CRYONICS

VOLUME 6(11) NOVEMBER, 1985 ISSUE # 64

Contents:

CRYONICS is the newsletter of the ALCOR Life Extension Foundation, Inc. Mike Darwin (Federowicz) and Hugh Hixon, Editors. Published monthly. Individual subscriptions: $15.00 per year in the U.S., Canada, and Mexico.; $30.00 per year all others. Group rates available upon request. Please address all editorial correspondence to ALCOR, 4030 N. Palm St., #304, Fullerton, CA 92635 or phone (714) 738-5569. The price of back issues is $2.00 each in the U.S., Canada, and Mexico, and $2.50 for all others.

EDITORIAL MATTERS

In January of 1980 I participated in two cryonic suspensions conducted at Cryovita Laboratories. That was almost six years ago, and at the time I was President of Soma, Inc, an Indiana cryonics company (now merged with Cryovita) with no thoughts of moving to Los Angeles. Clearly, a lot has happened since then. I bring this up by way of explanation as to **why** it has taken us so long to write these case histories up. The story is one of delay after delay and even a few (minor) catastrophes.

It took us nearly a year after the suspensions were completed just to sort everything out and get the data analyzed. We didn't have the equipment ourselves at the time, so we had to rely on others in the scientific community to help us, quietly and carefully, whenever they could. Then came integrating and interpreting the data. A fair amount of our recent animal research has in part been targeted at answering questions and firming up hypotheses generated as a result of these two suspensions. Also, there is the matter of pressing business in other areas—just keeping things running so that we can continue to do suspensions. Finally, about a year ago, when the paper was in rough draft stage, our computer gobbled it up (including backup copies) and we were back to square one--re-entering hard copy. After several false starts, the text was faithfully reentered by ALCOR Director Brenda Peters.-MD-

To make a long story short, we finally finished up and got the paper refereed by competent professionals. Much has changed in terms of patient care since these suspensions were carried out. Nevertheless, this work does represent a real benchmark in patient care, and many present procedures can be traced back to it directly. We are just sorry this report wasn't completed a lot sooner.

We wish to sincerely thank everyone who made these suspensions possible, especially to the team members who took (and continue to take) valiant risks to provide good care, and to the patients whose courage, trust, and love of life are the reason for it all.

URGENT ACTION NEEDED!

Many times in the last year or two you've seen discussion of so-called animal rights activities and the explanations of why ALCOR is engaged in animal research. To our suspension members, there is probably little explanation needed as to **why** continued animal research work is absolutely critical to our success. Thus, we urge you, as we have never urged you before, to pay close attention to what follows and to **do** something to prevent what we truly believe will be an unthinkable catastrophe from occurring.

In June of 1985, California State Senator David Roberti (D-Hollywood) introducted SB 1405 to amend the civil code governing animal experimentation. The bill is simply unbelievable. If you think we're engaging in hyperbole just because someone's stepping on our toes, think again and read on...

The Roberti bill tremendously expands the power of humane officers to interfere to prevent cruelty to animals in **all places** within the State of

California, including research facilities. It will enable humane officers to carry guns, make arrests, and seize animals—even to use deadly force to prevent cruelty to animals or to prevent a person from fleeing or resisting arrest. More incredible still, these humane officers can enter a research or other facility **at any time, on probable cause, and without a warrant,** and can seize animals or make arrests.

Who may wield such draconian power in such an unconstitutional manner? According to the Roberti Bill: "Any corporation incorporated for the purposes of prevention of cruelty to animals may by resolution of its board of directors or trustees duly entered on its minutes appoint any number of its members, who shall be citizens of the State of California, as humane officers."

Such humane officers "shall have power, at all places within the state, including but not limited to, research facilities administered under the federal Animal Welfare Act, and any place where animals are maintained for commercial, scientific or educational purposes, lawfully to interfere to prevent the perpetration of any act of cruelty upon any dumb animal and may use such force as may be necessary to prevent the same and to that end may summon to their aid any bystander."

What this means is that **any** organization dedicated to the "welfare" of animals may appoint its members humane officers and set them loose with **weapons** to enter research facilities at will **without a warrant!**

We first heard about this bill in a letter from the American Heart Association which stated, "Under SB 1405, animal protection agencies, some of whom have official positions in opposition to **all** medical research, could nominate members of extremist animal rights groups to carry out their missions of stopping research. The prospect of such people, who need have no professional qualifications, entering research facilities is frightening and dangerous." We echo the Heart Association's position.

We would tend not to take this crazy piece of trash seriously, but it has already passed the California State Senate! It is now up for consideration by the the State Assembly Judiciary Committee, where it will probably be voted on in January. Unbelievably, this insult to human rights and human decency has a reasonably good chance of becoming law. Roberti's district includes Hollywood, and many movie stars and starlets have provided strong support for this bill and have contributed substantial amounts of money for lobbying efforts.

If SB 1405 passes, it will mean a virtual end to medical research in California. Not just cryonics research, **medical** research as well. It will mean that animal rights groups can enter our facilities **armed** without a warrant and search at will—perhaps even opening patient care dewars and removing patients from storage in their search for evidence of cruelty to animals. This is

AMENDED IN SENATE MAY 30, 1985

AMENDED IN SENATE MAY 15, 1985

SENATE BILL **No. 1405**

Introduced by Senator Roberti

March 8, 1985

An act to amend Section 607f of the Civil Code, relating to animals.

LEGISLATIVE COUNSEL'S DIGEST

SB 1405, as amended, Roberti. Animals: research facilities: humane treatment.

Existing law provides that qualified humane officers have the power at all places to interfere to prevent the perpetration of any cruelty upon any dumb ani-

intolerable.

We urge you to call and write your Judiciary Committee members and to call and write your Assemblyman. In the center of the magazine you will find a sample letter to use for this purpose. Your telephone book or Directory Assistance can tell you the name of your Assembly representative. It is better if you rewrite the letter rather than use the form letter. But even a form letter is better than nothing at all.

☐ YES ☒ NO SB 1405 (Roberti)

The stupidity of SB 1405 is already costing us money. Our printing bill will be nearly $100 higher this month because of it. HELP US! We're under attack! WRITE YOUR ASSEMBLYMAN AND DO IT NOW.

If this bill comes up for a vote, we will probably make efforts to organize a demonstration in Sacramento. If you want to help with that let us know immediately. Don't let us down. We're counting on you.

NEW GIFT SUBSCRIPTION OFF

It's incomprehensible! It's nearly holiday time again and that means another year has swept by. And what have you done for cryonics in the last 24-hours let alone the last 300 days? Well, we've the perfect solution to both your gift giving and cryonics dilemmas: a gift subscription to CRYONICS magazine.

This year we're offering CRYONICS at 1/3rd off. An entire year for just $10.00. This offer is open to any ALCOR member or current subscriber to CRYONICS with only one condition: the person receiving the gift subscription cannot have previously been on our mailing list as a subscriber to CRYONICS or a member of ALCOR.

Perhaps there's someone who's shaped your life in some important way, and you want to repay them by telling them about cryonics. Or, perhaps you know someone who might be particularly receptive to cryonics, or who might be able to contribute to cryonics in some meaningful way--a writer, a newspaper columnist, a scientist? Now's the time to take action and get the word out.

We'd like to point out that gift subscriptions have been of tremendous help to us in the past. Several years ago John Krug sent a gift subscription to a fellow named Eric Drexler and cryonics and molecular engineering were brought together. More recently Luigi Warren gave a gift subscription to

science fiction writer Arthur C. Clarke and we received a letter of praise from Mr. Clarke for our coverage of molecular technology. In short, not only have some important new people become involved due to gift subscriptions, a number of other important people have had an opportunity to hear about cryonics in detail. Just raising consciousness can be of immense importance, and it may show the next time an author or scientist takes pen in hand and his or her thoughts drift below the freezing point of water.

Now's your chance to make a difference. Send the name and address of the person to whom the gift subscription is to be sent along with a check for $10.00 for each subscription ordered to ALCOR, 4030 N. Palm #304, Fullerton, California 92635.

Get your order in the mail today since this offer expires on January 1st, 1985!

SILCOOL

Last month we reported that the ALCOR Board approved a campaign to raise funds to purchase the silicone cooling fluid needed, for our suspension and research requirements. The Board also authorized $500 toward this goal to match the $500 contribution by Board member Jerry Leaf. Research by ALCOR has shown this compound to be vastly superior to alcohol in the post-perfusion cooling process. Alcohol apparently slowly replaces water in biological tissues, and is also known to dissolve lipids. The silicone fluid, in contrast, exhibits none of these traits, is nontoxic, and nonflammable. But unfortunately, it is expensive.

At the moment, we have $1,076 in the fund, against a goal of $2,700. We need this material to improve our suspension techniques and reduce the fire hazard which comes with keeping a 55 gallon drum of alcohol on hand. The alcohol is **not** safe, and the risk of keeping it for immediate use for suspensions is just barely tolerable. This is a problem affecting **all** of our members.

FOR THE PERSON WHO HAS EVERYTHING

Some things are hard to glamorize and some things just can't be--glamorized, that is. The leadership of ALCOR has repeatedly been asked "if there wasn't something that could be done about an alternative to drab, plain stainless steel ID tags." We've been slow to respond to requests for other tag designs or (more often) for tags made of gold for a variety of reasons.

First, we're busy. We lucked onto our source of ID tags after a lot of looking, and compared to delivering the coverage the tags represent, maintaining our patients, and putting out this magazine, plus a thousand other things, flashy bangles are not a high priority. Second, all that glitters is not gold, but don't count on a mugger or common thief to know that. Gold tags present a possible hazard: if you're done in in a hold up or disaster losing your Rolex may not be of any great concern, but losing your cryonics ID tag is quite another matter. In short, gold tags present a **theft** hazard. We're not anxious to market things that could present a hazard!

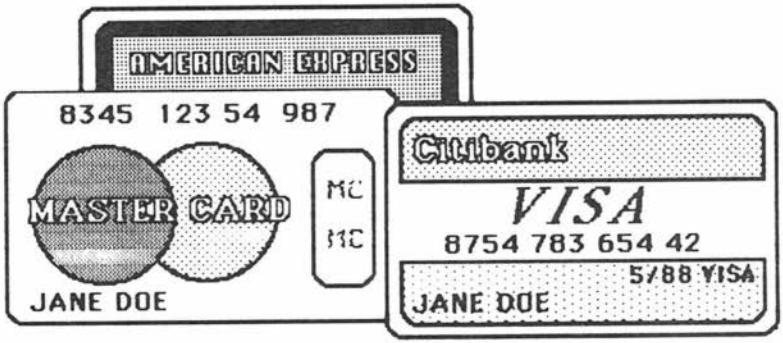
Nevertheless, some of our members have come up with some pretty cogent arguments about why they need gold tags. Some are business professionals where every article of dress counts (if you don't believe this, just read DRESS FOR SUCCESS). They simply **can't** wear a stainless steel tag, because it looks unprofessional and "cheap". Their only alternative to a gold tag is to wear nothing at all.

So we're now offering two kinds of gold tags. An expensive version and a cheap (or at least easily affordable) version. For the man or woman who has everything, solid gold bracelets are available on a custom basis with each link of 14 kt gold chain being handmade. The price on this tag is $500.

For those of more modest tastes or means, the standard ALCOR bracelet will be available as a gold-filled item (plated with 70/1000's of an inch of 14 kt gold), for a fee of $30.00 if you're willing to wait until we have an order for five or more, or for $60.00 if you want immediate gratification. Since we've no personal experience with this product, we did some checking to see how well gold-filled Medic-Alert bracelets hold up. The answer seems to be that they endure about 5 years of reasonably heavy wear, and may last as long as 10 to 15 years with reasonable care.

Response to the gold-filled bracelets has been good so far; at the October ALCOR meeting seven were ordered. Here's yet another holiday gift-giving idea for the cryonicist who has everything!

PAY FOR IT BY CREDIT CARD



You may now purchase the above items, or any items ALCOR offers, including paying your dues, by credit card. ALCOR now accepts Master Charge, Visa and American Express. To order by phone just give us a call and have your credit card ready.

SECOND HAND PRESS

Two news items relating to cryonics have come our way in the last few days; one is a typical piece of careless misinformation, the other, perhaps worth a

little more and potentially even some fun.

The Los Angeles Times runs a regular reader question column, called "Your Changing World," about the future. Readers are invited to ask questions and Edward Cornish of the World Future Society (WFS) attempts to answer them. Members of the WFS, for those who've never had any contact with them, usually have a view of the future about as appetizing and imaginative as any cross between technocracy and world socialism can be (lots of central planning and new gadgets--gee whiz, by 2100 we'll have space ships 10 times as big as now and everyone will be 10 times as rich too!). The question posed by a reader to the October 4, 1985 column was, "What method of burial will generally be used in the future...?"

After discussing rocketing ashes into space, Cornish brings up cryonics and disposes of it in the following way:

"Some remains are now stored in cryonic--deep freeze--containers in the hope that at some future date physicians may be able to thaw them , cure them and restore earthly life. So far, no dead person has ever been frozen and brought back to life. I believe the chances that any of those now frozen will ever be brought back to life are virtually zero."

So much for Mr. Cornish, his imagination, and his breathtaking vision of the future.

The second item may not be any more substantial, but it sounds like a lot more fun. The October issue of OMNI magazine contains a center pull-out map of the United States showing "America's quirks and quarks; your road map to the past, present and future of science and technology in these United States." The map is part of an OMNI sponsored contest to choose the site which aliens would be most likely to land--if indeed there are any aliens out there interested in visiting earth. OMNI has conducted a Delphic poll of UFOlogists to determine **their** answer. Essentially, the objective of the contest is to come closest to identifying the landing site OMNI's experts have suggested and to best justify that choice in an essay. You have 50 words or less to explain **why** the aliens would pick a given site.

What does any of this have to do with cryonics? Well, one of the sites on the OMNI America Map is "Fullerton, CA: Underground storage site for frozen bodies awaiting cures and the big thaw." We share Southern California with Edwards Air Force Base,

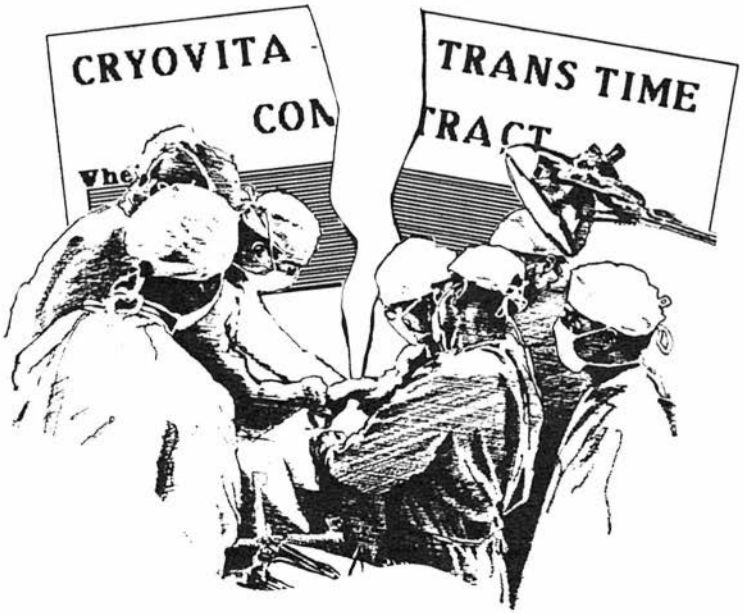
the Hughes Laser Research facility in Malibu and the infamous so-called Nobel Sperm Bank in Escondido.

First prize in the contest is an all-expenses paid Caribbean cruise for two with second and third prizes being $350 and $250 in cash prizes, respectively. We all know why the aliens would choose to land in Fullerton, CA. But does OMNI? Here's your chance to find out. Send your entry to Alien Landing, OMNI, 1965 Broadway, New York, New York 10023-5965. Additional details are available in the October issue of OMNI.

TRANS TIME AND CRYOVITA: NO CONTRACT

After months of lengthy negotiations, Cryovita Laboratories and Trans Time have still not reached an agreement concerning perfusion and cooling services. According to Cryovita President Jerry Leaf, contract negotiations are stalled over access to and use of video footage of suspension patients and cryonics operations (see "Ethics, Common Sense, and Human Dignity", CRYONICS 6(10), October, 1985).

American Cryonics Society and Trans Time members and clients **have not been covered by Cryovita for perfusion and cooling services since June 5, 1985.** According to Jerry Leaf, two notices have been sent notifying both Northern California groups that Cryovita is not currently responsible for any ACS or Trans Time members/clients and will not be responsible for their care until such time as a **written** contract is negotiated. Any ACS member or Trans Time client who has received reports to the contrary is urged not to heed such reports.



MUTUAL AID AGREEMENTS ?

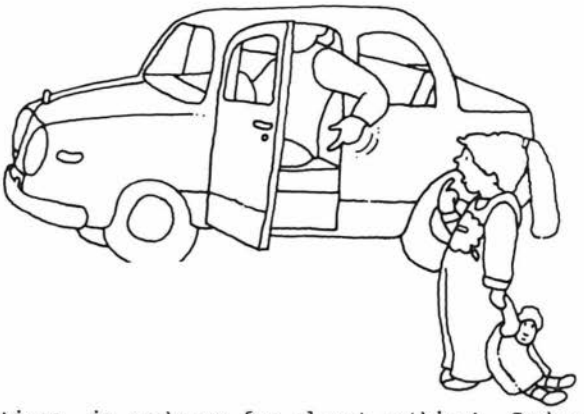
A few weeks ago, ALCOR was approached by a member of another cryonics organization and asked if we would respond with rescue and suspension services in the event of this individual's death. This request was made because this individual lived closer to ALCOR's facilities than to those of his own cryonics organization. On the surface, it seems like a reasonable thing to ask about and even to request. We all would like to know that if deanimation occurred suddenly while traveling or while in a city where cryonics facilities existed that there would be a response from the local organization--whether it was ALCOR or not.

On closer examination, things are not that simple. We've often heard it said that communism would be a wonderful idea, if only people would cooperate: from each according to his ability, to each according to his need. And yet, as we can see from practice, this sentiment doesn't work out very well in the real world. There are a lot of hidden traps between good intentions and reality.

Such is the case with mutual assistance agreements. Every organization has its own internal policies and ways of doing business. If two or more organizations are to cooperate with each other effectively, particularly in an emergency, extensive guidelines and standards need to be agreed upon in advance. Otherwise, misunderstandings and acrimony may occur. Protecting oneself against this isn't easy, as the odious history of so-called Good Samaritan laws attests. Such laws, designed to protect against liability, have failed in virtually every state in which they've been enacted, and in fact have encouraged innocent and well-meaning individuals to get involved in situations guaranteed to produce ruinous litigation (see, for example, "Why Good Samaritan Laws Don't Work," by Roger D. Curry, J.D., **Journal of Emergency Medical Services**, p. 26, (August, 1985)). Without lengthy, detailed, and time-consuming standards, and the confidence that all parties can and will carry them out, it's impossible to even begin considering mutual assistance. We have responsibilities for organizational effectiveness and continuity, both to our members who count on us for suspension and our members who are totally defenseless and completely dependent upon us because they are already in suspension. It would be a clear case of dereliction of these responsibilities to enter into an agreement that would expose us to litigation unnecessarily.

ALCOR has a history of promptly dealing with problems that jeopardize good legal and physical protection for our members. Years ago, when legal opinion changed regarding the use of the Uniform Anatomical Gift Act, ALCOR was the first to update its suspension paperwork and provide a new mechanism of coverage to members. For years we have also had skilled personnel available on-call by pager 24-hours a day. As far as we know we are currently the only cryonics organization with these safeguards. This is relevant because a mutual assistance agreement with other organizations with different standards or the absence of such safeguards puts **ALCOR** in a position of responsibility for **their liabilities!**

There is also another issue, less pleasant to confront, but nevertheless very real. ALCOR has facilities on both coasts with trained teams available to respond to emergencies. Our people have volunteered, month after month, year after year to participate in lengthy, grueling training sessions. Many **thousands** of dollars have been spent on equipment, animals, airfare, and other



expenses to make such training a reality. To the best of our knowledge, no other cryonics group has ever expended resources or energy on such a scale. Most other groups have had only one or two training sessions (relatively simple affairs compared to ALCOR's efforts) in the past three or four years! A mutual assistance agreement with such groups basically makes available the resources you, as an ALCOR member, have worked so hard to create, through volunteer effort, dues, and contributions, in exchange for almost nothing! Such an agreement puts us in the position of doing all the work and getting none of the rewards. We would also run a very high risk of shouldering potentially great liability should something go wrong--or even just be **perceived** to have gone wrong!

We have responsibilities to our own members first. We have responsibilities to **you.** If others require ALCOR quality and ALCOR services, they must join ALCOR. And we're not afraid to say the reverse either. If you want the services of another cryonics organization because you live near them, or feel they can do a better job than ALCOR, then make the appropriate arrangements. We always advise people to shop and compare. On the other hand, don't expect them or us to provide services for free and incur serious risk in the bargain!

For these reasons ALCOR cannot undertake, as an organization, any emergency response or services for members other than its own.

This does not mean that members of ALCOR, acting as individuals, cannot render assistance to other cryonics organizations in time of need. In fact, there may be instances where members of another cryonics organization are close friends, or even relatives; in such cases, not to help could be virtually unthinkable.

However, there are two precautions that apply to any ALCOR member's assistance of another cryonics organization. One is an absolute must, while the other would certainly be prudent and advisable. They are as follows:

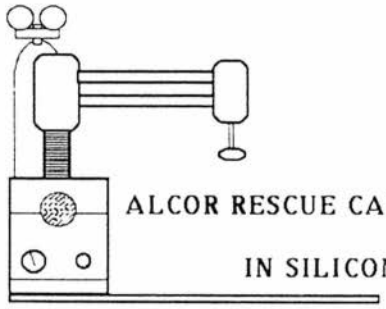
1. Under **no** circumstances may an Alcor member assist another cryonics organization as an official representative of the ALCOR Life Extension Foundation without the explicit approval of the ALCOR Board of Directors. This is absolutely prohibited, by a Board of Directors resolution approved October 6, 1985.

2. Under any circumstances where an ALCOR member chooses, as an individual, to assist another cryonics organization, it is advised that such assistance take the form of solely performing assigned tasks under immediate and direct supervision of an authorized official of the cryonics organization to be assisted.

It is impractical to discuss in detail here the full scope of situations which might arise where one would have to make judgments concerning the risks and benefits of assisting another cryonics organization. ALCOR members who feel they might have occasion to render aid to another cryonics organization, particularly under emergency conditions where critical decision-making might be required, are encouraged to discuss their circumstances with ALCOR officers prior to involving themselves with emergency assistance to other cryonics organizations.

We are making available a slightly modified copy of a release from liability form that we provide for our team members. If you do choose to become involved in assisting any other cryonics organizations, we urge you to get this form executed by an appropriate **officer** of the organization you are going to assist. In a very real sense, there is no such thing as protection from litigation, but an executed release from liability is certainly better than nothing at all. We value you, and we'd hate to see you involved in problems that might be avoidable by taking a little time to **plan in advance** before going into the trenches.

If you have any questions relating to ALCOR's position on this issue, please feel free to call us. We'll do our best to answer them.



ALCOR RESCUE CAPABILITY IN SILICON VALLEY

Recently, ALCOR has been adding members at a good rate in Northern California. At this time we have five members with completed suspension arrangements living in the Silicon Valley area. We have a number of other people who are in various stages of filling out their suspension paperwork and who, in our opinion, are high probability candidates for completing their arrangements in the immediate future. This growing concentration of ALCOR members in Northern California has left us without reliable, trained personnel who are capable of beginning the initial stages of suspension: cardiopulmonary support on a heart-lung resuscitator, administration of appropriate stabilizing medications, and external cooling. Several of our members have asked about getting this capability in Northern California and have indicated a willingness to participate in a team and attend training sessions.

Two of our members living in Sunnyvale, Thomas Donaldson and Cathy Woof, have agreed to serve as ALCOR team leaders in Northern California. Thomas and Cathy have had prior training, and formerly headed the Cryonics Society of Australia's suspension team. To this end, ALCOR has assembled and will soon deploy a rescue and stabilization capability in Sunnyvale consisting of oxygen, a heart-lung resuscitator, transport medications, ambulance cot, air shipping container, and appropriate monitoring equipment.

ALCOR members living in Northern California now have the benefit of much

faster response time in the event of an emergency. However, matters should not be left to rest there. More help is needed to firm up that team and provide coverage in the event key people travel. If you live in the Northern California area and would be interested in participating in the ALCOR Northern California Rescue Team, give us a call. We'll be holding a training session in the San Jose area within the next few months, and we'd like to know on what scale to start planning. So, if you want to help improve your chances, give us a call at (714) 738-5569.

SHE WAS YOUR MOTHER . . .

But now she's only a memory. In a cruel reverse of the cycle of birth, you watched her slip away. And the hardest thing of all to bear about it was the terrible awareness that in the future, perhaps in the very near future, she needn't have died at all. As technology moves forward, as our understanding of biology grows, it will increasingly be possible to treat and reverse most of the causes of illness and death which defeat us today. Even the aging process, relentless and hopelessly formidable as it seems now, will almost certainly be amenable to treatment or cure. But not for her. It was too late by a few years or a few decades. The answers simply weren't there when they were needed most, and she slipped away ...

It doesn't have to be that way. Right now, **today,** there is a technology which offers the prospect of a second chance. When today's physicians have given up and admitted defeat by pronouncing "death" the critical element of life, indeed the only one that matters, is still there: The molecular structure, the information content, the very basis of memory and personality, persists long after a physician "certifies" there is no hope.

Cryonic Suspension, the continued low temperature **care** of patients after legal "death" offers the only hope of getting to the future when contemporary medical know-how has been exhausted.

Contact us today. Keep those you love and care about, and yourself, from becoming just another fading memory ...

Please send information on ALCOR's program of cryonic protection.

Name _____

Address _____

City _____ State _____ Zip _____

Mail To:
ALCOR LIFE EXTENSION FOUNDATION
4030 N. Palm, No. 304
Fullerton, California 92635
Phone: (714) 738-5569

ALCOR COORDINATORS

If you want more information about cryonics or are interested in increasing cryonics activity in <u>your</u> area, contact the nearest ALCOR COORDINATOR for help. ALCOR COORDINATORS also serve as a base for establishing local rescue and resuscitation capability.

Bob Abernathy, P.O. Box 3757, Gaithersburg, MD 20078

Steve Bridge, 1720 N. Layman, Indianapolis, IN 46218

Fred and Linda Chamberlain, P.O. Box 16220, South Lake Tahoe, CA 95706

Mike Perry, 1035 Adams Circle #222, Boulder, CO 80303

Dave Pizer, 1355 E. Peoria Ave., Phoenix, AZ 85020

LETTERS TO THE EDITORS

ABOUT SCHROEDER: MY SIX MONTHS ARE UP

Some time ago, talking about the artificial heart, I wrote that I didn't expect Schroeder to survive for six months. I guess he has, although it's been a bit chancy.

I still do not feel that this direction of research is really the way to go. His heart may work perfectly, but his body is aging and eventually, not very long from now in the scale of years, Schroeder will die. I can't see that this kind of last ditch attempt to stave off defeat shows a lot of promise.

I don't mean that the life Schroeder has gained isn't valuable, but rather, there other things of even more value. Directly or indirectly, the money spent on Schroeder is NOT going to cryonic suspension. We have to make choices, collectively and individually. The collective choice is between aging research and cryonic suspension, which might even work, and artificial hearts (etc) which are doomed to failure. It is clear to me that if people ever WANTED (which they don't now) a massive cryonics program, we could afford it. BUT, we'd have to give up a lot of contemporary medical practices, dialysis and artificial hearts among them. THE MONEY JUST ISN'T THERE.

Of course, we'll all have to make our individual choices in the context of medical research as it stands at the time of our death. These choices are

certain not to be pleasant ones, especially with a scientific establishment thoroughly against cryonics and in favor of dialysis, artificial hearts, and computerized wheelchairs. The artificial heart may look really tempting. So long as I don't have to pay for it, I may very well accept one.

I would still feel intense rage against the medical establishment which put me in that situation, though. Where were their anti-aging treatments? Where is their cryonic suspension? What numbskulls, not to think out their problem and go for an obvious answer, rather than a futile delaying action! And then they attempt to convince me that my artificial heart and my old folks home is a TRIUMPH OF MODERN SCIENCE!!

Thomas Donaldson
Sunnyvale, CA

CASE REPORT: TWO CONSECUTIVE SUSPENSIONS, A COMPARATIVE STUDY IN EXPERIMENTAL HUMAN SUSPENDED ANIMATION

by Jerry D. Leaf, Michael Federowicz and Hugh Hixon

INTRODUCTION

The two suspensions reported on here were carried out in January of 1980 by Cryovita Laboratories. Both patients discussed in this report are now being maintained in long-term cryogenic storage by Trans Time Inc., of Emeryville, CA. Since these patients were placed into suspension within 24 hours of each other, essentially the same perfusion and cooling protocol was employed for each of them. There have been many changes in perfusion protocol since these patients were placed into suspension. Most of these changes are a direct result of information obtained during the course of these two patients' transport and perfusion.

The protocol used in these cases tested a number of hypotheses: 1) Glycerol, as a cryoprotective agent, should cause less edema than dimethyl sulfoxide (DMSO); 2) The "Smith Criterion" (Appendix A) can be approximated in ischemically injured patients; 3) An improved cryoprotective ramp can be achieved by using stepped recirculation rather than a single-pass technique; 4) Arterial/Venous differences in cryoprotective agent concentration can be held low; 5) A surface thermistor probe on the surface of the brain can be used to indicate the freezing point of the cerebral cortex; 6) A cranial burr hole can be used to make observations of the CNS response to cryoprotective perfusion.

These hypotheses were tested, as well as other minor ones. The methods used as well as the results are described in the text of this paper. The answers to these inquiries have suggested future hypotheses and improved our current state of the art.

The age, medical history, and transport protocol of these patients differ greatly and these differences complicate evaluation of the significance of any one of these factors. Nevertheless, an attempt will be made to relate these factors to significant differences observed in the two patients, (degree of blood washout, development of edema, and increase in vascular resistance).

This case report is intended to inform the public about the nature of cryonic suspension procedures (experimental human suspended animation). This kind of reporting is a necessary part of a larger body of information that would constitute being informed about cryonics. Most people making cryonic suspension arrangements today are signing a **consent form**, which implies that they are **informed** about the experimental nature of suspension procedures. The concept of an "informed consent" is a reasonable standard of practice that we would like to achieve. A complete "informed consent" approach is also being advocated by legal counsel James Bianchi (Bianchi, 1983). It is hoped that this information will add to the individual readers' empirical knowledge of these procedures to the end that they will truly be **more informed.**

In keeping with Cryovita's ethical practices, the identities of these patients are being maintained in confidence and for purposes of identification they will be referred to as Suspension Patient One (SP1) and Suspension Patient Two (SP2) in this report.

In December of 1983, one of these patients, SP2, was removed from whole body cryogenic storage and converted to neuropreservation. The body of SP2 from below approximately the 6th cervical vertebra was thus available for postmortem gross and histological examination, and the results of this study will be discussed as they relate to perfusion and preparation for cryogenic storage. A complete discussion of the autopsy findings from this patient has been reported previously (Federowicz, Hixon, and Leaf, 1984).

PART I
SUSPENSION PATIENT ONE (SP1)

MEDICAL HISTORY

SP1 was a male caucasian, 79 years old, weighing 59.1 kilograms. Details of past medical history are unknown because the next of kin has not provided medical records. Examination showed no evidence of previous chest or abdominal surgery. External examination was otherwise remarkable only in that the right arm had been amputated at approximately midforearm, reportedly as a result of an injury sustained during WWI.

Approximately 48 hours prior to deanimation SP1 had been admitted to a hospital in Wisconsin, at which time we were notified that his condition was probably terminal and clinical death was likely to occur within 72 hours. Suspension arrangements were made a few days prior to the patient's clinical death.

The patient's admitting diagnosis at the hospital was transient cerebral ischemia with probable recent stroke. Admitting chest films disclosed a large mediastinal mass which the attending physicians felt was a malignancy. Initial examination and laboratory work-up disclosed moderate cachexia with slight

jaundice and elevated liver enzymes and bilirubin, indicative of hepatitis secondary to obstructive biliary disease. The obstruction was thought to be a result of either primary or secondary hepatic carcinoma. The patient had a history of adult onset diabetes which had been managed with diet and oral medications.

TRANSPORT

Patient stabilization and transport were carried out by Soma, Inc. of Indianapolis, Indiana (now merged with Cryovita Laboratories). Initially a team of five people was dispatched to undertake transport/stabilization. Owing to economic constraints, all of these individuals with the exception of one was allowed to return to Indianapolis after the first 48 hours. Transport and initial stabilization were thus carried out by one team member (Michael Federowicz) with assistance of the hospital staff and a local mortician whose facilities were also used to carry out external cooling during extended, mechanically assisted CPR.

At the time the rescue/stabilization team arrived the patient was in the Intensive Care Unit (ICU) and still alert and communicative. He appeared to be in moderate distress at the time he was examined by Federowicz and emesis showed moderate amounts of bile-tinged fluid during the course of the brief (10 minute) examination. Heart sounds were normal and breath sounds were remarkable only for slight rhonchi present bilaterally. The patient was febrile with a charted rectal temperature of 38°C. The patient appeared to be fully cognizant of the severity of his condition and expressed relief and gratitude that cryonics personnel were present.

During the following 24 hours the patient's condition deteriorated and he demonstrated only intermittent episodes of consciousness and responsiveness. Periods of unconsciousness were often accompanied by Cheyne-Stokes respiration. Pupillary reflexes were present and cerebral perfusion appeared intact until cardiac arrest occurred at 4:00 pm on January 15th.

Cardiac arrest was initially determined by monitoring the patient's EKG. The ICU staff had agreed to promptly initiate cardiopulmonary support and summon a physician for a prompt pronouncement of legal death. CPR was carried out for approximately four minutes prior to the arrival of the physician, at which time it was interrupted for approximately one minute to allow the physician to auscultate the chest, determine the absence of any electrocardiographic activity, and pronounce legal death. CPR was then promptly resumed, and the patient was intubated by a respiratory therapist and coupled to an MA-1 ventilator. The patient was hyperventilated using pure oxygen at a rate of 25 respirations per minute and a tidal volume of 1.5 liters while manual CPR was continued.

Concomitant with manual CPR, medications were administered through an intravenous line which had been previously placed in the left forearm. A heat exchange blanket had been placed under the patient prior to deanimation, and immediately after pronouncement of legal death this blanket was connected to a Blanketrol unit which had been preset to circulate coolant at 4°C.

Transport medication consisted of intravenous administration of the following:

Heparin	507 IU/kg
Mannitol	2.12 g/kg
Anectine	0.88 mg/kg
Cimedtidine	5.0 mg/kg
Thorazine	50 mg
Methylprednisolone	250 mg
THAM (Tromethamine)	212 mg/kg (250 cc)

(All the above medications were given as boluses. Another 250 cc of THAM were given by continuous IV infusion over the next 3 hours.)

During administration of transport medications, the hospital staff began packing the patient in ice with special attention to the head, neck, groin, and axilla. After administration of transport medications was complete, the patient was coupled to a Travenol/Brunswick HLR 50-90 for continued cardiac support. Transportation from the ICU to the mortuary was via hearse, and HLR-supported CPR was continued throughout transport and subsequent external cooling. Immediately prior to removal of the patient from the ICU, respiratory support was transferred from the MA-1 to a bag-type manual ventilator. Hyperventilation using pure oxygen was continued by manual ventilation until the patient reached the mortuary.

Upon arrival at the mortuary, the patient was transferred from the ambulance cot to an embalming table, where he was completely covered in bags of crushed ice. HLR support was not interrupted during this transfer. The patient's temperature descent was monitored via a rectal thermistor (YSI Type 401) employing a YSI 42SL Telethermometer. Respiratory support during cooling alternated between hyperventilation with a manual resuscitator and use of the HLR respirator (which automatically imposes one ventilation between each five compressions) as dictated by operator fatigue. The patient's temperature descent during HLR supported external cooling is shown in Figure 1.

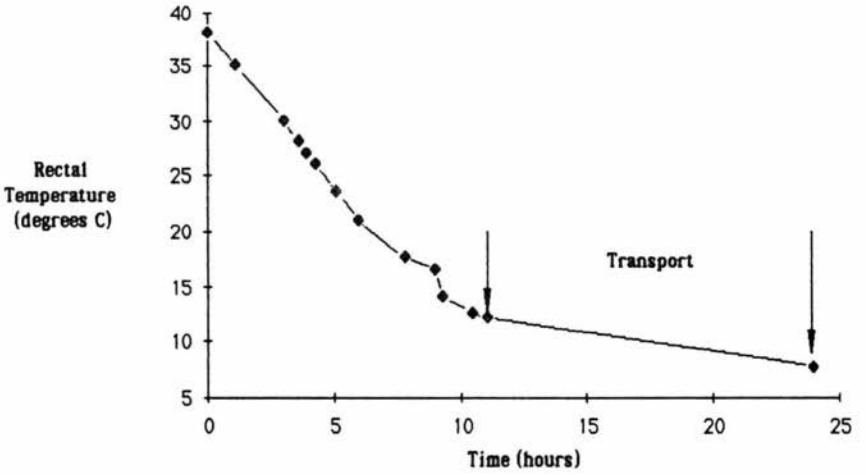


Figure 1. SP1 Cooling, 37-7°C.

Six hours following the start of the procedure, an IV drip consisting of 50,000 IU of sodium heparin in 1,000 cc of normal saline was begun. This additional heparin was administered as a safeguard against loss of anticoagulation due to acidosis-induced degradation of previously administered heparin.

Six and a half hours following the start of the procedure, phlebotomy was successfully performed on a peripheral leg vein which was distended using a tourniquet. Blood collected in a red-stopper Vacutainer demonstrated grossly visible clumping or agglutination of red cells which was initially thought to be possible intravascular coagulation. This clumping disappeared as the sample warmed to room temperature, indicating the presence of cold agglutinins.

Nine hours and twenty minutes after the beginning of the procedure the patient's rectal temperature was 13°C and it was noted that the jaws appeared to be in rigor mortis. Shoulders and limbs did not appear to be affected.

At 3:05 am on January 16th, CPR was discontinued at a rectal temperature of 12°C. The patient was then placed in a rubberized canvas "body bag", transferred to a metal Ziegler case nested in a styrofoam insulated box, and completely covered over in Zip-Loc plastic bags containing crushed ice. Transportation to Los Angeles was via commercial air freight at approximately 8:00 AM (CST) that morning.

SURGICAL AND PERFUSION PROTOCOL

Upon arrival at Cryovita Laboratories that evening, the suspension patient was placed on the operating table and fresh ice packs applied to maintain hypothermia. External examination of the patient showed no remarkable pathology relevant to the impending surgical procedure. A Foley catheter was in place and was connected to a urinometer. A rectal temperature probe was already in place from the transport. The temperature on arrival was 7°C.

Five surgical sites were prepared: sternum, right neck, scalp, and the middle anterior thighs, bilaterally. All sites were preped as previously described (Leaf, 1979, 1981). Plastic 3M drapes were used on all operative sites. The top of the scalp, left of the midline, was draped with surgical towels and an incision 3 cm long was made down to the periosteum. A Wietlaner retractor was placed to expose the periosteum. A periosteal elevator was used to expose the skull, approximately 1.5 cm left of the midline. A 19 mm burr hole was made with a neuro burr and drill. The dura and pia mater were opened to expose the surface of the brain.

The burr hole allowed direct observation of the brain during cryoprotective perfusion. To our knowledge this was the first time the human brain has been directly visualized during cryoprotective perfusion. This procedure was undertaken to determine what, if any, volume changes the brain undergoes during exposure to increasing cryoprotective agent (CPA) concentration, to determine if there is complete blood washout from the surface vessels of the brain, and to provide exposure for placement of a temperature probe directly on the surface of the brain (it was hoped that by doing this we would be better able to determine the cortical freezing point during subsequent subzero cooling and thus determine cortical CPA concentration).

A screen (Cohen Frame) and patient drapes were applied as previously described (Leaf, 1979, 1981). After sternotomy an arterial cannula was placed through a purse string suture in the aortic root for arterial perfusion. The venous cannula was placed in the right atrium through a purse string suture for venous return (Leaf, 1979). (Plates 1 and 2) A right jugular dissection was done and a 30 cm x 0.062 cm I.D. catheter (10) was introduced through a veinotomy and advanced as far toward the brain as possible for effluent sampling. This technique represents a mixed venous sample, but provides an approximation of CPA equilibration in the brain which can be compared to central venous CPA equilibration for the whole body.

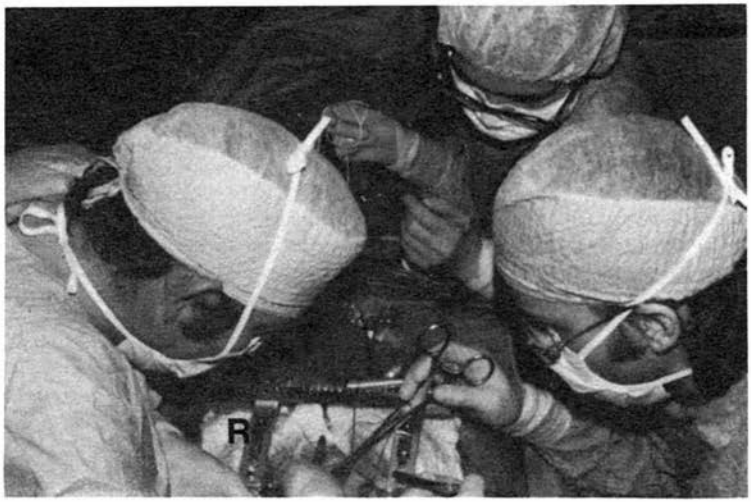


Plate 1. Cannulation of the vessels of the heart to connect the patient's circulatory system to the heart-lung machine for perfusion. The sternum has been divided for access to the heart, and is being held open by a retractor (R).

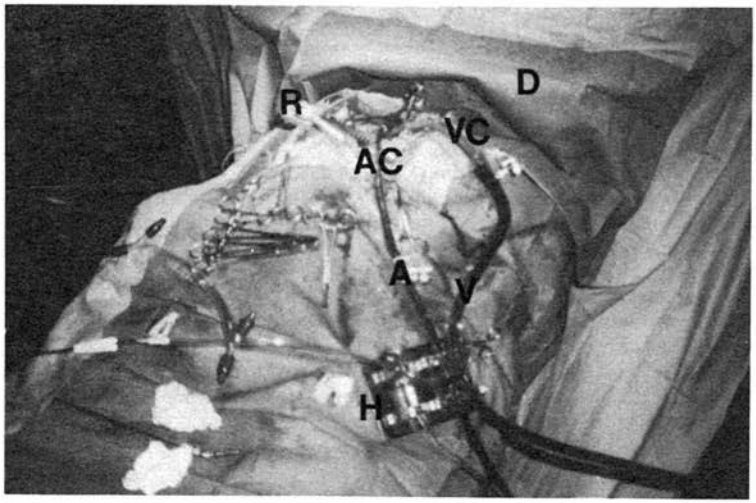


Plate 2. SP1 with the connections to the heart-lung machine in place. Arterial line (A), Venous line (V), Tubing holder (H), Sternal retractor (R), Arterial cannula (AC), Venous cannulea (VC), Drape (D).

Bilateral incisions, 2 cm long, were made in the middle anterior thigh, into the rectus femorus muscle. These provided fluid sampling sites for comparing the symmetry of perfusion in the extremities, using osmolality as an indicator. (This was not repeated in the suspension of SP2.) Venous samples were taken by venipuncture of the superficial foot veins to monitor the hematocrit during total body washout (TBW), and CPA perfusion. This technique provided a good indication of the mean arterial pressure (MAP) necessary to perfuse the extremities in order to achieve blood washout. Forty minutes into the perfusion, these samples showed higher hematocrits than the central circulation, 7 Hct vs. 2 Hct, indicating that blood washout occurred much more slowly in the limbs.

Perfusion to achieve TBW was done using a base perfusate containing 5% v/v glycerol, the base perfusate composition is given in Table 1. Medical Grade USP Water for Injection was used as the solvent in the perfusate. The specifications for USP Grade water are given in Table 2. Methylprednisolone, 250 mg/liter, was added as a membrane stabilizer. The extracorporeal circuit (Figure 2 & Plate 3) is modified from previous designs, the primary difference being the addition of a pre-filter/pre-cooling capability at the heart-lung machine.

Table 1. Base Perfusate Composition.

Component	Conc., mM
Dextrose	180.16
Potassium chloride	26.3
Potassium phosphate	7.2
Sodium bicarbonate	10.0
Glutathione	5.0
Magnesium chloride	2.0
Calcium chloride	1.0
Adenine	1.0
Polyvinylpyrrolidinone	6% w/v
Glycerol	0.54 to 3.0 Molar

Perfusate was made up with USP Water For Injection. Glycerol was USP grade.

Eighty liters of perfusate were used, having the following volumes and concentrations:

5% glycerol perfusate	30 liters
10% glycerol perfusate	10 liters
15% glycerol perfusate	10 liters
20% glycerol perfusate	20 liters
50% glycerol perfusate	10 liters

Table 2. Specifications, USP Water for Injection.

	Not to Exceed
Total Solids	10 mg/L
Heavy Metals	1.0 mg/L
Chloride	0.3 mg/L
Sulfate	0.3 mg/L
Ammonia	3.0 mg/L
Calcium	0.3 mg/L
Oxidizable Substances	0.8 mg/L
pH	5.0-7.0
Culture	STERILE
Pyrogens	FREE

Cryoprotective perfusion was achieved by gradual stepped increases in glycerol concentration up to 3.0 molar. Electrolyte and other solute concentrations were kept constant at all glycerol concentrations. A closed circuit perfusion system was used. The glycerol ramp was achieved by maintaining a constant volume, as measured in the oxygenator reservoir, while adding higher glycerol concentration perfusate. The use of glycerol, instead of DMSO, allowed longer perfusion time with a more gradual increase of CPA concentration. Previous suspensions in this laboratory were carried out using single pass stepped increases in perfusate, with recirculation at the terminal CPA con centration. Closed circuit systems will be used in the future due to the efficacy of this procedure as established during this perfusion.

Perfusate temperature averaged $4^{o}C \pm 1^{o}C$, and esophageal temperature averaged $6^{o}C \pm 2^{o}C$. Glycerol was selected as the CPA of choice, based on

A screen (Cohen Frame) and patient drapes were applied as previously described (Leaf, 1979, 1981). After sternotomy an arterial cannula was placed through a purse string suture in the aortic root for arterial perfusion. The venous cannula was placed in the right atrium through a purse string suture for venous return (Leaf, 1979). (Plates 1 and 2) A right jugular dissection was done and a 30 cm x 0.062 cm I.D. catheter (10) was introduced through a veinotomy and advanced as far toward the brain as possible for effluent sampling. This technique represents a mixed venous sample, but provides an approximation of CPA equilibration in the brain which can be compared to central venous CPA equilibration for the whole body.

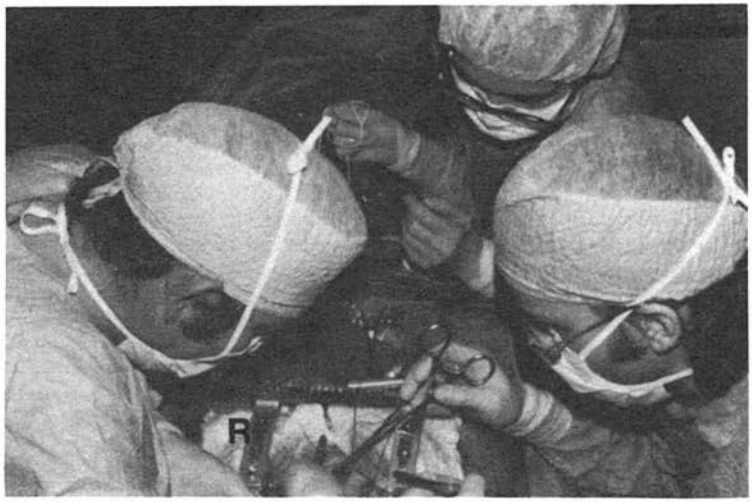


Plate 1. Cannulation of the vessels of the heart to connect the patient's circulatory system to the heart-lung machine for perfusion. The sternum has been divided for access to the heart, and is being held open by a retractor (R).

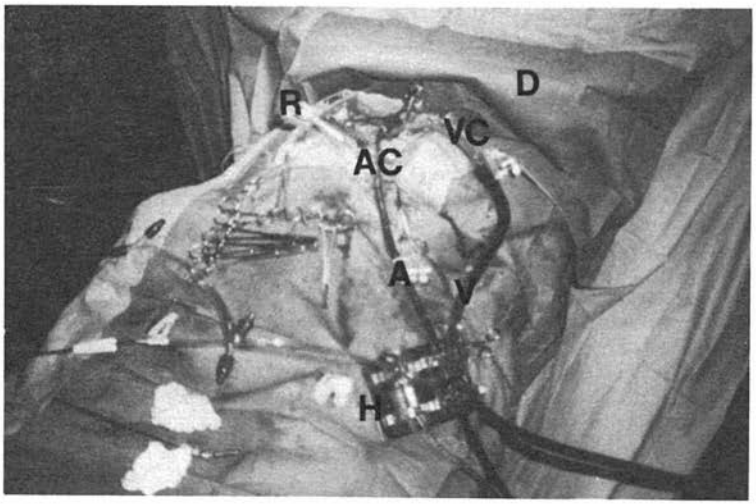


Plate 2. SPl with the connections to the heart-lung machine in place. Arterial line (A), Venous line (V), Tubing holder (H), Sternal retractor (R), Arterial cannula (AC), Venous cannulea (VC), Drape (D).

Bilateral incisions, 2 cm long, were made in the middle anterior thigh, into the rectus femorus muscle. These provided fluid sampling sites for comparing the symmetry of perfusion in the extremities, using osmolality as an indicator. (This was not repeated in the suspension of SP2.) Venous samples were taken by venipuncture of the superficial foot veins to monitor the hematocrit during total body washout (TBW), and CPA perfusion. This technique provided a good indication of the mean arterial pressure (MAP) necessary to perfuse the extremities in order to achieve blood washout. Forty minutes into the perfusion, these samples showed higher hematocrits than the central circulation, 7 Hct vs. 2 Hct, indicating that blood washout occurred much more slowly in the limbs.

Perfusion to achieve TBW was done using a base perfusate containing 5% v/v glycerol, the base perfusate composition is given in Table 1. Medical Grade USP Water for Injection was used as the solvent in the perfusate. The specifications for USP Grade water are given in Table 2. Methylprednisolone, 250 mg/liter, was added as a membrane stabilizer. The extracorporeal circuit (Figure 2 & Plate 3) is modified from previous designs, the primary difference being the addition of a pre-filter/precooling capability at the heart-lung machine.

Table 1. Base Perfusate Composition.

Component	Conc., mM
Dextrose	180.16
Potassium chloride	26.3
Potassium phosphate	7.2
Sodium bicarbonate	10.0
Glutathione	5.0
Magnesium chloride	2.0
Calcium chloride	1.0
Adenine	1.0
Polyvinylpyrrolidinone	6% w/v
Glycerol	0.54 to 3.0 Molar

Perfusate was made up with USP Water For Injection. Glycerol was USP grade.

Eighty liters of perfusate were used, having the following volumes and concentrations:

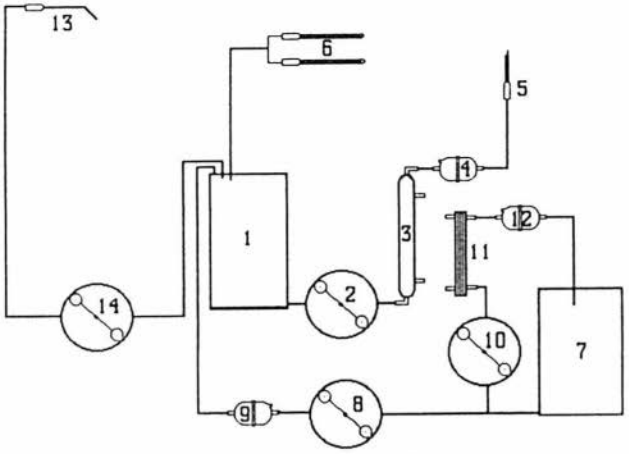
5% glycerol perfusate	30 liters
10% glycerol perfusate	10 liters
15% glycerol perfusate	10 liters
20% glycerol perfusate	20 liters
50% glycerol perfusate	10 liters

Table 2. Specifications, USP Water for Injection.

	Not to Exceed
Total Solids	10 mg/L
Heavy Metals	1.0 mg/L
Chloride	0.3 mg/L
Sulfate	0.3 mg/L
Ammonia	3.0 mg/L
Calcium	0.3 mg/L
Oxidizable Substances	0.8 mg/L
pH	5.0-7.0
Culture	STERILE
Pyrogens	FREE

Cryoprotective perfusion was achieved by gradual stepped increases in glycerol concentration up to 3.0 molar. Electrolyte and other solute concentrations were kept constant at all glycerol concentrations. A closed circuit perfusion system was used. The glycerol ramp was achieved by maintaining a constant volume, as measured in the oxygenator reservoir, while adding higher glycerol concentration perfusate. The use of glycerol, instead of DMSO, allowed longer perfusion time with a more gradual increase of CPA concentration. Previous suspensions in this laboratory were carried out using single pass stepped increases in perfusate, with recirculation at the terminal CPA con centration. Closed circuit systems will be used in the future due to the efficacy of this procedure as established during this perfusion.

Perfusate temperature averaged $4^{o}C \pm 1^{o}C$, and esophageal temperature averaged $6^{o}C \pm 2^{o}C$. Glycerol was selected as the CPA of choice, based on



1. Main (Circulating) Reservoir
2. Perfusion Pump
3. Sarns Torpedo Heat Exchanger
4. 40 Micron Pall Filter
5. Arterial Cannula
6. Venous Cannula
7. Glycerol Concentrate
8. Glycerol Ramp Pump
9. 0.20 Micron Pall Filter
10. Prefiltration and Precooling Pump
11. Travenol Miniprime Heat Exchanger
12. 40 Micron Pall Prefilter
13. Cardiotomy Sucker
14. Cardiotomy Pump

Figure 2. Extracorporeal perfusion circuit.

experience with previous animal and human perfusions. Continuous perfusion for 6.75 hours at 50 mm Hg arterial pressure was used. The average pump flow rate was 0.8 liters/min. Refractometer[1] measurements of arterial and venous samples were used as an indicator for increasing CPA concentration. (Table 3) Termination of the perfusion was determined by direct observation of the brain volume, as described below. Terminal arterial glycerol concentration was 2.85 Molar and venous concentration was 2.67 Molar. The jugular effluent, as an indicator of brain equilibration, and vena cava (body) effluent

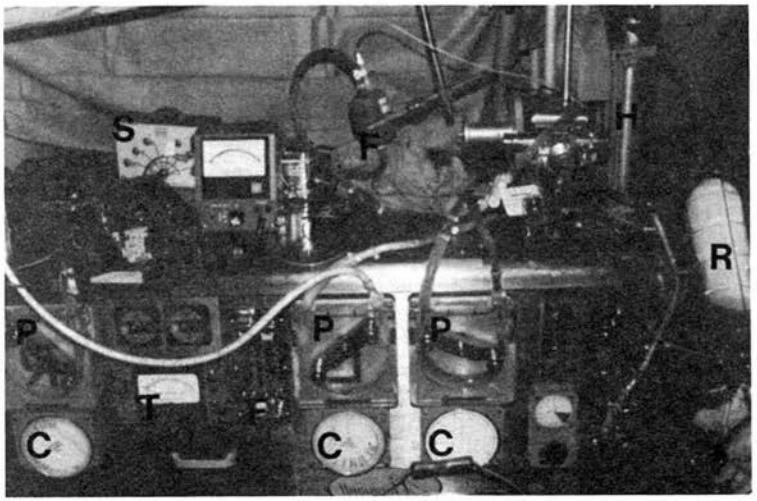


Plate 3. The heart-lung machine. Roller pumps (P), Pump controls (C), Gas flowmeters (F), Telethermometers (T), Thermometer switch (S), 40-micron blood filter (F), Oxygenator reservoir (R), Heat Exchanger (H).

samples at the final CPA concentration showed no difference, 2.67 molar for both. (Table 3) Molar glycerol concentrations were derived by measuring osmolality, subtracting the estimated osmotic contribution of the base perfusate, and using the empirically compiled graph shown in Figure 3, after first subtracting the estimated osmotic contribution of the base perfusate. (Table 3)

1) Refractometer was a temperature-compensated Atago, Model N-1, Cat #311-N

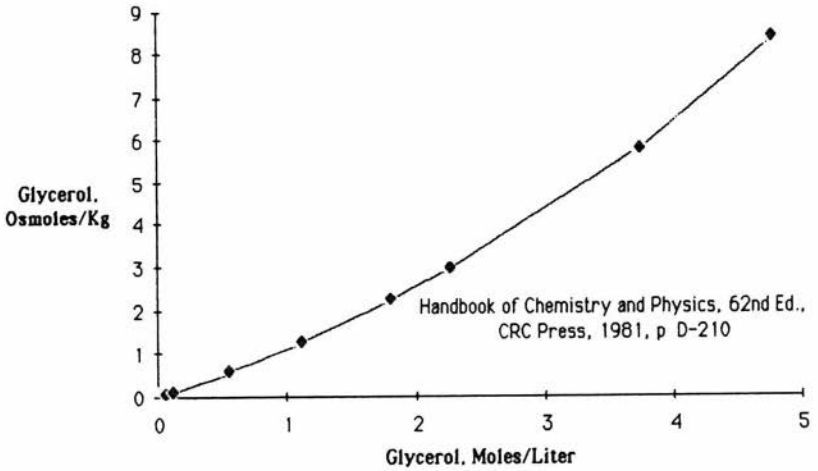


Figure 3. Glycerol concentration conversion. Molar <--> Osmoles/Kg.

The glycerol concentration data is plotted in Figure 4.

Changes in peripheral vascular resistance (PVR) were calculated from the standard formula,

$$PVR = \frac{(MAP-CVP)}{Flow}$$

where MAP is mean arterial pressure in mm Hg, measured at the aortic root, CVP is central venous pressure in mm Hg measured in the vena cava near the heart, and Flow is in liters per minute, measured with a calibrated occlusive arterial pump. Pressure measurement was done with Statham P23Db transducers. Figure 5 shows changes in PVR over the course of the perfusion. The initial rise in PVR reflects the resistance to washout of blood cellular components at low temperature. Of special relevance to PVR was the observed cold agglutination of red cells, particularly in the peripheral circulation. The identification of cold agglutination as a problem was first made during these suspensions. Specific changes in transport and perfusion protocols have been made to help eliminate cold agglutination problems (Leaf, 1984). The rise of PVR after it reached its lowest point was probably caused by

Table 3. **SP1 - Glycerol Concentration.**

Time (min)	15	113	200	500
Arterial				
Brix No. (1)	11.0	16.2	19.4	23.1
Moles (2)	0.68	1.13	1.71	2.85
Percent (3)	5.8	10.1	15.0	24.8
Time (min)	**15**	**213**	**288**	**504**
Venous				
Brix No. (1)	7.48	11.5	13.8	20.9
Moles (2)	0.296	0.712	1.26	2.32
Percent (3)	2.5	6.1	11.0	20.1

1) Measurements made at the time of perfusion with a hand-held refractometer, temperature compensated, Atago Model N-1, Cat. #311-N.
2) Molar glycerol concentration calculated at a later date on the same samples that the Brix measurements were made on. Measurements made with a Micro-Osmette Model 5004 freezing point osmometer.
3) Conversion of glycerol concentration, molar to w/w percent, from **Handbook of Chemistry and Physics, 60th Ed.**, CRC Press, 1979.

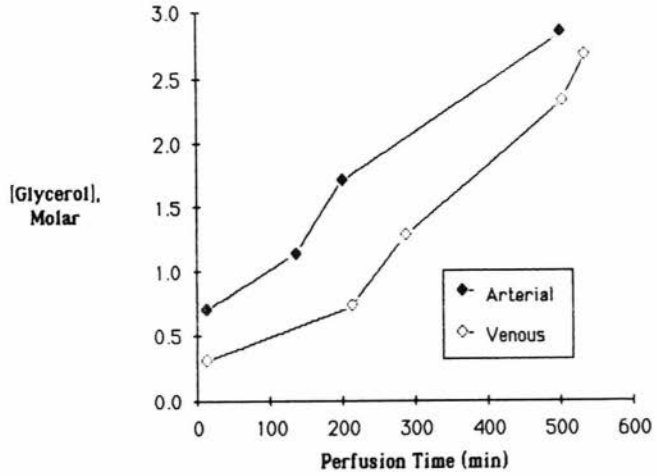


Figure 4. SP1 Glycerol Concentration vs. Perfusion Time

increased viscosity of the perfusate, i.e., higher CPA concentration, and/or increased tissue edema.

Arterial and venous perfusate pH values were measured during the course of perfusion. The results are shown in Table 4. The persistent fall in venous pH, despite use of a high arterial perfusate pH, appears to be the result of both respiratory and metabolic acidosis. The respiratory component was secondary to not oxygenating the perfusate. Since the perfusate provided abundant substrate for anaerobic metabolism, lactic acid production was the other major component of the acidosis (Lehninger, 1979, pp. 421-2, 485). A later measurement of lactate demonstrated 3.3 times the expected lactate

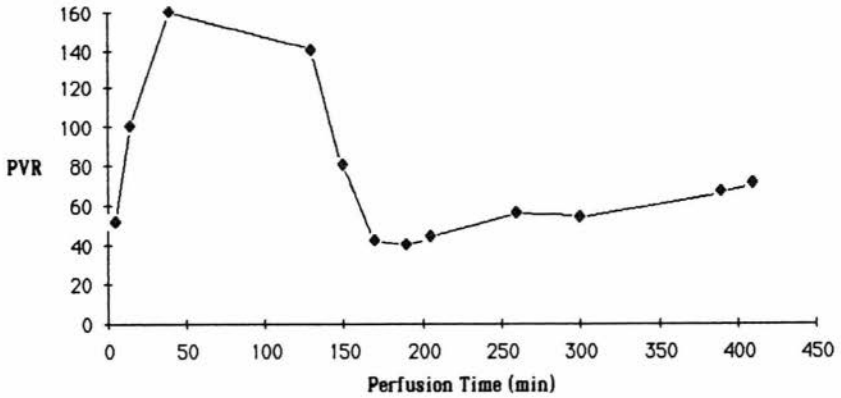


Figure 5. SP1 Peripherial Vascular Resistance (PVR).

Time (min)	10	124	184	268	388	426
Arterial	7.79	8.00	7.71	7.85	7.90	7.25
Venous	7.35	7.39	7.09	7.15	7.18	7.15

Table 4. SP1 Arterial/Venous Perfusate pH.

content of human blood (Lehninger, 1979, p. 831). The presence of high levels of lactate is evidence of active cellular metabolism, and is unexpected in view of the deep hypothermia employed. It seems likely that the persistently high lactate levels observed during perfusion were a result of metabolic activity rather than as a result of metabolic uncoupling. Metabolic uncoupling as a result of exposure to toxins or cellular death would have resulted in rapid loss of lactate. These data are a positive indication of biological viability. Subsequent animal experiments at Cryovita Laboratories using glycerol perfusion have demonstrated that continuous oxygenation of CPA containing perfusate (or other perfusates rich in metabolic substrates) is essential to control pH and that active metabolism continues in deep hypothermia even at terminal concentrations of 3.Ø molar glycerol. In future cryonic suspension operations patients should be perfused with oxygenated perfusates, and perfusate pH and blood gases monitored, if adequate metabolic support and control of pH is to be achieved.

During the course of perfusion, an attempt was made to maintain a close arterial/venous (A/V) glycerol concentration in order to minimize osmotic stress as much as possible. At the outset of perfusion, a target terminal glycerol concentration of 3.Ø M was selected. Unfortunately, due to increasing vascular resistance and the development of both generalized and cerebral edema, this goal was not achieved (Figure 4). The development of edema and the subsequent increase in PVR was probably to a large extent due to the patient's condition at the time of perfusion, as will be discussed later. In future operations of this kind the addition of pulsatile perfusion may help achieve better peripheral distribution of CPA. Research is currently underway to determine the effectiveness of such an approach. Lowering PVR will achieve better CPA equilibration by improving peripheral perfusion and consequently removing more body water by CPA exchange.

The deciding factor in terminating the perfusion was the development of cerebral edema as determined by direct observation of the brain. Early in the course of the perfusion, cerebral volume decreased by an estimated 20% as a consequence of osmotic removal of water with increasing glycerol concentration. The degree of reduction in brain volume observed was comparable to that seen in a clinical setting where mannitol is employed to reduce cerebral volume for neurosurgical procedures. The subsequent re-expansion of the brain indicates that at some point in the perfusion, significant amounts of glycerol began to cross the blood-brain barrier. Osmotic dilution of cellular contents plus glycerol then produced the swelling.

Decannulation and sternal and skin closures were accomplished in the usual fashion (Leaf, 1979). (Plate 4) A YSI Style 729 disk temperature probe was placed on the surface of the cerebral cortex approximately 1.5 cm to the right of the burr hole margin. Bone wax was used to fill the burr hole, and the temperature probe lead was securely sutured in place with subcutaneous scalp sutures. The scalp incision was closed with continuous 2-Ø Ticron suture and additional stay sutures were used to anchor the probe lead wires to the surface of the skin. Parke-Davis spray-on bandage was used on all suture lines.

Copper-constantan thermocouple temperature probes were placed in the esophagus and rectum, and on the foot, and the patient placed in double vinyl ethyl acetate plastic bags, as previously reported (Leaf, 1981). The patient was then placed in a dry ice/alcohol bath at $-22^{\circ}C$ for slow cooling to $-77^{\circ}C$. Figure 6 shows the temperature measured at probes in the esophagus and rectum,

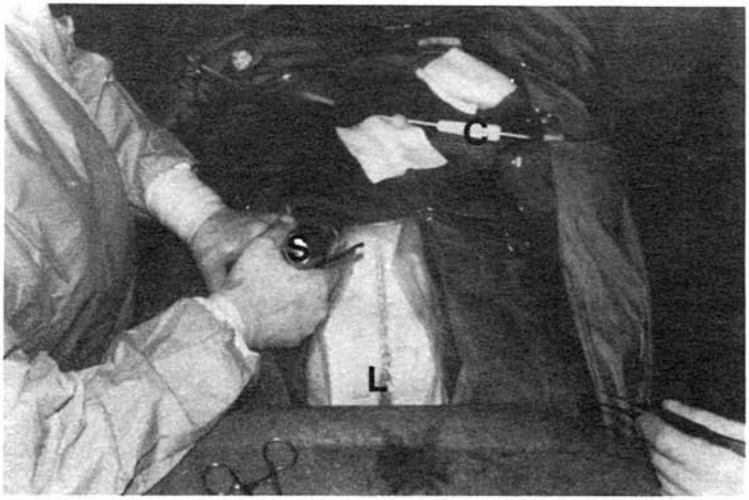


Plate 4. Skin closure with surgical stapler (S) at the end of the perfusion. The sternum has previously been approximated with stainless steel wire. Staple line (L), Cardiotomy sucker (C).

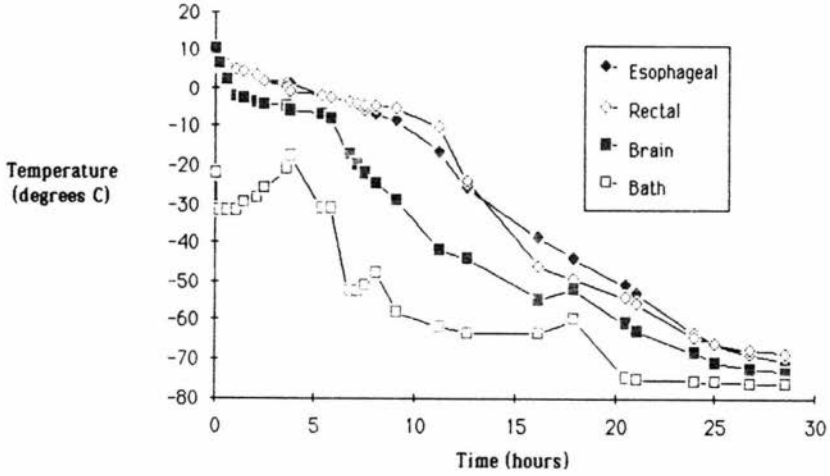


Figure 6. SP1 Dry ice cooling.

on the surface of the brain, and in the alcohol bath. The time required for cooling to a core temperature of -7Ø°C was 28 hours at an average cooling rate of 2.5°C per hour. Following cooling to -77°C, the patient was covered with dry ice for shipping in an insulated container. Liquid nitrogen vapor phase cooling and encapsulation for storage in liquid nitrogen was carried out in Emeryville, CA at a later date.

PART II
SUSPENSION PATIENT TWO (SP2)

MEDICAL HISTORY

SP2 was a female caucasian, age 36, weight approximately 65 kg. The following history from records was provided by the next of kin and represents only an outline of what was a very complicated and protracted course of illness.

In 1972, SP2 presented with a nasopharyngeal mass which biopsy subsequently demonstrated to be a squamous cell carcinoma. A concomitant finding was severe cervical lymphadenopathy. SP2 had a history of frequent respiratory infections and general poor health, including several surgeries for removal of benign breast masses.

A course of radiation treatment was decided upon as the best method to manage the patient's oropharyngeal malignancy. Radiotherapy resulted in complete regression of the tumor, and elimination of associated adenopathy Unfortunately, shortly after completion of this therapy the patient developed a moderately severe myelopathy and retinopathy which initially manifested as a loss of fine motor skills and bladder control, and ended in confinement to a wheelchair. Clinical findings were consistent with radiation myelopathy. There was a developing temporo-mandibular fibrosis, restricting the patient's ability to open her mouth. Lacrimal atrophy resulted in "dry cornea" and frequent eye infections. Brain stem and inner ear damage, presumably also a result of radiation therapy, caused vertigo and episodic severe nausea and vomiting.

The character and location of the malignancy, in addition to the long-standing history of frequent respiratory infections suggested the possibility of chronic Epstein-Barr Virus (EBV) infection. Subsequent evaluation of serum and cerebrospinal fluid confirmed the presence of chronic EBV infection. As a probable consequence of EBV infection and radiotherapy, the patient's immune status continued to deteriorate and her course over the following years was one characterized by moderately severe immunosuppression and numerous secondary bacterial and viral infections, many of which required hospitalization. The last few years of the patient's life were spent at home in strict reverse isolation in attempt to reduce the frequency of infection. Followup neurological examination revealed a pancerebellar syndrome characterized by truncal ataxia and marked limb ataxia affecting both the upper and lower extremities.

Other remarkable medical history was hypothyroidism of long duration and a total hysterectomy, the reason for and date of which were not available in the medical records provided us.

During the course of her illness, the patient was managed with a wide range of medications. In the period immediately prior to her deanimation the following medications were being taken: Ruvert for vertigo, 2 grains thyroid extract daily for hypothyroidism, multivitamin tablet, Percodan for pain, and antibiotics, including Keflex.

Additional details of the patient's condition will be described in the section on the surgical protocol. After a long course of chronic illness with steady deterioration of her condition, SP2 succumbed to an acute aspiration during a seizure episode which was felt to be secondary to sepsis. SP2 had been a Suspension Member of the Bay Area Cryonics Society for several years prior to

her deanimation.

TRANSPORT

At 1:30 AM, shortly after SP1 had begun cooling to dry ice temperature, we were notified of SP2's deanimation and were asked to prepare for her cryonic suspension. Arrangements were made for SP2 to be flown from Northern California, where she had deanimated, to the Orange County Airport by air ambulance.

Of necessity, the majority of the suspension team was released to get some sleep, during which time preparations for the perfusion of SP2 were carried out by three supervisory personnel. All of the team members present for the suspension for SP1 remained for the perfusion of SP2. In some instances personnel remained actively working without sleep in excess of 72 hours.

Negotiation with hospital personnel and arrangement of transport for SP2 were carried out by Art Quaife. In brief, SP2 had a respiratory arrest after aspiration of food following a grand mal seizure. At the time of her arrival in the hospital emergency room (ER) the patient was in full cardiac arrest. The ER staff agreed to administer such transport medications as they had on hand while giving CPR. A note attached to the patient when she arrived at Cryovita Laboratories listed the following medications as having been administered:

mannitol	500 cc
Anectine	60 mg
Tagamet	300 mg
Solu-Medrol	250mg

Heparin was verbally reported as given, but was omitted from the list of medications accompanying the patient. CPR was continued for 15 minutes following administration of the last medication, after which the patient was transferred to the refrigerated morgue of the hospital and packed in ice.

External examination of SP2 upon arrival showed remarkable pathology, the details of which will be discussed in the next section.

SURGICAL AND PERFUSION PROTOCOL

After the patient's arrival, surface cooling with crushed ice was maintained until preparations were completed for the perfusion. The patient's temperature upon arrival was measured using YSI Type 401 thermistor probes. Temperatures were as follows: vaginal, 12.5°C; esophageal, 12.0°C; and oral, 8.0°C. Vaginal rather than rectal temperature was taken owing to the presence of rigor and our inability to position or turn the patient in the ice-filled shipping container in which she arrived. Cursory examination of the patient disclosed the presence of fully developed rigor mortis. A more detailed examination revealed several lesions on the lower extremities which penetrated deeply into subcutaneous fat and in one instance into muscle. These lesions had been packed with iodophor gauze tape and 4x4 gauze sponges. The etiology of these lesions is unknown, but they presented the appearance of chronically infected decubiti. Bilateral fibrotic scarring and numerous vesicles filled with clear fluid were observed on both legs and the lower abdomen. The abdomen

was markedly distended and palpation (which was complicated by the presence of rigor and hypothermic stiffening) revealed a very firm, large, and immobile mass that was originally thought to be a large fibroma or other neoplasm, but was later discovered to be a massive enlargement of the liver (Federowicz, Hixon, and Leaf, 1984).

Following external examination, the patient was moved onto the operating table and thermistor temperature probes were placed in the esophagus and vagina. The procedure for surgical preparation was essentially the same as that employed for SP1: scalp incision with burr hole, right jugular cannula placement, and median sternotomy. No mid-thigh incisions were made, since the refractometer measurements of fluid filtrate on SP1 provided no significant information compared to arterial/venous differences.

When the median sternotomy was retracted open, the right diaphragm was found to protrude approximately 20 cm upward into the pleural space. The diaphragm was displaced by the massively enlarged liver, which compressed the right lower lobe of the lung.

Despite this anomaly, arterial and venous cannulation proceeded as described for SP1. However, an examination of the descending aorta and inferior vena cava, at the level of the diaphragm, indicated they were running through a solid mass. The inferior venous cannula was advanced beyond the diaphragm to confirm patency, then withdrawn to the normal position, above the diaphragm.

The perfusion protocol was the same as was used for SP1 in regard to extracorporeal circuit, base perfusate (except Solu-Medrol was omitted), and choice of glycerol as the cryoprotective agent. The average arterial perfusate temperature was 3.4°C, with a range of 3.0°C to 5.0°C. Esophageal temperature averaged 8.8°C, with a range of 4.2°C to 11.5°C. Continuous perfusion for 4 hours and 6 minutes at an average MAP of 40 mm Hg was used. Average pump flow rate was 0.7 liters per minute. Clumps of red blood cells typical of cold agglutination were also noted in this patient during the initial blood washout. A total of 80 liters of perfusate was used, with the following quantities and compositions:

5% glycerol perfusate	25 liters
10% glycerol perfusate	10 liters
15% glycerol perfusate	10 liters
20% glycerol perfusate	10 liters
25% glycerol perfusate	10 liters
50% glycerol perfusate	15 liters

Refractometry of paired arterial and venous perfusate samples was used to determine how rapidly glycerol concentration could be increased. An attempt was made to confine the A-V difference in glycerol concentration to a range of 150 to 200 mM. The data on glycerol concentration is tabulated in Table 5 and plotted in Figure 7. As can be seen, the objective of maintaining a 200 mM or less spread between arterial and venous glycerol concentrations was achieved. Introduction of glycerol was also achieved employing a substantially shorter perfusion time than was required for SP1. As with SP1, termination of perfusion was determined by observation of brain swelling through the burr hole in the skull. Terminal arterial glycerol concentration was 2.95 M, and venous glycerol concentration was 2.87 M.

Table 5. SP2 - Glycerol Concentration.

Time (min)	5	34	108	133
Arterial				
Brix No. (1)	11.7	10.3	16.2	20.0
Moles (2)	0.608	0.610	1.39	1.95
Percent (3)	5.2	5.2	12.0	17.0
Time (min)	**5**	**38**	**133**	**235**
Venous				
Brix No. (1)	9.0	10.6	17.2	26.0
Moles (2)	0.432	0.616	1.62	2.87
Percent (3)	4.0	5.5	14.1	25.0

1) Measurements made at the time of perfusion with a hand-held refractometer, temperature compensated, Atago Model N-1, Cat. #311-N.
2) Molar glycerol concentration calculated at a later date on the same samples that the Brix measurements were made on. Measurements made with a Micro-Osmette Model 5004 freezing point osmometer.
3) Conversion of glycerol concentration, molar to w/w percent, from **Handbook of Chemistry and Physics, 60th Ed.**, CRC Press, 1979.

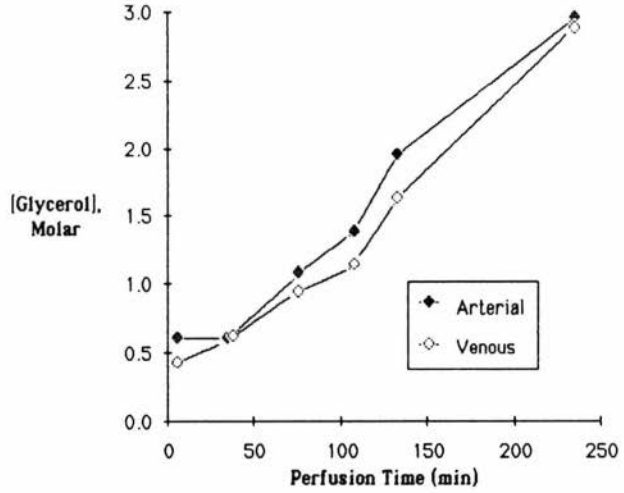


Figure 7. SP2 Glycerol Concentration vs. Perfusion Time.

Changes in peripheral vascular resistance (PVR) are shown in Figure 8. The significantly lower PVR probably made most of the difference in perfusion time requirements between SP1 and SP2, i.e., good peripheral perfusion was achieved, compared to SP1.

Table 6 shows arterial and venous pH during the course of the perfusion. We believe these values are indicative of the presence of active anaerobic glycolysis.

Observation of the cerebral cortex through the burr hole during perfusion revealed the same pattern of initial cerebral dehydration followed by cerebral edema as was observed in SP1 as glycerol penetrated the blood-brain barrier. Perfusion of both SP1 and SP2 was terminated at the point cerebral edema became pronounced enough to result in slight bulging of the cortex into the burr hole without injury to the brain. Values for PVR over the course of the perfusion are plotted in Figure 8. There was a significant correlation between terminal PVR values and maximum brain volume in both patients. These results and their importance to future cryonic suspension operations will be discussed in more detail below.

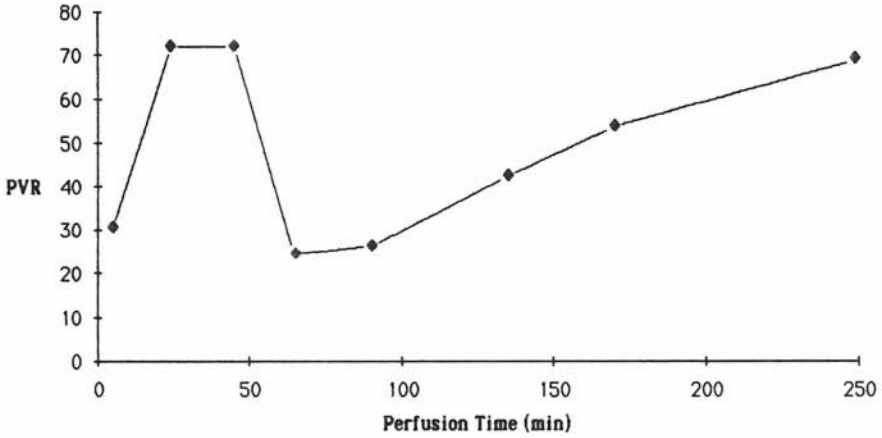


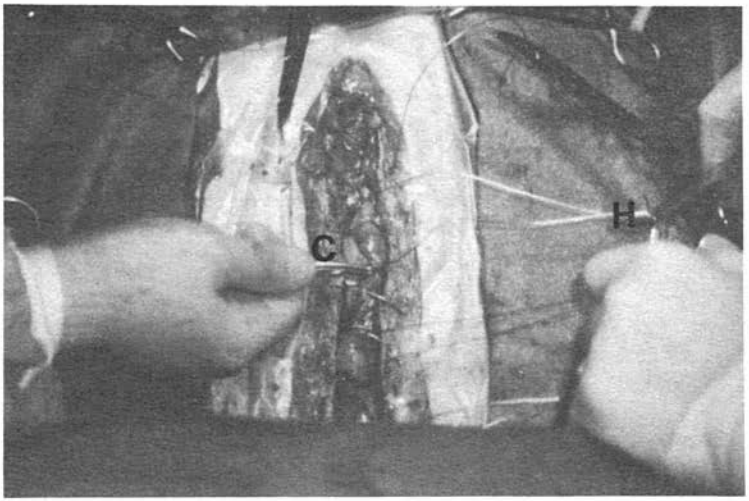
Figure 8. SP2 Peripherial Vascular Resistance vs. Perfusion Time.

Time (min)	1Ø	4Ø	142	164
Arterial	7.8Ø	7.9Ø	7.1Ø	7.Ø9
Venous	6.8Ø	6.89	6.99	7.Ø7

Table 6. SP2 Arterial/Venous Perfusate pH.

Decannulation and closure of surgical wound sites was accomplished. (Plate 5) External copper-constantan thermocouples were placed in the trachea and vagina, and on the foot, the patient was placed in double ethylene vinyl acetate

Plate 5. Closing the sternum with stainless steel wire. The wire has been driven through the sternum with a needle holder (H), and is being pulled tight with Kocher clamps (C).



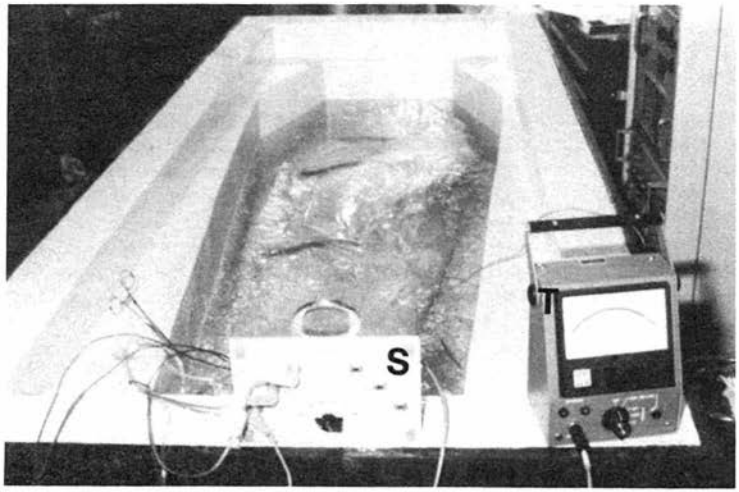


Plate 6. SP2 being cooled in an alcohol-dry ice bath in a foam insulated box. Telethermometer (T) and Temperature probe switch (S).

plastic bags, and cooling begun in a dry ice/alcohol bath precooled to -26°C. (Plate 6) Figure 9 shows the tracheal, brain, and alcohol bath temperatures during cooling. Approximately the same total time as for SP1, 28 hours, was used to achieve -70°C. (At the time, it was thought that a probe was being placed in the esophagus. Postmortem examination of SP2's remains following conversion to neuropreservation in 1983 disclosed that the "esophageal" probe had in reality entered the trachea and was not in close contact with tissue, which accounts for the slow change in the tracheal probe temperature seen in Figure 9 (Federowicz, Hixon, and Leaf, 1984)).

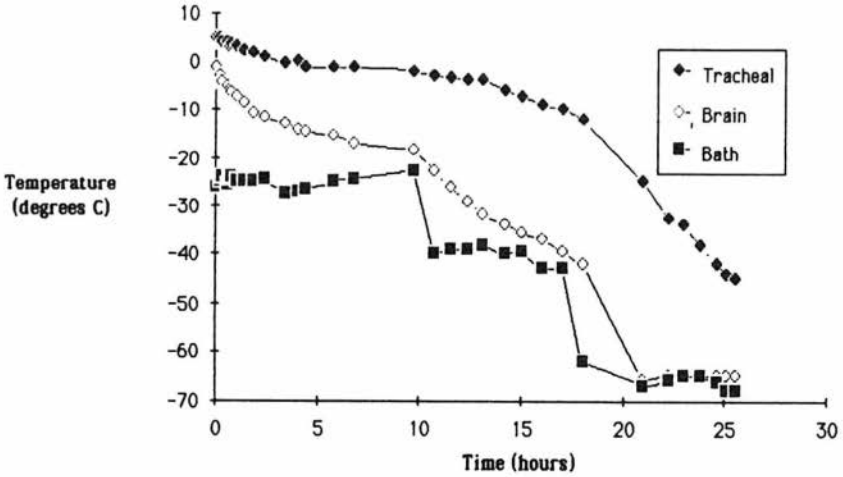


Figure 9. SP2 Dry Ice Cooling.

SP1 and SP2 were transported together to Emeryville, California for liquid nitrogen vapor phase cooling and placement in long term cryogenic storage,

PART III
COMPARISON OF PATIENTS

COMPARISONS

A list of factors are presented in Table 7 for comparison. Differences in age were probably the most important. SP1 was 79, and SP2 was 36. The general condition of the vascular system and the multiplicity of other age-related changes are probably of significance. Based on greater age alone, the presence of a less compliant vascular system, narrowing of the inner diameter of major arterial vessels, reduced permeability of vessel walls, and greater antibody activity (i.e., increased cold agglutination) would be anticipated. These are certainly major contributing factors to differences in the final glycerol concentration achieved and the duration of perfusion.

Table 7. Comparisons: SP1 and SP2.

	SP1	SP2
Age	79 years	36 years
Place of death	Hospital	Emergency Room
Cause of death	Cancer/MSOF	Cancer/Acute aspiration
Transport	HLR/Drugs/Hypothermia	Drugs/Hypothermia
Weight	59.1 Kg.	65 Kg.
Ischemic time	28 hours	24 hours
Av. Temp. (Trach.)	$6.0^{o}C \pm 2^{o}C$	$8.8^{o}C \pm 4^{o}C$
Perfusion MAP	50 mm Hg	40 mm Hg
Perf. flow rate	0.8 l/min	0.7 l/min
PVR	160 peak, 70 final	72 peak, 70 final
Perfusion time	446 min	240 min
CPA Equlib. Conc.	2.67 Molar	2.85 Molar
Metabolism	less lactate than SP2	lactate
Cold agglutination	Positive	Positive

Abbreviations: CPA-Cryoprotective Agent; HLR-Heart-Lung Resuscitator; MAP-Mean Arterial Pressure; MSOF-Multiple Systems Organ Failure; PVR-Peripheral Vascular Resistance.

Both SP1 and SP2 were in clinical environments when they were pronounced dead, and were not exposed to long periods of postmortem deterioration at ambient temperatures without transport medications and surface cooling. SP2 received only manual chest compression during the course of administration of the pre-transport pharmaceuticals. The patient was then packed in ice for transport to Cryovita. There was no metabolic support provided SP2 during surface cooling.

SP1 received a clearly better transport regimen. It is not possible to assess the relative contributions made by the differences in the administered transport protocols. The long distances these patients had to be transported would have made continuous support of circulation virtually impossible. HLR support is not well suited to lengthy transports due to low efficiency and marginal cardiac output. Only ECMO transport (Extracorporeal Membrane Oxygenator transport using a portable heart-lung machine), would have been adequate. ECMO capability will be available in the near future.

SP1 was a thin man with low body fat. Since muscle tissue is more vascularized than fat, we would expect a higher flow of perfusate and better distribution of glycerol in SP1. SP2 had a greater amount of fat, which is natural in women compared to men, but also a much greater amount due to the sedentary life style she led as a result of her long illness. Considering these factors, we would have predicted a better glycerol distribution and shorter perfusion time for SP1 compared to SP2. However, as shown by their respective glycerol equilibration graphs, SP1 required significantly longer perfusion time and achieved a slightly lower final glycerol concentration than did SP2, which is the opposite of what would have been expected if there were no other contributing factors.

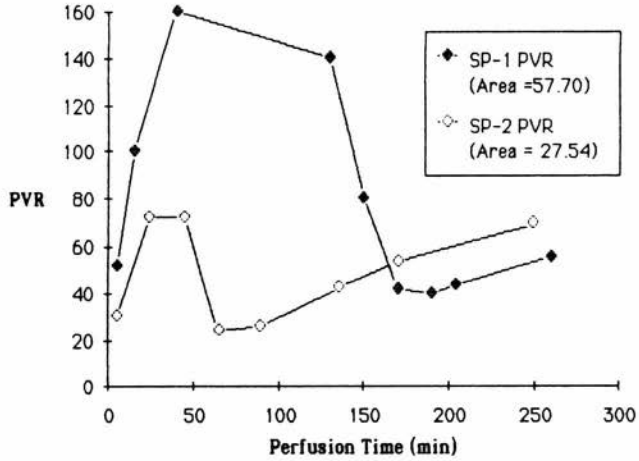


Figure 1Ø. Comparison of Peripherial Vascular Resistance, SP1 and SP2.

As previously shown, peripheral vascular resistance (PVR) was calculated for both patients over the course of the perfusion. Figure 1Ø shows comparative vascular resistance, in terms of PVR, for SP1 and SP2. The areas under the curves, for four hours of perfusion, were measured by planimeter and compared. The PVR of SP1 was 47.7% greater than SP2, quite significantly different. Factors contributing to the observed difference in PVR are as follows:

1) Normal aging pathology of arteries, including medial fibrosis and subsequent thickening of the endoarterial layer (Wolstenholme and Freeman, 1954, p. 17). Arterial wall thickening is at the expense of inside vessel diameter. Resistance to flow is related to vessel length and inversely related to vessel diameter, e.g., a small change in inside vessel diameter has a large effect on resistance to flow. Additionally, this kind of vessel pathology reduces vessel elasticity and further restricts flow, compared to the normally more compliant arterial vessels of younger individuals.

2) Rheology of the blood. Because of its cellular components, blood is a non-Newtonian fluid, and therefore there is a non-linear relationship between pressure and flow. Reduced blood flow thus causes increased viscosity and vascular resistance, in general. However, this would not be a significant factor after blood washout.

3) Low temperature, increasing blood cell rigidity and consequently reducing flow at the capillary level, further contributing to viscosity increases. Again, after blood washout this should not be a problem.

4) Long ischemic times produced very low blood pH's. SP2 showed an arterial blood pH of 6.1 before the beginning of perfusion. Red cell rigidity,

as well as rouleaux formation (stacks of blood cells), is increased by low pH.

5) The presence of cold agglutinins. Under some circumstances, which were present in both patients, blood cells stick together at reduced temperatures. A more complete discussion of these factors has been presented in the article on vascular obstruction and cold agglutinins published in the March, 1984 issue of CRYONICS (Leaf, 1984). We believe that Total Body Washout (TBW) before deep hypothermia would have been beneficial in both cases, in terms of preventing cold agglutination, but it clearly would have been of much more benefit in the case of SP1.

One final observation can be made concerning PVR. While there were considerable differences in PVR between SP1 and SP2 over the course of perfusion, there is one similarity. Both patients' perfusions were terminated at 70 PVR units. The criterion for termination of perfusion was brain size, without regard to PVR data, which was only calculated at a later date. However, if there were a reliable correlation between PVR and brain size, we could possibly use vascular resistance as an indication for perfusion termination. More data establishing the significance of this correlation will have to be acquired in humans before it can be validated. In any event, direct observation of the brain for developing edema will continue to be absolutely necessary, until other reliable criteria can be established.

Both patients' medical histories show chronic ailments. However, SP1 would be classed as a chronic death, and SP2 as acute. SP1 had active metastatic cancer that affected more than one organ system over an unknown period of time. The final stress of these failing organs resulted in cardiac arrest. SP2 had been successfully treated for cancer, but developed extensive fibrotic lesions, neurological deficits, and systemic infections. Death was acutely due to respiratory failure followed by cardiac arrest. Quantification of influences from the differences of pathology are not possible at this time. Only ischemic time is quantifiable, 28 hours for SP1 and 24 hours for SP2. To our knowledge, these are not significantly different.

Perfusion parameters, as shown in Table 7, are similar in terms of MAP and perfusate flow rates. Hypoxic perfusion time is quite different, SP1, 448 minutes, compared to SP2, 240 minutes. The effects of added hypoxia for SP1 at the temperature of perfusion are unknown, since we do not have comparable morphological data. In any case, it is extremely doubtful that hypoxic effects could be separated from other complications.

The final CPA concentrations given in Table 3 were achievable because we used glycerol rather than DMSO. No suspension patient has tolerated perfusion times close to these when DMSO was used. The added perfusion time of SP1 was well tolerated, in terms of edema, compared to DMSO-perfused patients, or compared to SP2.

Tables 3 and 5 show comparisons of arterial and venous determinations of glycerol concentration from samples taken from SP1 and SP2 respectively. The measure of CPA concentration in arterial and venous samples is important in determining how fast CPA concentration can be increased to the final value desired. Too rapid an introduction of CPA can cause cellular dehydration and damage. Figures 3 and 11 are the graphs used to convert osmolality and percent glycerol to moles, for the data given in Tables 3 and 5.

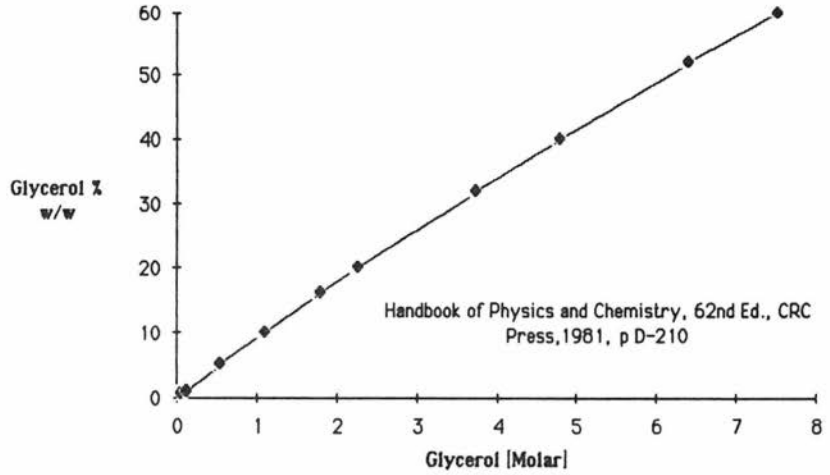


Figure 11. Glycerol Concentration. Molar <---> w/w%.

CONCLUSIONS

Table 8 lists some of the new information gained, and modifications in suspension protocol we shall institute, if possible, in future cryonic suspensions undertaken at Cryovita Laboratories.

Table 8. Conclusions.

1) Control surface cooling
2) ECMO transport, if possible
3) Total body washout at 16°C
4) Oxygenation for metabolic support
5) Glycerol perfusion at 8-12°C
6) Glycerol does cross the blood-brain barrier
7) Brain swelling is an end-point determinant for perfusion
8) Less edema results with glycerol than with DMSO in extended perfusion
9) Pulsatile perfusion should be tested, to reduce PVR
10) An improved cryoprotective ramp can be achieved using an improved extracorporeal circuit and direct on-line refractometry

The presence of cold agglutination in both of these patients demonstrates the importance of controlling surface cooling. Ice packs should only be used as long as necessary to achieve safe core body temperatures for transport. Unrestricted application of ice packs results in blood sludging, cold agglutination, high peripheral vascular resistance, restricted perfusate flow, poor CPA distribution, and prolonged perfusion time, (i.e., unnecessary exposure to high concentrations of CPA).

ECMO transport on portable heart-lung machines should be used when possible, in preference to HLR support. If suspension patients cannot be transported with circulatory support, they should undergo total body washout before being packed in ice and shipped to a facility for cryoprotective perfus-

ion. TBW before shipping would also be desirable because: 1) Platelets and granulocytes could cause problems even with the stabilization medications present: and 2) Plasma is a poor cellular support compared to artificial solutions. If TBW is not possible, ice packs used in shipping should be removed from patients before TBW, and flushing perfusate temperature should be between 16-20°C to avoid inducing cold agglutination (Leaf, 1984). Administration of Dextran-40 and methylprednisolone in normal clinical amounts during transport will help reduce the degree of cold agglutination experienced.

The presence of persistent and pronounced lactic acidosis indicates the importance of oxygenating perfusates employed during ECMO transport, TBW, and cryoprotective perfusions. For short-duration transports (those 4 hours or less) or for TBW followed by air shipping, a bubble-type oxygenator such as the Shiley S-100A is preferred. A bubble-type oxygenator should always be employed where there is any possibility of intravascular coagulation, as the porous defoaming column can act as a coarse prefilter of large surface area. For transports involving extended periods of extracorporeal support (greater than 4 hours) a membrane type oxygenator such the Sci-Med spiral-wound silicone membrane is preferred, because of this oxygenator's ability to preserve cellular blood components for extended periods of perfusion. Another means of controlling pH is the use of perfusates containing only physiological levels of glucose.

The long perfusion times possible, and the high CPA concentrations achieved with these patients, as contrasted with previous perfusions carried out in this laboratory employing DMSO (Leaf, 1979, 1981), indicate the clear superiority of glycerol as the cryoprotective agent of choice for perfusion of ischemically injured suspension patients. Cryoprotective perfusion should be carried out at 8-12°C to allow for adequate intracellular penetration of glycerol and to minimize cellular dehydration.

The deciding factor in terminating the perfusion was the direct observation of brain size. As CPA concentration increased, the brain began to lose volume due to osmotic removal of water. Brain volume reduction was approximately 20%, and had the same appearance as in neurosurgical patients one of us (Leaf) has seen in the UCLA operating rooms after the patient was given 1-2 gr./kg. IV mannitol. This technique is used for neurosurgery when the optic nerves must be exposed. While the brain can tolerate considerable volume reduction, it cannot tolerate high pressures created by expansion against the constraining cranial vault. When the blood-brain barrier is opened by high enough CPA concentration, the brain assumes its normal size. If cerebral edema occurs during perfusion, then the obvious point to terminate perfusion will be before the brain is subject to elevated intracranial pressure with the associated risks of no-reflow and herniation of the brain stem or of the cortex through the burr hole. It would in any case be useless to continue perfusion, in terms of trying to increase CPA concentration in the brain, because cerebral perfusion will cease as the intracranial pressure exceeds the mean arterial pressure. Therefore, observation of brain size is the best method for determining the end point of perfusion for suspension patients. This is the criterion we used for SP1 and SP2. This is also now our standard criterion for termination of perfusion. The second standard will remain achievement of the desired terminal CPA concentration. Since brain volume decreases promptly when perfusion is discontinued after the development of cerebral edema, it has been proposed that higher terminal CPA concentrations might be achieved by reinitiating perfusion after a "rest period" to allow spontaneous reversal of brain swelling. Given

enough stop-start cycles, the proper CPA concentration may be achievable despite the development of cerebral edema.

The most likely solution to the high PVR encountered in SP1, aside from controlling cold agglutination, is the application of pulsatile perfusion during TBW and cryoprotective perfusion. This is a known, effective method employed during clinical perfusion of patients for reducing PVR (Taylor et al, 1978). Cannulation, through median sternotomy, of the inferior and superior vena cava for perfusate return, and the aortic arch for perfusate delivery are desirable, particularly if pulsatile flow is to be used. In the future we will employ left ventricular venting in an effort to improve heart and lung perfusion by reducing left atrial pressure and potential left ventricular distension.

A technique of recirculating perfusate is superior to single pass stepped increases in CPA concentration for establishing a more controlled cryoprotective ramp. Several types of mixing systems that would provide a continuous ramp are available. We have used a system for animal work with a large reservoir, to which perfusate of high glycerol concentration is added continuously. This produces a ramp that increases quickly at the beginning, and slower and slower as more concentrated perfusate is added. Other more complicated systems that produce linear and upward-curving ramps are also possible. These might allow much better control of the brain edema.

Inability to monitor cryoprotectant concentration continuously interferes seriously with any attempt to actively control edema. Monitoring may be done either with osmometry or refractometry. Our experience with osmometry since these suspensions has been unsatisfactory in that they balk at measuring cryoprotectant solutions with high concentrations of colloid and cryoprotectant. Hand-held refractometers have been unsatisfactory because they are usually designed for a single application and work in a fairly narrow range. A good general purpose bench refractometer would be much more useful. Even better would be a recording system with process refractometers in the arterial and venous lines that could monitor cryoprotectant concentration continuously.

As noted at the beginning of this article, observations made during the course of these suspensions have been implemented both in animal work and the human suspension carried out since that time.

The goal of cryoprotective perfusion has been to replace enough water with cryoprotective agents to keep the amount of water available in tissue for freezing to approximately 50%. There is evidence from whole mammal research that this amount of ice is the maximum tolerable, or at least significantly more injury occurs if more than 50% of available water is frozen (Lovelock and Smith, 1956; Noble, 1980).

The changes in technique discussed above are all aimed at improving the primary goal of good cryoprotective perfusion. Every case of experimental human suspended animation, like every scientific experiment, offers its grain of truth that will hopefully lead to new understanding and knowledge that can be employed to achieve better perfusion of cryonic suspension patients.

We would like to thank Brenda Peters and Al Lopp for major help in entering and proofreading this paper.

REFERENCES

Bianchi, J., (1983), Cryonics and the Law, Part II, **CRYONICS**, #40, (Nov, (1983), p. 24.

Federowicz, M., H. Hixon, and J.D. Leaf, (1984), Postmortem Examination of Three Cryonic Suspension Patients, **CRYONICS**, #30, (Sept, 1984), p. 16. (A reprint of this article is available from ALCOR Life Extension Foundation, 4030 N. Palm, #304, Fullerton, CA 92635.)

Leaf, J.D., (1979), Cryonic Suspension of Sam Berkowitz: Technical Report, **Long Life Magazine, 3**, 30-35, (March/April, 1979).

Leaf, J.D., (1981), Case Study: KVM Suspension, **CRYONICS**, #13, (Aug, 1981).

Leaf, J.D., (1984), Perfusion: Acute Vascular Obstructions and Cold Agglutinins, **CRYONICS**, #44, (Mar, 1984), p. 20.

Lovelock, J.E., and Audrey U. Smith, (1956), Studies in Golden Hamsters During Cooling To and Rewarming From Body Temperatures Below 0°C. Part III: Biophysical Aspects and General Discussion, **Proc. Roy. Soc., Ser. B, 154**, 427-42 (1956).

Noble, C., (1980), Letter to **CRYO-LETTERS** (Dr. Felix Franks), **THE IMMORTALIST, 11(10)**, 2-5 (Oct, 1985).

Taylor, K.M., W.H. Bain, K.J. Maxted, M.N. Hutton, W.Y. McNab, and P.K. Caves, (1978), Comparative Studies of Pulsatile and Non-Pulsatile Flow During Cardiopulmonary Bypass, **Journal of Thoracic and Cardiovascular Surgery, 75**, 569-73 (1978).

Wolstenholme, G., and J.Freeman, Eds., (1954), Peripheral Circulation in Man, A CIBA Foundation Symposium, J. & A. Churchill, Ltd., London, 1954, p.174

Appendix A: The "Smith Criterion" for adequate cryoprotection.

Audrey Smith's hamsters survived if: 1) $\leq$ 50% of total body water froze; or, 2) $\leq$ 60% (rounded up from high 50's) of brain water froze.

This suggests that if 40-50% of liquid **volume** remains (**NOT** liquid water), **mechanical** injury from ice will be avoided. (Smith's results do not speak to the effect of **dehydration** injury, i.e., the effect of replacing water by glycerol. Perhaps this is a good thing, because it is **impossible** to prevent 50% of the **water** from freezing, since even a 50% glycerol solution will freeze! So will a 60% glycerol solution.)

Accepting the goal of preventing mechanical injury then, and forgetting about "solution effects" injury, we compute the following:

Let V_v = the concentration of glycerol (in %v/v) that is unfreezable.

Let V_s = the concentration of glycerol (in %v/v) one **starts** with.

During freezing, we let half the volume of the **solution** be converted into ice, during which time $V_s \dashrightarrow V_v$. Since the volume has changed by a factor of two, and the volume of glycerol is unchanged, the concentration of glycerol as %v/v has doubled. Therefore, $V_s = 1/2\ V_v$. According to Rasmussen and Luyet, a 73% w/w glycerol solution will not freeze (**Biodynamica, 10**, 329 (1969)).

Converting to %v/v units gives:

$$\frac{73 \text{ ---> } 57.94 \text{ ml}}{73 \text{ ---> } 57.94 + 26 \text{ ---> } 26} = \frac{57.94}{83.94} = 69.0\%$$

Therefore $V_S = 69/2 = 34.5\%$ v/v ≃ **4.72 Molar.**

If we relax the "Smith Criterion" from the body's 50% requirement to the brain's ~ 60% requirement, then:

$$V_S = (40/100)\ V_V = 0.4\ V_V = 27.6\% \text{ v/v} \simeq \textbf{3.78 Molar.}$$

NOVEMBER - DECEMBER 1985 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 NOVEMBER meeting will be at the home of:

(SUN, 3 NOV 1985) Maureen Genteman
524 Raymond Avenue, #12
Santa Monica, CA

DIRECTIONS: Take the Santa Monica Freeway (Interstate 10) to Santa Monica and get off at the 4th Street exit. Turn south (left) on 4th. Go south on 4th to Ocean Park Ave. (4-way flashing stop). Go left on Ocean Park, down ramp to stop and up to 6th St. on Ocean Park. Turn right on 6th. Raymond is the second street. Turn right on Raymond. 524 is on the left. #12 is on the second floor.

The DECEMBER meeting (Annual Turkey Roast) will be held at the home of:

(SAT, 7 DEC, 1985) Brenda Peters
(FIRST SATURDAY) 8150 Rhea
Reseda, CA

DIRECTIONS: Take the San Diego Freeway (Interstate 405) north into the San Fernando Valley, to Roscoe Blvd. Go west (left) on Roscoe 3-4 miles. Rhea is 2 blocks past Reseda Blvd. Turn south (left) on Rhea, which has a geodesic dome church on the corner. 8150 is the second house in the second block, on the left.

ALCOR LIFE EXTENSION FOUNDATION
4030 NORTH PALM #304
FULLERTON, CALIFORNIA 92635
(714) 738-5569

ADDRESS CORRECTION AND FORWARDING REQUESTED