The Arrest of Biological Time as a Bridge to Engineered Negligible Senescence

JERRY LEMLER, STEVEN B. HARRIS, CHARLES PLATT,
AND TODD M. HUFFMAN

Alcor Life Extension Foundation, Scottsdale, Arizona 85260, USA

ABSTRACT: Biological systems can remain unchanged for several hundred years at cryogenic temperatures. In several hundred years, current rapid scientific and technical progress should lead to the ability to reverse any biological damage whose reversal is not forbidden by physical law. We therefore explore whether contemporary people facing terminal conditions might be preserved well enough today for their eventual recovery to be compatible with physical law. The ultrastructure of the brain can now be excellently preserved by vitrification, and solutions needed for vitrification can now be distributed through organs with retention of organ viability after transplantation. Current law requires a few minutes of cardiac arrest before cryopreservation of terminal patients, but dogs and cats have recovered excellent brain function after 16–60 min of complete cerebral ischemia. The arrest of biological time as a bridge to engineered negligible senescence, therefore, appears consistent with current scientific and medical knowledge.

KEYWORDS: cryopreservation; vitrification; cryonics; cryogenics

In 1971, the eminent gerontologist, Dr. George Martin, made the following observations:[1]

> a comparatively modest investment in research could theoretically provide man with a partial and interim solution to the "terrible problem of death awareness" recently discussed by Sir John Eccles…. I must confess that the only solution which appeals to me is one which preserves the central nervous system. The spectacular success of cryobiological procedures in the long-term preservation of viability at the cellular level suggests that, in principle, satisfactory whole organ preservation may yet be achieved.… Of course,… preservation will of necessity have to be carried out *in situ*, presumably using perfusion techniques.

This suggestion, based on an original proposal by R. C. W. Ettinger,[2] is based on one fact and two assumptions. The fact is that at the boiling point of liquid nitrogen, changes in biological systems generally are agreed to be negligible for periods of hundreds to thousands of years. The first assumption is that it is possible to cool a human being to such a temperature without fundamentally destroying the essential information underlying memory and personality in the brain. The second assumption is that medical and scientific progress will continue until medical resuscitation tech-

Address for correspondence: Jerry Lemler, Alcor Life Extension Foundation, 7895 E. Acoma Drive, Scottsdale, AZ 85260. Voice: 480-905-1906; fax: 480-922-9027.
jlemler@alcor.org

Ann. N.Y. Acad. Sci. 1019: 559–563 (2004).
doi: 10.1196/annals.1297.104

nology is limited only by physical law. If these assumptions are correct, the memories and personalities of people preserved by today's methods should be intact after revival by future technology, and medical time travel can be used as a bridge to a time in which senescence can be controlled. Let us now briefly consider evidence pertaining to the validity of the two assumptions underlying the possibility of medical time travel.

REACHING SAFE HAVEN

Technology in the field of cryopreservation is currently undergoing revolutionary change. In 1971, the only method available for preserving viability for indefinite periods involved freezing, but today a radically different preservation method, vitrification, is available. As the name implies, vitrification allows systems to be preserved in the vitrified or glassy (noncrystalline solid) state, which eliminates the structural disruption caused by ice crystals.[3] Studies that are still ongoing have shown, using both transmission and scanning electron microscopy, that the ultrastructure of rabbit brains is well preserved using current methods to both vitrify and rewarm entire cephalic preparations (FIG. 1). The extension of similar techniques to clinically dead human beings at the Alcor Life Extension Foundation has indicated, based on visual inspection and other observations, that the human brain indeed can be vitrified even after extended periods of clinical death. Furthermore, recent studies (Y. Pichugin *et al*., submitted for publication) have shown that not only the ultrastructure but also the viability of rat hippocampal slices can be preserved by vitrification. In addition, rabbit kidneys transplanted after being perfused with advanced vitrification solutions have supported life with little injury (G.M. Fahy *et al*., submitted for publication). These observations in combination with the fact that human synapses are hardy enough even to survive after freezing and thawing[4] provide powerful support to the proposition that the essential information content of the human brain can now be kept intact during the processes required to reach low and stabilizing temperatures.

OVERCOMING LEGAL OBSTACLES

To actually implement medical time travel, the preservation process must currently be applied after the declaration of legal death. However, legal death is normally pronounced upon the cessation of heartbeat and breathing, and in our experience never involves the criteria for brain death required for organ donation. Although a brief period of cerebral ischemia is necessitated to permit the declaration of legal death, this is not an obstacle in view of recent observations that it is possible to completely resuscitate dogs after 16 minutes of unpretreated normothermic cardiac arrest with no lasting neurological deficits (TABLE 1; S.B. Harris *et al*., in preparation). Furthermore, it was demonstrated many years ago that damage induced by 60 min of complete normothermic cerebral ischemia in the cat could be reversed using simple methods, resulting in the permanent survival of the cat with retained locomotor, self-cleaning, and purring behaviors and with recognition of laboratory personnel.[5] Modern methods of cardiopulmonary bypass can be applied shortly after legal

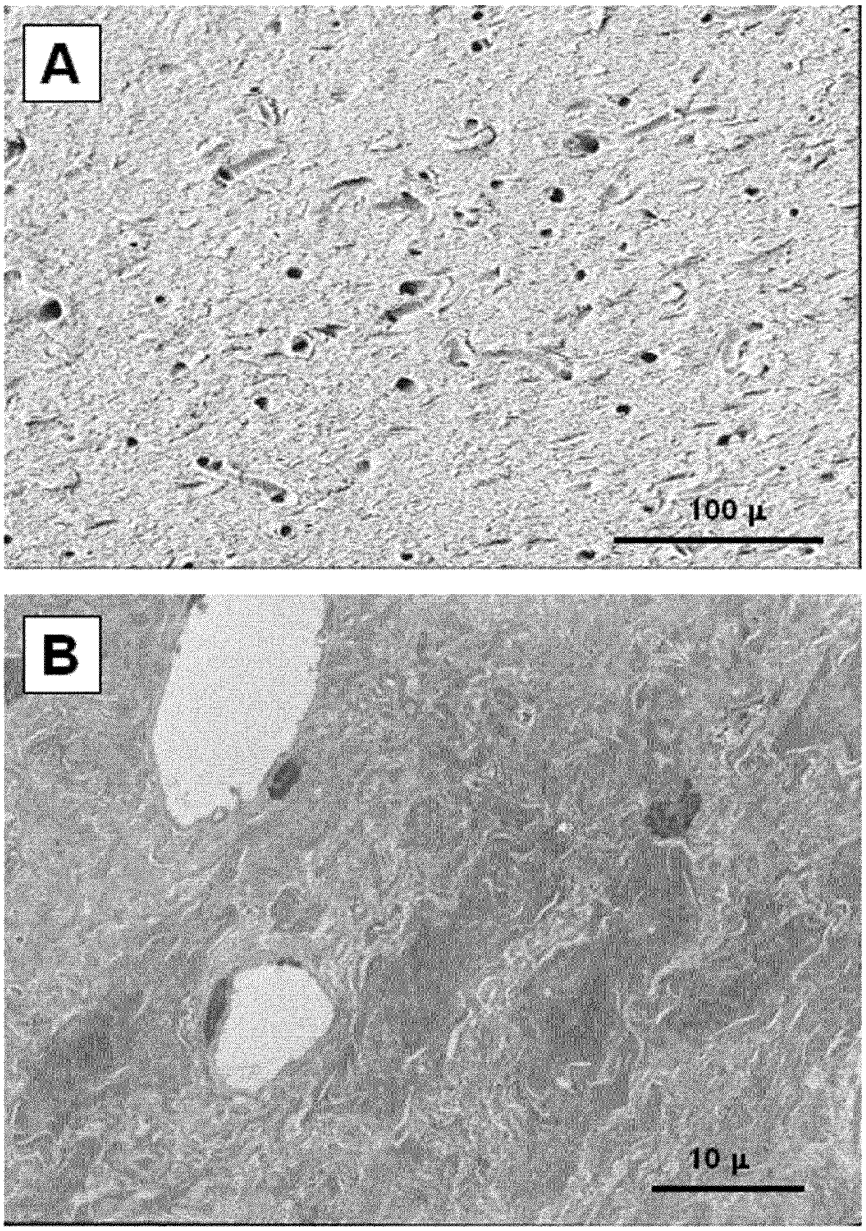

FIGURE 1. (**A**) Scanning electron microscopic image of the cerebral cortex of a New Zealand white rabbit after perfusion with M22 vitrification solution, cooling to below the glass transition temperature, and slow rewarming. Note dilated but normal capillary structure, smooth neuropil, and absence of large (~20–200 μm) disorganized cavities in the tissue that normally result from ice formation. (**B**) Transmission electron microscopic image of the hippocampal dentate gyrus, showing shrunken but preserved features. The brain was fixed with a solution containing cryoprotectant and then slowly diluted in low-osmolality Karnovsky's fixative until all cryoprotectant was removed before being processed for scanning or transmission electron microscopy.

TABLE 1. Dogs surviving with no neurological deficit after prolonged normothermic cardiac and circulatory arrest induced by ventricular fibrillation[a]

Dog number and name	Tympanic temperature[b]	Time with MAP below 30 mmHg
2 (Cerberus)	35.9	14 min 15 s
5 (Scroffy)	37.3	14 min 45 s
6 (Claudia)	38.0	14 min 48 s
10 (Maude)	37.7	15 min 45 s
14 (Bob)	37.7	15 min 25 s
16 (Stuart)	37.6	16 min 15 s

[a]Dogs were resuscitated after the periods shown by immediate cardiopulmonary bypass, rapid postinsult cooling to 34°C, and a complex pharmacological support protocol that will be described elsewhere (Harris *et al*., in preparation). All dogs were allowed to survive for at least 6 months after resuscitation.

[b]Temperature just before electrically induced ventricular fibrillation. Tympanic temperature closely approximates intracerebral temperature in canines. Courtesy of Critical Care Research, Inc.

NOTE: MAP, mean arterial pressure (objective marker of circulatory arrest).

(clinical) death and are unequivocally able to maintain the biological viability of both the brain and the body for extended periods until cryopreservation is initiated. Therefore, application of advanced vitrification methods to human beings after legal death is not medically invalidated by warm ischemic injury.

THE LIMITS OF REPAIR

Once cooled to safely below the glass transition temperature, there is no known time limit beyond which safe storage cannot continue.[6] Therefore, the possibility of successfully reviving would-be time travelers must be considered in the light of technological advances of the indefinite future. Assuming technological progress continues until fundamental physical limits are reached, any required repair process that is consistent with physical law should become available to rescue contemporary people.

In considering the possibility of repair, we can distinguish between two fundamentally different kinds of injury. The first kind of injury involves, in essence, the rearrangement, misfolding, or chemical modification of the molecules constituting the patient, but especially of molecules constituting the patient's brain. The reversal of this kind of injury will require the ability to recognize and correct molecular changes. The fact that biological systems already perform these functions on a continuous basis implies that repairs of this nature are consistent with physical law, and detailed engineering calculations and designs for molecular recognition and manipulation systems of the kind that would be capable of effecting the required repair processes are available.[7–9] Quantitative descriptions of possible repair scenarios also have been described.[10]

The second kind of injury involves the outright loss of biological information, such as might be induced by major gunshot wounds to the brain or several days of postmortem autolysis. Although any injury may be repairable in which the original

state of the patient can be inferred from the damaged state, there are clearly modes of death in which complete or even partial inference of the correct structure will be impossible, and in this case no repair technology, no matter how advanced, can be successful. Complete erasure of the patient's identity in this way has been called "information theoretic death"[10] and, unlike "clinical death," represents true death of the individual. Unfortunately, current knowledge is insufficient to determine whether information theoretic death has taken place in some cases, or whether partial loss of information is sufficient to render future repair pointless. However, in most cases, these uncertainties and dilemmas need not arise.

CONCLUSIONS

Medical time travel is consistent with current medical and scientific knowledge and may offer a bridge to the future for those who cannot wait for the development of engineered negligible senescence. Information on the many facets of this procedure that cannot be discussed in this short space can be obtained at <http://www.merkle.com/cryo/techFeas.html>, <http://www.nanomedicine.com/NMI.htm>, <http://www.nanomedicine.com/NMIIA.htm>, and <http://www.alcor.org>.

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