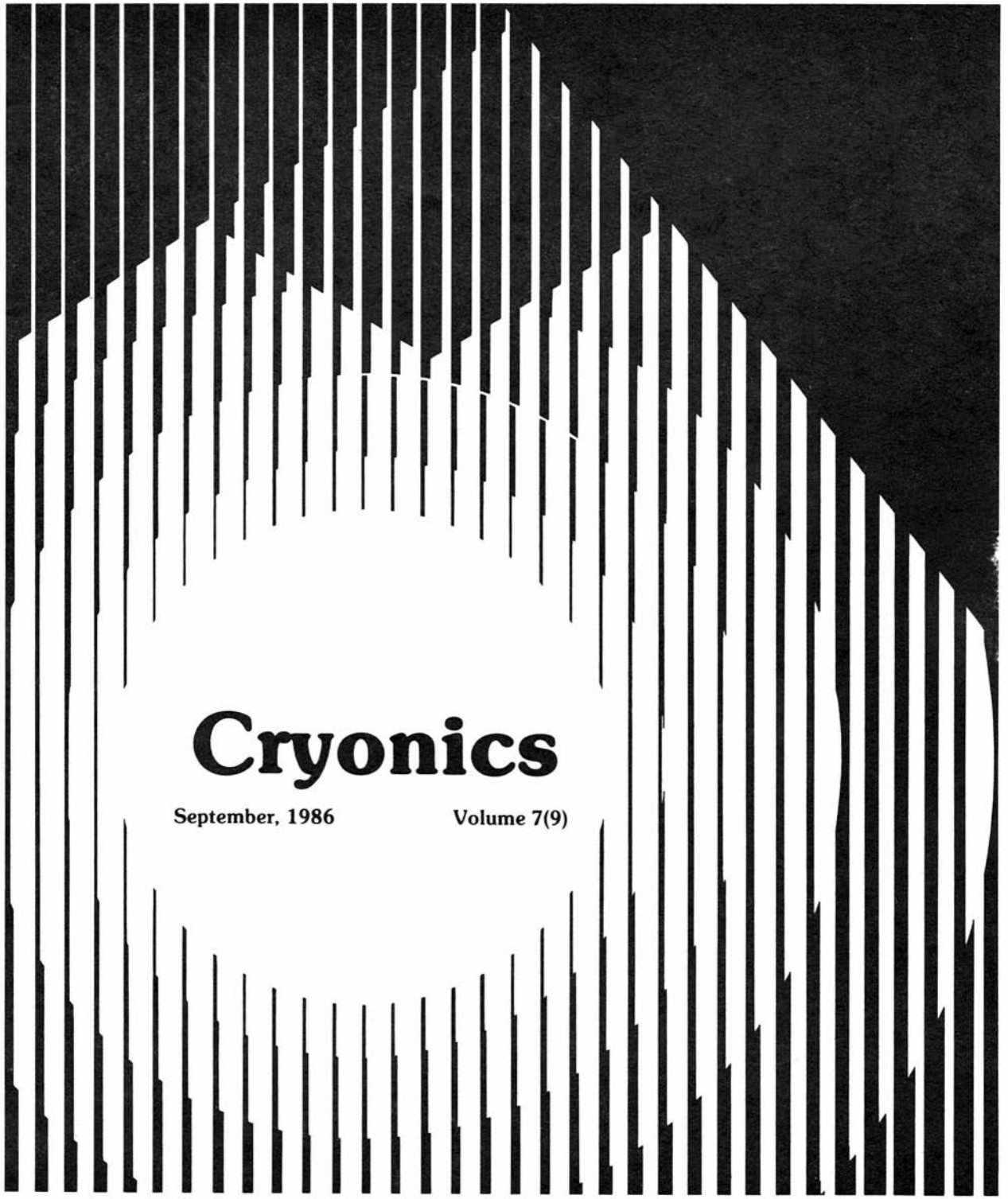

Cryonics

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EDITORIAL MATTERS

We have received a number of entries in our Bracelet Message Contest. Some of them have been really outstanding. Unfortunately, a snag has developed. The large company with the nationwide marketing network whom we were counting on to provide tags and engraving appears to be in the process of going belly-up. Initially they were quite responsive to us, sent along sample tags and appeared to be very reliable. A check of local vendors carrying their tags reported a long history of good business dealing with them.

Subsequently, we've had nothing but trouble -- unreturned phone calls, broken promises and now — the last straw, a disconnected phone when we call! We are going to continue to look for tag vendors. In particular we are trying to track down the companies that **manufacture** the blanks. This information is kept as a tight secret by the tag vendors (for obvious reasons) and so far we haven't been able to crack this lock hold.

We are increasingly finding that wherever possible it is important to eliminate the middleman when essential services are concerned. Tomorrow, Medical ID tags, next year, a liquid nitrogen supply!

We still intend to proceed with the contest — selecting the best message and awarding the prizes. But, it may be awhile before we can upgrade the ER system by making new tags available.

If you have information or can help us locate either new medical ID tag vendors or manufacturers, please let us know. We'd really like to get this problem solved!

1981-1984 CRYONICS Indexes Available

Psssst, buddy. Remember that article in CRYONICS two years ago that you really liked, but you just can't remember the title, or the subject, or the author, or the issue. Now we can offer a solution. Steve Bridge's **Indexes to CRYONICS** for 1981 through 1984 all together in one place. If you can't remember which of your issues has the previous year's annual index (they **are** irregular), or if you're new to cryonics and CRYONICS and want to know what we were doing back when, this collected index may be the answer. It is still grouped by year, unfortunately, but it's a lot easier than Easter Egging the Table of Contents of each issue. The price for the 1981 - 1984 Combined Index is $2.00.

LEGISLATIVE UPDATE

Several readers have inquired about what happened to SB 1405: the Roberti "animal rights" bill which would allow humane officers to carry guns and enter our premises armed and at will — with or without probable cause. We haven't reported on this bill because until recently nothing much was happening with it. Due to unfavorable mail to legislators (some of it generated by cryonicists!) and pressure from university and industry groups, the bill has been radically modified.

On July 8th the Assembly Judiciary Committee unanimously passed a heavily modified version of the bill. SB 1405 now provides only for a **supplemental** inspection program to be provided by the state and for that program to be used only in instances where the federal government is not carrying out frequent enough inspections of research facilities. It requires that a Humane Officer (as defined in the bill) be invited to accompany the state inspector. The role of the Humane Officer is limited strictly to that of an observer, although the bill does allow for the Humane Officer to add comments to the official inspection report.

The bill still has a way to go before becoming law. Because the revised bill contains provisions for state financing of "supplementary inspections" the bill now goes to the Assembly Ways and Means Committee for consideration of its financial impact. As it stands now, the bill has been largely gutted of its more objectionable components and probably will not make a lot of difference to researchers if it is passed. Except, perhaps, to allow animal rights raiders to "case" facilities, and select targets.

However, if you live in California and don't much like the feel of the Franchise Tax Board's hand in your pocket every year, you might write another letter to your Assemblyman suggesting this is a service you really feel you can do without.

NMR--A QUANTUM ADVANCE

by Mike Darwin

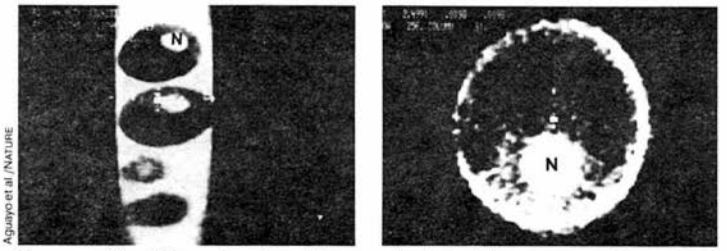
About 8 months ago a cryonicist who also happens to have a Master's Degree in biochemistry (as well as a good background knowledge of engineering and

physics) and whose initials are Hugh Hixon, sneered at me when I mentioned the possibility of getting NMR resolution to the cell level. It should also be noted that a lot of other people in the know "sneered" at this suggestion as well. (Since I seldom sneer, the accuracy of this account is in considerable doubt. I **do** recall expressing an opinion that medical NMR imaging equipment must be pushing the limits of resolution because of the difficulty of localizing the imaging signals to that degree. I probably also delivered a disclaimer concerning my ignorance of the specific technology. Obviously, my ignorance was worse than I thought. This will change. -HH)

For those of you who don't know what Nuclear Magnetic Resonance (NMR) and Magnetic Resonance Imaging (MRI) are, NMR is a technique which allows you to determine the structure of chemicals, and MRI uses the same technique to "look" inside living systems by sweeping them with a very strong magnetic field while pulsing with a radio frequency signal. At a certain combination of frequency and field strength certain types of atoms resonate, or return a detectable signal. It is a particularly exciting analytical and imaging technique because it does not involve the use of damaging radiation, radioactive tracers, or "analog" chemicals which can interfere with metabolism.

The principal problem with MRI has been the limits of its resolution. Currently, the resolution limit on clinical machines is about 2 mm. This is great for seeing tumors, cerebral hemorrhages, and so on, but it doesn't really let you look inside cells -- or even resolve the outlines of individual cells for that matter.

Well, Hugh and the others have gotten a surprise! In a stunning tour de force, James Aguayo of Johns Hopkins University in Baltimore has reported the development of an MRI **microscope**! Reporting in the July 10 issue of **NATURE**, Aguayo has presented an incredible series of photos of single large cells (ova of the African clawed toad) showing nuclei and membrane structure, and of the interior structure of a mouse eye. In the best case, the image resolution is 10 x 13 microns! Their instrument is a modified high resolution NMR spectrometer (designed for analytical chemistry rather that imaging).



Four ova of the African clawed toad, Xenopus laevis, *at different stages of development, are NMR-imaged at a resolution of 16×27 microns (the smallest dimensions at which the object can be distinguished). The nucleus (N) of the cells is distinct from the dark cytoplasm, as it is also in a single ovum (right), imaged at 10× 13 microns.*

This is potentially a very powerful technique. It means being able to evaluate the structure and biochemistry of living organisms and living tissue without disturbing them in the process. With phosphorus MRI you should be able, for example, actually to look at the energy biochemistry of individual cells, as well as their structure, and evaluate a tissue's ATP level. This new technique

should be capable of giving an incredibly detailed picture of the workings of the cell. One of the more intriguing pictures in the **NATURE** article shows a cell, and off to the side, a "ghost" that defines the distribution of fat in the cell, which the researchers noted slowly disappeared as it was metabolized.

It also has profound implications for clinical medicine. It will now probably be possible to someday tell if critical brain cells are missing, or if a growth deep inside the body is malignant or benign. In embryology it should be possible to follow the development and differentiation of cells. It is hard to exaggerate the potential importance of this technique. In cryobiology it should be possible to examine cells during freezing and in the frozen state, and to look at membrane structure both in natural cells and in artificially created cells. The key question at this point is: what is the ultimate limit on MRI resolution? Since Aguayo's work appeared in **NATURE**, that's a question I'm finding fewer and fewer takers willing to speculate on. (Another question is, how fast the image can be constructed. The images in the **NATURE** article took 4-8 minutes to build up, because the resonating atoms take a long time to settle down after they're pulsed. I don't know if this will be a fundamental physical limit or not. -HH)

It is immediately obvious that data collection at this resolution is going to require data processing on a massive scale, and that display of the information gained in any comprehensible form will require even more computer power. In another article that has been pointed out to us (**Science News, 130,** 52 (July 26, 1986)), researchers at MIT have produced the first **computed** hologram, an event which clearly presages the ability to produce solid-appearing images of microscopic objects. And will also require large amounts of computer time. So, while the MRI microscope appears relatively easy to implement, really dramatic performance is going to have to wait until the instrument is coupled to a good-sized computer.

WHATEVER HAPPENED TO THE OMNI ARTICLE?

Some months ago, we reported that OMNI was going to run an article on cryonics (and in particular on ALCOR and neuropreservation) in the Antimatter section of the magazine. That article was scheduled to appear in the June '86 issue of OMNI. No doubt some of you must be wondering what happened.

The article initially came about as a result of select mailings ALCOR did to a number of publications. OMNI expressed an interest, but ALCOR was very dissatisfied with the notion that coverage would be in the Antimatter section, cheek by jowl with the likes of cattle mutilations, extraterrestrial abductions, and psychic surgery. Mike Darwin, in particular, argued interminably with the OMNI reporter doing the story that: a) cryonics was a more interesting and provocative issue than a three paragraph blurb could cover, and b) cryonics did not need or deserve the company of the "lunatic fringe" kooks who normally appear in the Antimatter section.

The reporter, Nancy Lucas, agreed to try to persuade her editor that cryonics raised broader issues and that it really was a more serious subject which merited greater coverage. After much effort, she succeeded. The

Antimatter story was canned and OMNI made contact with ALCOR at the LIFE EXTENSION BREAKTHROUGH CONFERENCE to talk over doing a more detailed story.

A few weeks later Mike Darwin was contacted by OMNI reporter Paul Bagne. Mike turned Bagne on to the annual Society for Cryobiology meeting which was going on in Augusta, Georgia. To his credit, Bagne dropped everything, hopped on a plane (an all-night "red eye" flight) and attended the final two days of the Cryo '86 session. A few days later he arrived at ALCOR's facilities in Fullerton and interviewed Mike Darwin. He also gathered information from cryonics organizations in Northern California and Michigan in researching the article.

The article which resulted from these peregrinations is an **interesting** one. It is **not** a glowing testimonial to cryonics. But it is reasonably fair. It is a well written article, and Bagne did get most of his facts right (an amazing achievement for most journalists covering cryonics). But, most importantly, the article exposes the issue of conflict between cryonicists and cryobiologists -- and it does so in a thoughtful and reasonable manner.

We have seen a rough draft of the article (a very unusual courtesy -- the first time EVER we've had such a courtesy extended to us by any journalist anywhere) and, on balance, we like it. We particularly like the way it ends (we hope they retain this ending in the final article, and, if they don't, we'll share "our version" of it with you).

The article is scheduled to appear in the October issue of OMNI, which will be a "life extension issue" and will feature a wide range of articles on efforts to extend the human lifespan.

We understand that Bob Guccione (OMNI's publisher) is planning to begin a monthly newsletter on life extension similar to the one published by the Life Extension Foundation. We have met and spoken with the editor-to-be of this newsletter and it is possible, just possible, that there will be additional opportunities for a broad cross-section of people to be exposed to cryonics in a more detailed and comprehensive manner than in the "one-shot", one dimensional articles the media has given us in the past.

We don't know if the OMNI article will do us any good. Certainly it is the first major national "feature" press coverage that cryonics has had for a long, long time. At least it lets people know we're still out there. One thing it **has** demonstrated to us: if you push real hard for quality and try to get good reporters to thoughtfully explore an idea, sometimes you get lucky.

ADVENTURE IN SUNNYVALE

Saturday, July 26th and Sunday, July 27th brought nine ALCOR Suspension Members together in Sunnyvale, California for a hands-on weekend of training in cryonic suspension transport procedures. The session was hosted by Cathy Woof and Thomas Donaldson in their lovely home, located very conveniently about a mile off of El Camino Real, the main thoroughfare through Sunnyvale. The session was a very productive one, and Mike Darwin reports that this group of students was by far his most outstanding.

The trainees consisted of Fred and Linda Chamberlain (the dynamic duo who founded ALCOR in 1972), Thomas Donaldson and Cathy Woof (Thomas is a Ph.D. mathematician and Cathy is a comparative biochemist working for the Alza Drug Company), Keith Henson and Arel Lucas (Keith is an engineer and a founder of the L5 Society and his wife Arel has a comprehensive medical background), and Roger Gregory and Naomi Reynolds (software engineers and pioneers in the development of Hypertext). With a group like that, such outstanding performance is not surprising. This team proved not only sharp of mind but quick of hand -- and they made many useful suggestions for improving transport procedures. Mike was very impressed by the speed at whic this group picked up the manual skills required to complete the course, particularly the folks with engineering backgrounds who seemed to find it a real piece of cake.

Thomas Donaldson, Cathy Woof, Arel Lucas, and Naomi Reynolds work with Mike Darwin on the intubation trainer.

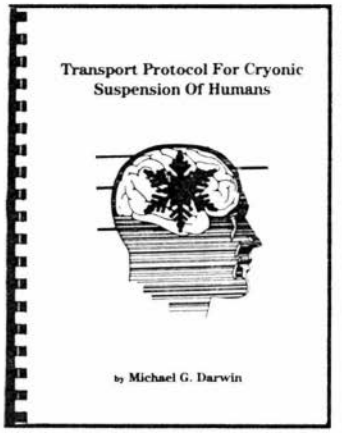
The session went smoothly and was reasonably well organized. This is a little surprising considering what went on in the 12 hours or so prior to it. There's a bit of an adventure story, and it's worth sharing.

Several weeks prior to the training session Thomas Donaldson contacted Mike to ask about arranging lodging. Mike suggested something simple and inexpensive: a Motel 6, which is located not far from the Donaldson's residence. Reservations were made, but a few days later Thomas called back to say that Motel 6 had cancelled the reservation due to a "biker's convention" which was going to be in Sunnyvale that weekend. Thomas did a little investigating and found a small "mom and pop" style place about a half mile from his home, located right on the El Camino real, conveniently close to nice restaurants and other amenities.

Mike Darwin arrived in Sunnyvale in the afternoon on the Friday before the session and stopped at a gas station to ask directions to the motel. That was the first hint that he was in for interesting night, in a very Chinese sort of way. The station attendant arched his eyebrow and made a few coy remarks before responding with remarkably precise directions.

Mike arrived at the motel, checked in, found the accommodations acceptable and adjourned to the Woof-Donaldson's for an evening of conversation. When he returned to the motel around midnight he found it a changed place. In fact, what he found was a "brothel" operation in full swing. The quiet little "mom and pop" business turned out to be the base of operations for a group of call girls -- complete with stretched white Cadillacs and the other associated trappings. Mike's room was sandwiched between those of two very busy working girls. The walls were paper thin.

When Mike got up around 2 AM to take a good, long cold shower he noticed that the management (or perhaps the last guest) had thoughtfully laid out prophylactics next to the clean towels! Finally, around 4:30 AM the commotion settled down and Mike began to drift off to sleep. At which point someone began madly pounding on his door, demanding that he send "Millie" out. Despite Mike's assurances through the closed door that "Millie isn't in here", the fellow refused to take no for an answer. A word of caution about inexpensive motels: there are no phones in the room and that means no easy way to call for assistance at 4:30 in the morning. Finally, Mike opened the door and after a brief confrontation the drunken guest or customer departed, satisfied that Millie was indeed not in the room, or not worth pursuing if she was.



Thus, Mike ended up conducting the Saturday session sans sleep. We hasten to point out that Thomas and Cathy do not live "in that kind of a neighborhood". They have a lovely home on a quiet, solidly middle class, tree shaded street. As Mike pointed out, few people who didn't **know** what they were looking for would have suspected that sleepy little motel of being what Cathy Woof delicately referred to as a "bawdy house." Despite the lack of sleep, Mike has no regrets about the experience. He was able to make many interesting observations which unfortunately we cannot share with you here, and he reports that on the balance it was an experience he would not have missed — but would also not repeat!

Despite the handicap of a somewhat sleepy instructor, a tremendous amount of course material was covered in the 20 hours or so of session time. The new TRANSPORT PROCEDURES manual was employed as the textbook, and the students had plenty of opportunity to practice applying the HLR, set up IV's, open medical packaging, use esophageal airways and generally get acquainted with ALCOR's administrative and technical procedures. Cathy Woof provided her superb hospitality in generous doses and arranged for excellent box lunches to be delivered to the famished crew on a daily basis. She also provided a lovely backyard (she's quite a gardener) for the picnic-style lunches (and for **once** Northern California weather obliged by providing us with spectacular sunny days in the 80's with crystal blue skies to match).

Lunch Break — Clockwise from lower left; Mike Darwin, Thomas Donaldson, Roger Gregory, Naomi Reynolds, Keith Henson, Arel Lucas, Linda Chamberlain, Cathy Woof. Picture by Fred Chamberlain.

Mike reports leaving the Northern California ALCOR crew with the definite certainty that if any emergency arose that they would be able to respond to it with competence and confidence.

BUILDING PROGRESS

There's been a lot of progress on the construction site for ALCOR's new home, but none of it is very dramatic in terms of visual impact -- consequently we'll skip photos this month. All three sets of walls have been poured (stacked one atop the other) and the concrete is up to the required 2500 psi test strength required for "tilt-up". Tilt-up is scheduled for Wednesday, August 13th, and we hope to be on hand with a camera to record the action. Once the walls are tilted into position, placement of the roof and interior work will proceed apace. We're still hoping to see the superstructure completed by the first half of September and we hope to have our interior modifications done within a month or so afterwards.

We'll keep you posted!

TBW-14: A MAJOR ADVANCE RAAHPed UP

by Mike Darwin

Photographs by Luigi Warren

Introduction

On Saturday, August 2nd ALCOR conducted the first canine perfusion employing what we have christened "reversible ametabolic asanguineous hypothermic perfusion" ("RAAHP" for short). To translate, we performed a total body washout (TBW) using a radically modified perfusate which contained **no oxygen and no glucose.** In other words, the perfusate was substrate free — it provided no nutrients or oxygen to the tissues. There are several reasons for carrying out such an experiment. The most pressing is the problem of "reperfusion injury." After a period of no blood flow at normal body temperatures (i.e., clinical death) when circulation is later restarted (i.e., by CPR or attaching the person to a heart-lung machine), major damage occurs to tissue as a biochemical "cascade" is set in motion. This is particularly a problem for cryonicists since we almost invariably suffer varying periods of ischemia prior to our suspension.

Nitrogen and oxygen cylinders used in different stages of the operation.

Background

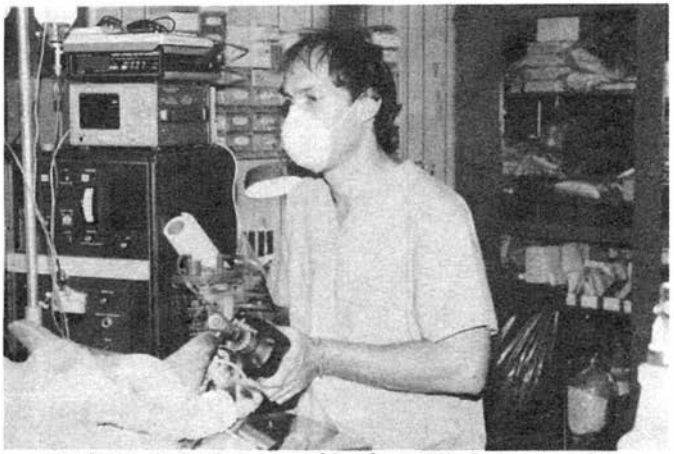
ALCOR researchers have been very anxious to find ways around the reperfusion injury problem. We had tried using calcium channel blockers and free radical quenchers in a previous experiment conducted with an ischemic animal (administered after 30 minutes of clinical death) -- but the results, at least as far as the brain was concerned, were not encouraging. Of course, in many situations ischemic periods may be far longer than 30 minutes, and strategies for dealing with extensive ischemic injury during subsequent cryoprotective perfusion need to be developed. We don't want to destroy a lot of cell structure while trying to "reperfuse" with cryoprotective agent.

This is a serious problem and it is related to another serious problem, which is how to best stabilize patients who deanimate far away from ALCOR's facilities. Even with the best of existing field support methods, it is eventually necessary to stop CPR or perfusion and pack the patient in ice for air shipment -- during which time there is an interruption of delivery of substrate and oxygen to the tissues. What are the alternatives?

About a year ago, University of Wisconsin organ preservationist James Southard suggested an approach which we've been very anxious to try (and would have tried a lot sooner were it not for our recent spate of technical problems with our dog TBW model). We have noted for some time that a tremendous amount of anerobic (nonoxygen using) metabolism seems to be going on in our TBW animals, and that this metabolism is responsible for the acidosis we've been experiencing. Increasingly we've come to believe that this metabolism is "nonproductive". We have reason to believe that such anerobic metabolism observed during deep hypothermia is the result of uncoupled mitochondrial activity — rather like racing an automobile's engine with the gearshift in neutral position.

In talking over these problems with Dr. Southard a year or so ago, he had some interesting observations of his own to add. It seems that the kidneys of **nonhibernators** do much worse if you supply them with metabolic "sparking" agents such as pyruvate while attempting to store them in the hypothermic state. In fact, the better you try to support metabolism in hypothermia the worse the organs do. Why? Well Southard has evidence that nonhibernators try to use a hibernator's trick unsuccessfully — they try to metabolize lipids and they get these lipids by scavenging them from the cell membrane. This doesn't do the cell membrane any good. Quite the reverse. It can destroy its integrity and kill the cell.

Southard's approach to solving this problem was to try to **not play** the hibernator's game. In other words, to **really induce suspended animation** or an **ametabolic** state. He has done this by a variety of means, including depriving organs of substrate and oxygen and by using an ATP analog called deoxycoformycin. The latter is a competitive inhibitor, which works by "looking" enough like ATP to trick the cell into thinking it is ATP, and then having been accepted as such, by **not** acting like ATP. This conserves the ATP (which is the cellular equivalent of gasoline) and it also acts to **inhibit metabolism** across the board, including the lipid metabolism which causes degradation of the cell membrane.

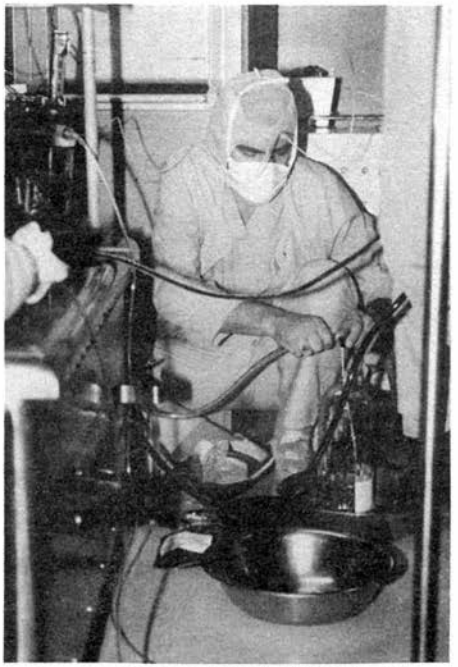


Arthur McCombs ventilating the dog at the beginning of the procedure.

Southard's approach intrigued and excited us. It offered the possibility of getting around the reperfusion injury question as well. It is already well documented that you can reperfuse ischemically damaged organs for extended periods of time without exacerbating the damage or causing reperfusion injury as long as the perfusate does not contain **oxygen, glucose or other cell substrates** (nutrients). If we could develop a reliable ametabolic approach to perfusion, all sorts of possibilities open up -- including deployment of inexpensive flush systems for field TBW of cryonic suspension patients. The question was, would RAAHP work? Could we really get away with RAAHPing a dog for, say, several hours? Normally, at a temperature of 6°C to 10°C you would expect to be able to hold an animal for about one hour with no blood flow (and thus with little or no substrate and oxygen available). But not for any longer. This is just about what the Arrhenius equation and the Q_{10} law would predict: every 10°C drop in temperature decreases the metabolic rate by 50%. The question was, could we get away with much longer periods of substrate-free cold storage if we supported the cells properly?

Jerry Leaf during surgery.

Since there would be no oxygen or glucose available to run metabolic machinery we would have to prevent cell swelling by replacing small sodium chloride molecules with larger molecules to bind and hold water outside the cells. To some extent this is the approach we had been taking in the past with our use of mannitol. However, mannitol is freely permeable to liver cells (and we have evidence that it penetrates pancreas cells as well) and previous TBW dogs had shown high post-procedure liver and pancreatic enzyme levels (evidence of ruptured, inadequately protected cells). Mannitol also leaks slowly into other body cells as well.



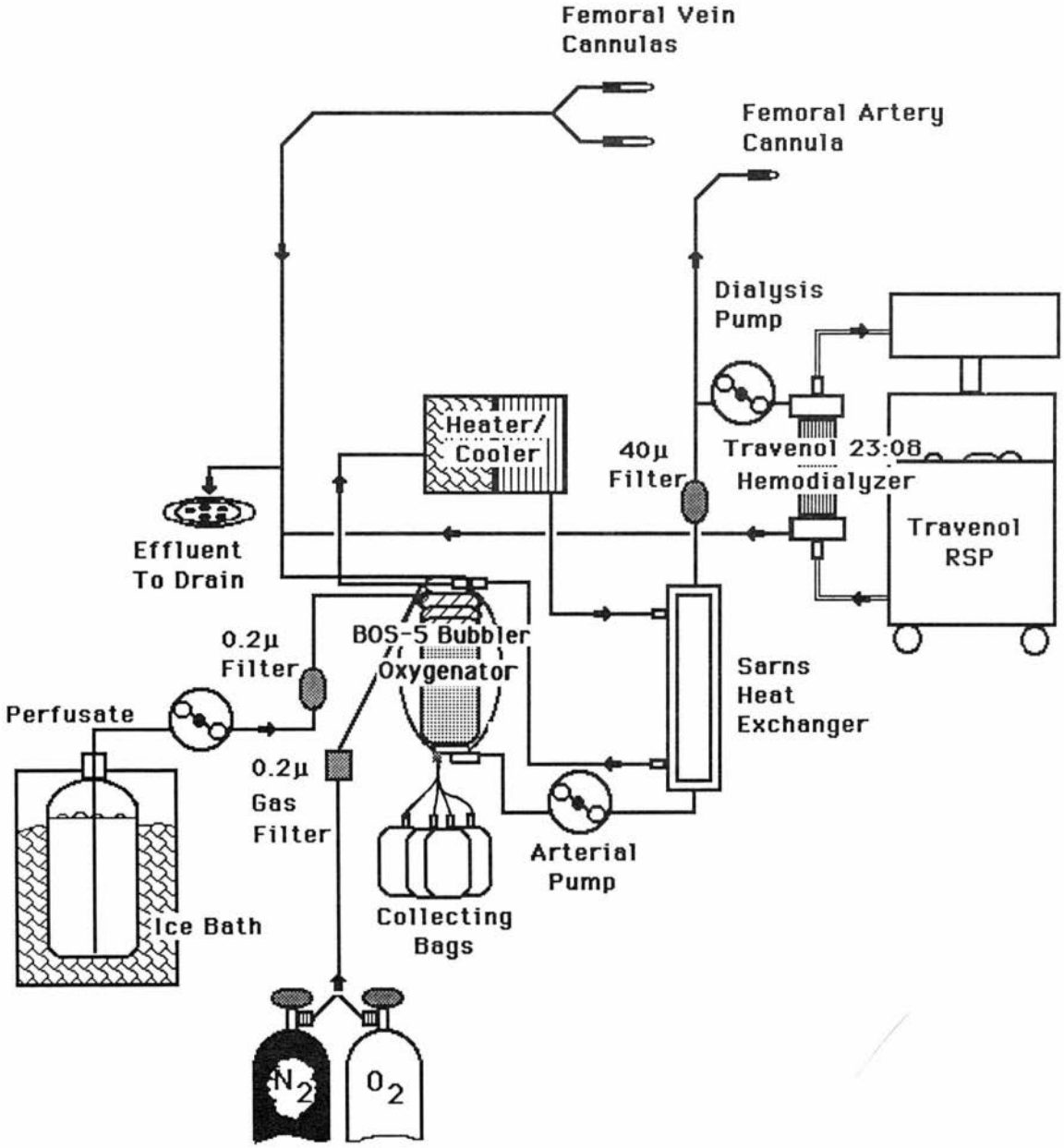
Jerry Leaf collects blood at the beginning of the asanguineous period for use on rewarming.

A decision was made to radically modify the composition of the perfusate. The mannitol was replaced with sucrose (common table sugar), the buffering capacity of the perfusate was tripled and the potassium concentration was doubled to a whopping 60 mM: about 13 times normal body levels. (In hypothermia or metabolic arrest the potassium and sodium pumps in the cell membrane are shut down. If you don't want potassium to leak out of the cells you have to raise the concentrations outside the cells to the level you want to be present inside). A somewhat technical description of the procedure follows. If you are just interested in the results of the experiment and what they mean, you can skip to the end of this article.

The Procedure

We perfused the animal (a 32 kilo Golden Labrador/Shepherd mix) with a substrate-free and oxygen-free solution for 2 hours and 16 minutes at an esophageal temperature of between 6° and 6.4°C. Patency of the bubbler oxygenator frit was maintained by bubbling the perfusate with 100% nitrogen gas. We have found in the past that if we fail to keep gas running through the oxygenator, perfusate saturates the frit and this badly compromises gas exchange during rewarming. During perfusion the animal was ventilated with humidified nitrogen using a bag-valve device once a minute to guard against atelectasis (collapse of the tiny lung air sacs (alveoli)), with the endotracheal (ET) tube being cross-clamped at the end of each inspiration and the lungs being allowed to deflate only immediately before the next inflation. The lungs were thus kept inflated most of the time to provide some "positive end expiration pressure" (PEEP) and reduce the likelihood of intra-alveolar water accumulation (we don't know if this **really** works or not, but it doesn't seem to hurt).

We premedicated the dog with cimetidine (150 mg given the night before the experiment and again about three hours prior to perfusion), Atropine (0.3 mg/kg), sodium bicarbonate (prn up to 250 cc to a prebypass blood pH of 7.50),



Perfusion circuit for TBW-14.

mannitol (20 g), metubine iodide (0.07 mg/kg), methylprednisolone (3.4 mg/kg), erythromycin (14 mg/kg — all other broad spectrum antibiotics we've tried cause cold agglutination during deep cooling), verapamil (0.15 mg/kg), Maalox (50 cc via gastric tube), and heparin, which is given prior to cannulation (420 IU/kg). These medications were given to help induce hypothermia and stabilize the animal for the induction of deep hypothermia.

Following premedication we surface-cooled the animal to an esophageal temperature of about 30°C while ventilating manually and then pump cooled the dog with a heart-lung machine to an esophageal temperature of 6.75 °C. We carried out a blood washout with approximately 4800 cc of perfusate and recirculated with an oxygenator volume of between 650 and 700cc.

The perfusate we employed in this model was a major modification of our usual mannitol-HEPES based solution: sucrose, 88.8 mM; sodium HEPES, 20 mM; sodium bicarbonate, 10 mM; potassium chloride, 60 mM; magnesium chloride, 1 mM; calcium chloride, 1 mM; glutathione, 5 mM; HES, 55 g/L; and sodium heparin, 6,000 IU; pH 8.2. Since we decided to run a high osmolality on this one (404 mOsm, normal is about 290 mOsm) we raised the volume of this mixture only up to 5500 cc (consequently the figures given above are a little lower than we actually ran).

Following asanguineous recirculation (hematocrit << 1) the animal was warmed up to an esophageal temperature of 10.3°C, perfusate was displaced with blood, and the animal was dialyzed with a bicarbonate dialysate for 32 minutes to normalize serum electrolytes (sodium, 138 mEq; potassium, 4.5 mEq; calcium, 5.5 mEq; magnesium, 1.5 mEq; acetate, 4.0 mEq; bicarbonate, 39 mEq; chloride, 106 mEq; and dextrose, 2.0 g/l; pH = 7.45, mOsM = 320). We dialyzed using an old Travenol RSP "batch type" machine converted for single pass hollow fiber dialysis. We used a Travenol 23:08 high ultrafiltration, high clearance dialyzer and hard ultrafiltration (TMP = 500 mm Hg) to achieve hemoconcentration (post pump hematocrit was 34) and avoid pulmonary or systemic edema as we dropped our serum osmolality back towards normal.

Anybody Home? It's 10 PM and Mike Darwin checks the dog for signs of consciousness while Brenda Peters ventilates it. Looking on are Max O'Connor (top) and Garret Smyth.

Results and Discussion

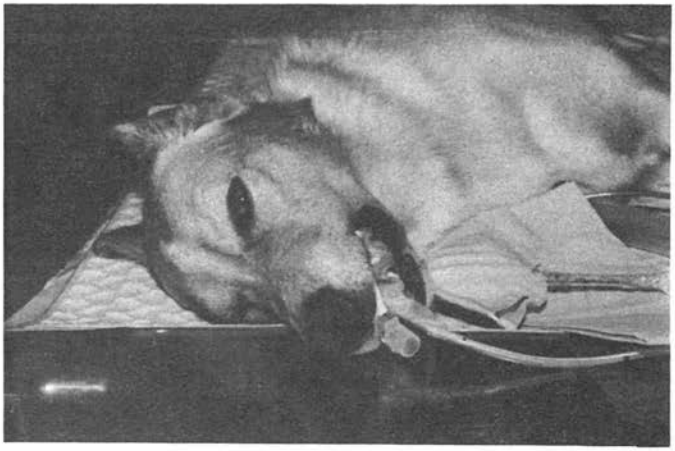
The animal did astoundingly well, considering that he was unsupplied with substrate or oxygen for over two hours! Blood sugars on our small in-house meter taken during asanguineous recirculation were unreadable (with the strip not even showing the vaguest color change). Our pO_2s were predictably low: 5 to 6 (!), which is the limit of accuracy of our Radiometer blood gas system. Surprisingly

our pCO_2s were higher than expected: 18 to 20, and we did have to use small amounts of bicarb (about 30 cc of 5%) to hold a pH of 7.4. We'd like to know where this CO_2 was coming from, and on the next animal we'll probably run some blood lactates. Unfortunately, we failed to draw a proper lab sample for the recirculating period. We made an error in drawing the sample and it ended up contaminated with ACD (acid citrate-dextrose anticoagulant) blood from the prime. In general TBW-14's lab work looks good -- his SGOT, SGPT, and amylase (liver and pancreatic enzyme levels) are far lower than we would expect on even a one hour dog perfused with our previous mannitol-HEPES based perfusate. We also didn't experience the hypoglycemic crash we sometimes see post procedure (presumably due to pancreatic islet lysis) followed by transient hyperglycemia. We are hoping this means we may have provided better support for the pancreas as well -- but once again, we won't know until we do more animals and run them longer.

TBW-14's heart began to beat very slowly at 15°C (as evidenced by EKG and pressure readings) and spontaneous respiration resumed at an esophageal temperature of about 27°C! This is about the best we've ever done (however, we've done mostly 4-hour dogs in the past, so it's hard to say how things will stack up when we get into longer runs). Postoperatively the animal was confused and unresponsive to visual stimuli (unable to "track" with his eyes) for about 24 hours, which is a little longer than our 4-hour dogs are usually in this state. However, the dog improved markedly post procedure after being given 500 cc of Veinamine (intravenous amino acid mixture) and an ampule of Berocca with C (B and C vitamins). We are now reasonably well convinced that this period of disorientation following the procedure is a result of "osmotic disequilibrium syndrome" — a result of the tremendous osmotic shifts experienced during blood reperfusion and dialysis.

Right now, five days post procedure TBW-14 is fully ambulatory, eating well, and has only one complication: draining groin wounds which we are treating vigorously with antibiotics.

We are very excited by the success of this pilot project. We hope to attract funding for more extensive and more innovative experiments in the future. In the meantime, TBW-14 has demonstrated that the RAAHP approach is one which merits a lot of additional attention -- and it has hopefully pointed up a possible pathway to greatly reducing the risk of reperfusion injury and providing yet better biopreservation for suspension patients.



Waking up at 4 AM after a bad day.

CRYO '86: A REVIEW OF THE ANNUAL SOCIETY FOR CRYOBIOLOGY MEETING

The Society for Cryobiology met in Augusta, Georgia this year on June 17-20 at the Augusta Hilton. No papers supported by cryonics organizations were offered this year, and no official representatives of any cryonics organization were in attendance. In fact, attendance in general was low, far under the standards of the '85 meeting and on a par with the '84 attendance bomb in San Diego. This was offset to some degree by a program which was roughly equal in quality to the program in Madison last year (which was very good), and superior to the program in '84.

The program was divided into the following symposia and general sessions: Cryoinjury in Membranes (Steponkus); Gamete and Embryo Preservation (Leibo); Poster Session; Vitrification vs. Freezing of Aqueous Solutions: Physical and Biological Aspects (MacFarlane); Defense Strategies Against Hypoxia and Hypothermia (Southard); The Cornea: Special Considerations for its Cryopreservation (Taylor); Preservation of Organs and Tissues (May on Thursday, Bank on Friday); Cryopreservation of Blood Cells (Fahy); Insect Cold Hardiness: Concepts and Conjecture (Baust). There were a total of 87 abstracts, few enough to permit the entire meeting to be run without concurrent sessions so that every participant could take in every presentation of interest.

Cryoinjury in Membranes

Steponkus' session introduced Martin Caffrey (Cornell University), an expert on lipid phase transitions and membrane rearrangements who discussed a computer data base he is generating on the effects of different environments on the phase behavior of various lipids and lipid mixtures. This will be of great interest and help in the future, but is in a very early stage of development currently. Data on the molecular interactions underlying the membrane-protective actions of proline and trehalose were presented by Rudolph (Naval Research Lab). Daniel Lynch of Steponkus' group gave an exhaustive account of the membrane composition of acclimated vs. nonacclimated plants. This monumental study is of importance because the behavior of the membrane in response to freezing is radically different for the acclimated and nonacclimated cells, and this difference in behavior can only be understood in the light of the changes in membrane composition during acclimation. Even though this research is directed at plant cryobiology, a better knowledge of the effects of ice formation on membranes in general will be essential for a complete understanding of mammalian cryobiology.

Additional contributed papers of great importance were presented in this session. John McGrath (Michigan State University) presented a fascinating study showing that artificial cells (liposomes) are strongly attracted to an approaching ice front and stick to the ice so tightly that 30% are lysed (broken) by the contact alone! The main reservation is that the study was done in distilled water, which may alter the results compared to what would occur in

a concentrated cryoprotectant/salt medium as would be relevant for cryonics. McGrath presented a second paper also describing a new device he has invented which should enable fundamental new work in cryobiology to be done which may finally make it possible to sort out the various damaging phenomena associated with freezing and thawing. Basically, the device uses a porous membrane to separate cells from a flowing stream whose temperature and composition can be controlled so as to simulate freezing both in terms of temperature and in terms of concentration. The effects of ice can be added in, as mentioned above. Great promise for the future.

M. Toner (MIT) presented a direct way of solving "the Mazur equation" which avoids successive approximations. (The Mazur equation is the basic equation of cryobiology. It predicts how cells shrink when they are frozen at different cooling rates.) K. Diller (University of Texas at Austin), who earlier appeared on the mass media to discuss cryobiology, used a completely different method (network thermodynamic model using nonlinear bond graphs) to arrive at solutions for the same equation and to include cryoprotectant fluxes during freezing, in a manner so efficient that results could be generated quickly on an IBM personal computer.

Embryos

By far the most interesting paper in Leibo's session was W.F. Rall's paper on "Cryopreservation of Mouse Embryos by Vitrification". Rall found that embryos would survive vitrification not only in VS1 (a mixture of DMSO, acetamide, propylene glycol, and polyethylene glycol) but also in either of two new solutions, VS2 (5.5 M propylene glycol plus 6% PEG) and VS3 (6.5 M glycerol plus 6% PEG), both of which actually appeared to be less toxic than the VS1 solution. Furthermore, the VS3 solution **did not devitrify** during warming even at the rate of 10 deg per min.! Interestingly, Rall now seems to be trying to claim credit for the idea of vitrification itself. His abstract reads, for example: "Cryomicroscopical observations . . . had indicated that, under some conditions, partially dehydrated cytoplasm would supercool during rapid cooling and solidify into a glass by a process termed vitrification (Rall, Reid, & Polge, 1984, Cryobiology 21:106). **These observations suggested an alternative approach to cryopreservation: The complete vitrification of a suspension of cells at practicable cooling rates. . . .Rall and Fahy. . . .developed such a 'vitrification solution'. . . ."** (emphasis ours). Obviously, such comments give no credit for this idea to Fahy, who originally presented and published on this subject in 1981. We understand that Rall's oral presentation used the same sort of language, emphasis, and omission as well, even though Fahy was sitting in the audience listening. In any event, it is interesting to note that Rall is vigorously pursuing and contributing to cryopreservation by vitrification and thereby giving tremendous help to us as cryonicists even though he personally has a particularly strong dislike of cryonics due to his quasi-fundamentalist Christian beliefs (even bordering on Creationism, we understand).

In this same session, Mazur presented data indicating that embryos behave as ideal osmometers during freezing, that is, that they shrink to exactly the volume they ought to at all temperatures. This kind of result is important because it gives us some indication that current theories are leading in the right direction.

Posters

The poster session was held on Tuesday evening and was in the same room as a buffet dinner. There were 19 posters in all. Kruuv and Glofcheski (University of Waterloo, Ontario) reported that DMSO can block the protein-denaturing effects of ethanol and that cells frozen in ethanol+DMSO showed synergistically improved survival. They and co-workers also found hydroxyethyl starch to protect against membrane blebbing. They used innovative techniques to look for protein denaturation in intact cells, finding DMSO and glycerol to protect against freeze-thaw-induced denaturation. They will next look at membrane proteins in particular to get more details concerning the sites of denaturation in intact cells.

Jack Layne and Richard Lee (Ohio Univ., and Miami Univ.) found that wood frogs could survive 48 hours of whole-body freezing to -3°C but not to -5.5°C. Freezing was very slow, taking 24 hours to reach completion, and they suggested that this might be important for allowing the cryoprotectant glucose to diffuse through the body after freezing begins.

Th. Forster (Berlin Technical University) et al. submitted an abstract indicating that DMSO blocks membrane rearrangements/phase transitions during freezing.

R. Rajotte et al. (Univ. of Alberta) reported measuring DMSO permeability of human islets (the parts of the pancreas that control blood sugar levels and may help to reverse diabetes). The results were similar to the results obtained with rat islets.

G. Fahy et al. (American Red Cross Biomedical R&D Labs) reported successful cryopreservation of peripheral nerves. They found 20% "DF" (DMSO + formamide) and 20% DMSO to be effective agents for the whole nerve. All cellular elements, including the Schwann cells (which add myelin to axons), the perineurium, and the vasculature survived based on histological examination 1 to 3 months after transplantation. Conventional freezing was used. Interestingly, the nerves did not fracture when cooled to -196°C.

Takahashi et al. (American Red Cross Biomedical R&D Labs) reported that hydroxyethyl starch may be cryoprotective because of its ability to vitrify the extracellular medium at a high temperature (-20°C), preventing the cells from shrinking to death during freezing to lower temperatures. They also reiterated their work on vitrification of human monocytes recently published in Cryobiology. Takahashi also reported a novel method of enhancing cryoprotection, namely, increasing the intracellular levels of the natural chemical messenger known as cAMP.

C.L. Guy and Dale Haskell (Univ. of Florida) reported finding two proteins made by cold spinach which may confer cryoprotection on the spinach. This may seem humorous, but in fact discovery of specific mechanisms of cryoprotection such as these are of fundamental importance in cryobiology.

It is worth noting that W.F. Rall also had a poster discussing fracturing, but his results are not helpful to us.

T. Tamaki et al. from Pegg's group reported successful 48-hour preservation of rat livers by using perfusion, fluorocarbon, and an isotonic citrate base solution.

Finally, the organizer of the meeting, S. Randolph May, had an interesting non-scientific poster discussing the abstracts presented at annual meetings of the Society. For the first decade or so, papers came from the USA primarily, with 4-6 other countries making a small number of contributions. This situation has changed greatly, so that now papers come in roughly equal numbers from the USA and from other countries (8-10 countries in the last decade). This is due to both an increase in foreign contributions and a decline in US contributions. It looks like, as in so many other areas, the US is losing its competitive edge in cryobiology!

Vitrification vs. Freezing

In the session on vitrification vs. freezing, Doug MacFarlane, who represents one of the best things that has happened to cryobiology in recent years, gave a good paper on vitrification and devitrification. With respect to the latter, he found, using new techniques, that high pressures reduce the magnitude of devitrification in unexpected ways. Greg Fahy talked about the relationships between chemical structure, physical properties (glass-forming ability, for example), toxicity, and membrane permeability of cryoprotectants. Allen Hirsh (also of the Red Cross R&D Labs) spoke about his work with plants showing that the plants can survive anything once they get below -20°C because at about -20°C they vitrify intracellularly and thereby become cryobiologically inert. They can do this by accumulating the simple sugars raffinose and stachyose as well as water soluble sugar binding proteins. The above 3 papers will be published in Cryobiology and can be reviewed in more detail when this happens.

David Reid and William Rall contributed a paper backing up Rall's work with VS2 and VS3 but also leading to the suggestion that the PEG in VS2 may crystallize during warming. This paper was followed by a paper by Alan MacKenzie showing that, in fact, PEG crystallizes readily upon warming. Consequently, it may not be a good solute to use in vitrification solutions.

Pierre Boutron gave a talk about vitrification using new possible cryoprotectants (polyalcohols with 4 carbons). After considering several different factors, he concluded that 1,3 butanediol may be the best new cryoprotective agent studied, and this agent appears similar to propylene glycol in usefulness.

Finally, Ch. Korber gave an elegant paper on the production of gas bubbles during freezing.

This was a particularly well attended session of obviously great general interest and attests to the rapidly growing interest in vitrification, which can only be helpful for cryonics because it may accelerate successful organ cryopreservation.

End of part 1. Conclusion in next issue.

WHO IS MARVIN MINSKY?
Thomas Donaldson Reviews Eric Drexler's ENGINES OF CREATION

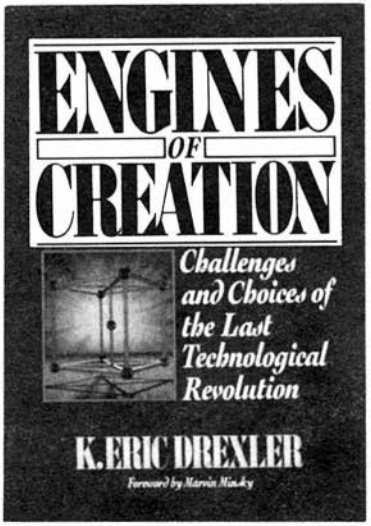
As a cryonicist this book made me feel like an Indian in 1492 A.D. As he rests on the beach near his village, he sees a party of men in a longboat rowing to shore. Gesticulating excitedly, the men unfurl a large flag, fall to the beach to pray, and exclaim at the New World **they** have discovered.

Much of this book was not new to me. A few parts were awfully familiar. Virtually all the nanotechnology parts were commonplace, not in the sense that I had thought exactly those things before. I had not. Eric has carried these ideas further in some directions my own thoughts had not taken. I will say, though, that the **approach** was commonplace to me: like my village, my beach.

Eric has written an excellent book. It conveys the meaning of nanotechnology very well. We'll achieve many wonders with this technology. Eric describes these wonders, with many specific examples.

It's so good I feel chagrined because I had not written it myself. In a sense it is a book I could have written years ago. I'm not the only one. Mike Darwin or Jerry White could have written such a book. Mike Darwin once even suggested that we collaborate on such a book. On the other hand, there's another sense in which we could not have written such a book. We became cryonicists instead.

Everyone who has been a cryonicist for over ten years will remember their first discovery of cryonics. It was wonderful, it was an important insight. We all went around telling everyone we knew of this idea. And then we discovered something very disagreeable about other people, cryonics, and the world. They would not have a word of it. What! This idea says we should freeze the dead? Then it must be wrong, wrong, completely wrong, wrong at all costs, under any conditions, to or for anyone, with no reservations, unredeemably false. All of its consequences must also be wrong, all of its antecedents also, and any idea in the least connected with it must be **wrong!**



Eric is quoted by some as saying that he finds the old cryonicists bitter and twisted. I think cryonicists are about the **least bitter** and **least twisted** people I know. But it is true that we acquired some hardness of thought and habit in those days. One habit which I think we all learned was a loss of belief in intellectual authorities. We tried to tell Marvin Minsky and the rest about this idea. That did not work. So we could either choose to forget them completely and have immortality, or to follow them in ignoring cryonics and lose immortality. It was utterly clear which choice to make. Look, folks! Marvin Minsky, Arthur Kantrowitz, Philip Abelson, etc, etc, are **just a bunch of guys.** Their

opinions command no more automatic assent than those of a bus driver. Maybe less. Who is the bus driver? Or as Jerry White once said: "I haven't seen their signature on a check."

We've lived in cryonics for a long time. We're not excited by it any more. One of the most wonderful things about this technology (or any technology) is the way in which it becomes a commonplace. People fly to Thailand in a day and complain because their baggage was delayed.

But if you as a cryonicist want to read Eric's book, the best thing about it (to a cryonicist!) isn't the ideas on nanotechnology. It is the tale of discovery. It is the way we all felt when we first discovered cryonics for ourselves, laid out to read. Yes, that is the **wonder** of what has now become everyday commonplace. It's well worth reading just for that alone. After all, the Indians discovered America once, too. Yes, cryonics **is** wonderful.

Furthermore, this book is very important for what it tells us about public attitudes. When we started cryonics, discussion of these topics was forbidden out of hand. Eric has just demonstrated that times have changed. Our old attitudes, hard learned, need changing. Maybe Marvin Minsky would listen now. For us, that's **far more important** than what Eric has to say to us. The ice age is over. We've got to accommodate to a **much** warmer climate.

And the fact is that Eric has carried many details forward. In fact, Eric's own most novel, positive contribution to nanotechnology is the idea of putting **numbers** on these things. Unfortunately, his calculations on these limits, which would make an excellent appendix, are not included in the book.

How small can we make this machine? How fast? Anyone thinking about the potential of molecular technology can see that these machines will be **very small** and **very fast.** I found it illuminating to see just how small and how fast. For the problem of reviving a suspendee, in fact, I think that much of this ability is overkill. We don't really need to insert all that power inside a cell, for instance. We can easily do repairs from outside. But that's not important.

As far as I know, Eric has pushed this quantifying idea much farther than others. Furthermore, he has some good ideas for applications of the technology. I liked his spacesuit, how it worked and what it meant. His rocket motor didn't feel at all new to me, but contained lots of details I hadn't thought about. His discussion of cell repair machines will seem quite familiar to any cryonicist.

The most outstanding characteristics of the technology Eric discusses are **grace** and **economy.** The ability to make things with a microstructure comparable to that of living things means that all of those objects we can imagine for the future, spaceships, airplanes, and houses, won't really do anything **qualitatively** different from what a cruder technology could accomplish. What they can do could be done by a far more crude approach. In his notes, Eric discusses a starship which could metamorphose in flight, turning into a design for decelerating rather than accelerating. We can see crude ways to accomplish the same goal. The striking thing is the economy of it, not the basic idea. The original idea of self replicating machines was of **big** machines, self-replicating starships of 100,000 tons each. Eric's idea is much smaller, more graceful. Its superiority is like that of transistors over vacuum tubes. Grace and economy aren't trivial at all. Even with vacuum tubes, **enough** economic

growth would eventually give us personal computers. Grace and economy brought that day far closer.

Where the **practical** limits are is very interesting. I have a persistent feeling on reading Eric's book that he overestimates the multiplication rates which will be possible. After all, bacteria and other creatures have been highly optimized. They are all over the place. They have not turned the world into a gray goo. Eric writes, for instance, of how his spacesuit will produce enough energy from sunlight to power itself and its occupant. I'd like to see some figures on that one. It is true, again, that self-replicating machines ought to allow many transformations. We could terraform Mars with self-replicating machines. What isn't clear is how fast we can do it. The idea of microstructure tells us how to achieve these things, but there are limits due to energy availability and dissipation.

I also respect biological entities more than Eric seems to. Specifically, I believe that protein and calcium are not all the poor materials Eric seems to think. We think slowly compared to computers not because protein and calcium are such poor materials, but because we think as fast as we need to think. Selection hasn't developed faster brain processes because there's been no need for them. Pound for pound, bone is comparable to steel. True, steel has an advantage in bulk. But we aren't optimized for bulk anyway. Even in terms of thermodynamic limits, the fact that living things don't grow as fast as Eric seems to suggest makes me want to look very closely at Eric's figures. Bacteria know about limits to growth rates in a way that human theoreticians don't.

The materials out of which a microstructures spaceship is built may well consist of "wood" and "bone". And yes, it will metamorphose in flight.

In fact, there's a broader view about growth rates and growth limits where I part completely with Eric. In Chapter 10 Eric discusses "limits to growth". He is describing "fundamental physical limits" which provide an absolute upper bound. I don't see how this is useful, since they are so far away. Historically, every century has believed that they completely understood the universe and the limits of technology. . . .except for a few trivial nagging problems. Every previous century has been **WRONG!** We should not believe that we are any different.

Furthermore, this has happened because **every** statement of "physical law" must involve some vagueness in formulation. When finally we examine this vagueness, we suddenly see the supposed "law" fall apart. For instance, at one point Eric states (p. 271) that it has been "mathematically proven" that we can't use quantum effects to communicate faster than light. This choice of words is an oversight. But I think it is is significant. We can't mathematically **prove** anything about the universe. We can only make proofs based on our **assumptions.** We have to decide these assumptions are true, and **even decide if they are well formulated,** from experiments. We are no different from 19th Century physicists in this respect.

The real kick in the groin comes from another kind of limit to growth which Eric doesn't discuss so much. It's the **important** one. That is, what are the limits to **rate** of growth. Will microstructured machines and artificial intelligence (Eric's book is just as much about AI as about microstructure.) give us a significant increase in the rate of growth.

This is a lot more subtle than it seems, very important, and a point I wish Eric had discussed at much more length. It's true that as we grow wealthier, the absolute amount we'll have available to invest on further growth will increase. But will the **proportion** increase?

I will explain myself here in much more concrete terms.

I believe that Eric's discussion here suffers from a **fundamental** fallacy, put about by Marvin Minsky among others. It is an issue which has been completely confused by Herbert Dreyfus and still needs airing. The **relevant** question in AI isn't really whether or not we can build machines capable of thought. Of course we can. The relevant question is how we **control** our machines. We cannot simply tell them to design us a wonderful world, step back, and then see it done. It can't work like that. It is **our** choices and **our** wants, not those of these machines, which we wish to implement. The problem is that every single design involves making such choices. We have to deal with the issue of what is possible. Not the **limits** of the possible, but what is possible **here, now, at this instant.** We can't make choices without understanding the alternatives. Hence the real limits on rate of growth have to do with our speed of thought, not that of our machines.

Nor does this fundamental limit have to do only with technology. We can't tell our superintelligent machines just to go out and discover "true facts about the world", either. We really want "**interesting** true facts about the world". This **also** involves choices, which **we** must make.

So we increase our own speed of thought? Yes, that could be done. It would not, however, speed up the subjective rate of progress. That is after all what really interests us.

Perhaps these limits aren't operative yet. There may be other limits. The question is complex and **important.** My own belief, which I can document but not prove, is that the exponential rate of technological progress has remained substantially the same for centuries. We do not live in a time of particularly rapid progress. Microstructured machines will not make any difference to this rate of change. Historically, the arrival of nanotechnology will seem very brief. But in terms of the human lifespan, it will take two to three generations at least.

I have a quote from someone in the 14th Century about how rapid "modern" progress had become. "Everywhere inventions crowd upon us. I have met myself the man who invented eyeglasses . . ."

Finally, Eric's book makes me amused at myself. It tells me how different I have become from all the commonsensical noncryonicists around me. You see, I thought that the early parts, about AI and nanotechnology, were very sensible and commonplace. It was the latter parts, about "due process", refereed journals, science courts, proposals to politely divide up the universe among everybody living in 2011, and social methods of controlling this technology which struck me as fantastic nonsense. Doesn't this guy know that these issues will be decided by the usual treacherous gory melee? I'm not in the least worried about nanotechnology. But like every other technology before it, the battles it causes will certainly remind us all of our emotional kinship with the apes from which we sprang.

INTERVIEW WITH JERRY LEAF
PART III

CRYONICS Magazine: You've been involved in a long-standing battle with the Society for Cryobiology over the legitimacy of cryonics and over cryonicists presenting conventional cryobiological research at Society meetings and publishing scientific papers in their journal CRYOBIOLOGY. Could you discuss your point of view on these issues?

Jerry Leaf: Some years ago I heard that some members of the Society for Cryobiology were totally opposed to cryonics. I've been a member since 1970 and occasionally I'd hear offhand remarks about cryonicists from a few members of the Society. Nothing very serious, just offhand negative comments which indicated that they knew almost nothing about cryonics — usually comments made in the context of talking about other things.

It only became an issue with me during the 1982 meeting in Houston, Texas when there was a policy statement about cryonics put before the Board of Governors for approval which I considered to be inappropriate. It stated that cryonics was not scientific in nature, and while it was not the business of the Society to judge what people's beliefs should be, they nevertheless considered cryonics to be inappropriate. Basically they wanted to disassociate themselves from cryonics.

CM: What was the reason given for this action?

JL: They stated that they had had inquiries about cryonics from the general public and the news media and that they needed a formal way to respond to these. By directly questioning them at the time I learned that these inquiries had amounted to a grand total of three over the previous year. This is not what I would consider a nuisance level of inquiries about cryonics. I considered that the reason they were making this policy statement was not because the inquiries were a nuisance to them or likely to result in cryonics being associated with the Society in the media or public mind. Rather, I feel it was because there were specific individuals on the Board who were antagonistic to cryonics — for reasons which were never stated.

CM: But don't you feel the Society has the right to distance itself scientifically from activities of which it doesn't approve and of which it doesn't feel are workable or ethical?

JL: I certainly think that the Society has the right to do anything that it wants in the context of its stated purposes and Bylaws. I do not feel it is the purpose of the Society to make pronouncements about activities (such as cryonics) about which they are not well advised. It has been my personal experience that they are not advised about what cryonics is about, or about what we are doing of a scientific nature — or where the science leaves off and where aspects they would consider nonscientific begin. So, they have some sort of personal views which cause them to be antagonistic. I don't know what those views are, since I'm not in their confidence.

However, there have been statements from people such as Dr. Harold Meryman (a founder and past President of the Society) in the written form in which he

has expressed the opinion that cryonics and the idea of biological immortality are mischievious in the extreme and socially undesirable. The general flavor of his written statements has been that he feels cryonics has the potential of diverting funds from what he considers legitimate research in low temperature biology. He seems to feel that if cryonics was accepted as a legitimate endeavor, then money which would go to laboratories such as the one he oversees would be diminished.

CM: The Society's initial policy statement seems fairly benign. Certainly it's one that ALCOR has no trouble with. It seems a fair policy statement and it is our opinion that Society for Cryobiology has the right to distance itself from cryonics or from other endeavors which they deem unscientific or unworkable.

JL: There was something else that occurred at that meeting in 1982 and that was a general overhauling of the Bylaws of the Society. I felt that there were a number of issues touched on in the Bylaws that reflected on the control that the Board of Governors would be able to exercise with regard to membership and the possibility of practicing exclusionary policies towards individuals who might be known to be engaged in cryonics activities.

It is one matter to issue a statement of "nonsupport" or to express your opinion about an area of endeavor, and quite another to interfere with presentation of legitimate, conservative scientific research or to interfere with access to cryobiological research by others just because you don't endorse or approve of their "nonscientific" endeavors.

CM: Why do you feel that it's important for cryonicists to be able to participate in the Society for Cryobiology and to attend meetings and become members?

JL: I think that it's important for anyone who's doing research on suspended animation and who's interested in the effects of low temperatures, cryoprotective agents and so forth on mammalian tissue to be involved with the Society as a scientist. I think that there is absolutely no conflict of interest between a cryonicist who's doing actual animal research on the cryobiology of mammals and his membership in the Society just because he **also happens to be a cryonicist.**

Participation in the Society offers a public platform in which an investigator can present his findings and get feedback at scientific meetings from some of the world's foremost experts in cryobiology. If an investigator is doing good work — work they would normally accept as legitimate and be willing to listen to -- then what difference does it make if he is also involved in cryonics or if the ultimate aim of that work is to further cryonics? What they are doing is making a moral judgement about the motivations and purpose of that investigator and his work. That is totally outside the realm of their charter, their Bylaws, or accepted practice in such matters. I challenge them to show that the goal of cryonics, which is survival, is either unscientific or unethical.

CM: If the Society for Cryobiology decides to prohibit the attendance and participation at meetings and the publication of papers by cryonicists, papers which deal strictly with so called "legitimate" or "conventional" cryobiology, what sort of action do you feel should be taken?

JL: It is my understanding the a new resolution has been formulated and approved by the Board of Governors in which members can be expelled from the Society and forbidden from participating at meetings if they have a known public association with cryonics. It is my belief that my chances of having any additional work presented before the Society is minimal because they know that I am associated with cryonics.

I simply must wait to see if they prevent any more of my work from being presented. At that time I will have to consult with a lawyer and see what can be done. UCLA has paid for my attendance at Society for Cryobiology meetings for a number of years, and the reason that they did that was because our work at UCLA involves the effects of hypothermia on the heart. As a consequence we need someone in the laboratory who is current on the effects of hypothermia on the myocardium and on other tissues as well. It's important to UCLA that I attend those meetings and remain current in that area. Part of keeping current on any endeavor is the opportunity to present research and to interact with others at the meetings — to experience peer review.

It is also of critical importance to realize that work that's being presented at scientific meetings is considerably ahead of what's being published in journals and books. It's cutting edge stuff — and that can be essential to providing good patient care in cryonics as well as to a successful professional career. So, I would have to take real exception to being excluded from meetings and membership.

CM: Do you really feel that litigation is a constructive approach here? Do you think that people can, in essence, be forced to cooperate with you?

JL: I don't consider it forcing people to cooperate with me. I consider it trying to prevent people from taking unjust action against me. There's no loss to them as a result of my participation in the meetings of the Society for Cryobiology. But there is a personal loss to me -- professionally -- if I'm unable to attend the meetings. I'm only asking that they cease and desist in taking action against me. The purpose of a scientific society is to promote and disseminate information -- not pass judgment about people's philosophical, personal, or political beliefs.

The legitimacy of my participation, or any other person's, should be judged on the basis of my scientific work. That is the standard that is accepted in science and it is the only standard which should be applied.

CM: Litigation against the Society would be an extremely costly, time consuming, and draining affair. Do you feel it will be worth the effort considering the many other pressing issues which need to be addressed in cryonics?

JL: I think that when you take the overall effect of the kinds of actions the Society would be taking in order to exclude me from membership and meetings and to prevent scientifically valid and useful research information from being disseminated to peers and the public, then I think there are substantial ethical, economic, scientific, and personal issues at stake. Not to fight is to tacitly endorse such witch hunting. It also cuts off our access to minds which have the ability to improve the state of the art with respect to cryonics and suspended animation. I don't think the issues are just personal ones by any means. They are very practical ones as well in the long run.

As to the costs, I have limited funds and I would be willing to commit some of these to such a fight. I would no doubt need help from others: financial support, free legal advice, and so on. How far I would get would depend upon how much support I would get from others in the cryonics community who feel as I do.

CM: What do you feel is the future for cryonics as a whole?

JL: Since I've been involved in cryonics there have been ups and downs. This involves a fairly short period of time so I can't really say what the future will hold. However, there certainly has been a real growth in membership over the last few years and there certainly is more research going on than has ever gone on before in the history of cryonics. Even when we were hitting lows in membership and public interest in the years preceding these last few, the research work continued to advance. I think we're becoming more professional in almost every aspect of our operations and that bodes well for our future. The better our research base becomes, the more convincing our program will become. That should lead to greater public involvement and even faster rates of growth.

Of course, the media have long had a romance with cryonics and I don't see that changing. So, if things continue as they have and cryonics continues to grow, I think its future looks great!

CM: What do you see as the prospects for cooperation in the future between the various cryonics groups?

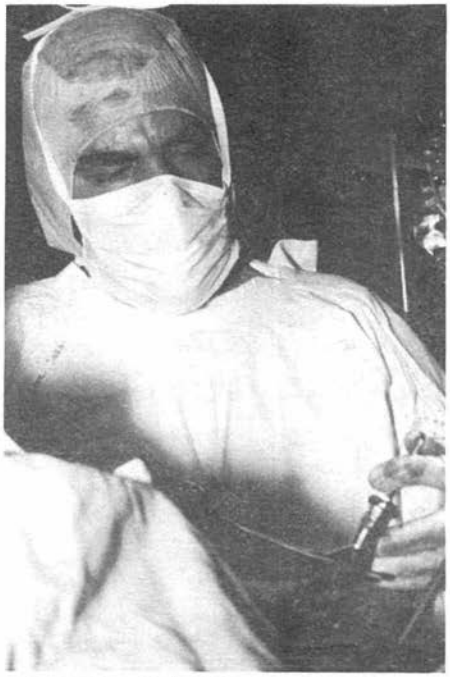
JL: Well, historically the various groups have always had different individuals who had different philosophies of how to make cryonics work in terms of selling the idea to the public. Cryonics groups have tended to have a single individual which each local group has rallied around. Those were largely personal issues rather than substantive philosophical or procedural issues which determined how the various groups got along.

However, in later years there have been increasing differences based on issues rather than personalities. In particular issues involving investment in technology, doing research, safe practices of patient storage and handling, these began to evolve into real differences.

In Southern California with ALCOR we've tended to push for advancing technology both in terms of perfusion and greater safety in terms of patient storage and handling. I think these advances and concerns will stand us in good stead when we go to the public and try to interest them in cryonics. Others have taken the reverse view that if you can just get people interested in cryonics you can raise the money to pay for the technology. Well, when you're intimately involved in patient care the technological issues become more acutely appreciated.

I've been involved in doing most of the cryonic suspensions which have been done over the past few years and to me those are the critical issues, issues which have to be addressed up front. In other words, we have to show that we can do something before we can convince people that there is a degree of hope and the prospect of success.

CM: So are you saying that you don't see the likelihood of cooperation between the various groups as being good until the underlying philosophical and



Jerry Leaf during surgery in a recent ALCOR Total Body Washout experiment.

technical differences are resolved?

JL: I think that cryonics is a scientifically and technologically demanding process. I think it simply cannot be done without using certain minimum standards of technology. If there is anyone out there who thinks that you can rely on future medical advances to restore what you've lost by your lack of technology or effort, there will never be a unified front in cryonics which will form a basis for mutual cooperation. I certainly am unwilling to yield on the issue of good patient care. Anyone who wants to do less than I already know should be done can look elsewhere to achieve unity and political cooperation.

At ALCOR we find it impossible to wait for every cent of money to be raised for research or to do other things that need to be done. That's why a lot of us put our personal money into it. In Michigan they seem to have a point of view which relies almost completely on future technology to make up for their own inadequacies now. That is a view which I find there is no room for agreement with. It is not a view I can accept or cooperate with.

The stated reason for the differences in the level of technology between Northern and Southern California is that the Northern California group has said that when they have enough money to support high technology then they will do so. But until then, no.

CM: In fairness to CI, that's essentially the position they claim they are in. They say they have many retired members who do not have the money to afford the kind of technology ALCOR offers. They do not believe the neuro option is acceptable and they say they would rather accept the extra injury rather than go neuro.

JL: If they're maintaining that it is appropriate to maintain a low level of technology because some of their members cannot afford the higher level then what about the new members that are coming? What about the consideration that the charges being used by everyone else in cryonics are much higher than theirs? Where is their supporting information and data? Where are the case histories and technical information which offer their members the information they need to make a choice about what kind of service they want? People can't make an informed decision in a vacuum.

Their statement that they are willing to back high technology when the money becomes available is acceptable. What is not acceptable is that they are

not willing to arrange a cooperative relationship with another organization which already has the technological capability to serve their members. That's a consideration that maybe they should give more thought to. When they start talking about those issues, then we can start talking in a positive way.

In regard to their position on neuropreservation vs. whole body suspension: Historically, neuropreservation has been perceived as the low cost option in cryonics. However, there are those who think that it is perhaps a safer long term method of cryonic suspension due to ease of handling patient storage and the less likelihood of failure of storage systems and so on. It's a complicated issue, but I consider it untenable of them to take the view that the neuro option is not feasible or unlikely to succeed. I've never seen them give any evidence to support their views on that. At least none that was of a scientific or technical nature. The only view I've heard them give was one of a social nature. They felt that espousing neuropreservation would be unacceptable to the public and therefore would affect their ability to deal with the public in terms of acquiring new members.

Since that is contradicted by the reality that ALCOR is able to acquire new neuro as well as whole body suspension members, to me that's a nonissue and one that represents some prejudice on the part of the leadership in Michigan.

CM: Do you have any regrets about your life? About the lives you've taken, your war experiences or about your involvement in cryonics?

JL: I'll start with the last part first. I have absolutely no regrets about my involvement with cryonics and science. I think for the most part that I've probably taken an adequate course to contribute to the history of cryonics and suspended animation. As things have evolved these are activities which are not being pursued by very many and a career in medicine would not have allowed me to pursue these things in an institutional environment. So, my involvement in cryonics has worked out better than if I had taken other courses in a professional life.

As far as my war experiences are concerned I have no regrets about my involvement in the war or the activities that I participated in. The only thing that even remotely would be considered a regret in that respect would be the effect that it has had on my life over the past two years in which I found myself returning to those memories of that conflict. Memories not of activities which I thought were not appropriate, but rather to the feelings that I had about the friends that I lost in that conflict. Secondarily, re-experiencing those losses and dealing with those emotions, which is something I didn't do completely before because of the social environment that was imposed on soldiers returning from that conflict, cost me a relationship, one that I valued very much. The loss of that romantic relationship is something that I'll probably regret the rest of my life. Even so, I do not regret having fought against an organized political system, which, even today, threatens the freedom of its own citizens and those of neighboring countries.

CM: What do you plan to do if this thing really works? What are your long term goals and ambitions?

JL: To be a free man who is allowed to pursue whatever in life allows me to

contribute to my wellbeing. I've done a lot of things in the life that I've already lived. I suppose the outstanding things in my own mind about my life are things that have been adventurous in one way or another. I think the things that have impressed me the most have been things which stimulated me both intellectually and physically.

I'm probably like most people who enjoy living. I like to use all my senses. I like to see things that look good, smell things that smell good and use my body and mind to the fullest.

If I wake up in the future some time and I have to get a job on the basis of what I've already done I'd probably become involved in science and technology on some level. Although I would like to have also the romance and adventure that I've already experienced on some occasions in my life -- only more of it and more lasting in the future.

CM: That surprises us a little. We figured you more as a spacedog or soldier/adventurer, solar sail ship captain...

JL: I was getting to that (laughter). As a soldier, as someone who has worked in secret military operations and as an assassin I would be able to get a job perhaps as a blade runner (laughter). That would be an easy one for me because that's the kind of job that by its very nature only requires a limited amount of specialized skill and capability. It mostly requires good senses, guts, and physical ability. The environment that you operate in is the only thing that requires specialized training and that can be acquired rapidly. So, yes, when I was asked the question as to what I would be in the future at one of the Tahoe meetings I said that I would like to live long enough to become an Interstellar Smuggler — such as Han Solo of STAR WARS. That would suit my lifestyle well. Particularly if I could find a Princess Leia out there among the stardust.

SCIENCE UPDATES
by Thomas Donaldson

HYPOTHERMIA AND CELL DEATH

When cryobiology began we had only empirical understanding of treatments to protect cells from cold. By now it's quite clear that if we want to progress much farther we'll need a much more fundamental understanding of why freezing and cold in general damage cells. Even now, however, such fundamental studies are more rare than they should be.

J. Kruuv at the University of Waterloo in Canada has published many papers already on possible mechanisms for damage. In a recent paper (**CRYOBIOLOGY, 22,** 484-489(1985)) Kruuv and his coworkers present some information on cell survival for **cold** (nonfrozen) preservation. The issue these scientists addressed is: are media made high in osmotic strength more or less harmful to the cells? As background, many methods for **organ preservation** use media containing mannitol or other osmotic chemicals. These chemicals tend to prevent water from entering the cells and therefore prevent swelling.

His results are paradoxical. Even though adding agents such as mannitol (which make the medium **hypertonic** and therefore help to prevent cell swelling in cold) greatly improves ORGAN preservation, it turns out that it harms the individual cells. We shouldn't really be surprised at this. Methods for organ preservation require us to find a BEST CHOICE among many different treatments, ALL of which cause some harm.

Kruuv et al exposed Chinese hamster lung cells to hypertonic agents such as mannitol and potassium chloride (KCl). They then kept these cell cultures at low (but not freezing) temperatures for varying periods of time. With this information, these experimenters could work out some indications of two different processes for cell damage.

If they kept their cells at temperatures from 10°C to 25°C, damage seemed proportional to the total metabolism of the cell, i.e.--it decreased for the same length of time if the temperature went down. Plotted curves for survival did not fit such a model at all when they held their cells at temperatures at or below 7°C. BHT (yes, butylated hydroxytoluene!) improved cell survival at temperatures below 7°C but had no effect above that.

Kruuv et al believe that their results give some support for proposals to store cells and organs in media rich in potassium ions, because KCl was the least damaging hypertonic chemical. KCl did not however actually **improve** survival compared to controls kept in a medium with the same degree of osmotic strength as the cell interior (iso-osmotic medium). Kruuv et al say that inferences about possible mechanisms of cell injury aren't clear cut. However it seems to me that they have shown that AT LEAST TWO (possibly more) processes are involved in cell injury by cold. Furthermore, their media did prevent cell swelling. It follows that cell swelling probably doesn't relate to cell damage by cold.

These scientists can also say something about the clinical situation. One striking fact from cold preservation of kidneys is that it doesn't last beyond 72 hours. In their control media, survival was high for 72 hours, followed by an abrupt die-off. It seems likely that this die-off accounts for the magic number 72 in the case of organs also. We can't expect to preserve organs in nonfrozen cold past this time unless we understand the process much better than we do now.

NEURON ACTIVITY CAUSES ISCHEMIC DAMAGE

Classically, neurons are very susceptible to damage through deprivation of nutrients or oxygen. Only a short period of ischemia (blockage of blood flow) will permanently destroy brain neurons (so says the classical theory).

However even within the classical theory there are problems. One problem obvious to any close scrutiny is that not all brain regions seem equally susceptible to this damage, even if blood flow is equally blocked off to all of them. So we are to say not that ALL neurons are easily damaged but only SOME neurons? That doesn't sound nearly so universal or bleak.

Furthermore, it is simply not true that this supposed fatal damage to

neurons happens visibly all at once, as if (people have seriously proposed this account to me as THE WORD on brain damage) blood flow is cut off, and 5 minutes afterwards the brain is so much custard. One study (R. Suzuki et al, **ACTA NEUROPATH, 60,** 217 (1983)) finds that it took as long as ONE DAY for any microscopic cell changes at all to occur after ischemia, even in a case in which all neurons were destroyed (**four days** later). I have not discussed here the work of Hossmann and others. I believe that even without the more spectacular advances of neurology in recovering function after ischemia evidence such as this ought to tell us that excellent possibilities for restoring full function exist. We only need to work for it.

A recent paper by Myron Ginsberg, D. Graham, and R. Busto in **ANNALS OF NEUROLOGY (18,** 470-481 (1985)) brings out still more evidence of this. It also, of course, gives us more understanding of the actual reasons for injury and prospects for preventing them.

These authors studied the metabolism of glucose in different brain regions immediately after cutting off blood flow (ischemia) to one hemisphere of the brains of rats. In this model, it turns out that not all brain regions suffer equally from equal ischemia. The **neocortex** suffers relatively little from this cutoff of blood flow, while another region, the **striatum**, suffers very severely. By 4 hours after restoring circulation, virtually all cells in the striatum of almost all animals showed the characteristic changes of cells on the way to death.

Ginsberg and his coworkers are able to partially answer the question of why it is the striatum which suffers so much. They used radioactively labelled glucose to measure the metabolism of these brain cells. It turns out that cells in the striatum started furious metabolism right after blood flow was restored, even though they weren't getting very much blood flow. In contrast cells of the neocortex remained subdued. The immediate cause of injury to neurons after ischemia is likely to be their hyperactivity, rather than the simple failure of metabolism due to lack of nutrients and oxygen.

Other scientists have also found evidence to suggest that hyperactivity causes this brain damage (R. Suzuki et al, **ACTA NEUROPATH** (cited), and also S.M. Rothman, **SCIENCE, 220,** 536 (1983); **J NEUROSCIENCE, 4,** 1884 (1984)).

This work may explain why barbiturate anesthetics like sodium pentothal tend to protect against brain damage. It's also, of course, extremely hopeful news about means to prevent this damage, even after ischemia. Rothman in particular could prevent death of neurons in culture by giving them an antagonist of their neurotransmitter chemical. Hopefully we'll see attempts to find and use such antagonists clinically.

A NEW WAY TO DEAL WITH CLOTTING

One significant technical problem in carrying out cryonic suspensions has been the problem of **clotting.** Once our heart stops, our blood starts forming clots. These can clog up the circulatory system, making perfusion difficult. We can't deal with these clots by using **heparin.** Heparin only prevents the formation of clots, it won't help when clots are already there. Suspension

protocols use heparin now as a preventive. What we need is a means to dissolve clots which have already formed.

An article in **SCIENCE** (**230**, 1289 (1985)) by J.A. Zivin and others at the Department of Neurosciences reports success with **tissue plasminogen activator** (**tPA** for short). tPA is part of the chemical-biological system we have for dealing with clotting. As a side benefit, tPA may also considerably help in reducing the damage from strokes.

One proposal to deal with blood clots in the circulation has been to administer the enzymes **streptokinase** or **urokinase**. As a treatment for stroke, these haven't worked. First, they generally cause multiple hemorrhages elsewhere in the circulation. This is hardly useful for someone who is already endangered by a stroke. Second, even if there were no problem with hemorrhage, we'd need to catheterize the local artery. This takes a lot of time, during which brain damage proceeds.

Zivin and his coworkers prepared blood clots from rabbit blood. They withdrew rabbit blood from the arteries of prepared animals, allowed it to clot, and made up a preparation of small clot particles for injection into test rabbits. Control animals just receive an injection of blood clots. Experimental animals got tPA too, within 2 minutes after they received blood clot preparation.

During the two hours after receiving their clot injection many of these animals started to show neurological problems such as seizures. A significant number, though not all, died outright. The severity of damage in both the treated and the control animals of course depended on just how much blood clot they had received. Out of 12 control animals, 4 died 24 hours after receiving the clots and 3 became grossly abnormal. Out of 11 animals getting both blood clots and tPA, 10 remained normal (no visible neurological damage) up to 24 hours afterwards. One animal died.

Zivin and his colleagues killed all their animals after a week to look at their brains. Among surviving animals, ALL had areas of dead tissue scattered through their brains. There was some blood leakage to brain spaces in both treated and control animals. No animal showed any large hemorrhages.

In a separate study, these workers could show that tPA would dissolve blood clots within 15 minutes. The concentrations of tPA needed resembled those which their animals received at a dose of 2 mg/kg.

For suspensions, clotting is a major problem particularly in cases in which the suspension team only reaches the patient some time after cessation of circulation. Given all the logistical problems, this can happen to anyone, not just those who have neglected their preparations. tPA may be a great help in such cases. Of course, it's also true that Zivin's rabbit model differs in many respects from the case of a suspension patient who is only reached one hour after all circulation ceases. We'll therefore have to wait for practical availability of this drug and explicit clinical studies of its use in suspension. Still, prospects for it seem good.

Availability of tPA in the amounts we'll need (and which neurologists will need for treating stroke) comes about because of genetic engineering. Zivin et al used tPA made by Genentech.

SEPTEMBER 1986 MEETING CALENDAR

ALCOR meetings are usually held on the first Sunday of the month. Guests are welcome. Unless otherwise noted, meetings start at 1:00 PM. For meeting directions, or if you get lost, call ALCOR at (714) 738-5569 and page the technician on call.

ALCOR

ALCOR LIFE EXTENSION FOUNDATION

4030 NORTH PALM #304
FULLERTON CALIFORNIA 92635
(714) 738-5569

The SEPTEMBER meeting will be at the home of:

(SUN, 14 SEPT 1986) Allen J. Lopp
(SECOND SUNDAY) 13354 Veracruz St.
Cerritos, CA

DIRECTIONS: Take the Artesia Freeway (State 91) to Cerritos (Between the San Gabriel Freeway (I-605) and the Santa Ana Freeway (I-5)), and get off at Carmenita Road going north. Veracruz is the third street on the left after 183rd St. 13354 is on the southwest corner of Carmenita and Veracruz. You may park on Veracruz or in the lot of the Thrifty Drugstore on the opposite side of Carmenita.

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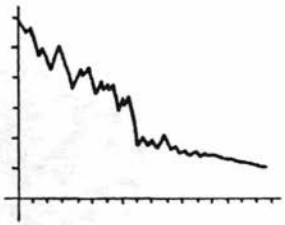

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