncement.

9. The Biological Basis of Cryoprotection

News stories about cryonics often include quotes from scientists who state that ice damage is irreversible. Unfortunately, in almost every case, these scientists are not cryobiologists. Consequently they are not properly informed or qualified to give an opinion on the inevitability of ice damage in brain tissue.

The field of cryobiology was established fifty years ago by British scientists who derived its name from the Greek word "kryos," meaning "cold." Their early work demonstrated that some types of cells could be rewarmed and revived successfully if they were soaked in a solution of glycerol before freezing. The glycerol functioned as a "cryoprotectant," replacing some of the water and minimizing ice damage that would normally occur.

Today, glycerol is used routinely to protect semen samples and very small human embryos before the cells are immersed in liquid nitrogen. Not all embryos survive this procedure, but many have been rewarmed and implanted, and have matured as normal, healthy human beings. These people—many of them now grown to adulthood—



Advances in Brain Cryopreservation: *Left, electron micrograph shows severe damage in brain tissue by traditional protection from freezing. Either side of a capillary, massive tears (white areas) have been caused by ice. A naked cell nucleus with no cell membrane is visible (dark rounded object). This is the kind of damage that many commentators assume is common among cryonics patients. Their assumption is outdated and inaccurate.*

Right, brain tissue preserved with a modern vitrification solution shows virtually no ice damage. Whole neurons are visible with intact membranes and well defined structure. This is the excellent preservation which Alcor can achieve in human patients. Most commentators who complain about irreparable damage caused by cryonics procedures are unaware that such preservation is now possible, under optimal circumstances.

demonstrate that human life can resume after weeks, months, or years in stasis at a very low temperature.

Unfortunately, glycerol is toxic at high concentrations and cannot provide sufficient protection to guarantee 100 percent survival. Also, while it is reasonably effective on individual cells or small clusters of cells that retain some individual mobility, it does not provide adequate protection for large, highly structured organs such as the brain. For decades this problem seemed intractable, but in the late 1990s some scientists working in the field of cryobiology developed vitrification solutions that can prevent ice in large organs under ideal conditions. Instead of forming ice crystals, the water becomes a uniform, "vitreous" substance.

While today's vitrification solutions have not received certification yet for use with living patients, Alcor uses the solutions to preserve the human brain because they cause far less toxicity than would occur with other methods of morphological preservation, such as chemical fixation. Preliminary electron micrographs indicate excellent preservation of ultrastructure in animal brain samples. Ice damage no longer needs to occur, so long as the patient's vascular system is sufficiently robust and unobstructed to permit cryoprotective perfusion.