Ethics in Biology, Engineering & Medicine - An International Journal, 3(1-3): 9–28 (2012)

Cryonic Life Extension: Scientific Possibility or Stupid Pipe Dream?

D. John Doyle

Professor of Anesthesiology and Staff Anesthesiologist, Department of General Anesthesiology, Cleveland Clinic Foundation, 9500 Euclid Avenue - E31, Cleveland, Ohio, 44195, Phone: (216) 444-1927, djdoyle@hotmail.com.

ABSTRACT: The central quest in cryonics is to preserve brain-encoded information essential to personhood after cryonic preservation. Advocates of cryonics seek to use cryoprotectants, vitrification, and extreme cold to extend the life of an individual when conventional methods fail. This means of life extension is employed for an intended period of decades, or even centuries, until safe reversal of the preservation process, as well as treatment for the underlying medical condition, becomes feasible.

Such an undertaking is predicated on three principles, only one being well established. The first is that life can be suspended as long as attention is directed at preserving the basic biological structures upon which life is based. The second is that technology will become available to extend the first principle to human organisms. The third is that post-thawing cellular damage might be repaired, for example using nanomedicine.

However, a number of problematic scenarios may emerge as the required innovations are developed. Consider some possible outcomes where only the head is cryopreserved: (1) failure to reanimate the individual, (2) existence as a reanimated head attached to a new body, and (3) existence as a reanimated head existing independently from a body. Additional issues emerge: What moral standing does the cryopreserved individual now have? What is the legal and moral status of individuals who end up technically alive but with severe neurological damage? And finally, who should be responsible for the care of a thawed patient who requires complex medical care?

KEY WORDS: Cryonics, cryopreservation, death, moral standing, reanimation

"I've long thought it a pity that non-transhumanists equate trying to conquer death with a childish fear of death and a lack of wisdom. This is like saying Sir Edmund Hillary had a childish fear of mountains."—Philip Goetz

I. WHAT IS CRYONICS?

The central scientific quest in cryonics is to develop, test, and validate technology that would preserve brain-encoded information essential to personhood after cryonic preservation. Advocates of cryonics seek to use cryoprotectants, vitrification, and extreme cold (such as immersion in liquid nitrogen) to extend the life of an individual who can no longer be sustained for long periods by conventional medical technology (Figs. 1–3). This cryonic life extension is employed for an intended period of decades or even centuries, until safe reversal of the preservation process, as well as treatment for the underlying medical condition, becomes feasible as a result of new advances in medicine and technology. Such an under-

FIGURE 1. The bodies or severed heads of a number of "patients" in cryogenic storage await future cures for their conditions at the Alcor Life Extension Foundation in Scottsdale, Arizona. Each of these liquid-nitrogen-filled steel "Dewars" can hold up to four "whole-body" patients and five "head-only" preserved patients at –196° Celsius. Cellular damage is reduced through a process of "vitrification," which inhibits the formation of cell-damaging ice-crystals by producing glassy molecular arrangement within the cells. Photograph courtesy Alcor Life Extension Foundation.

taking is predicated on three important principles, only one of which is currently well established at this time.

The first principle of cryonics is that life can be stopped or suspended as long as appropriate attention is directed at preserving the basic biological structures upon which life is based. Although this principle is well established for a number of animal species as well as for human embryos,[1] much needs to be done to extend the principle to include full human beings. That said, this is a field of active research in medical science and it is reasonable to expect researchers in these fields will continue to unveil interesting developments.

A second principle is that the use of cryoprotectants and vitrification will be useful in extending the first principle to larger organisms such as adult human beings. Progress on this second principle is now occurring at the level of entire organs. One particularly important scientist in this field is Gregory M. Fahy, who has achieved successful vitrification and autotransplantation of a rabbit kidney using his (proprietary) M22 vitrification solution.[2]

ALCOR
LIFE EXTENSION FOUNDATION SINCE 1972

Understanding the Cryopreservation Process

An overview of our procedure is below with full details available here: http://www.alcor.org/procedures.html

The clinically and legally deceased patient is placed in an ice water bath, and blood circulation and breathing are artificially restored by a heart-lung resuscitator. The combination of simultaneous cardiopulmonary support (CPS, similar to CPR) and rapid cooling are known to be especially effective for protecting the brain during cardiac arrest. Intravenous lines are established and protective medications are administered.

If the patient is in a hospital, the patient is moved to an alternate location while CPS anc cooling are maintained without interruption. Femoral arteries and veins are surgically accessed and the patient is placed on cardiopulmonary bypass. This means that blood is circulated through a portable heart-lung machine that takes over the function of the patient's own heart and lungs. External CPS is no longer necessary and is discontinued.

Within minutes, a heat exchanger in the heart-lung machine reduces the patient's temperature to a few degrees above the freezing point of water. The blood is replaced with an organ preservation solution that is specially designed to support life at low temperature. If the patient is located outside of Arizona, they are covered in ice for air shipment to Alcor's facility in Scottsdale, Arizona.

At Alcor a surgeon connects major blood vessels to a perfusion circuit. A perfusate similar to the preservation solution used during transport is circulated through the patient at a temperature near 0°C (the freezing point of water) for several minutes. This washes out any remaining blood. The cryoprotectant concentration is then linearly increased over two hours. This slow introduction minimizes osmotic stress and allows time for the cryoprotectant concentration to equilibrate inside and outside cells. A rapid increase to the final concentration is then made. Temperature, pressure, and cryoprotectant concentration data are continuously monitored by computer.

The status of the brain is visually monitored through two small holes in the skull made using a standard neurosurgical tool (14 mm Codman perforator). This permits verification of brain perfusion and observation of the osmotic response of the brain. A healthy brain slightly retracts from the skull in response to cryoprotectant perfusion. An injured brain swells, indicating that the blood-brain barrier has been compromised. This injury is often seen in patients who suffered a long period of untreated cardiac arrest.

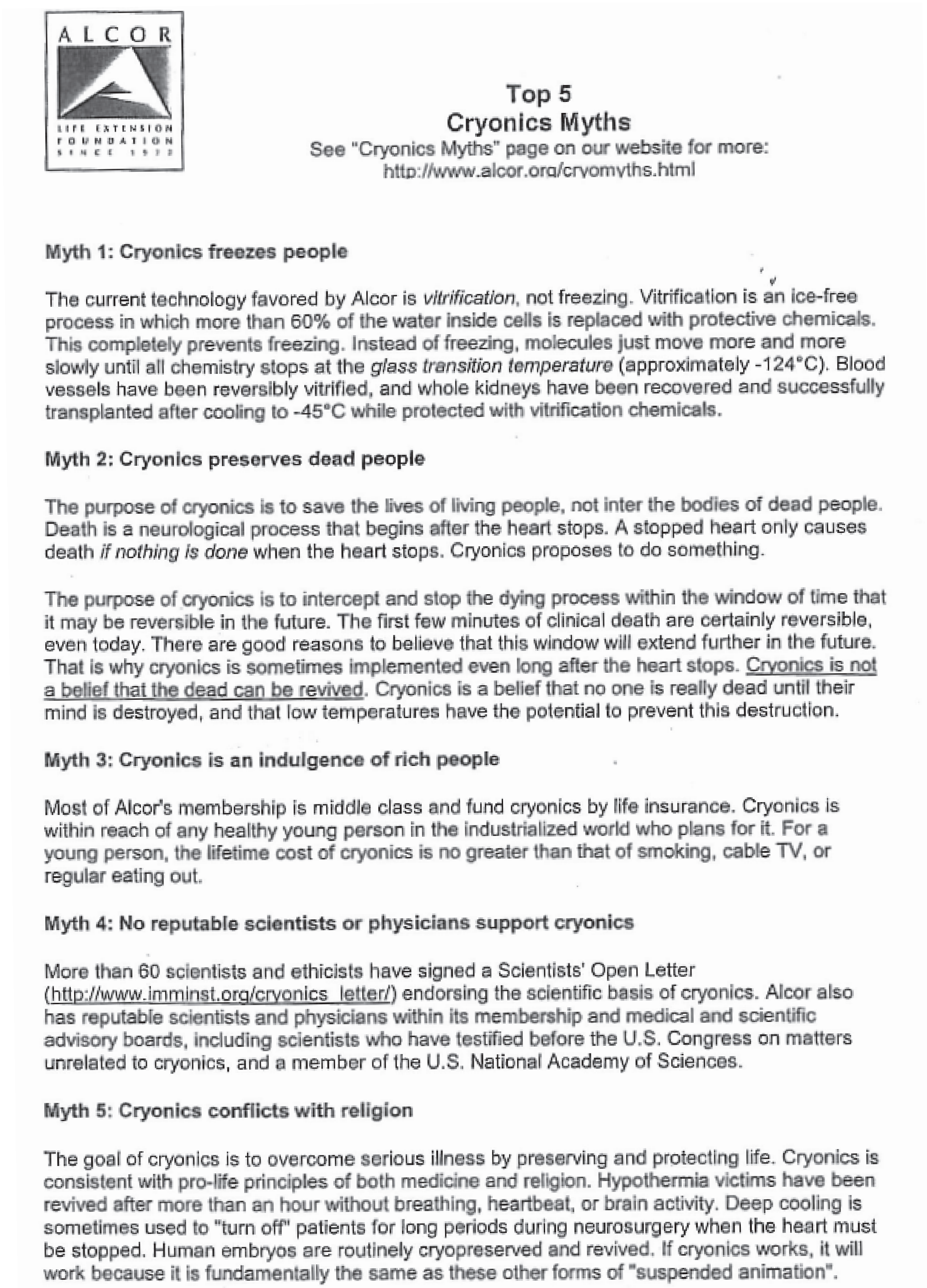
After cryoprotective perfusion, if the patient has selected whole body preservation, the patient is immersed in silicone oil for cooling to -79°C (the temperature of dry ice) at a rate of approximately 0.1°C per minute. This slow cooling is necessary to allow time for cell water movements that accompany freezing to occur. The patient will then be transferred to a cryogenic dewar for further cooling in nitrogen vapor to a temperature of -196°C over two weeks.

Neuropatients are cooled under computer control by high velocity nitrogen gas at a temperature of -130°C. The goal is to cool all parts of the patient below -124°C (the glass transition temperature) as quickly as possible to avoid any ice formation. This requires approximately three hours, at the end of which the patient will have "vitrified" (reached a stable, ice-free state). The patient is then further cooled to -196°C over approximately two weeks.

Patients are monitored by sensitive instruments during this long cooling period to detect fracturing events that tend to occur when large objects are cooled below the glass transition temperature. Contrary to media reports, fracturing is not a result of mishandling. It is a universal problem for large organs cooled to liquid nitrogen temperature.

Following cooling, patients are then transferred into liquid nitrogen at a temperature of -196°C. They are thereafter kept in Alcor's Patient Care Bay. Since Alcor uses liquid nitrogen to keep cryonics patients cold, electricity is not required for current patient care systems.

FIGURE 2. Synopsis of the cryopreservation process used at Alcor. Courtesy Alcor Life Extension Foundation.



ALCOR
LIFE EXTENSION FOUNDATION

Top 5
Cryonics Myths
See "Cryonics Myths" page on our website for more:
http://www.alcor.org/cryomyths.html

Myth 1: Cryonics freezes people

The current technology favored by Alcor is *vitrification*, not freezing. Vitrification is an ice-free process in which more than 60% of the water inside cells is replaced with protective chemicals. This completely prevents freezing. Instead of freezing, molecules just move more and more slowly until all chemistry stops at the *glass transition temperature* (approximately -124°C). Blood vessels have been reversibly vitrified, and whole kidneys have been recovered and successfully transplanted after cooling to -45°C while protected with vitrification chemicals.

Myth 2: Cryonics preserves dead people

The purpose of cryonics is to save the lives of living people, not inter the bodies of dead people. Death is a neurological process that begins after the heart stops. A stopped heart only causes death *if nothing is done* when the heart stops. Cryonics proposes to do something.

The purpose of cryonics is to intercept and stop the dying process within the window of time that it may be reversible in the future. The first few minutes of clinical death are certainly reversible, even today. There are good reasons to believe that this window will extend further in the future. That is why cryonics is sometimes implemented even long after the heart stops. Cryonics is not a belief that the dead can be revived. Cryonics is a belief that no one is really dead until their mind is destroyed, and that low temperatures have the potential to prevent this destruction.

Myth 3: Cryonics is an indulgence of rich people

Most of Alcor's membership is middle class and fund cryonics by life insurance. Cryonics is within reach of any healthy young person in the industrialized world who plans for it. For a young person, the lifetime cost of cryonics is no greater than that of smoking, cable TV, or regular eating out.

Myth 4: No reputable scientists or physicians support cryonics

More than 60 scientists and ethicists have signed a Scientists' Open Letter (http://www.imminst.org/cryonics_letter/) endorsing the scientific basis of cryonics. Alcor also has reputable scientists and physicians within its membership and medical and scientific advisory boards, including scientists who have testified before the U.S. Congress on matters unrelated to cryonics, and a member of the U.S. National Academy of Sciences.

Myth 5: Cryonics conflicts with religion

The goal of cryonics is to overcome serious illness by preserving and protecting life. Cryonics is consistent with pro-life principles of both medicine and religion. Hypothermia victims have been revived after more than an hour without breathing, heartbeat, or brain activity. Deep cooling is sometimes used to "turn off" patients for long periods during neurosurgery when the heart must be stopped. Human embryos are routinely cryopreserved and revived. If cryonics works, it will work because it is fundamentally the same as these other forms of "suspended animation".

FIGURE 3. Alcor informational brochure. Courtesy Alcor Life Extension Foundation.

The third and most controversial principle is that post-thawing damage to individual cells (especially neurons) might be repaired one molecule at a time using the emerging sciences of nanotechnology and nanomedicine. However, to the extent that cryonic preservation might eventually be achieved without damage to cellular structures, or may be achieved through naturally occurring biological repair mechanisms, the advanced molecular repair methods referred to above may not be necessary.

Additionally, it should be emphasized that—at least in principle—damage to individual cells may not always result in loss of the information needed to reconstruct a viable post-suspension organism. Should advanced methods become available to reconstruct the entire human organism from information reliably preserved and subsequently exploited despite the presence of cellular damage following cryonic suspension, this problem might be expected to vanish. One scenario here would be to clone an entire new body but with the special proviso that the information / identity / memories of the original organism be transferred to the new organism. In such cases the patient would emerge rejuvenated and "better than well" and without the lifespan limitations of the original cryopreserved tissue. Yet another possibility, should mind uploading and downloading ever become feasible, is that an individual become recovered in virtual reality.[*]

II. IS CRYONICS POSSIBLE IN PRINCIPLE?

Although so far alien to humans, the ability to endure winter freezing has developed in several species of frogs and turtles as well as in a number of species of insects and microorganisms. This suggests that with appropriate scientific advances reversible freezing of larger organisms might be possible in principle.

The evidence that reversible freezing of humans may eventually be possible comes from several sources. First, there is support from nature. For instance, the wood frog *Rana sylvatica* (Fig. 4) utilizes naturally-occurring cryoprotectants in order to survive low temperatures during winter months. This natural process utilizes glucose, derived from hepatic glycogen, as well as urea, as cryoprotectants.[3-5] As a result, these frogs can "endure freezing for at least 2 weeks with no breathing, no heart beat or blood circulation, and with up to 65% of their total body water as ice."[6] The spring peeper (*Pseudacris crucifer*) and the gray tree frog (*Hyla versicolor*) are other species that can withstand freezing temperatures during winter.[7]

*I am indebted to High Hixon for identifying this intriguing possibility. Mind uploading (whole brain emulation) is the hypothetical process of transferring a conscious mind from a biological brain to a non-biological substrate (e.g., silicon computer) via as yet uninvented technical innovations (scanning, mapping, simulation). The new substrate would run a simulation so faithful to the original that it would behave indistinguishably from the native brain. For additional discussion on this fascinating issue the interested reader is invited to read a discussion from Bostrom's Future of Humanity.Institute: http://www.fhi.ox.ac.uk/Reports/2008-3.pdf. One interesting issue is whether or not the Heisenberg uncertainty principle in physics—which precludes one from simultaneously knowing the exact position and velocity of any particle (such as an atom)—makes this possibility impossible in principle. This issue arises because, accepting physicalism for discussion purposes, the mind is not just a set of particles with positions w, x, y, and z, but a set of particles with both position and velocity.

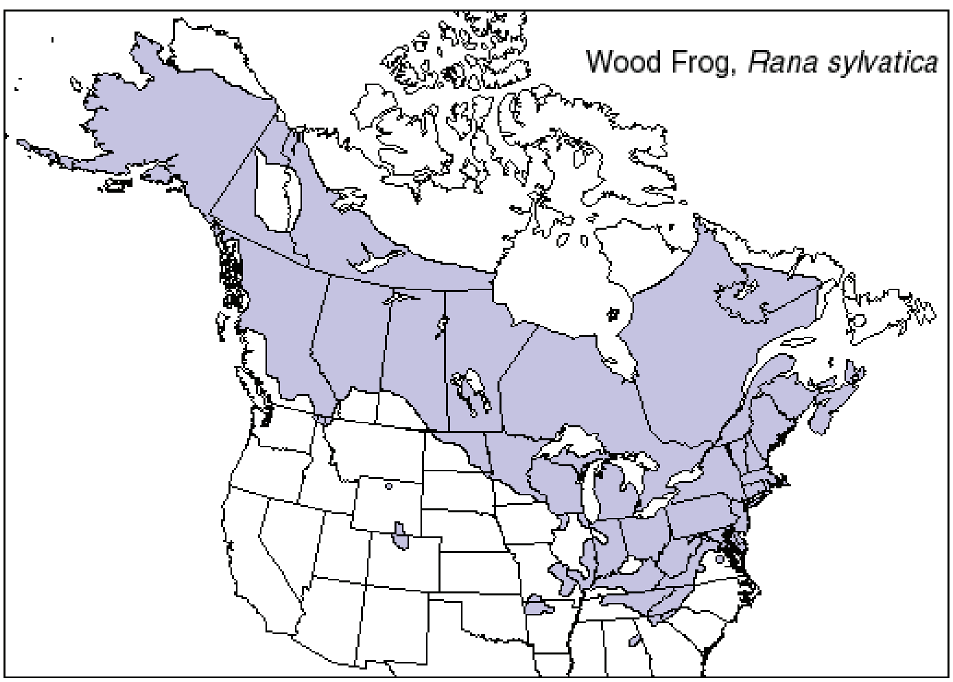


FIGURE 4. Top. A wood frog *Rana sylvatica* found in Gatineau, Quebec, Canada. Image Credit: http://en.wikipedia.org/wiki/File:Ranasylvatica.JPG **Bottom.** The wood frog *Rana sylvatica* lives predominantly in cold northern climates where freezing frequently occurs. Image Credit: http://commons.wikimedia.org/wiki/File:Rana-sylvatica_Range.gif.

In recent years, the application of gene screening technology to animals that tolerate freezing has allowed scientists to identify proteins that contribute to freeze tolerance in animals.[6-8] These proteins are in turn coded for by genes (DNA sequences) such as *fr10*, *li16*, and *fr47*.[7] As our scientific understanding of these processes improves over time, it is interesting to speculate as to whether it might be possible to use genetic engineering means to add these genes to the human genome (if they do not already exist), or to activate them should they be present in the human genome but not expressed.

The idea would be that should a patient be diagnosed with an untreatable terminal illness, genetic engineering interventions aimed at inducing natural cryoprotection might be expected to be more effective than the methods currently in use. Another possibility would be to create new babies with the required cryoprotectant genes as a risk mitigation measure against dying from accidental hypothermia in cold climate regions like northern Canada.

(Although this all might seem quite outlandish, consider that as of this writing (2012) the structure of DNA has been known only six decades. Consider also that it took only seven decades for humankind to progress from the first powered flight by the Wright brothers (1903) to the first manned moon landing in 1969.)

A second line of argument that the safe freezing of humans may eventually be possible stems from the fact that human spermatozoa, oocytes, and even embryos are already routinely frozen in *in-vitro* fertilization clinics around the world. Indeed, a great many individuals alive today were at one time cryopreserved embryos. In fact, two embryo cryopreservation methods are in common clinical use: slow freezing and vitrification.[9-10]

III. VITRIFICATION

Vitrification is the technology that advocates of cryonic suspension hold as having the most promise for eventual success. In vitrification, cellular water is largely replaced by one or more cryoprotectants. In addition, rapid cooling is carried out so that any remaining water is transformed directly from its liquid phase to a glassy, vitrified state that occurs with minimal formation of damaging ice crystals.

This process involves a number of special challenges. First, there are biological limitations to the degree to which cryoprotectant chemicals will be tolerated by cells undergoing vitrification. Second, while vitrification of cell clusters has been achieved, it is much harder to do this with an entire organ or an entire organism. Finally, the required cooling rates can be a challenge. For instance, for embryo vitrification, cooling rates between 15,000 and 30,000 °C/min are often used.[11†] Despite these challenges, as noted earlier, the success-

†For vitrification on the human-scale, thermal mass and heat conduction properties conspire to limit the rate of cooling, with the consequence that novel approaches to vitrification must be sought. Recognizing that there is non-covalent competitive binding of water molecules between the biomolecules (which incorporate water as an integral component of their structure), the various components of the cryoprotectant, and crystalline ice, may be the basis for future developments. Note that the goal of cryoprotection is to avoid irreversible alteration of biomolecular structures, which ice does by competitive dehydration; the affinity of the water molecules for the ice is greater than for the biomolecules. (I am indebted to Hugh Hixon for pointing this out).

ful vitrification and subsequent transplantation of a rabbit kidney by Fahy[2] suggests that eventual success is mostly a matter of effort, money, and imagination.

IV. SUBSTRATE PRESERVATION VS. INFORMATION PRESERVATION

In dealing with cryonics, is helpful to distinguish between the information preserved in a person's brain and the substrate used to hold that information. The information that makes us a person includes our longitudinal memories, as well as our hopes, our dreams, and countless other mental events. This information is unique to us—it is what makes us persons. How exactly this information is encoded into the brain substrate is a field of active neurologic research. The reader interested in this complex question might start by looking at some of the articles published in the academic journal *Learning and Memory*, which maintains an online presence at http://learnmem.cshlp.org. For individuals who would like a brief sketch on this matter, the following commentary is offered.

One popular theory of how memory is encoded in the brain is based on a hippocampal synaptic plasticity model.[12-14] The support for this theory comes from a number of sources. First, in Alzheimer's disease the hippocampus is one of the earliest brain structures to suffer damage. That memory problems appear among the first clinical findings in Alzheimer's disease suggests that the hippocampus has an important role in memory formation.

Second, lesions of the hippocampus in humans may prevent the acquisition of new memories, as in the well-known case of HM. (In 1953, a man known as HM lost substantial portions of his hippocampus, parahippocampal gyrus, amygdala, and anterolateral temporal cortex in a neurosurgical procedure aimed at stopping his intractable epileptic seizures. While the surgery was successful in eradicating the seizures, HM ended up with complete anterograde amnesia, although his working memory and procedural memory remained intact.)

Third, hippocampal synapses are known to have "activity-dependent synaptic plasticity" that provides neuronal level evidence of a possible role in memory. In this arena, a particularly attractive family of molecular candidates for modulating synaptic plasticity during learning and memory processes are neurotrophins (NTs).

Finally, the importance of the hippocampus to neuroscience in general and memory research in particular is evidenced by the fact that there is a journal devoted specifically to it (called, appropriately, *Hippocampus*). Information about the journal is available at http://www.wiley.com/WileyCDA/WileyTitle/productCd-HIPO.html.

A computer analogy may be helpful in explaining this distinction between the information preserved in a person's brain and the substrate used to hold that information. In order for a computer to be useful, its hard drive (or equivalent memory) must be loaded with a number of kinds of information. For example, the hard drive will contain an operating system, as well as a number of applications (such as word processing and spreadsheets), as well as a number of data files (such as the text file containing these very words). For the computer to be useful, it must contain both the hardware as well as the information constitutes its "identity" (programs and data). If the computer is destroyed, for example by fire, mere replacement of the hardware would be insufficient to restore the computer to its previously useful state. Instead, all the information that was unique to that computer would have to be added as well.

In the world of computers, restoring this information is a relatively simple task using backup programs that are commonly available. In the case of the brain, there is as yet no way to achieve this task. In the realm of science fiction, brains are backed up using methods whereby the state of the brain is measured in sufficient detail that it can be reconstructed on demand. In this sense, there is a rough analogy to teleportation, another popular science fiction theme.

The importance of this distinction between the substrate and the information encoded on the substrate is that it could turn out that cryonic brain preservation ends up preserving brain tissue (substrate) but might still not be sufficient to preserve the information that the brain retains.

V. THE TWO USUAL CRYONICS SCENARIOS

In the USA, Alcor, a facility located in Scottsdale, Arizona, is one of several companies offering a cryonic suspension service. Candidate patients carry an alert bracelet requesting that as soon as possible after death, a large dose of heparin (an anticoagulant) be given intravenously and the newly "dead" patient be placed on cardiopulmonary bypass to allow continuing organ perfusion prior to freezing. Two options are offered: a whole body option (cost: $200,000 and up) and a less expensive option where only the head is cryonically suspended (cost: $80,000 and up). In either case, the hope is that at some future time the body (or head) will be able to be unthawed and repaired, although, in the case of the head only option, the problem of finding a matching body exists unless (1) a new body can be constructed (perhaps via a variant of cloning or by advanced tissue engineering methods) or if (2) the newly reanimated head is configured to exist as an isolated perfused preparation (*vide infra*), or (3) the head's information contents are transferred to an entirely new biological entity (again, perhaps constructed via a variant of cloning) or (4) somehow a new organism is made to exist entirely *in silico*.

VI. LIVING AS AN ISOLATED HEAD

In the situation where only the head would be preserved, one can imagine three possible outcomes: (1) failure to successfully reanimate the individual in question (certainly a possibility, at least in the early experimental phases of any cryonics research), (2) existence as a conscious, reanimated head attached to a new body (a situation with numerous challenges beyond mere successful thawing of the head), and (3) existence as a conscious, reanimated head existing independently from a body via an artificial cardio-pulmonary-renal-endocrine support system. Although this last possibility—that of a conscious human existence somewhat like the "brain in a vat" scenario so often discussed in introductory philosophy courses—seems to be almost ludicrous, the situation may be technically possible, at least for moderate periods of time.

About 50 years ago, White et al. were able to isolate a series of five monkey brains by surgically removing all anatomical structures surrounding each brain except a small basal plate of bone and the central portion of the skull.[15-18] These brains were completely isolated from the donor monkey's body neurogenically and vascularly, and were perfused *in vitro* for 30 to 180 minutes via extracorporeal circulation using an immunologically compatible second monkey. That the isolated perfused brain remained alive and working in this setting was demonstrated by showing persistent electro-encephalographic activity at the cortex as well as by showing that the brain was appropriately extracting oxygen from its blood supply (by obtaining expected differences in oxygen content between the blood entering the brain and the blood leaving it).

A year later, White's team successfully repeated the experiments using a mechanical extracorporeal system (instead using the body of another monkey as a life-support system for the isolated monkey brain). In addition, White's team was able to transplant the head of one monkey onto the body of another. The procedure was a success to the extent that the transplanted head was able to smell, taste, hear, and see, even though the animal was quadriplegic (since the spinal cord was not connected). The animal even occasionally tried to bite some of the staff.

White's team was not the first to show that conscious existence as a severed head was possible. Many years earlier, in 1928, Bryukhonenko and Tchetchuline at the Institute of Experimental Physiology and Therapy in the USSR showed that life could be maintained in the isolated head of a dog for a moderate period by connecting the carotid arteries and jugular veins to a system for extracorporeal perfusion and oxygenation that used the lungs from a second dog as part of the setup (Fig. 5).[19-21]

Evidence that the isolated perfused dog head was alive and responsive to stimuli comes from the following *New York Times* report:[22]

"When the eye was touched it twitched. After twenty minutes there were more signs of life. The eyes were open by that time and looked alive. The head responded to a whole series of stimuli. Eyelids blinked when hairs on the brow were plucked. Particularly noticeable was the response when the mucous membrane of the nose was irritated. In fact, it was often necessary to hold the head on the plate by force. The muzzle was opened and the teeth were bared in a snarl. When quinine was placed on the tongue there was every sign of repugnance. Pieces of sausage were swallowed and ejected through the top of the alimentary canal. In short, the head behaved just as if it were attached to the body. And in this condition it remained for about three and a half hours."

Bryukhonenko went on to pioneer a number of important clinical developments that lead to the first Soviet open-heart operation in 1957. For these achievements, Bryukhonenko was posthumously awarded the Lenin Prize.

VII. AN INTERESTING HYPOTHETICAL SCENARIO

It is 2045. Generalissimo Sanchez rules the nation of Sanchiva with an iron fist. Unfortunately for him (but perhaps not for his subjects) he is diagnosed with metastatic melanoma with an exceedingly poor prognosis. He now has only a few months to live, de-

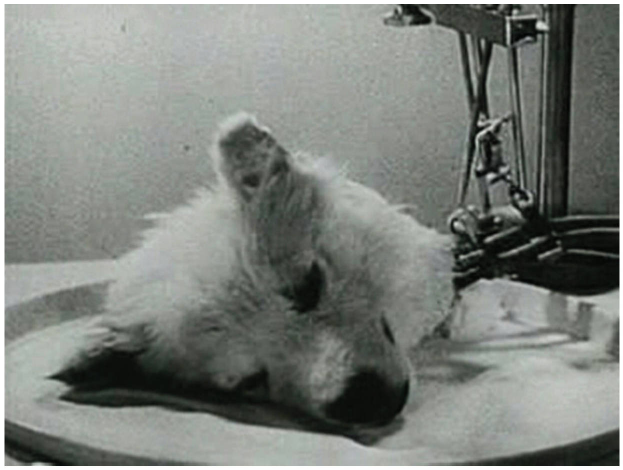


FIGURE 5. Screenshot from the 1940 public domain film "Experiments in the Revival of Organisms" showing an isolated perfused dog head exhibiting signs of consciousness. The film is available at the Prelinger Archive (http://www.archive.org/details/prelinger). The film may also be viewed at http://www.youtube.com/watch?v=ap1co5ZZHYE Image Credit: http://upload.wikimedia.org/wikipedia/en/f/f3/Experiment1940.jp.

spite having access to the best possible medical care and a massive personal fortune. To everyone's surprise he decides to step down and put his eldest son in power. Even more surprising, he decides to be cryonically suspended before his anticipated death, with a view to be reanimated at some future time when effective treatment becomes available. To this end, he hires a team from the Mayo Clinic and from Alcor to induce general anesthesia, establish anticoagulation and cardiopulmonary bypass, and then freeze his body under general anesthesia according to the Alcor protocol, which now has advanced to the point that their technology to prevent cell damaging ice crystal formation has become very reliable (at least in animal studies). Following this, the Generalissimo has his frozen body placed in a special mausoleum featuring triply redundant cooling systems and advanced electronic monitoring, as well as a well-guarded viewing station for the convenience of the populace.

This bizarre and macabre scenario raises a number of interesting questions: Is the Generalissimo Sanchez now dead or alive? What moral standing does the Generalissimo now have? How would one gauge the success of any reanimation efforts?

VIII. A SECOND HYPOTHETICAL SCENARIO

Field Marshal Perrera has adeptly but firmly ruled the oil-rich European island nation of Novacia since he overthrew the democratically elected but corrupt government over a decade ago. He now wishes to institute a uniquely bizarre form of capital punishment. To avoid criticisms that his shady judicial system might kill innocent citizens via capital punishment, he sentences people found guilty of capital crimes to indefinite cryonic suspension. That way, should exculpatory evidence clearing the accused ever arise, resulting in a more favorable judicial outcome, there is at least a theoretical chance of a post-thaw recovery. On the grounds that a better outcome would be expected if the freezing is done before death has actually occurred, a protocol identical to that described in the earlier scenario is used.

As in the previous scenario, some interesting questions are raised. What are the legal and moral standings of such cryonically suspended individuals? Based on the argument that the suspended individuals are not really dead, would such an arrangement still be acceptable if Novacia sought admission to the European Union (which forbids capital punishment)?

IX. CRYONICS AS "BORDERLINE SCIENCE"

The information and scenarios presented so far raises a number of intriguing scientific, philosophical, social, and ethical questions. Let us explore some of these questions, starting with the question of whether cryonics is real science.

Not every knowledgeable scientist takes cryonics seriously, particularly when the possibility of nanobots carrying out post-thaw cellular repairs is raised. For instance, since cells contain thousands upon thousands of components that may be damaged, some authorities argue that developing the required nanobot for each conceivable type of cellular damage may be impossible, or at least highly impractical. As another example of the skepticism raised by scientists, consider the words of Shermer, writing in Scientific American:[23]

"Cryonicists believe that people can be frozen immediately after death and reanimated later when the cure for what ailed them is found. To see the flaw in this system, thaw out a can of frozen strawberries. During freezing, the water within each cell expands, crystallizes, and ruptures the cell membranes. When defrosted, all the intracellular goo oozes out, turning your strawberries into runny mush. This is your brain on cryonics."‡

Shermer also writes: "This is what I call 'borderlands science,' because it dwells in that fuzzy region of claims that have yet to pass any tests but have some basis, however remote, in reality. It is not impossible for cryonics to succeed; it is just exceptionally unlikely. The rub in exploring the borderlands is finding that balance between being open-minded enough to accept radical new ideas but not so open-minded that your brains fall out. My credulity module is glad that some scientists are devoting themselves to the problem of mortality. My skepticism module, however, recognizes that transhumanistic-extropian cryonics is uncomfortably close to religion. I worry, as Matthew Arnold did in his 1852 poem 'Hymn of Empedocles,' that we will 'feign a bliss / Of doubtful future date, / And while we dream on this / Lose all our present state, / And relegate to worlds yet distant our repose.'"

Shermer is arguably unfair, however, in some of his criticisms of cryonics, especially in his strawberry analogy. He fails to mention, for instance, that it is the goal of vitrification science to avoid irreversible denaturation of cell biomolecules at low temperatures, and that this process does occur in nature in some organisms (as discussed earlier in this paper).

‡In cryonics circles this is known as the "strawberry man" argument.

X. CRYONIC REINCARNATION?

Another issue is that it is conceivable that a thawed individual might end their lengthy cryonic slumber with a substantial degree of information loss, so that the longitudinal memories that define us as persons would be substantially gone. The thawed individual would in a way have become a *tabula rasa* ready for "reprogramming" with new experiences and memories but unaware of his or her past. This is a possibility I call "cryonic reincarnation." To the extent that the long-term goal of cryonics is to develop technology to reversibly preserve brain-encoded information essential to personhood, it should be clear that cryonic reincarnation would actually be a form of failure. After all, the goal of cryonics is to preserve both the substrate and the information held by the substrate—mere preservation of the substrate alone, while a marvelous biotechnical achievement is still a failure of cryonics. Also, the simpler objective of mere substrate preservation could likely be achieved by human cloning, a process much simpler than cryonic preservation.

XI. SOME PHILOSOPHICAL CONSIDERATIONS

Smith[24] has argued that both cryonics and genetic engineering, in replacing natural processes with technological processes, "disturb the delicate balance of the triad of life which each individual experiences—faith, health, and justice." As a consequence, Smith argues, these new biological technologies raise a number of difficult legal, social, and philosophical issues, such as how should the legal system deal with faith and religion issues surrounding the cryonics patient and how should it respond to the cryonics physician "who views death as a disease which is curable?" One problem with Smith's analysis is that from the dawn of time man has been in replacing natural processes with technological processes. Would Smith have us live like Stone Age creatures? The limiting cases are "in a state of nature," which humans departed from many thousands of years ago, and—at the other extreme—"anything allowed by physics."

One particularly interesting issue concerns the legal and moral status of cryonically suspended individuals. It is completely unwarranted to argue that cryonics patients *will* certainly be resuscitated in the future. On the other hand, it would be wrong to unconditionally rule out the possibility of eventual success. In this sense, cryonically suspended individuals lie somewhere on a continuum between being unequivocally alive and being irreversibly dead. However, neither our legal system nor our conventional approaches to medical ethics are currently well-equipped to deal with uncertainties of this kind.

Another unresolved issue concerns the legal and moral status of any thawed individuals who end up technically alive but with severe neurological damage, such ending up in a chronic vegetative state (*vide infra*).[§]

---

§Arguably, though, before thawing is attempted, the brain should be repairable to the extent that basic functioning would likely be fully restored, even if pre-preservation memories are not. In addition, such memories in turn might be reconstructed to an extent from records, especially if the patient made a special effort to record past experiences. (I am indebted to Mike Perry for making this observation.)

XII. SOME BIOETHICAL CONSIDERATIONS

As discussed earlier, central to cryonics is that notion that life and death are not always simple binary events. Similarly, some authorities have argued that the classic notion of basing the definition of death on cessation of the heartbeat is philosophically problematic. This is because death is not an event that happens instantaneously when the heart stops, but rather is a complex process involving a series of biochemical events at the cellular level that takes time to complete once tissue perfusion stops because of the cessation of cardiac contractions.

In fact, in cases where the heart can be restarted, the clinical result may sometimes still be excellent, without any obvious neurological impairment or damage to other organs. For instance, cold water drowning victims have been resuscitated without clinical sequelae after periods of submersion and cardiac arrest in excess of 30 minutes. Some critics such as Donaldson[25] have argued that the concept of death based on classical criteria such as cardiac asystole or resuscitation failure is, in fact, a mere social construction lacking a rigorous scientific foundation. Consider similarly the following commentary from Whetstine et al.:[26] "…few if any patients pronounced dead by today's physicians are in fact truly dead by any scientifically rigorous criteria." It is with this approach to death that cryonicists work, hoping to cryopreserve their patients before sufficient brain damage has occurred that irreversible death has set in.

In this regard, Hershenov[27] has emphasized that most definitions of death—whether cardiopulmonary or on neurological grounds—implicitly require irreversibility. Thus, mere cessation of cardiac or neurological function should be insufficient grounds to declare death. However, current clinical rules for the declaration of death do not actually require that irreversibility be rigorously established. For instance, in the case of organ donation after cardiac death, it might well be possible to restart the heart after the required period of asystole for the declaration of death has passed. And even if the heart might not be restartable, one could emergently institute cardiopulmonary bypass and install one of the fully implantable artificial hearts now commercially available. (In my opinion, the AbioCor artificial heart would show special promise in such a scenario).

Hershenov also emphasizes that the thorny issue of the definition of death likewise arises in the context of cryonic suspension: "in the future, millions of cryogenically frozen human beings could spend centuries in a non-dead state because of the future technological breakthroughs; or large numbers of 'frozen' people are dead for eons but coroners are not able to declare them so because they are unaware of what biological conditions science will never be able to reverse."

It would thus appear that true irreversibility of death is incompatible with successful cryonic revival. Fortunately for enthusiasts of cryonics, however, true irreversibility is not always present at the time that death is declared in most clinical situations. Accordingly, cryopreservation with the possibility of future resuscitation requires a "window of opportunity" between legal death and irreversible death.[28]

XIII. SOME NEGATIVE BIOETHICAL CONSIDERATIONS

One aspect to the debate hinted at above, but not emphasized in the cryonics literature, is the very real possibility that any initial "successes" with cryonic reanimation may be accompanied by severe neurological injury, such that the revived individual would remain comatose or in a minimally conscious state, or exhibit other profound impairments that would render life too degraded to be worthwhile. The result would be that the revived individual would not get the outcome that was hoped for, with the additional complication of now having a patient who requires complex medical care with very little likelihood of improvement.

Possible counterarguments to this concern are twofold: first, the expectation is that a "last in, first out" process will take place where the oldest cases will be the most difficult and the last to be attempted. Secondly, if technology able to resuscitate cryopreserved people comes to be developed, then it is hoped that other companion technologies will also become available so that the worst likely deficit will be some degree of amnesia.

Other potential objections to cryonics exist. For instance, Shaw[29] has summarized some of the practical and ethical objections to cryonics: it "would change the very concept of death"; "it is 'against nature'"; "no friends or family of the 'freezee' will be left alive" following thawing; the science of cryonics "might not advance enough to ever permit revival"; "reanimation might not take place due to socio-political or catastrophic reasons"; and "cryonics could lead to premature euthanasia in order to maximize chances of success."

After reviewing these and other arguments, Shaw offers a variation of Pascal's Wager as an argument in favor of utilizing cryonic suspension. (Recall Pascal's Wager: Even though the existence of God cannot be established through pure recourse to reason, one should still live life as though God exists, because in doing so one has eternal life to gain, and little to lose.)

However, I disagree with Shaw in this matter. My clinical opinion is that the *likely* outcomes following thawing, at least in the early years, will be predominantly negative, consisting variously of a recovered individual with no memories, a recovered individual with severe neurological impairment, or a thawed individual with some organs working but no brain function at all. Pascal's Wager is worthwhile only if there is little to lose if the wager is lost. In my opinion, these likely negative outcomes hardly constitute "little to lose."¶

XIV. BURDEN ON SOCIETY?

Dr. John Baust has made the comment that an "individual who freezes himself or herself to come back in the future makes the assumption he will be a contributor to that society and that they would want him".[30] Such a comment carries with it both interesting practical and ethical perspectives. The practical aspect here is that the recovered individual might require complex, lengthy, and expensive medical care to fix the problems that led

---

¶I should point out that many in the cryonics community don't think these are "likely outcomes." They argue that should cryonic resuscitation become possible, contemporaneous technological developments will also make it possible that an individual will awaken without neurological deficits.

to them undergoing cryonic suspension in the first place unless means such as growing new bodies via tissue engineering become perfected. Patients who were frozen as severed heads would have the special challenge of finding (or constructing) a body to which their head would be attached. Also, funding to deal with all of these issues this would likely not be in place, resulting in a burden on society.

The ethical issues involved in Baust's comment run deep. Many individuals, especially those who regard human life as being sacred, would take issue with the implied notion that human beings have value to society only to the extent that they are wanted (for example by family members) or are able to make social contributions. On the other hand, Corlett[31] argues that in health care contexts "there is a moral duty to die inexpensively." Certainly, cryonic suspension would be viewed by a great many of its detractors as a particularly expensive way to die.

XV. A WASTE OF MONEY?

Dr. Kenneth Goodman, a bioethicist writing in the Miami Herald, has commented "If you have enough money (for cryonics), then you have enough money to help somebody in need today."[32] In a similar vein, Jean Medawar is said to have commented that "Money invested to preserve human life in the deep freeze is money wasted, the sums involved being large enough to fulfill a punitive function as a self-imposed fine for gullibility and vanity."[33**]

Both these comments raise interesting ethical issues. The first comment about not spending money on membership in a "cryonics club" so that others might benefit from that same money applies equally well to a number of more costly expenditures that most ethicists do not criticize. For instance, as of this writing, the annual cost of membership with Alcor for adults in the United States is $800. Additional adult family members pay $490, minors, $156. This is in addition to the whole body preservation cost of $200,000, which is often achieved from a life insurance policy payout.

While these are not small sums, many Americans maintain (for example) luxury estates or second vacation homes at much higher costs than that of a cryopreservation plan without being seen as being unethical for not having given this money to help others.

On the other hand, Peter Singer has argued exactly this—that we in the West are morally obligated to live a relatively modest life, living below our means so that the resulting discretionary money can be used to substantially improve the lives of others. In his book *The Life You Can Save: Acting Now to End World Poverty*,[34] Singer suggests that we are not required to choose between asceticism and self-indulgence, but that a middle solution based on unpretentious living can free up money to allow us to donate to charities where mere few hundred dollars can save a life.

Singer provides the following example to make his point. Imagine that you are walking in the park and you find a little girl drowning in a water fountain. Do you help? Almost everyone would agree that that would be the right thing to do. Similarly, argues

**Many have said the same for donating to religious institutions.

Singer, the same reasoning applies to helping solve global poverty. The only difference is that in the former case the person being helped is located directly in front of you while in the other case the person being helped is far away.

A related ethical issue arises with the suggestion implied by the second comment (by Medawar) that paying for cryonics services is a form of "fool's tax" or a "tax on hope." But arguably similar issues arise with other experimental endeavors with very uncertain outcomes. Would one label Louis Washkansky, the recipient of the first heart transplant (Cape Town, 1967), as being "gullible and vain" because he took a great gamble but lived only 18 days after the transplant? Similarly, does the use of newly developed genetically engineered drugs that cost thousands of dollars per dose yet is not fully guaranteed to be helpful constitute a waste of money?[35]

XVI. SOME LEGAL CONSIDERATIONS

The legal issues that arise in cryonics will vary from location to location, and usually depend, to a large extent, on applicable definitions of death and protocols regarding interment. In the United States a particularly interesting legal case pertaining to cryonics was the case of *Donaldson v. Van de Kamp*.[36] Donaldson, suffering from an inoperable brain tumor, sought the legal right to obtain antemortem cryonic suspension of his body, knowing that this was technically preferable to a postmortem suspension. However, both the trial court and the appellate court ruled against Donaldson, arguing that the cryonic process in this case would be a form of physician-assisted suicide, and that Donaldson did not have a constitutional right to such a form of death. Specifically, the court determined that "the state's interest in preserving life, preventing suicide, protecting innocent third parties, and maintaining the ethical integrity of the medical profession" trumped Donaldson's interest in cryonic suspension until treatment for his brain tumor was available.[37]

This case suggests, however, that should physician-assisted suicide ever become legal in the United States, antemortem cryonic suspension, with its greater likelihood of favorable outcomes compared to postmortem cryonic suspension (at least theoretically), could be legally practiced.

XVII. RELIGIOUS PERSPECTIVES

Like a belief in an afterlife found in many religions, participants in cryonics take a leap of faith that resuscitation with a worthwhile outcome will be possible sometime in the future. In truth, however, the future repair technologies assumed by cryonics enthusiasts remain, at best, hypothetical and are certainly unproven, in a manner similar to a number of religious beliefs.[††]

Likewise related to religion, for many thinkers a fundamental issue is whether cryonic suspension should be regarded as a form of interment or as a form of medical

††That being said, cryonicists' expectations fall within the realm of physical law, while most religions place faith in the supernatural.

intervention. Some religious thinkers who define death in terms of the soul leaving the body argue against cryonics because "only God can resurrect the dead." However, a potential counter-argument that can be offered to believers in such a setting is that the soul leaves the body only with the onset of *irreversible* death. As with the above discussion concerning organ donation after cardiac death, a "window of opportunity" between ordinary clinical death and irreversible death once again can be seen to exist, with the soul fully leaving the body only with the onset of irreversible death.

XVIII. CONCLUSIONS

In conclusion, the possibility of human cryonic suspension, while admittedly remote and far-fetched to many, raises a number of fascinating philosophical and ethical questions about moral standing, the nature of personhood, and what it means to be a living human being. Central to the possibility of successful human cryonic suspension is the idea of a "window of opportunity" between legal death and irreversible death. Of course, even better from a purely technical point of view would be antemortem cryonic suspension.

REFERENCES

1. Pegg DE. Principles of cryopreservation. Methods Mol Biol. 2007; 368:39–57.
2. Fahy GM, Wowk B, Pagotan R, Chang A, Phan J, Thomson B, Phan L. Physical and biological aspects of renal vitrification. Organogenesis. 2009;5:167–75.
3. Costanzo JP, Lee RE Jr. Cryoprotection by urea in a terrestrially hibernating frog. J Exp Biol. 2005; 208:4079–89.
4. Costanzo JP, Lee RE Jr. Urea loading enhances freezing survival and postfreeze recovery in a terrestrially hibernating frog. J Exp Biol. 2008; 211:2969–75.
5. Muir TJ, Costanzo JP, Lee RE Jr. Osmotic and metabolic responses to dehydration and urea-loading in a dormant, terrestrially hibernating frog. J Comp Physiol B. 2007; 177:917–26.
6. Storey KB, Mosser DD, Douglas DN, Grundy JE, Storey JM. Biochemistry below 0 degrees C: nature's frozen vertebrates. Braz J Med Biol Res. 1996; 29:283–307.
7. McNally JD, Sturgeon CM, Storey KB. Freeze-induced expression of a novel gene, fr47, in the liver of the freeze-tolerant wood frog, Rana sylvatica. Biochim Biophys Acta. 2003; 1625:183–91.
8. Storey KB. Strategies for exploration of freeze responsive gene expression: advances in vertebrate freeze tolerance. Cryobiology. 2004; 48:134–45.
9. Kolibianakis EM, Venetis CA, Tarlatzis BC. Cryopreservation of human embryos by vitrification or slow freezing: which one is better?. Curr Opin Obstet Gynecol. 2009; 21:270–4.
10. Loutradi KE, Kolibianakis EM, Venetis CA, Papanikolaou EG, Pados G, Bontis I, Tarlatzis BC. Cryopreservation of human embryos by vitrification or slow freezing: a systematic review and meta-analysis. Fertil Steril. 2008; 90:186–93.

11. García-Velasco JA, Pellicer A. Cancer treatment and fertility: a time to reassess realistic opportunities. Clin Transl Oncol. 2007; 9 681–2.
12. Bliss TV, Collingridge GL. A synaptic model of memory: long-term potentiation in the hippocampus. Nature. 1993; 361:31–9.
13. Shapiro M. Plasticity, hippocampal place cells, and cognitive maps. Arch Neurol. 2001; 58:874–81.
14. Conner JM, Franks KM, Titterness AK, Russell K, Merrill DA, Christie BR, Sejnowski TJ, Tuszynski MH. NGF is essential for hippocampal plasticity and learning. J Neurosci. 2009; 29:10883–9.
15. White RJ, Albin MS, Verdura J. Isolation of the monkey brain: in-vitro preparation and maintenance. Science. 1963; 141:1060–1.
16. White RJ, Albin MS, Verdura J. Preservation of the viability in the isolated monkey brain utilizing a mechanical extracorporeal circulation. Nature. 1964; 202:1082–3.
17. White RJ, Albin MS, Locke GE, Davidson E. Brain transplantation: prolonged survival of brain after carotid-jugular interposition. Science. 1965; 150:779–81.
18. White RJ, Albin MS, Verdura J, Takaoka Y, Massopust LC, Wolin LR, Locke GE, Taslitz N, Yashon D. The isolation and transplantation of the brain An historical perspective emphasizing the surgical solutions to the design of these classical models. Neurol Res. 1996; 18:194–203.
19. Brukhonenko S, Tchetchuline S. Expériences avec la tête isolée du chien. I. Technique et conditions des experiénces. Journal de Physiol. et de Pathol. Génér. 1929; 29: 31–45.
20. Brukhonenko S, Tchetchuline S. Expériences avec la tête isolée du chien. II. Résultats des experiénces. Journal de Physiol. et de Pathol. Génér. 1929; 29: 64–79.
21. Adamenko NP. [Technic of experimental resuscitation of dogs with a variant of the method of extracorporeal circulation using S S Briukhonenko's autojector pump and a live parabiotic donor]. Patol Fiziol Eksp Ter. 1969;13:69–71.
22. Kaempffert W. Process of Dying. New York Times Nov 14, 1943; pg. E9 Available from http://blogfiles.wfmu.org/KF/2006/01/NY_times_1943.pdf.
23. Shermer M. Nano nonsense and cryonics. Sci Am. 2001; 285:29.
24. Smith GP 2nd. The iceperson cometh: cryonics, law and medicine. Health Matrix. 1983;1:23–35.
25. Donaldson T. "Neural Archeology". Cryonics (Alcor Life Extension Foundation) February 1987: 24–33. http://www.alcor.org/Library/html/NeuralArcheology.html.
26. Whetstine L, Streat S, Darwin M, Crippen D. Pro/con ethics debate: when is dead really dead? Crit Care. 2005; 9:538–42.
27. Hershenov D. The problematic role of 'irreversibility' in the definition of death. Bioethics. 2003;17:89–100.
28. Best BP. Scientific justification of cryonics practice. Rejuvenation Res. 2008; 11:493–503.
29. Shaw D. Cryoethics: seeking life after death. Bioethics. 2009;23:515–21.
30. Baust J. 2002. Quoted at http://www.alcor.org/notablequotes.html.

31. Corlett JA. Is there a moral duty to die? Health Care Anal. 2001;9:41–63.
32. Goodman K. 2002. Quoted at http://www.alcor.org/notablequotes.html.
33. Quoted at http://people.ucalgary.ca/~kmuldrew/cryo_course/cryo_chap15_1.html#02.
34. Singer PA. The Life You Can Save: Acting Now to End World Poverty. New York, NY: Random House; 2009.
35. Burrows R, Crippen D, Dellinger RP, Kelly DF, Streat S, Whetstine LM. Ethics roundtable: Using new, expensive drugs. Crit Care. 2002; 6:473–8.
36. Pommer RW 3rd. Donaldson v. Van de Kamp: cryonics, assisted suicide, and the challenges of medical science. J Contemp Health Law Policy. 1993;9:589–603.
37. California Court of Appeal, Second District, Division 6. Donaldson v. Van de Kamp. Wests Calif Report. 1992;4:59–65.