CRYONICS

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A Non-Profit Organization

ALCOR LIFE EXTENSION FOUNDATION

$9.95
Improve Your Odds of a Good Cryopreservation

You have your cryonics funding and contracts in place but have you considered other steps you can take to prevent problems down the road?

- Keep Alcor up-to-date about personal and medical changes.
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- Wear your bracelet and talk to your friends and family about your desire to be cryopreserved.
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Your source for news about:

- Cryonics technology
- Cryopreservation cases
- Television programs about cryonics
- Speaking events and meetings
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Connect with Alcor members and supporters on our official Facebook page:

http://www.facebook.com/alcor.life.extension.foundation

Become a fan and encourage interested friends, family members, and colleagues to support us too.
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Resuscitation Research Can Start Now!

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**IN PERPETUITY**

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The James Bedford Society recognizes those who make a bequest of any size to the Alcor Life Extension Foundation. If you have already provided a gift for Alcor in your estate, please send a copy of your relevant documents to Alcor’s Finance Director, Bonnie Magee.

If you’d like to learn more about setting up a bequest, send an email to bonnie@alcor.org or call 480-905-1906 x114 to discuss your gift.

2013 Annual Giving Program

Alcor provides a wide array of services for you the member, and the general public. We inform and educate, we protect and preserve, and we strive to remain at the forefront of cryonics technology.

Since its founding, Alcor has relied on member support to maintain its mission and attract new members. Your support, regardless of size, can provide a better future for all cryonicists. Please act now.

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- $60  Junior Supporter
- $120  Sustaining Supporter
- $500  Advocate Supporter
- $1,000  Leading Supporter
- $2,500  Visionary Supporter
- $5,000  Silver Supporter
- $10,000  Gold Supporter
- $25,000  Titanium Supporter
- $50,000  Vanguard Supporter

We encourage every member to donate. Even if you can only afford $5 right now, you will make a significant contribution to Alcor’s future.

Donations may be made via the Donations button on the Alcor website or by contacting Alcor’s Financial Director, Bonnie Magee, at bonnie@alcor.org. Your donation may be made as a lump sum or divided into easy monthly payments.
A major obstacle to strengthening the case for cryonics is the perception that meaningful research aimed at resuscitation of cryonics patients cannot be done today. Attempts to be more specific than evoking the need for a technology that can manipulate matter at the molecular level are considered to be vague and unproductive. Clearly, such a stance is an open invitation for skeptics to claim that cryonics advocates have not much more to offer than hope and optimism. Nothing could be further from the truth. Not only is there a lot of relevant empirical research that can be conducted today, a focused investigation into the technical and logistical challenges of resuscitation can also define cryonics research priorities and refine the stabilization and cryopreservation procedures that we use today.

The first thing that needs to be recognized is that if we want to say something specific about the nature and limits of repair we need to be able to characterize the damage in detail. There has been a lot of general discussion of damage but there have been few writers that have systematically characterized the forms of damage that can occur prior to and/or during cryopreservation and then linked those forms of damage to contemporary or envisioned repair strategies. A notable exception is the 1991 article “Realistic Scenario for Nanotechnological Repair of the Frozen Human Brain” (http://www.alcor.org/Library/html/nanotechrepair.html) where the individual forms of mechanical and biochemical damage (ice formation, protein denaturation, osmotic damage etc.) are catalogued and repair strategies are discussed in biological terms.

Describing the various forms of damage at such a detailed level provides a meaningful context within which to discuss the technical feasibility of cryonics in rather specific terms, too. If someone would claim that cryonics is hopeless because of the “toxicity” of the vitrification agents we can ask for more specifics about what kind of biochemical damage is being alleged and why such alterations irreversibly erase identity-critical information.

Even when it is admitted that theoretical and empirical investigations into damage associated with (crude) cryonics technologies is possible it surely would be preposterous, wouldn’t it, to claim that repair of the damage itself can be done today. Well, not quite. Granted, we do not have the biological or mechanical cell repair technologies that would be required for repair of the brain at the molecular level but we can simulate a specific kind of damage (ice formation, ischemia) and create three dimensional neural wiring maps that can be compared to controls. Often this is not even necessary because we understand the universal language of biology and, for example, if we observe a ruptured cell membrane wall we know how it is supposed to look.

From here it is a short step to what I would call “reconstructive connectomics,” a sub-discipline of the field of connectomics that studies pathological changes of neural connections in the brain with the aim of “in silico” repair. Computational limitations currently constrain the scale and complexity at which we can do these reconstructions but it is not necessary to do reconstructive connectomics in a human-sized brain to obtain a much greater understanding of the mechanisms of damage, the type of repair required, and the empirical content of concepts like information-theoretic death.

It is important to point out here that the idea that resuscitation research can start today does not require taking sides in debates about the relative merits and limitations of biological versus mechanical cell repair technologies. The primary objective here is to show that meaningful resuscitation research can be done today and that the absence of such research only provides our critics easy targets.
Overview
A-2091, an Alcor member living in southern California, was diagnosed with a glioblastoma in 2010. Chemotherapy and medication administration were prescribed; however they were discontinued in June 2011. With the assistance of a local home healthcare agency the member received 24 hour care within the comfort of her home. In mid-June, Alcor prepared and shipped a mini-med kit to her home in the event of a sudden clinical death.

Arrangements were made with Suspended Animation (SA) to provide standby services when required. These arrangements were made at the specific request of the family who agreed to pay any and all additional costs from early deployment. Alcor’s Medical Response Director, Aaron Drake, arranged a charter flight and made a special arrangement with the Health Department so that we could call after hours to secure a transit permit. Aaron visited the patient and her family at her home in late July, while also meeting with a nearby mortuary and working out logistic details.

SA initiated a standby on August 9, 2011 with at least two team members on site at all times. Shortly before noon on August 18, it was clear that clinical death was imminent. The charter flight was set in motion, but a dust storm in Scottsdale/Phoenix delayed its departure—fortunately only briefly.

Immediately following pronouncement, the patient was cooled quickly over the first hour after cardiac arrest. This cooling rate appears to be one of the two fastest yet achieved. No one was answering the phone at the Health Department; however the private, after-hours number prompted a quick return call which allowed the paperwork to be processed, despite the office being closed. The patient was loaded onto a private plane at 8:57pm and reached Alcor at 10:22pm. The surgery was challenging due to extensive medical issues, however target cryoprotectant concentration was reached in the brain. Member A-2091 became Alcor’s 107th patient.

Personnel
Field stabilization team: Aaron Drake, Alcor’s Medical Response Director; Catherine Baldwin, Suspended Animation’s Standby Team Leader; three SA staff members, a cardiac perfusionist, and a cardiothoracic surgeon. They were supported by Max More, CEO; and Steve Harris, M.D., Chief Medical Advisor.

Alcor’s surgery team: Dr. Nancy McEachern, DVM, Surgeon; Aaron Drake, NREMT-P, Surgical Assistant; Hugh Hixon, Cryoprotection Perfusionist; Steve Graber, Assistant Cryoprotection Perfusionist; Max More, Ph.D., Scribe; R. Michael Perry, Ph.D., Cooldown Coordinator; Bonnie Magee, Refractometry. Surgical support staff: Bruce Cohen and Richard Cremeens.

Pre-Deployment
A-2091 was physically active and healthy prior to being diagnosed with a glioblastoma multiforme in her brain during the spring of 2010. Subsequently, she underwent fifteen months of conventional tumor therapies and one experimental medication. These treatments may have slowed the course of the tumor but were unable to prevent its spread. Slowly, she was losing her ability to walk, talk and eat.

Alcor Life Extension Foundation (Alcor) was notified in June 2011 that the member had decided to discontinue further tumor treatments. A local concierge medical provider, Premiere Home Health Care, coordinated her physicians, nursing, physical therapy and other support in her home.

Over the next few weeks, Alcor’s Medical Response Director made advance preparations with a local funeral home, a private air charter for transport and the Orange County Health Department for expedited paperwork, even in the event these were needed after-hours. Local Alcor volunteers were on alert with a vehicle and equipment nearby in the event of a sudden and unexpected clinical death.

Alcor notified Suspended Animation (SA) that member A-2091 was discontinuing treatment for her terminal condition and might require SA standby services soon. Alcor monitored the situation closely and informed local volunteers and officials as changes precipitated. SA also began coordinating preparations directly with the member’s medical providers and family. The family agreed to cover all extended costs associated with having SA deploy a full team to the home well in advance to handle the patient’s standby, stabilization, surgery and field perfusion.

SA visited the member and her family and positioned a vehicle and equipment to support stabilization, surgery and perfusion at the patient’s home. Staff from Premiere and SA worked closely over the following weeks to monitor the patient’s condition and create an action plan.

The patient’s condition declined incrementally over June and July; she lost her ability to communicate verbally and to move on her own, and spent more and more time sleeping. Her physician ordered...
placement of a supra-pubic urinary catheter and a peripherally inserted central catheter.

By early August, the patient was having increasing difficulty swallowing and fewer lucid periods, although her vital signs and blood test values remained within normal ranges. Her neuro-oncologist said her brain scans indicated tumor intrusions further into her brain that would likely begin to interfere with her body's basic life support functions.

On the evening of August 8, 2011, the member’s medical staff and family felt that her death would occur within a few days although it was clinically possible for her to survive much longer. The member’s spouse requested that SA deploy to avoid any risk of not having a full team onsite at the time of clinical death. SA sent a surgeon, a cardiac perfusionist, two staff EMTs and two additional staff to begin the standby at the patient’s home on August 9.

Deployment
As the team arrived, the patient was sitting up, alert and responsive. She was still able to swallow soft foods and thick drinks, but was receiving minimal oral hydration and nutrition. Her vitals remained steady. Her temperature was normal. Blood pressure was 122/98. Pulse 91. Her oxygen saturations were 96% with a nasal cannula delivering oxygen from an oxygen concentrator. Respirations were 23 per minute. A blood draw and analysis in the afternoon showed lab values largely within normal ranges.

In pre-planning, nearby funeral homes either had no room suitable for surgery or declined to support the case “on the advice of corporate legal counsel.” The closest cooperative funeral home was nearly an hour’s drive away from the patient’s home and from the closest airport. If the patient had to be moved there for surgery and perfusion, it would result in unnecessary ischemic time, add dependencies on funeral home personnel and impose extended transport times in traffic.

The member’s home had a clean, well-lit and air-conditioned garage that was barely 30 feet from the room where she was being cared for. The member’s spouse agreed to have SA set up in the garage space for performing stabilization, surgery and field perfusion.

After cleaning and mopping a suitable space, the team set up the ice bath, AutoPulse and ventilator and the perfusionist prepared the Stockert SCPC mini heart-lung bypass machine. A scrub in area was prepared for the surgeon at a corner sink. A large, deep freezer held enough ice for cooling the patient and insulated coolers were set up to chill the organ preservation perfusate solution and keep stabilization medications cold.

Team members divided into two 12-hour shifts between the patient’s home and the closest local hotel, ten minutes away by car. Two Premiere Home Health Care nursing staff also remained with the patient in shifts 24 hours a day.

After determining that the patient’s physician would not be readily available to provide a prompt pronouncement of legal death, Premiere obtained independent 24-hour hospice nurse coverage at the patient’s home. The hospice nurses had authority to pronounce legal death, so SA could begin procedures immediately afterward.

Over the next week, the patient continued to remain fairly stable. Her periods of alertness varied but generally grew shorter. Her breathing grew more labored but respiratory rate stayed at 24. Her vitals often dipped precipitously around 2am, as her blood pressure would drop from around 120/80 to 70/60, her pulse would climb from 90 to above 100 and her oxygen saturation would fall from 95% to below 90% if the nasal cannula were dislodged or removed. Since her hydration was minimal, urine output was also minimal and grew concentrated.

On August 15th, the seventh day of the standby, the initial surgeon SA deployed had to return to regular work and was replaced by another SA surgeon. An eight-hour overlap of the incoming and outgoing surgeon was arranged to avoid gaps in coverage. The perfusionist and remaining team members asked to be allowed to remain on the case to see the patient through.

On August 17th, as the patient’s health appeared to be declining more rapidly, Aaron Drake flew from Scottsdale to Orange County, CA and arrived at the family’s home by mid-afternoon. Over the course of that evening, the patient’s breathing grew more labored interspersed with long periods of apnea. By the morning of August 18, obvious mottling appeared on her feet and her lower left leg became cool. Finger and radial pulses were undetectable. All team members were summoned to the house.

That same afternoon, the ninth day of the standby, the patient stopped breathing. The hospice nurse attempted to detect a heartbeat using a stethoscope. After listening for two full minutes and detecting no heartbeat, the nurse pronounced the patient legally dead at 4:12pm on August 18th, 2011.

Stabilization, Field Surgery and Perfusion
Immediately following pronouncement, the patient was moved from her bed into the portable ice bath and manual chest compressions were given as she was moved down the hall and into the garage area. The AutoPulse chest compression device was started and ice and circulating water applied to the patient once inside the garage.

The rectal occluder and nasopharyngeal temperature probe were inserted and the EZ IO needle set into the left tibial tuberosity. The PICC line was no longer patent. The patient’s nasopharyngeal temperature was 36º C.

Over the first 15 minutes following pronouncement, medications were administered through the intravenous line: 200mg Propofol, 50,000 units Heparin, 250,000 units Streptokinase, 300mg Aspirin, 100 units Vasopressin, 1mg of Epinephrine every three minutes, 400mg S-methylthiourea, 500mg Nicardipine, 1.5g L-Kynurenine, 1.5mg Keterolac, 80mg Gentamicin.

Over the next 15 minutes, the patient received 100ml of THAM, less than 70ml of Vital Oxy, 250ml of 6% Hetastrarch, 100g of Mannitol. Epinephrine continued to be administered every three minutes.

The patient was intubated with a Combitube. Initial insertion encountered resistance. The tube was withdrawn and dried globules of food and mucus were observed in the mouth and on the tube. Visible food was swept from the mouth and the tube was reinserted while mild cricoid pressure was applied. After verification of tracheal placement, approximately 200mls of Maalox was added through the esophageal lumen.

While initial stabilization procedures were delivered, the surgeon scrubbed in. After the first medications had circulated for 15 minutes, the surgeon prepped the right groin area with Chloraprep and Steri-Drape and began a right femoral cut down. Braided silk ligatures were placed around
the femoral artery and vein. A longitudinal arteriotomy was performed releasing an arterial spray. The surgeon inserted a 19Fr arterial catheter into the artery. After several attempts to gently advance the catheter into the aorta without success, the catheter was secured in the common iliac artery. A 21Fr venous catheter was placed into the right femoral vein through a longitudinal venotomy. This catheter could not be manipulated into the vena cava and was secured in the iliac vein. Some venous blood flowed into the catheter. The surgeon then connected the catheters to the patient perfusion circuit. The patient’s temperature was 34º C.

The perfusionist briefly applied light vacuum assist for venous drainage. As drainage began, the perfusionist filled a serum collection kit from which the patient’s stem cells would later be isolated and stored. The remaining venous drainage partially filled a 30 liter waste bag.

Open circuit perfusion continued for 10 minutes with forward flow rates of 700-800mls per minute. The perfusionist maintained circuit pressures between 200-216mmHg. Over this initial period, the patient’s nasopharyngeal temperature dropped from 34º C to 24º C.

Attempting to improve flow, the surgeon requested the perfusion pump be shut off and clamped the circuit. He then removed the 21Fr venous catheter to insert a 17Fr catheter into the inferior vena cava. Removal of the initial catheter brought out a large blood clot. The surgeon suggested that the vessel thrombosed pre-mortem. To try to remove additional clot, the surgeon passed a long clamp proximally into the vein to remove another 20-30cc of clot and then inserted the 17Fr catheter and connected it to the circuit. When the pump was turned on again, however, flows did not change significantly. Some abdominal swelling was noted. The pump was turned off for the last time after a total of approximately 35 minutes of perfusion, using 17L of perfusate.

While the stabilization and perfusion procedures commenced, Aaron called the Orange County Health Department, only to find that their office has closed 12 minutes earlier. As he had earlier obtained the personal cell phone number for the department’s director, he called the private number but only received her voice mail. Aaron left an urgent message with the news and requested her assistance in the matter. He then contacted the private jet company to provide them with a progress report. They asked to be called again when there was approximately one hour remaining before the procedure was finished and the patient would be arriving at the airport. They would alert their pilots now but wait for our phone call before activating them.

The next call was to the mortuary so they could begin processing the death certificate through the California Electronic Death Registry System. Although it was after hours, he instructed them to send the paperwork electronically anyway as someone from the health department would be there to receive and complete the necessary forms required to issue a transit permit – the legal document that was required for the airplane to cross the California state line.

A short while later, the director of the health department returned the call. She had received the voice message while she was driving home from her office. She immediately turned her car around and returned to reopen the building and begin processing the paperwork personally. As Premiere Home Health Care staff...
arrangements for the patient’s physician to sign off on the death certificate, Aaron provided the health department official with the contact numbers for the physician as well as the shipping and receiving mortuary representatives. She said once she had everything completed, she would send both a facsimile and an electronic copy.

Transport
Team members removed the patient from the ice bath into a body bag packed with bags of water ice. This bag with the patient was then placed inside a heavier duty body bag and loaded into the vehicle for transport. Catherine and Aaron departed for the FBO section of John Wayne Airport in Orange County with the patient secured in the back of the vehicle. Aaron called the private jet charter dispatcher while en-route only to find the flight had been delayed by a sudden sand storm in Scottsdale prior to departure. Fortunately, the delay was only around 20 minutes.

When the plane touched down at the airport, the patient was driven out to the private charter area on the tarmac and loaded onto the plane for the flight to Scottsdale, accompanied by Aaron. The flight duration was slightly less than an hour and unremarkable. Upon arrival in Scottsdale, Alcor staff members were waiting with the response vehicle to transport the patient the three blocks to the Alcor facility.

Surgery
The patient arrived at Alcor’s surgery suite at 22:22 and was transferred to the operating table which was covered with a base layer of ice. Additional bags of ice were placed on top of the patient. Aaron Drake disinfected the sternum and an extensive area surrounding it using Betadine surgical scrub applied in expanding concentric circles. Simultaneously, Dr. McEachern shaved and prepped the head in anticipation of establishing burr holes later in the procedure.

Dr. McEachern returned to the chest to perform a median sternotomy. She made a vertical inline incision along the patient’s sternum from the suprasternal notch to below the xiphoid process. Aaron placed the guide of the Sarns sternal saw under the sternum at the suprasternal notch. Steve Graber operated the foot pedal on the floor as Aaron lifted and guided the saw to divide the sternum. After the sternum was separated, the chest was opened with Finochietto rib spreaders, exposing the pericardial sac. Dr. McEachern accessed the heart by making an incision through the pericardium.

Dr. McEachern performed an arterial cannulation of the heart by sewing a purse-string suture in the wall of the aortic arch,
puncturing the vessel within the purse-string, and advancing and securing the catheter. She then repeated this process for the venous cannulation of the heart, going into the right atrium and advancing the cannula into the inferior vena cava. The purse-strings were tightened around the cannulae and secured.

The procedure took 23 minutes from start to finish. Dr. McEachern noted that the patient had a very thick atrium, bilateral hypertrophy in the ventricles and roughly a 4 cm aortic aneurism.

While the perfusion tubing was connected to the cannulae and the ramp was initiated, Dr. McEachern and Aaron moved to the head. Dr. McEachern made two vertical incisions with a scalpel to expose the skull. The scalp was parted with retractors and Aaron created two burr holes using a Codman perforator. Dr. McEachern cleaned each of the burr holes with a Kerrison rongeur prior to inserting two crack-phone elements bilaterally and a thermocouple which were secured using a surgical stapler.

**Cryoprotection Summary (by Hugh Hixon)**

On completion of the right burr hole, clear fluid gushed from the hole, eventually settling down to a leakage of >200 ml/min. There was additional leakage from the left burr hole. Squeezing the neck caused cryoprotectant to gush out of the burr holes. There was no blood in the initial gush of fluid.

The cryoprotectant concentrate pump was adding ~600 ml/min concentrate, running at full speed, but could not maintain the mixing reservoir level. There was almost no venous return and abdominal distention was present. The lungs were massively edematous and fluid was leaking from the mouth.

Since the addition pump could not keep pace with the perfusate losses, pumping air was inevitable. Steve Harris, Alcor's Chief Medical Advisor, was contacted and he recommended concentrating on the head, by clamping the aortic arch at both ends. Hugh decided to go further and simply go to straight carotid perfusion, using perfusate on hand for the field neuro step ramp procedure. Aaron raised the carotids while the switch was organized. Perfusion of the whole body was discontinued to assist the carotid cutdown and to avoid
### TIMELINE

#### Stabilization (by Suspended Animation)

**Thursday, August 18th, 2011, PDT**

<table>
<thead>
<tr>
<th>Time</th>
<th>Event Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>16:12</td>
<td>Pronouncement</td>
</tr>
<tr>
<td>16:13</td>
<td>Ice bath with patient moved into garage</td>
</tr>
<tr>
<td>16:14</td>
<td>Autopulse running</td>
</tr>
<tr>
<td>16:15</td>
<td>Rectal occluder in</td>
</tr>
<tr>
<td>16:16</td>
<td>EZ-IO set</td>
</tr>
<tr>
<td>16:18</td>
<td>200mg Propofol in</td>
</tr>
<tr>
<td>16:18</td>
<td>50,000 units Heparin in</td>
</tr>
<tr>
<td>16:19</td>
<td>250,000 units Streptase in</td>
</tr>
<tr>
<td>16:20</td>
<td>300mg Aspirin in</td>
</tr>
<tr>
<td>16:20</td>
<td>100 units Vasopressin in</td>
</tr>
<tr>
<td>16:20</td>
<td>Ice water recirculation started</td>
</tr>
<tr>
<td>16:20</td>
<td>Dual LogR started, nasopharyngeal 36°C</td>
</tr>
<tr>
<td>16:21</td>
<td>1mg Epinephrine in</td>
</tr>
<tr>
<td>16:21</td>
<td>400mg SMT in</td>
</tr>
<tr>
<td>16:21</td>
<td>Nasopharyngeal temp probe in</td>
</tr>
<tr>
<td>16:22</td>
<td>500mg Niacinimide in</td>
</tr>
<tr>
<td>16:24</td>
<td>1mg Epinephrine in</td>
</tr>
<tr>
<td>16:24</td>
<td>50ml L-Kynurenine in</td>
</tr>
<tr>
<td>16:25</td>
<td>50ml L-Kynurenine in</td>
</tr>
<tr>
<td>16:25</td>
<td>7.5mg Keterolac in</td>
</tr>
<tr>
<td>16:25</td>
<td>Combitue in, ventilator on</td>
</tr>
<tr>
<td>16:28</td>
<td>80mg Gentamicin in</td>
</tr>
<tr>
<td>16:26</td>
<td>1mg Epinephrine in</td>
</tr>
<tr>
<td>16:29</td>
<td>Maalox in</td>
</tr>
<tr>
<td>16:30</td>
<td>1mg Epinephrine in</td>
</tr>
<tr>
<td>16:33</td>
<td>1ml Epinephrine in</td>
</tr>
<tr>
<td>16:35</td>
<td>First incision</td>
</tr>
<tr>
<td>16:36</td>
<td>Nasopharyngeal temp 35.0°C Rectal temp 38.9°C</td>
</tr>
<tr>
<td>16:37</td>
<td>THAM in</td>
</tr>
<tr>
<td>16:38</td>
<td>1ml Epinephrine in</td>
</tr>
<tr>
<td>16:39</td>
<td>Nasopharyngeal temp 34.7°C Rectal 39.0°C</td>
</tr>
<tr>
<td>16:41</td>
<td>1mg Epinephrine in</td>
</tr>
<tr>
<td>16:44</td>
<td>1mg Epinephrine in</td>
</tr>
<tr>
<td>16:47</td>
<td>1mg Epinephrine in</td>
</tr>
<tr>
<td>16:47</td>
<td>21Fr cannula in venous side</td>
</tr>
<tr>
<td>16:50</td>
<td>19Fr cannula placed in artery</td>
</tr>
<tr>
<td>16:50</td>
<td>1mg Epinephrine in</td>
</tr>
<tr>
<td>16:51</td>
<td>Drainage</td>
</tr>
<tr>
<td>16:53</td>
<td>1mg Epinephrine in</td>
</tr>
<tr>
<td>16:57</td>
<td>Perfusion pump off, venous cannula swapped, clots removed</td>
</tr>
<tr>
<td>17:03</td>
<td>Perfusion pump on</td>
</tr>
<tr>
<td>17:06</td>
<td>Autopulse off – battery swap</td>
</tr>
<tr>
<td>17:08</td>
<td>Nasopharyngeal temp 13.3°C</td>
</tr>
<tr>
<td>17:11</td>
<td>Nasopharyngeal temp 12.7°C</td>
</tr>
<tr>
<td>17:15</td>
<td>Abdominal swelling noted</td>
</tr>
<tr>
<td>17:15</td>
<td>Nasopharyngeal temp 11.0°C</td>
</tr>
<tr>
<td>17:18</td>
<td>Nasopharyngeal temp 9.9°C</td>
</tr>
<tr>
<td>17:20</td>
<td>Nasopharyngeal temp 7.6°C</td>
</tr>
<tr>
<td>17:27</td>
<td>Nasopharyngeal temp 6.6°C</td>
</tr>
<tr>
<td>17:32</td>
<td>Perfusion pump off</td>
</tr>
</tbody>
</table>

#### Cryoprotection (by Alcor)

**Thursday, August 18th, 2011, PDT**

<table>
<thead>
<tr>
<th>Time</th>
<th>Event Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>22:22</td>
<td>Patient arrived Alcor</td>
</tr>
<tr>
<td>22:33</td>
<td>Patient transferred to operating table, covered in ice</td>
</tr>
<tr>
<td>22:38</td>
<td>Nancy prepped head for burr holes while Aaron prepped chest for separation</td>
</tr>
<tr>
<td>22:55</td>
<td>Nancy made sternal incisions, opened chest, Aaron assisted</td>
</tr>
<tr>
<td>23:00</td>
<td>Aaron spreads chest</td>
</tr>
<tr>
<td>23:07</td>
<td>Nancy and Aaron begin to insert cannula</td>
</tr>
<tr>
<td>23:15</td>
<td>Cannulated right atrium. Very thick atrium and ventricles noted</td>
</tr>
<tr>
<td>23:19</td>
<td>Patient had abnormal heart, bilateral hypertrophy in ventricles, ~4 cm aortic aneurism</td>
</tr>
<tr>
<td>23:26</td>
<td>Cleared bubbles out of tubing</td>
</tr>
<tr>
<td>23:30</td>
<td>Tied off aorta after cannulation</td>
</tr>
<tr>
<td>23:47</td>
<td>Started ramp</td>
</tr>
<tr>
<td>23:51</td>
<td>Mixing reservoir @ 6 liters</td>
</tr>
<tr>
<td>23:53</td>
<td>Nancy made incisions for burr holes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time</th>
<th>Event Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>23:57</td>
<td>Aaron drilled bilateral burr holes, right then left</td>
</tr>
<tr>
<td>23:59</td>
<td>Huge leak from right burr hole, suggesting a subdural hematoma</td>
</tr>
<tr>
<td>00:12</td>
<td>14.2 liters in the dump, 3 liters/4 minutes</td>
</tr>
<tr>
<td>00:21</td>
<td>20.2 liters in the dump, 6 liters/9 minutes</td>
</tr>
<tr>
<td>00:23</td>
<td>Rectal temperature dropped from 25 C to 12 C, indicating some circulation</td>
</tr>
<tr>
<td>00:29</td>
<td>Mixing reservoir volume: 4 liters. Pump speed maxed out</td>
</tr>
<tr>
<td>00:31</td>
<td>Abdomen distended</td>
</tr>
<tr>
<td>00:47</td>
<td>Switched to neuro step ramp, starting with bag #7</td>
</tr>
<tr>
<td>00:56</td>
<td>88mm perfusion pressure @ 0.75 liters/min.</td>
</tr>
<tr>
<td>01:04</td>
<td>Left jugular located</td>
</tr>
<tr>
<td>01:05</td>
<td>Perfusion stopped to help view surgical field</td>
</tr>
<tr>
<td>01:15</td>
<td>Isolated and raised both carotids</td>
</tr>
<tr>
<td>01:35</td>
<td>Perfusion of neuro restarted. Venous return from left side is good</td>
</tr>
<tr>
<td>01:43</td>
<td>Transferred to second bag. 56.68 Brix</td>
</tr>
<tr>
<td>02:04</td>
<td>Steve switched bag</td>
</tr>
<tr>
<td>02:52</td>
<td>Switched bag – last bag</td>
</tr>
<tr>
<td>03:08</td>
<td>Last bag completed</td>
</tr>
<tr>
<td>03:27</td>
<td>Right side of brain retracted 1 cm, left side of brain not retracted</td>
</tr>
<tr>
<td></td>
<td>Both eyes well retracted</td>
</tr>
<tr>
<td>04:03</td>
<td>Begin plunge to -100º C</td>
</tr>
<tr>
<td>04:33</td>
<td>Change Cooldown program to plunge to -80º C</td>
</tr>
<tr>
<td>13:43</td>
<td>Moved patient to pod, restart Cooldown 1º C/hr to LN2</td>
</tr>
</tbody>
</table>

**Thursday, August 25th, 2011, MST**

<table>
<thead>
<tr>
<th>Time</th>
<th>Event Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>00:51</td>
<td>All thermocouple traces flattened out - endpoint</td>
</tr>
<tr>
<td>09:25</td>
<td>Begin LN2 fill</td>
</tr>
<tr>
<td>13:23</td>
<td>Cooldown dewar full</td>
</tr>
</tbody>
</table>
pumping air. The first bag selected (bag 7, ~67% CNV) was at roughly the M22 concentration in the WB circuit. Since the patient was on the operating table, the hook for the field neuro bags had to be elevated nearly to the 10° OR ceiling, and was lowered for each bag change.

At the end of the cryoprotection the eyeballs were collapsed (normal dehydration response).

The right hemisphere was retracted about 1 cm, under the burr hole, but the left hemisphere under its burr hole did not retract significantly. The skin of the body was tanned, and the head and neck, indicating that the skin was cryoprotected. There is some inflection in the cooling curve that may indicate incomplete cryoprotection (indicated in blue box below).

The glioblastoma was on the left side of the brain surface and had been surgically debulked in the past. There were probably adhesions to the dura and the vasculature was ripped apart when the brain was shrunk by hyperosmolar MHP-2 washout solution or the very hyperosmolar cryoprotectant, and pulled away from the skull, leading to the major leakage observed. This might well result in only partial cryoprotection to portions of the right side of the brain.

The right crackphone element was spring-loaded against the brain (retraction ~1 cm beneath burr hole). The left crackphone element was placed under the dura toward the centerline (no retraction of brain under burr hole). There was a cluster of events on the right side in the -120° C to -130° C portion of the cooldown, but the meaning of this is somewhat uncertain.

The sternal approximator worked very well, but the edematous lungs had to be inserted back into the chest cavity (as is not uncommon).

Field washout: while the brain cooled quite quickly once perfusion was begun, there was no effect on the rectal temperature. 17 liters of organ preservation solution were pumped into the patient, with some coincident abdominal swelling. Conclusion: while the head was perfused, the body was not, for reasons unknown. Given the clots that the washout surgeon removed from the inferior vena cava, we speculated that there may have been pre-mortem clotting.

Issues and Actions

Issue: PICC line, although maintained regularly pre-mortem, was no longer patent after pronouncement. No additional intraosseous line was set.
Action: Always set two intraosseous lines (added to protocol and training September 2011).

Issue: Second dose of vasopressin was not given.
Action: Acquire and use low volume, multi-port extension sets to leave epinephrine and vasopressin syringes in place on line with high volume meds for easier administration (Y connector sets acquired October 2011).

Issue: Lower flow and slower cooling through femorals; major thrombi present.
Action: Surgeon recommends acquiring field-appropriate thoracotomy instruments to allow catheterization of aorta and vena cava to speed procedure and cooling. (Portable thoracotomy instruments acquired October 2011).
The latter half of therapeutic cryopreservation involves three “R”s: resuscitation, rehabilitation, and reintegration. Of the three, reintegration receives the least attention as to its content, so permit me to deconstruct it a bit before diving straight in. First off, it’s r-s-integration, so like r-susitation and r-habilitation, we are talking about some present state or condition that we want to return to – in this case, a state of integration, of being part of a larger whole. By identifying a need for something called reintegration, we are predicting that being awakened from a cryonic slumber, even with every memory intact and in perfect health, is not going to be the same as going to sleep one night and waking up the next morning. The world around us will have changed – possibly quite dramatically – and all that we were prior to cryopreservation may not be enough to immediately begin operating as part of the larger whole as we did before. However, none of us is integrated into all subsystems and sub-communities of the larger human social organism at the same time, and to the same degree. So when we talk about reintegrating revived cryonics patients, are we talking about bare, functional integration into the community immediately around the cryonics facility, or something more than that? And either way, how will we measure success of reintegration? According to the norms at the time of revival, or somehow relative to the individual’s first integration?

I think it is problematic to think of reintegration as a general, one-size-fits-all process that will not require extensive, non-medical background knowledge of the individual patients. Reintegration is as much about how to fit resuscitated patients back into tomorrow, as it is about how they already fit into today. By leaving the reintegration problem entirely to our friends in the future, we may be allowing data about the patients which would greatly assist with reintegration slip through our fingers to be lost in the sands of time.

But there is another problem that is closely related to the reintegration problem, and that is fear of dis-integration, which is really combination of two things: separation from features of one’s present integration, especially family, friends, but also wealth and possessions; and fear of not having a “place” in the future, of not having a reason to get up in the morning, or as the Japanese call it, ikigai.

This problem was very well encapsulated in a recent segment on cryonics on the television show “The Doctors,” when one of the panelists was asked if she would want to be cryopreserved. After her resolute “No,” she was asked why not, so she quickly elaborated, “Well, everybody else you love is not there. Why would you want to be around without people you love?” In reply, one of the more open-minded panelists suggested, “Well, freeze everyone then!” There is a certain logic to this, but social inertia being what it is, it is not a very persuasive argument to someone on the fence (or the other side of it) today.

Nor is such fear soothed by simply telling people that we (or our successors) will figure out how to tackle the reintegration problem closer to the relevant time. And by not addressing people’s fear of disintegration more effectively by making tangible efforts today to assist reintegration tomorrow, we may be hampering our own growth, potentially hindering the pace of development and thus prolonging revival for all patients – making the task of their eventual reintegration all the more difficult.

**Personhood**

It probably goes without saying that reintegration has legal components to it. The one which has received the most attention thus far is asset preservation, but this and most other legal aspects of reintegration rely on the threshold issue of personhood. Legal personality is quite fundamental to our current integration, as is the continuity of that legal personality over time, based on various identifying data like our names, unique appearance, date of birth, etc. Maybe some of us wouldn’t mind fresh starts, but for the sake of exploration I’m going to assume that, given the choice, most cryonicists will want to be recognized as continuations of who they are today, same as we would for any other lapse of consciousness. But for all the good of waking up feeling like we are the same person we were prior to cryopreservation, and expressing that feeling, how do we prove that is what we are? We wouldn’t expect to have much of a problem in an idealized (and impossible) revival scenario that just involved thawing the patient, waking them up with a sharp pinch, and going about curing the disease that caused their initial legal death – but clearly more is going to have to be done...
for today’s patients than that. So the question is, how much deviation from that fictional ideal will the legal system of the day be able to tolerate before concluding that the resuscitated patient is not a continuation of the previous person – or maybe not a person at all? Those who are setting up trusts for their resuscitation may be able to work around the issue of continuity of legal personality by dictating that their cryonics organization and trust advisors are responsible for “recognizing” them, but without legal personality, the resuscitated patient may have rather a difficult time using those saved resources, not having recourse against those who might try to take them away, or even being able to enter into simple contracts.

Law is highly contextual, and particularly sensitive to place and time. We can only make predictions about what the legal result will be of certain facts tomorrow or the next day because we can predict with a reasonably high degree of certainty what the governing rules will be tomorrow or the next day. This gets a lot harder when we are talking about some decades in the future, though we can certainly try to make reasonable guesses about the larger context to which the system will have already had time to react and adapt. For example, it seems improbable that a cryonics organization would attempt an uploading method of resuscitation without it being previously established that apparently self-aware, conscious, intelligent beings can exist on substrates other than biological brains. Thus, the political and legal organs of the day should have already had opportunity to develop a rule on whether such beings are “persons,” and rules governing the effect of copying and transferring them, etc. But is it reasonable to assume that the rules arrived at will be the ones we want, when and where we want them? We can think ahead to all sorts of good arguments supporting our positions on the matter, but we can’t argue them unless and until we actually get there. It seems more practical to advocate for greater recognition and protection of cryonics patients now, through public awareness campaigns, lobbying and legal efforts.

Our Living Family

Some of the more logistical aspects of reintegration are equally ripe for present action. Practically speaking, the closest analogues to revived cryonics patients today are survivors of very long comas. However, only the longest of long comas are remotely comparable to the scale of temporal displacement cryonics patients are looking at, and survivors of such long comas are very rare. As such, good evidence for successful reintegration strategies is unfortunately lacking. However, one shared feature of several of the cases I found was extraordinary commitment of the patients’ families and/or spouses.[1] In fact, this is usually cited as the reason the patient recovered at all – and to some extent that may be true, given that long-term coma patients without such persistent advocates and caregivers might not be expected to receive the same quality of care, and thus survive long enough to reawaken. But surely reintegration, too, is facilitated by involvement of family, just as it is during our first integration in childhood. This got me thinking about whether my family (and friends) would remain connected to me and my care, if I were cryopreserved tomorrow. Would they scan the science headlines for relevant advancements? Would they check in periodically on the health of my cryonics organization? And even if they did at first, how long would their interest last? Would I have any connection to the people at my bedside upon resuscitation?

Well, maybe I would, because I am fairly integrated with the cryonics movement itself – but that is not going to be the case for everyone, and by leaving it entirely up to the patients’ families and friends to remain engaged… well, results may vary. Here, we have a real opportunity to personalize integration. What if cryonics organizations were to track their patients’ family trees, periodically reaching out to new members of the family (once they are old enough to understand) to inform them that they have a relative being cared for in cryostasis? Sadly, there are probably many cryonicists today whose immediate family are resistant or indifferent to their wishes, but perhaps the next generation will find the novelty intriguing. Ongoing family engagement could potentially benefit the patients’ cryonics organizations in the form of donations, and even new members. The real payoff, though, would be to have relatives of the patients on hand to greet them upon resuscitation, and hopefully assist with the reintegration process – maybe even hosting them with some financial assistance from the Patient Care Trust (and/or personal resuscitation trusts, where existing). Even if average human lifespan does not increase significantly in the decades ahead, the older living relatives of revived patients may not be very many generations removed from them.

Right now, the familial data collected by Alcor and CI as part of the sign-up process is significantly less than what most people can rattle off the top of their heads in the way of names of grandparents, aunts, uncles, and cousins. While a cryonics organization may have some ability to obtain this kind of information via medical records after the patient’s legal death, it would certainly be much easier to get it while they are alive. And that still only gets us part of the way. Where I live, at least, vital statistics information on births, marriages and deaths is not made publicly available for genealogical research until many decades after they occur. Part of keeping the family engaged with the patient would involve asking for their assistance in filling in our picture of the patient’s family tree as it grows new branches. This information may also be obtainable by scouring the web and social media, but the point is not to passively track the patient’s living genealogy in the most efficient manner possible – it is about the cryonics organization maintaining an active relationship with the family, keeping the connection between patient and family alive.

Arguably, this is a lot of work to identify relatives who might be tracked down with the aid of genetic data closer to the day, but I think the power of this idea is more than just the possibility of having patient relatives at bedside for resuscitation, but rather in the effort we make in keeping the family informed, and if they’re willing, engaged. It’s about what we can say we are doing, to the person who expresses to us that, in effect, their fear of being revived permanently separated from their families and loved ones is greater than their fear of death.

These are only some of multiple aspects of reintegration that I think can be constructively brainstormed and worked on today. I will be exploring more at the upcoming Symposium on Resuscitation and Reintegration of Cryonics Patients, hosted by the Institute for Evidence Based Cryonics in Portland, Oregon on May 12, 2013.

Endnotes

[1] Annie Shapiro, 30 years. Jan Grzebski, 19 years. Terry Wallis, 19 years. (Wallis was actually in a minimally conscious state, but the effect is the same, for our purposes.)
In this short article I will discuss two distinct developments in contemporary cryonics that are setting the stage of how cryonics is going to be practiced in the foreseeable future.

First, there is the recognition that the most formidable obstacle for people to make cryonics arrangements is not scientific or technological, but psychological. We know this because people tell us so. It is a form of anxiety about the future and social alienation that is even a concern for people who have made cryonics arrangements. Ignoring this and/or telling people to “toughen up” is simply not an effective response.

Second, there is an increasing interest in long-term wealth preservation among people who have made cryonics arrangements and this interest is no longer confined to wealthy Alcor members. In addition, there is also a growing interest in preserving biographical information, ranging from personal memories to tangible objects. This development can reflect a desire to prevent “disintegration” (see Keegan Macintosh’s excellent article in this magazine) during cryostasis or may be motivated by the use of such information for damage repair or validation of resuscitation attempts.

It seems clear to me that these two developments are closely associated and that Alcor can address the desire of their members to preserve biographical information, remain “connected” and make cryonics a less anxiety-inducing choice at the same time.

In the April 2013 issue of Cryonics magazine Mike Anzis contributed a useful review of very long-term storage alternatives for personal information and materials and all these options have their pro’s and con’s. I suspect that many people not only have reservations about the long-term survival of many of the organizations and companies reviewed, but also have concerns about privacy and the alignment of the goals of these entities and the objective of personal survival.

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While it is unrealistic to expect that Alcor can be involved in all matters concerning personal data storage and reintegration (there is an argument for diversification and redundancy, too) it seems rather obvious that Alcor has a more substantial role to play than it does today. It needs to play a substantial role if we want Alcor to be perceived as an organization that does not just see reversible cryopreservation and rejuvenation as a technical problem to be solved, but one that will also do its best to give its patients a face, maintain the social integration of its patients, and facilitate means to protect personal assets and personal information.

I cannot do justice to the practical aspects of this objective in this short article but let me conclude with a number of specific suggestions.

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I cannot do justice to the practical aspects of this objective in this short article but let me conclude with a number of specific suggestions.

We do not know whether email in its current format will still exist in the future but we do know that Alcor owns a domain name and can issue email addresses to their cryopreservation members and provide secure storage of email messages.

We do not need to speculate as much about the nature and compatibility of very long-term data storage technologies if Alcor starts offering such services and will ensure to upgrade them as times change. In addition, Alcor can allow its members to securely edit their personal information and medical records to allow for a better response in time of need.

“By giving our members a visible place and the tools to remain relevant we will also communicate to the rest of the world that we are serious and that we will not let our members slide into oblivion – even during cryostasis.”
COOLER MINDS PREVAIL

APOLIPOPROTEIN E GENOTYPE AND VIRAL INFECTIONS

By Chana de Wolf

Last month this column considered current and future progress in Alzheimer Disease (AD) diagnosis, management, and treatment. Because AD is a terrible brain disease with an increasing rate of prevalence with age, and because it represents one of – if not the – worst conditions that can afflict a person with cryopreservation arrangements, I would like to continue our consideration of this well-known and widely-feared neurodegenerative disease. Specifically, our focus will be on apolipoprotein E (apoE) and research regarding its role in the modulation of physiological responses to certain viral infections.

ApoE is primarily synthesized peripherally in the liver and mediates cholesterol metabolism systemically, but it is also made in the central nervous system by astroglia and microglia (non-neuronal cell types) where it transports cholesterol to neurons. In the CNS, neurons express receptors for apoE that are part of the low density lipoprotein receptor gene family. Historically, apoE has been recognized for its role in lipoprotein metabolism and its importance in cardiovascular disease. Of course, apoE carrier status is also widely known as the major factor determining one’s risk of developing late-onset Alzheimer disease (AD). But more recent research has indicated that the various isoforms of apoE may also have significant immunological impact by conferring different susceptibilities to other diseases, as well.

The human apoE gene is located on chromosome 19 and is composed of 79 individual single nucleotide polymorphisms (SNPs). The three major alleles of apoE, named Epsilon-2 (Ɛ₂), Epsilon-3 (Ɛ₃), and Epsilon-4 (Ɛ₄), are determined by differences in SNPs s429358 and rs7412. The products of these alleles are the protein isoforms apoE2, apoE3, and apoE4, which differ only by a single amino acid at two residues (amino acid 112 and amino acid 158). These amino acid substitutions affect noncovalent “salt bridge” formation within the proteins, which ultimately impacts on lipoprotein preference, stability of the protein, and receptor binding activities of the isoforms (see Table 1).

There are also two minor alleles, Epsilon-1 (Ɛ₁) and Epsilon-5 (Ɛ₅), which are present in less than 0.1% of the population. The three major alleles are responsible for three homozygous (Ɛ₂/Ɛ₂, Ɛ₃/Ɛ₃, Ɛ₄/Ɛ₄) and three heterozygous (Ɛ₂/Ɛ₃, Ɛ₂/Ɛ₄, Ɛ₃/Ɛ₄) genotypes. [I will pause to mention here that it is now quite easy to determine one’s genotype through services such as 23andme.com.]

An interesting document in the field is the literature review by Inga Kuhlman, et al. (Lipids in Health and Disease 2010, 9:8) which assesses hepatitis C, HIV and herpes simplex disease risk by ApoE genotype. An important finding is that the Ɛ₄ allele is found less frequently in populations as they age (e.g., 14% of the general German population vs. 5% in centenarians), indicating that Ɛ₄ is a major mortality factor in the elderly. This is assumed to be a result of the Ɛ₄ allele’s well-known predisposition to Alzheimer and cardiovascular diseases. The authors explain that “apoE4 carriers have a tendency for 5-10% higher fasting total cholesterol, LDL-cholesterol and triglyceride levels relative to homozygote Ɛ₃/Ɛ₃” and that this tendency towards higher lipid levels is probably responsible for the 40-50% greater cardiovascular disease risk in Ɛ₄ carriers. They also point out that “although the molecular basis of the pathology is poorly understood, and likely to be in part due to apoE genotype associated differences in brain lipid metabolism, an apoE4 genotype has been highly consistently associated with the...”
risk of an age-related loss of cognitive function, in an allele dose fashion.” This means, of course, that $\varepsilon_4/$ $\varepsilon_4$ carriers are at greatest risk for cognitive dysfunction with increasing age.

In the field of immune regulation, a growing number of studies point to apoE’s interaction with many immunological processes. In their article, Kuhlman, et al., summarize the impact of the $\varepsilon_4$ allele on the susceptibility to specific infectious viral disease. The authors review a number of studies of the effects of apoE genotype on hepatitis C (HCV), human immunodeficiency virus (HIV), and herpes simplex (HSV) infection and outcome in humans.

In general, apoE4 was found to be protective against hepatitis C infection vs. (E3/E3) controls. Though the exact mechanisms of apoE genotype-specific effects on HCV life cycle remain uncertain, apoE seems to be involved because “available data indicate that the outcome of chronic HCV infection is better among $\varepsilon_4$ carriers due to slower fibrosis progression.”

Concerning the possible influence of apoE genotype on HIV infection and HIV-associated dementia, the authors call attention to the fact that “cholesterol is a crucial component of the HIV envelope and essential for viral entry and assembly.” Given that apoE is essential for cholesterol transport, they hypothesize that apoE genotype influences HIV-induced effects on neurological function. Subsequent review of available research suggests that the 4 allele is associated with higher steady-state viral load and faster disease progression due to accelerated virus entry in 4 carriers, but a correlation between apoE4 and HIV-associated dementia “remains controversial and needs to be clarified by further studies.”

Lastly, a review of the literature regarding the effects of apoE4 genotype on herpes simplex virus (HSV)-1 infection and outcome in humans indicates that apoE4 enhances the susceptibility for HSV-1 “as well as the neuroinvasiveness of HSV-1 compared to other apoE variants” (i.e., HSV-1 is found in more frequently in the CNS of 4 carriers). Importantly, the authors also note that “the combination of apoE4 and HSV-1 may lead to a higher risk of Alzheimer disease (AD) than either factor in isolation.”

Due to its generally being associated with higher risk of cardiovascular disease, dementia, and increased susceptibility to and/or accelerated progression of various viral infections, one may wonder why the 4 allele has not been eliminated by evolutionary selection. This may be explained, in part, by the protective and beneficial effects it exhibits in certain harmful infectious diseases, as demonstrated for hepatitis C.

The exact mechanisms of apoE influence on susceptibility to and course of viral infection remain shrouded. Because the mechanisms of HCV, HIV, and HSV infection are quite similar (i.e., all three viruses compete with apoE for cell attachment and receptor binding), it is interesting to find differences in receptor binding among them.

Involvement or interaction between the immune system, cognition, and brain diseases such as AD is an as-yet widely untouched field of inquiry. Further elucidation of the mechanisms by which apoE may influence the pathogenesis of infectious viral diseases can lead to new developments in the treatment of disease based on an individual’s apoE genotype.

Aside from the role that ApoE plays in susceptibility and progression of infectious disease, there is growing interest in the role that infection or a compromised immune system plays in the development of dementia. For example, despite the successful management of HIV with anti-retroviral drugs, some patients are showing signs of memory impairment and dementia at a relatively young age. Interestingly, these people seem to show accelerated aging, too, which raises important questions about the relationship between the immune system, immunosenescence, and aging.

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<table>
<thead>
<tr>
<th>Isoform</th>
<th>Amino acid 112</th>
<th>Amino acid 158</th>
<th>Relative charge</th>
<th>Lipoprotein preference</th>
<th>LDL receptor binding affinity</th>
</tr>
</thead>
<tbody>
<tr>
<td>apoE2</td>
<td>cysteine</td>
<td>cysteine</td>
<td>0</td>
<td>HDL</td>
<td>low</td>
</tr>
<tr>
<td>apoE3</td>
<td>cysteine</td>
<td>arginine</td>
<td>+1</td>
<td>HDL</td>
<td>high</td>
</tr>
<tr>
<td>apoE4</td>
<td>arginine</td>
<td>arginine</td>
<td>+2</td>
<td>VLDL, chylomicrons</td>
<td>high</td>
</tr>
</tbody>
</table>

Table 1. ApoE isoform amino acid differences and resulting chemical and physiological changes

"An important finding is that the $\varepsilon_4$ allele is found less frequently in populations as they age (e.g., 14% of the general German population vs. 5% in centenarians), indicating that $\varepsilon_4$ is a major mortality factor in the elderly."
Ancient China may seem an unlikely place to search for roots of immortalism, if we restrict the term, as I will here, to mean the idea that humans themselves are to engineer a greatly or infinitely extended life span (rather than a divine or other outside source being the main agency). Yet there was a movement known as Daoism (older, alternative spelling: Taoism; pronounced *dowism*) in which some interesting precursors of modern immortalist thinking can be seen. Daoism was far from a unified system and also shared territory with Confucianism, the other great indigenous Chinese philosophy (both still alive today and not mutually exclusive). Both originated several centuries BCE, Confucianism with Confucius (551-479 BCE), Daoism reputedly with Laozi (“the old one,” pronounced *loh-tsuh*, dates and historicity uncertain, lived possibly a century or two after Confucius). Confucianism offered a blueprint for living as part of a community and considered the state and one’s relations with it important. Daoism was more individual-oriented. Named for the Dao or “Way” of things, the way things work, a universal Ordering Principle though not usually considered a sentient agent or God, Daoism stressed approaches to life which would interface and harmonize with the forces of nature to one’s betterment.

There were three main subdivisions of Daoism which offered rather different prescriptions for using the De (*pronounced day*, older spelling Te) or power of the individual for interfacing with the Dao and securing desired benefits, mainly a long and happy life. Philosophical or Quietist Daoism stressed the idea of creative quietude or *wu wei*, “effortless action,” or we might say, “going with the flow.” One’s power was to be cultivated to the fullest, conserved and not spent on wasteful distractions. Married life with children was not discouraged, but in later centuries there were monasteries enforcing celibacy where devotees could spend their time in quiet contemplation and research. Life and death were viewed as part of a seamless whole, and should be accepted for what they are. In particular death was not something to be feared or resisted — you were born when the time was right and similarly, living a good life as best you could, you departed when it was also the right time, all in accordance with Nature (Dao).

Religious Daoism was also devoted to living well and harmoniously with Nature, as were all Daoisms, but it additionally incorporated appeals to supernatural agents to help with life’s various challenges including natural calamities and threats thought to exist from other supernatural sources. Religious Daoism especially appealed to the broad masses of mainstream society who demanded the usual sort of help and consolation with everyday problems and were not prepared to “go it alone.”

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1 Gruman, 53.
2 Smith, 199-200; 207-11.
3 Smith, 199; 204-06.
In addition to these two Daoisms there was a rather motley group of practitioners of what can be called Bootstrapping or Vitalizing Daoism, who sought augmentation of the power of the individual through self-help programs. In this way they tried to extend the life span as well as stay fit. There was a widespread belief that life and health might be extended indefinitely if one only knew the right technique. There thus came into being an early version of prolongevity – the seeking of a significant extension of the length of human life through human action.

Bootstrapping techniques were varied, ranging from dieting, gymnastics and sexual techniques to various elixirs and potions. There were many groups of practitioners with little in common beyond the overall commitment to some form of self-help in seeking a better, longer life. There were skeptics, in particular the quietist group who, much like some modernd, called in question the desirability of extending life beyond the usual limits.

Ge Hong (pronounced gab hoon; older spelling: Ko Hung; 283-343 CE) was a colorful court official who advocated an eclectic approach to the problems of life. On one hand he was a Confucian who thought the state was necessary for securing the greatest benefit in our imperfect world. On the other, after assimilating Confucianism in his youth, he became interested in the quest of some of the Daoists for physical immortality and became an important advocate of their cause while still insisting Confucianism had its place. For the problems of increased life span and immortality, his approach was also eclectic, subject to insistence that one must attain these benefits on one’s own rather than leaving it up to outside help such as gods (though their blessing on the endeavor might be sought). The benefits of long life were thus open to all who were willing to make the effort and not just a privileged elite.

As a starting point, Ge Hong had to contend with those who insisted that radical life extension, finite or unlimited, wasn’t worth having anyway. His response was a combination of “don’t listen to them” and a recounting of evidence that rebutted the conclusion that lives could never be much lengthened. Much of his “evidence” consisted of hearsay reports that ranged over a wide compass. Certain plants and animals had prodigious life spans: the pine, the cypress, the crane, the tortoise, the tiger, the snake, and so on. Certain historical records verified the existence of immortals known as xian (pronounced SHE-ahn) who lived unobtrusively among their mortal contemporaries, unrecognized by all but a few adepts. Then there were transformations of life forms: pheasants into oysters, snakes into dragons, and so on. Certain historical records verified the existence of immortal substances at least some of which would be longer-lived.

Much of the rationale for the Daoist longevity practices and beliefs related to qi (pronounced chee), the life force, which was associated with breath. Breathing exercises and gymnastics were obvious ways to enhance and sustain this life force; modern variants are still widely practiced today, with verified medical benefit. The same is true for sensible eating habits; nourishing the body

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4 Gruman, 37-49; Smith, 199-204.
5 Cf. Gruman, 6.
6 Cf. Gruman, 52-53; Lee.
7 Knapp; Gruman, 51-54.
8 Gruman, 52-53.
9 Knapp.
10 Gruman, 56.
11 Gruman, 47.
was nature’s way of furthering the life force. (Actually there were some very restrictive dieting practices that could have been harmful applied rigorously. But at least some of the Daoist programs, stressing restraint and emphasizing low-starch vegetables, no doubt were helpful.) As for sexual practices, there were ways allegedly of concentrating the life force and increasing longevity by withholding sexual climax through repeated “performances,” with questionable verification (and there was some Daoist opposition to these practices). Then there was alchemy, to nourish the body or otherwise affect it to achieve enhancements well beyond nature’s usual limits. Alchemy we have to say was a resounding failure, despite any hopes and any attempted reasoned approach. (That Ge Hong himself died at age sixty, unremarkable for his times as well as ours, underscores this futility.)

On the plus side, the early Bootstrapping Daoists did achieve some benefits and no doubt longer lives through exercise, hygiene and good dieting. And they did take the stance that radical life extension was desirable and tried to achieve it through a reasoned approach rather than just appealing to extrahuman agents. Though their methods were not scientific they could be called protoscientific and their accomplishment amounted to a protoscience of prolongevity. In other ways their practices prefigured sciences that would follow: chemistry, mineralogy, botany, zoology, and pharmaceutics.

With this in mind we may draw some inspiration from these early immortality seekers even as we try to do better at bootstrapping ourselves into genuine radical life extension through the tools of modern science. Our stated intentions meet much the same dichotomy of opposition and support as happened long ago. Some say that death is “natural,” one should accept it and shun the “impossible” task of resisting it, while others, notably including cryonicists, beg to differ. It is interesting that this division of views carries over into modern Daoism. There are quietists today who echo every bit of the anti-immortalist sentiments Ge Hong encountered and caution against the wish for life beyond the usual limits. Other Daoists however would welcome any radical life extension and see it as a gratifying vindication of still-respected traditions. Perhaps they would approve the thought that a new kind of scientific Daoism is possible and arguably in the works, with real prospects of success in the conquest of death.

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**Bibliography**


In all, the ancient Daoists attempted through a reasoned approach to enhance longevity and if possible achieve immortality. Their means, at least for more radical life extension, suffered from a number of defects that disqualify them as scientific in a modern sense. Among these were beliefs that vast life extension was achieved in remote past times or currently is enjoyed by certain individuals either in remote geographical locations or nearby but concealed from public notice. Coupled with this were a host of fanciful beliefs not backed by hard evidence – for example that cinnabar could make one immortal by a transformation related to its (alleged) ability to transmute metals into gold. Ge Hong in particular appears to have been more a compiler of results claimed by others than a researcher himself. (After his time there was a marked decline in Chinese references to life-extension practices based on alchemy.)

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12 Ibid.

13 Gruman, 52.
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www.alcor.org  Cryonics / May 2013 21
Older Brain Is Willing, but Too Full

Learning becomes more difficult as we age not because we have trouble absorbing new information, but because we fail to forget the old stuff, researchers say. Mice whose brains were genetically modified to resemble those of adult humans showed no decrease in the ability to make the strong synaptic connections that enable learning — a surprise to neuroscientists at the Medical College of Georgia at Georgia Regents University, whose findings appear in the journal *Scientific Reports*. Yet as the modified mice entered adulthood, they were less capable of weakening connections that already existed, and that made it hard for them to form robust new long-term memories. Think of it as writing on a blank piece of white paper versus a newspaper page, said the lead author, Joe Z. Tsien. “The difference is not how dark the pen is,” he said, “but that the newspaper already has writing on it.” The researchers focused on two proteins – NR2A and NR2B – long known to play a role in the forging of new connections in the brain.

Douglas Quenqua / New York Times
21 Jan. 2013
http://www.nytimes.com/2013/01/22/science/older-brain-is-willing-but-too-full-for-new-memories.html?_r=3&

One Form of Neuron Turned into Another in the Brain

A new finding by Harvard stem cell biologists turns one of the basics of neurobiology on its head by demonstrating that it is possible to turn one type of already differentiated neuron into another within the brain. The discovery by Paola Arlotta and Caroline Rouaux “tells you that maybe the brain is not as immutable as we always thought, because at least during an early window of time one can reprogram the identity of one neuronal class into another,” said Arlotta, an associate professor in Harvard’s Department of Stem Cell and Regenerative Biology (SCRB). The work, which uses a mouse model, is being published online Jan. 21 by the journal *Nature Cell Biology*. The experiments targeted callosal projection neurons, which connect the two hemispheres of the brain, and turned them into neurons similar to corticospinal motor neurons, one of two populations of neurons destroyed in Amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig’s disease. To achieve such reprogramming of neuronal identity, the researchers used a transcription factor called Fezf2.

Harvard University
21 Jan. 2013
http://news.harvard.edu/gazette/story/2013/01/new-avenue-in-neurobiology/

Three-Photon Microscopy Improves Biological Imaging

Scientists may be a step closer to cracking one of the world’s most compelling mysteries: the impossible complexity of the brain and its billions of neurons. Cornell researchers have demonstrated a new way of taking high-resolution, three-dimensional images of the brain’s inner workings through a three-fold improvement in the depth limits of multiphoton microscopy, a fluorescence-based imaging technique with Cornell roots. Publishing in the journal *Nature Photonics* Jan. 20, senior author Chris Xu, associate professor of applied and engineering physics, and colleagues have demonstrated high-resolution, 3-D imaging of the subcortical region of a live, intact mouse brain. They have broken the fundamental depth limit of standard two-photon microscopy, which is a widely used imaging technology invented in 1990 by Watt Webb and Winfried Denk at Cornell. Xu and Webb demonstrated three-photon fluorescence imaging while Xu was a graduate student in Webb’s lab in 1995, but its advantages were not fully recognized then, Xu said.

Anne Ju / Cornell University
21 Jan. 2013
http://www.news.cornell.edu/stories/Jan13/3mpm.html

Researchers Map Emotional Intelligence in the Brain

A new study of 152 Vietnam veterans with combat-related brain injuries offers the first detailed map of the brain regions that contribute to emotional intelligence – the ability to process emotional information and navigate the social world. In a study of Vietnam veterans, the researchers found that many of the same brain regions are important to general and emotional intelligence. The study found significant overlap between general intelligence and emotional intelligence, both in terms of behavior and in the brain. Higher scores on general intelligence tests corresponded significantly with higher performance on measures of emotional intelligence, and many of the same brain regions were found to be important to both. The study appears in the journal *Social Cognitive & Affective Neuroscience*. “This was a remarkable group of patients to study, mainly because it allowed us to determine the degree to which damage to specific brain areas was
related to impairment in specific aspects of general and emotional intelligence,” said study leader Aron K. Barbey.

Diana Yates / University of Illinois
22 Jan. 2013
http://news.illinois.edu/news/13/0122emotional_intelligence_AronBarbey.html

Progress in Delivering Large Molecules to Cells

Living cells are surrounded by a membrane that tightly regulates what gets in and out of the cell. This barrier is necessary for cells to control their internal environment, but it makes it more difficult for scientists to deliver large molecules such as nanoparticles for imaging, or proteins that can reprogram them into pluripotent stem cells. Researchers from MIT have now found a safe and efficient way to get large molecules through the cell membrane, by squeezing the cells through a narrow constriction that opens up tiny, temporary holes in the membrane. Any large molecules floating outside the cell – such as RNA, proteins or nanoparticles – can slide through the membrane during this disruption. Using this technique, the researchers were able to deliver reprogramming proteins and generate induced pluripotent stem cells with a success rate 10 to 100 times better than any existing method. They also used it to deliver nanoparticles, including carbon nanotubes and quantum dots, which can be used to image cells and monitor what’s happening inside them.

Massachusetts Institute of Technology
23 Jan. 2013

Patent Application Filed for All-in-One Robotic Fabricator

While some 3D printing manufacturing processes are currently automated, most still need human intervention and labor to complete the process and assemble the fabricated parts into the final product after printing. Bedford based Roomba maker iRobot Corporation, founded in 1990 by

Massachusetts Institute of Technology roboticists, has filed a US patent entitled “Robotic Fabricator,” a completely autonomous all-in-one product fabrication robot that handles manufacturing (including 3D printing) and all the post printing work from seed component to mature product. Connectors, fasteners, seams, and similar interfaces are frequently a source of failure in the end product of standard 3D printing. Furthermore human intervention and labor are required for assembling a finished product. iRobot’s Robotic Fabricator is going to change all that: it automates the manufacture and assembly processes aiming to reduce the need for human labor, decrease manufacturing costs and improve product quality.

www.3ders.org
23 Jan. 2013

Computer Breakthrough: Code of Life Becomes Databank

Scientists in Britain Jan. 23 announced a breakthrough in the quest to turn DNA into a revolutionary form of data storage. A speck of man-made DNA can hold mountains of data that can be freeze-dried, shipped and stored, potentially for thousands of years, they said. The contents are “read” by sequencing the DNA – as is routinely done today, in genetic fingerprinting and so on – and turning it back into computer code. “We already know that DNA is a robust way to store information because we can extract it from bones of woolly mammoths, which date back tens of thousands of years, and make sense of it,” said Nick Goldman of the European Bioinformatics Institute (EBI) in Cambridge. “It’s also incredibly small, dense and does not need any power for storage, so shipping and keeping it is easy.” To prove their concept, the team encoded an MP3 recording of Martin Luther King’s “I Have A Dream” speech; a digital photograph of their lab; a PDF of the landmark study in 1953 that described the structure of DNA; a file of all of Shakespeare’s sonnets; and a document that describes the data storage technique.

Richard Ingham / AFP
24 Jan. 2013
http://www.google.com/hostednews/afp/article/ALeqM5iczH1amyegBGTWTGbwxvUDEbrQsdolC-G4d421a2b487699b43ec004738ea055a9b101

Doctor’s Office Replaced with Telepresence Kiosk

Telepresence physicians have been predicted since Hugo Gernsback foresaw the “radio doctor” in the 1920s. HealthSpot of Dublin, Ohio takes this idea a step further with its HealthSpot Station. It’s a telepresence kiosk that acts as an alternative to the traditional doctor’s office. In the United States, there is increasing pressure on the health system, yet the Association of American Medical Colleges predicts that by 2025 there will be a physician shortage of 130,000. Billed as a telehealth system, the HealthSpot Station is a telepresence kiosk designed to take pressure off a beleaguered health care system by providing a private area where acute care patients can speak to a physician over a high-definition video conference system. Its purpose is to act as an alternative to urgent care centers and emergency rooms while giving physicians an alternative to urgent care centers and emergency rooms while giving physicians a way to use their time more efficiently. There is an attendant on duty and inside is a suite of digital instruments to aid diagnosis, such as a pulse oximeter, blood pressure cuff, dermascope, patient touchscreen, video conference screen, otoscope and stethoscope.

David Szondy / Gizmag
27 Jan. 2013
http://www.gizmag.com/healthspot/25972/
There's no debating the power of omega-3 fatty acids. From support for heart health and brain function to help with inflammation, their broad-spectrum benefits have been firmly established in a wealth of studies.19

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A bottle containing 120 softgels of Super Omega-3 EPA/DHA with Sesame Lignans and Olive Fruit Extract retails for $32. If a member buys four bottles, the price is reduced to $21.00 per bottle. If 10 bottles are purchased, the cost is $18.68 per bottle. (Item #01642)

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Supportive but not conclusive evidence shows that consumption of EPA and DHA omega-3 fatty acids may reduce the risk of coronary heart disease.

References

These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure or prevent any disease.
**About the Alcor Foundation**

The Alcor Life Extension Foundation is a nonprofit tax-exempt scientific and educational organization dedicated to advancing the science of cryopreservation and promoting cryonics as a rational option. Being an Alcor member means knowing that—should the worst happen—Alcor’s Emergency Response Team is ready to respond for you, 24 hours a day, 365 days a year.

Alcor’s Emergency Response capability includes specially trained technicians and customized equipment in Arizona, northern California, southern California, and south Florida, as well as many additional certified technicians on-call around the United States. Alcor’s Arizona facility includes a full-time staff, and the Patient Care Bay is personally monitored 24 hours a day.

Although monthly meetings are not held regularly, you can meet Los Angeles Alcor members by contacting Peter.

**San Francisco Bay:**

Alcor Northern California Meetings are held quarterly in January, April, July, and October. A CryoFeast is held once a year. For information on Northern California meetings, call Mark Galeck at (408) 245-4928 or email Mark_galeck@pacbell.net.

**FLORIDA**

Central Florida Life Extension group meets once a month in the Tampa Bay area (Tampa and St. Petersburg) for discussion and socializing. The group has been active since 2007. Email arcturus12453@yahoo.com for more information.

**NEW ENGLAND**

Cambridge:

The New England regional group strives to meet monthly in Cambridge, MA — for information or to be added to the Alcor NE mailing list, please contact Bret Kulakovich at 617-824-8982, alcor@bonfireproductions.com, or on FACEBOOK via the Cryonics Special Interest Group.

**PACIFIC NORTHWEST**

Cryonics Northwest holds regular meetings for members of all cryonics organizations living in the Pacific Northwest.

For information about upcoming meetings and events go to: http://www.facebook.com/cryonics.northwest

A Yahoo mailing list is also maintained for cryonicists in the Pacific Northwest at http://tech.groups.yahoo.com/group/CryonicsNW/.

**British Columbia (Canada):**

The contact person for meetings in the Vancouver area is Keegan Macintosh: keegan.macintosh@me.com

**Oregon:**

The contact person for meetings in the Portland area is Chana de Wolf: chana.de.wolf@gmail.com

**ALCOR PORTUGAL**

Alcor Portugal is working to have good stabilization and transport capabilities. The group meets every Saturday for two hours. For information about meetings, contact Nuno Martins at n-martins@n-martins.com. The Alcor Portugal website is: www.alcorportugal.com.

**TEXAS**

Dallas:

North Texas Cryonauts, please sign up for our announcements list for meetings (http://groups.yahoo.com/group/cryonauts-announce) or contact David Wallace Croft at (214) 636-3790 for details of upcoming meetings.

**Austin/Central Texas:**

We meet at least quarterly for training, transport kit updates, and discussion. For information: Steve Jackson, 512-447-7866, sj@sijgames.com.

**UNITED KINGDOM**

There is an Alcor chapter in England. For information about meetings, contact Alan Sinclair at cryoservices@yahoo.co.uk. See the web site at www.alcor-uk.org.
**What is Cryonics?**

Cryonics is an attempt to preserve and protect human life, not reverse death. It is the practice of using extreme cold to attempt to preserve the life of a person who can no longer be supported by today’s medicine. Will future medicine, including mature nanotechnology, have the ability to heal at the cellular and molecular levels? Can cryonics successfully carry the cryopreserved person forward through time, for however many decades or centuries might be necessary, until the cryopreservation process can be reversed and the person restored to full health? While cryonics may sound like science fiction, there is a basis for it in real science. The complete scientific story of cryonics is seldom told in media reports, leaving cryonics widely misunderstood. We invite you to reach your own conclusions.

**How do I find out more?**

The Alcor Life Extension Foundation is the world leader in cryonics research and technology. Alcor is a non-profit organization located in Scottsdale, Arizona, founded in 1972. Our website is one of the best sources of detailed introductory information about Alcor and cryopreservation (www.alcor.org). We also invite you to request our FREE information package on the “Free Information” section of our website. It includes:

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