

CRYONICS

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Trans Time Place 6th Patient Into Liquid Nitrogen Storage

On June 26th, 1982 Trans Time placed its 6th whole body patient into liquid nitrogen (LN2) storage. This patient had been perfused and placed on dry ice storage approximately two and a half years ago. Due to prolonged negotiations with the next of kind, cryogenic storage was delayed far beyond the amount of time normally considered necessary or desirable.

I was present both to help out with the encapsulation and to have an opportunity to see the Northern California team in action. I was especially anxious to see this patient's transfer to LN2 storage since I had been with him just prior to deanimation and was responsible for his resuscitation and transport to the perfusion facility in Southern California. Over a space of three years I had seen this patient through virtually every phase of cryostasis; resuscitation, transport, perfusion, cool down to -79°C and cool down to -196°C. Though I am no stranger to the phenomena, there is still something awesome about seeing someone virtually unchanged after two and a half years of "so-called" death.

The transfer operation consisted of removing the patient from the dry ice chest, placing him in a mummy type sleeping bag and nesting him in a custom made aluminum box designed to provide thermal and mechanical protection on all sides. These boxes are made to fit each individual patient by Frank Rothacker, Treasurer of BACS and a very competent engineer

as well. The interior of the boxes are lined with open cell urethane foam, and after the patient is in place additional open cell foam is packed around him to provide extra mechanical protection and to act as an absorbent for liquid nitrogen. This last feature is extremely important should transfer of the patient to another dewar become necessary in the future. The open cell foam slowly saturates with liquid nitrogen and then acts to hold large quantities of the refrigerant around the patient during subsequent transfers. Protection of the patient from any exposure to rewarming at liquid nitrogen temperatures is extremely important since the thermal stresses set up as a result of surface exposure to elevated temperatures can result in cracking or fracturing of tissues.

An impressive crew of people turned out to assist with operations including Art Quaife, John Day, Betty Symanski, Michelle Navarette, and Wes and Judy Walton. the team was well organized and the operation was carried out smoothly with no more than the usual minor glitches which are to be expected in any once or twice a year operation. M.D.

Give a Friend a Gift Subscriptions to CRYONICS and Save!

IABS announces a special offer for members of IABS, Alcor, and BACS. Do you have a friend who is interested (perhaps marginally) in cryonics and is not a member of either IABS, Alcor, or BACS? If so, we invite you to sponsor them for a special gift subscription to CRYONICS for one year for only \$5.00. All you must do is send us 1) your friend's name and address, 2) a \$5 check (yours and theirs) and 3) a statement saying you are a member of IABS, Alcor, or BACS and that you wish to sponsor their gift subscription. If you have several friends, sponsor a subscription for all of them at \$5 each -- there's no limit. However, all new subscriptions must have a mailing address inside the United States and your subscription letter must be postmarked on or before August 31, 1982. So help "get the word out" and save some \$\$\$ in the process!

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Cost Reduction for Neuropreservation

Oddly enough one of the significant factors affecting the cost of neuropreservation is the fee for disposing of the remains which are not placed into liquid nitrogen storage. Since the time of the Nelson scandal here in Southern California we have been forced to pay a very inflated price in order to get a mortician to cooperate with us in arranging for cremation of the patient's "remains." Before the Nelson scandal this service was available to Cryovita Laboratories for a fee of several hundred dollars. After the award of large judgements in the Nelson/Klockgether case the rate for this service was increased to over \$1,000 not including transportation and various other handling costs.

In an attempt to find an alternative to this outrageous situation Mike Darwin contacted a number of low cost cremation societies with an eye to negotiating a group rate for IABS and Alcor members. After many meetings, much frustration and countless hours of discussion an organization with a good reputation and reliable management was found which will accept neuropreservation members into their organization and cremate their remains following perfusion and apcision at Cryovita.

We are thus pleased to announce that memberships in the Omega Cremation Society are available for members of IABS or Alcor for a \$15.00 one-time initiation fee. The Omega Society's current fee for cremation is approximately \$350.00. This represents a savings to the patient's trust fund of \$650.00. IABS of Alcor neuropreservation members wishing to take advantage of this savings should contact IABS for a membership application

and instructions by writing to IABS, 4030 N. Palm #304, Fullerton, California 92635. You will be sent a special application for membership in the Omega Society along with some literature about the Society's services and operations. DO NOT WRITE TO THE OMEGA SOCIETY DIRECTLY! We have a special administrative arrangement with them in order to eliminate the possibility that you might be picked up directly from the place of your deanimation and be CREMATED BEFORE NEUROPRESERVATION WAS CARRIED OUT! Applications for membership in the Omega Society should be obtained only from IABS (they are a different color from the rest of the Society's application forms).

This same arrangement is available to the members of other nonprofit cryonics groups with an additional \$5.00 handling fee payable to IABS to defray printing and administrative costs. Other groups interested in obtaining this service for their members should contact IABS for additional information.

Included in the cost of cremation is a service which allows the individual to select whether he wishes his ashes scattered in the mountains, desert, or sea. With payment of the \$15.00 membership fee a tree will be planted in the member's name in the Cleveland National Forest. Alternative means of disposition for the ashes such as shipping to the next of kin or other responsible party are also included in the basic fee for cremation.

We urge all IABS and Alcor neuropreservation members to contact us promptly about participation in this plan. This is an IMMEDIATE and CONCRETE way YOU can help to reduce the cost of cryostasis for yourself.

New IABS/Alcor Emergency Service

On June 22, 1982 a new paging system covering all members which Trans Time has responsibility for was put into effect. This system was acquired and set-up by IABS and Alcor. The system consists of a paging

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unit which can be reached anywhere in the Los Angeles basin, Trans Time's 24-hour answering service and the bracelets or wallet cards being carried by the individual suspension members. A technician who has been specially trained in cryonics rescue procedure will be carrying the pager at all times. Should an emergency occur the answering service will patch the rescue technician through to medical personnel or next of kin within a matter of minutes after the call was received. This service will be of benefit even to members living a great distance from Southern California as it will allow the rescue technician to be in touch with a member's medical facilities within minutes of his admission.

An additional advantage of the system is that the dialer alarms which monitor patient storage dewars are also hooked into this system so that in the event of fire or vacuum failure cryonics personnel are immediately notified.

Well Preserved Brains

We have received a prepublication copy of a paper documenting good morphological preservation of rabbit brains perfused with six molar (6M) glycerol and frozen to -60°C. The purpose of the paper was not to demonstrate preservation of brain "viability" on rewarming, but rather to develop a freezing technique which does not destroy cell membranes. Intact cell membranes are necessary in allowing a new neurophysiological technique to be used. this technique, called 2-deoxyglucose mapping allows neurophysiologists to determine which areas of the brain are metabolically

active at a given time. In this procedure an experimental animal is stimulated while radioactively labelled 2-deoxyglucose is given. Active brain cells pick up this nonmetabolizable analog of glucose and concentrate it. It then becomes possible to make ultrathin sections of the brain and coat them with film emulsion in order to develop a "fingerprint" of metabolic activity. Unfortunately, this technique has been somewhat limited in its application by the amount of time it takes to create such a picture on a cellular level. The technique has worked quite well for larger brain regions, but has not yet been successfully applied to brains on a cell-by-cell basis. The need to carry this procedure out at below freezing temperatures has proved a stumbling block due to breakdown of brain cell membranes secondary to freezing. What the authors have demonstrated is a technique that should allow neurophysiologists to tell just which individual brain cells are involved in a given function. Thus, it should soon be possible to pull the whisker on a rat, give it radioactively labelled 2-deoxyglucose, kill it, section its brain, and discover just which cluster of cells is responsible for processing this stimuli. Obviously this will be a very powerful technique for gaining insight into brain function.

Of particular interest to cryonicists is the finding that brains perfused with 6M glycerol are virtually indistinguishable from control brains even after they have been frozen to -60°C. The authors also examined brains which were perfused with 3M glycerol (the same concentration currently used in human cryostasis operations) and brains which were simply "straight frozen" in the absence of cryoprotectant. Surprisingly, brains that were simply straight frozen looked remarkably good with most cells still visible. The cell membranes on these straight frozen cells were not as crisp, and there were numerous gaps in the dendritic weave, presumably as a result of large ice crystal formation. The brains treated with 3M glycerol appeared much better preserved than straight frozen brains but still were not as well preserved as the brains treated with 6M glycerol.

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Unlocking the Directorates -- BACS and TT Disagreement

It's an age-old problem, especially with beginning organizations: too many positions to fill with not enough people competent or willing to fill them. It has certainly been a characteristic of most cryonics organizations, which have generally worsened the problem with a proliferation of organizations. The typical set-up has been to have one organization responsible for acquiring members and accepting donations and the contracting the second organization to provide suspension services. The argument for this arrangement is that the membership organization can qualify for non-profit and tax exempt status to save money and pursue research funding, while the second company can be for-profit to encourage the development of professional cryonicists.

The problem is that if you have two corporations of this nature, you need two separate boards of directors -- yet, all past and present cryonics organizations began with a small number of members, usually less than ten. Besides, few people wanted to be the "altruistic" non-profit directions and watch everyone else get rich if cryonics were to capture the public fancy. Therefore, several organizations put the same people on the boards of both the non-profit and for-profit organizations with the idea that they would worry about it in the future if it became a problem. Most of the organizations set up in that way have now ceased to exist. Other groups found or were forced into alternate solutions. Cryonics Association and Cryonics Institute are both non-profit, so it doesn't matter if the boards

of directors are interlocking. The Institute for Advanced Biological Studies (non-profit) and Soma, Inc. (for profit) managed to scrape up enough people to prevent interlocking directorates. (Soma no longer exists, so IABS is not now paired with an organization.) The Alcor Life Extension Foundation (NFP) was formed with Manrise Corporation (FP) and had some interlocking directorates, although Fred Chamberlain was careful to formalize the relationship between the two. Manrise later merged with Trans Time, leaving Alcor essentially independent (although one Alcor board member is also a TT board member, and most Alcor board members own TT stock).

For the Bay Area Cryonics Society and Trans Time, however, the solution has not come that easily. BACS was formed in 1968 as a membership and mutual aid organization. In 1972 a group of BACS members decided to form Trans Time in order to make quality suspension services available in the San Francisco area. The officers of both organizations were different, but the directorates were essentially the same. Most suspension members of BACS (the only class of member eligible to be on either board) invested in Trans Time, interlocking the organization even more deeply. As long as organizations remain small, they can probably get away with this kind of set-up. However, the potential for income tax evasion and other types of fraud makes the interlocking arrangement between not-for-profit and for-profit corporations strongly discouraged by the Internal Revenue Service and the Securities and Exchange Commission. The main objection is that it would be very easy for a non-profit corporation to become a front for a for-profit corporation. The NFP takes in donations and pays the FP more than fair value for services. The FP then pays salaries and/or gives stock to its employees, who also happen to be NFP board members. A tidy system for turning ordinary donations into personal profits -- and quite illegal.

As BACS and TT became more successful (in terms of membership and cash flow), the potential for this kind of situation grew; so that, under

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the advice of their own attorneys and under some pressure from government agencies, in 1981 the two boards were reformed with differing members. There were no allegations of actual fraud or misconduct (and none are implied in this article). This action was taken to avoid the possibility of future fraud.

The division of the boards has brought to light a number of problems. The contract between BACS and TT was allowed to expire in 1976 and no new contract was agreed upon to replace it. Since that time BACS and TT have informally acted under the basic terms of the old contract and whatever understanding have been added since. Informality may be nice at parties; but in business and legal relationships, it is likely to create two situations: neither organization really knows what is being done, and whichever one knows more can easily take advantage of the other one.

Of course, this was not seen as a problem while BACS and TT were functionally one organization. But now BACS has a new board with some members committed only to the interests of BACS, and they have discovered that BACS has no written agreement with its chief business associate, little record of many past administrative decisions, and no strength from which to negotiate a new agreement. The Trans Time board is in the uncomfortable position of being forced to negotiate with a now more or less independent organization which has traditionally functioned as what amounted to a feeder system for TT. To further tangle the situation, TT owns the dewars in which the patients are stored, but BACS has legal possession of the bodies and the trust funds. TT cannot exist long without BACS payments for storage and other services; yet BACS cannot effectively negotiate with anyone else for storage or perfusion. (No one else has that

many storage dewars, and the only other California company capable of performing perfusions -- Cryovita -- is currently tied up in an exclusive contract with Trans Time.) Neither group is happy with this situation, and the resulting disagreements have led to calls for binding arbitration and even a hint of the possibility of litigation by one BACS board member, Frank Rothacker. Obviously, neither group wants to take their troubles to the courthouse; but at present they appear to be far from a compromise. The situation is coming to a head in part because of BACS's longstanding financial problems which have forced BACS to raise annual dues.

The most serious points of contention appear to be these:

1. BACS Treasurer Frank Rothacker feels strongly that the interlocking boards and informality of the past led to more potential advantages for Trans Time than for BACS. TT was also run as a much more efficient and effective operation than was BACS. Rothacker feels that the relationship between the two organizations was structured such that most potential losses were passed on to BACS while potential profits and windfalls were directed to TT.

2. BACS members now in suspension have paid an amount equal to or in excess of the cost of the storage dewars as an "encapsulation fee," but ownership is retained by Trans Time, making it almost impossible for BACS to pursue suspension services with any company other than TT. Trans Time, on the other hand, is free to negotiate with any non-profit group to acquire patients. This arrangement, whereby TT retains ownership of the dewars would have been an innocent enough matter if the boards of the two organizations were not interlocking at the time this policy was adopted. The virtual congruence of the boards at the time this decision was made raises the spectre of conflict of interests.

3. In the past, BACS has paid a \$700 commission (out of the \$1000 membership fee) for each suspension member that TT recruited. This was to be an incentive for TT to market BACS and cryonics. Once again, BACS's

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role was as little more than a feeder for Trans Time's operations.

4. Frank Rothacker and a few other BACS directors feel that TT has put itself in an unstable financial situation by misapplying its income to expansion and the purchase of nonessential equipment, such as a microcomputer, rather than using recent income to pay off debts, build cash reserves, and otherwise increase stability.

5. Both BACS and TT want to put themselves on a much more formal basis with each other. Little progress on this matter appears to be forthcoming from either organization. BACS has yet to respond to TT's contract proposal of over a year ago with a written counterproposal and TT does not appear to be cooperating with BACS's request for detailed itemization of TT's charges for perfusion, storage, and emergency responsibility.

All of this puts quite a burden of response on the Trans Time board of directors. They are being asked to assemble eight years of informality into a coherent body of information -- a difficult and intimidating task. All of this is at a time when TT has its own set of headaches and responsibilities.

The situation is further complicated by the fact that the BACS board is by no means in agreement on all or even most of these issues. Even the fairest description would have to acknowledge a considerable degree of fragmentation of the BACS board on all of these key issues.

We hope that BACS and TT are able to find ways to formalize their relationship to the benefit of each other. But whatever the outcome, we also hope that other cryonicists may learn from this situation. Even with

interlocking directorates, much of the current crisis could have been eased if a more formal attitude had been adopted by each organization. It is ironic that cryonics, an idea which so depends on planning for the distant future, has led to the formation of so many organizations which could not plan for the near future (IABS included; our insights are from our own past problems).

If one of our readers decides to start a cryonics organization or a pair of cryonics organizations, he should remember:

1. Get a good lawyer with organization experience.
2. Pay attention to him.
3. Follow his advice when he tells you to hold formal monthly meetings, to keep detailed minutes, and to keep a policy manual. (To a great extent both BACS and TT have done this.)
4. Do not do business, even as friends or relatives, without a contract. Friends do not always stay that way; and even a brother may sell his interest to a guy who ships you down the river.
5. No one else will watch out for your interest if you don't.
6. If you do not have enough people to run two organizations, do not start two organizations. (To be honest, if you don't have enough people to start two organizations, perhaps you shouldn't even start ONE. You will need substitutes eventually. Probably sooner than you think.)

Steve Bridge

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Do Android Film Makers Dream of Electric Audiences?
by Al Lopp

If you are one to pay attention to movie reviews in the general press such as national news magazines and major newspapers, it is likely you have encountered some of the bad to lukewarm opinions which have been written about "Blade Runner," the latest science fiction epic from the director of "Alien," Ridley Scott. It is my honor to tell you that you are a special person -- an immortalist -- and therefore ignore the mumblings of all those pre-immortalist consciousnesses, most of whom never caught what this movie was about. As an immortalist you will take to the theatre the insights they lack, and you will find this a powerful and artistically rewarding film. So I encourage you to reinforce the rightness of your desire to live indefinitely and go see "Blade Runner."

Not to imply that this film will lift your spirit. It is set in the year 2019 in a Los Angeles crowded shoulder to shoulder with semi-literate street people of indeterminate nationalities and composed of militaristic archeopolises and decaying apartment houses. There monolithic supercorporations huckster their products at you constantly from entire sides of skyscrapers or from the undersides of gargantuan aircraft. They make L.A. into a high-technology slum so depressing you will think twice about wanting to live to see it.

Harrison Ford plays a blade runner, a special cop who pursues and exterminates "replicants." Replicants are pseudo-humans, products of 21st century genetic engineering, who are manufactured for various types of slavery and therefore are created as well as possible to be emotionless. It has been found that after several years replicants develop emotions similar to our own and often become hard to control, so they have been outlawed on Earth and are used only in space or in off-world colonies. They are also manufactured with a genetic lifespan of only four years, supposedly so that their emotions cannot develop fully.

Four replicants make their way back to Earth to confront the men who designed them and to be reprogrammed for longer life. The blade runners

have no idea what the replicants are up to and don't care to find out, since their job is to execute them regardless.

The story follows Ford on his trackdown of the replicants through street markets, strip joints, and department stores. He is shown to be fed up with his world and haunted by his killing without the awareness of why. He gets the usual detective-story experiences: impersonates others, performs mental acrobatics of deduction, gets beaten up to within an inch of his life, and falls in love with a woman the unthinking viewer will consider his enemy.

It is here where so many moviegoers will falter, for if they are looking only for a detective story there have been better. Few among the denizens of 1982 will see that there is a message here as Ford races through a humanity of zombies to exterminate the few creatures who love living so much they will do anything and risk everything to hold onto it. The reviewers in "Newsweek" and the "L.A. Times" illustrate that 20th century society is just as lost for a reason to stay alive as this fictitious society of the 21st century. But then, what kind of idiot looks for messages in movies or in life?

The s.f. fans among us will recognize that "Blade Runner" is based on "Do Androids Dream of Electric Sheep?" by the late Philip K. Dick, for it is a faithful rendering, one in which Dick himself played a major part.

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Science Updates by Thomas Donaldson, Ph.D.

PITUITARY CHANGES DURING DIETARY RESTRICTION

As all cryonicists will know, dietary restriction and particularly calorie restriction will definitely prolong the lifespan of rats, and similar treatments if instituted would probably prolong the lifespan of human beings, though at considerable cost. Exactly how this may happen remains a mystery, although it may happen because of changes in the output of hormones of some kind by either the hypothalamus or the pituitary. Segall in particular has suggested that dietary restriction may act in some way similar to surgical removal of the pituitary in its effect on aging (Segall, P.E. MECH AGING DEVL 9 (1979) 515). An interesting paper in EXPERIMENTAL GERONTOLOGY (16 (1981) 432) by B.J. Merry and Anne M. Holehan gives us some empirical data on this question; as it turns out, dietary restriction does cause some changes qualitatively similar to surgical removal of the pituitary (known as hypophysectomy) but these changes differ in other ways. The total effect of the paper is to give us some fascinating clues as to how dietary restriction may act.

Merry and Holehan studied the production of luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone, and another testosterone related hormone, dihydrotestosterone, both in normally fed rats and in other rats existing under 50% of the normal dietary content of calories. All of these to fertility in male rats. For instance, FSH is a pituitary hormone controlling sperm production.

Their detailed results were quite complex. In normal control rats, testosterone levels decreased with age after puberty, in accord with results of a large number of other scientists. In restricted rats, testosterone was lowered and the time at which it reached its peak concentration was delayed, but nevertheless there was a definite occurrence of puberty and peak in testosterone levels. By age 100 days, Merry and Holehan found no

difference in fertility between the normal and restricted rats, and their serum testosterone concentrations were the same. However compared to the normal rats, the restricted rats didn't show a decrease in testosterone levels.

For pituitary hormones LH and FSH, results were also interesting. It is these hormones which control production of testosterone and puberty; Merry and Holehan found that FSH was markedly depressed in the restricted rats, but levels of LH were HIGHER than those of normal rats. This last observation shows quite definitely that whatever the effects of dietary restriction may be, they clearly are much more complex than a simple "turning off" of the pituitary.

While at present we can only speculate, some speculations are in order. It would seem that these results suggest that rather than a wholesale decrease in hormone production by the pituitary, dietary restriction causes some quite specific changes in hormone production. It seems unlikely that any of the hormones studied by Merry and Holehan connect directly with aging; but what their results would strongly imply is that we need to study the precise hormonal output of the pituitary of restricted rats and rats fed low-tryptophan diets. One suggestion might be that hormones connected with tryptophan metabolism may decrease selectively during dietary restriction, and it is these hormones which may relate closely to aging.

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CELL AGING AND THE HORMONAL ENVIRONMENT *

Almost all cryonicists will recall the very interesting experiments of David Harrison, in which he showed that blood-forming cells could be transplanted from mouse to mouse for up to 6 times the normal lifespan of mice; and that by implication aging at the level of the cell had at best an indirect influence on the total lifespan of mammals (Harrison, D.E. J. GERONTOLOGY 30 (1975) 279). Cell lines transplanted according to Harrison's technique will eventually die off; although they apparently last for several years beyond the time that an equivalent cell culture would last. As yet we don't know why such cells die off, whether there may be any relation between this eventual failure and the aging of the animal, and what there may be in, which preserves or destroys them. What we DO know, however, is that answers to these questions might tell us a lot about aging: they would clarify exactly what changes may be involved in hormonal aging and also in cellular aging if indeed cellular aging takes place.

To study this problem more closely, we have needed work relating the environment of these blood-forming cells to their capacity to grow and multiply. A recent paper in MECHANISMS OF AGING AND DEVELOPMENT (17 (1981) 289) by Kim Mathews and D. Crouse has begun the study of interrelations between the bloodforming cells and the other cells of the bone marrow both in aging young mice. It is these marrow cells which form the immediate environment of transplanted hematopoietic cells (blood-forming cells); Mathews and Crouse made a cell culture of such cells and then introduced into these cell cultures the actual bloodforming cells themselves. They made cultures of the marrow cells from both young and old mice, introducing into them hematopoietic cells from both young and old mice. They then studied the growth of the blood-forming cells from these different environments.

Mathews and Crouse found some very clear differences between hematopoietic cells cultured in a young environment versus those cultured in an old

environment, although surprisingly these differences were not of a kind we might have expected. As it turns out, blood-forming cells cultured in an OLD environment seemed to grow FASTER than those cultured in the young environment. However the types of cells produced in the old environment did clearly differ from those produced in the young environment; aged environments contained fewer lymphoid cells and a moderate increase in the number of cells of one type, the megakaryocytes. Furthermore, the old environments produced a greater variability in numbers as between different cultures.

The cells of the megakaryocyte type will definitely fail to grow in a normal young environment (Williams, N. et al BLOOD 51 (1978) 245). Furthermore, if young bloodforming cells are transplanted into old mice, they will produce a significantly greater number of megakaryocytes (M.L. Davis PROC SOC EXP BIOL MED 137 (1971) 1452). The eventual exhaustion of a transplanted cell culture may have something to do with this production of megakaryocytes, as may hormonal changes in the aging mice also. Mathews and Crouse speculate about possible other changes but so far their ideas are speculations only.

It would be of considerable interest, though also of great experimental difficulty, to attempt a duplication in vitro of the experiments of Harrison. The normal cellular environment clearly differs from the environment of a cell culture in which most of the work on cell lifespans has been done. We may hope that Mathews and Crouse pursue this work with a view to clarifying possible hormonal effects on cell lifespans.

* TYPIST'S NOTE: THIS ARTICLE IS DUPLICATED FROM LAST ISSUE.

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A NONINVASIVE AND SIMPLE MEANS TO VERIFY CIRCULATION TO THE BRAIN

Cryonicists will all know of the risk that in a hospital we may be placed upon an HLR and attending doctors may refuse to take us off for legal or other reasons until our brains are destroyed by prolonged lack of oxygen at a high temperature. Besides the legal steps which we might take to forestall this possibility, there are also several existing means to directly measure and verify whether or not circulation has been restored to our brains by the HLR. Obviously this is important: none of us actively wants to be frozen except as a last resort, and if we are frozen in a circumstance in which we might have actually recovered we would have undergone a loss!

The problem with existing methods of verifying circulation is that they are cumbersome difficult, and sometimes even dangerous. Even the best of these existing procedures, radionucleide scintigraphy, requires equipment not normally available in the same ward as HLR's, and while on an HLR we are not easy to move (not to mention the delay in getting us to the location of the equipment in the first place). Doctors may refuse to perform this procedure; particular hospitals may lack the necessary equipment and therefore be unable to perform it.

A very interesting paper in ARCHIVES OF NEUROLOGY (39 (1982) 136) by E.W. Kreutzer et al presents us with a much improved test for whether or not HLR treatment has restored circulation to the brain, in particular a test which greatly improves the possibilities for practical measurement.

The procedure is simple; they use a Doppler velocity meter to measure velocity of blood flow in the common carotid artery. They record their results on a simple strip chart recorder, and then with the aid of a desk calculator and a ruler they can make their diagnosis. Their procedure turned out to be 96% accurate in distinguishing patients for which brain circulation had not been restored from comatose patients, normals, and patients whose carotid arteries were narrowed or blocked. They had no false-negative diagnoses (brain-dead patients declared not to be brain dead) but did have one false-positive, a comatose patient who became clearly brain dead 24 hours after their measurements. The procedure in fact did have some ability to predict future developments with the patients studied. Their total test group consisted of 60 patients, of whom 8 were known to be brain dead by other tests, and another 8 were comatose.

At present, due to the large number of suspension patients arriving already deanimated and clearly "dead" (whatever that means), we lack as much experience as we would like in dealing with the problems of freezing someone whose suspension is already arranged in advance. However it appears that placement on an HLR is a significant risk; it may even prove advisable to acquire the necessary equipment and the ability to use it so as to strengthen our hand in any arguments with recalcitrant physicians.

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A central theme throughout much of Dick's writings is the two-part question of what does it mean to be human and what do we do to stay human. It is so unfortunate that this fine movie will be met by such mediocre crowds, for if the makers of this android film want for an electric audience they will find it only in our world of immortalists -- or in their dreams.

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EXPERIMENTAL STRATEGIES IN LIFE EXTENSION RESEARCH

Paul Segall, Ph.D.

Director of Biological Research, Trans Time, Inc.

Visiting Research Scientist, University of California at Berkeley

Rapid evolution in the fields of Gerontology, Suspended Animation, and Cloning is essential if most of us are to benefit from today's life extension efforts. I have spent much of the last twenty-two years developing strategies to deal with aging and the problems of suspended animation. I would like to summarize some of our latest finds, their implications, and a few thoughts about how we may most benefit from them.

The history of gerontology suggests that only by severely restricting the diet of the juvenile rat or mouse has a very large (up to 70%) extension of the maximum lifespan of a mammal been achieved. In a variant of this technique first employed by Monsanto Chemical, immature chickens and mice were fed diets extremely deficient in the amino acid tryptophan. The result was a substantial retardation of aging. These findings originate from a mysterious set of non-published experiments performed more than twenty years ago by Monsanto scientists under the supervision of Dr. Richard S. Gordon, Director of Research for Monsanto's St. Louis laboratories. Their studies revealed that when immature chickens and mice were fed on tryptophan deficient diets, the aging process could be substantially delayed. The tryptophan deficient diets are more convenient

to administer than the calorie restricted diets (one needs only to re-stock each cage of animals periodically with the deficient diet, rather than to weight a specific amount of diet each day for each animal caged separately, as in the classical caloric restriction studies). Their use also has a distinct theoretical advantage, in that radioactive tryptophan can be introduced into the body of the deficient animal and carefully followed along a few well documented pathways, in order to gather information about the underlying mechanism of this effect.

For these and other reasons, I have been actively involved in studies designed to reveal how the low tryptophan diet modifies aging. My experiments initially began when, as a graduate student at New York University during the fall of 1967, I was invited to work at the Medical College of the University of Pittsburgh. Although it was initially agreed that I would write my doctoral dissertation on the tryptophan deprivation phenomena, my professors felt the project was too involved, too complicated, and too expensive to be done competently on a small budget, and therefore was unacceptable. However, during the few months I was there, working at nights and on Sundays, I managed to develop a tryptophan deficient diet which would dramatically slow the growth of rats

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without killing them. This was a necessary first step, as Monsanto refused to discuss any of the work they did on mice (although they did release information on the chicken studies). I soon returned to New York determined to further explore the effects of tryptophan deprivation and found that the only way this could be done was to do research in my own laboratory. So, along with the help of some friends (including my partner in our present work, engineer and biophysicist Harold Waitz), I created a garage laboratory in a small house which I had purchased in Lindhurst, New York. Here I began studying the effects of the low tryptophan diet on mice. I was also able to initiate, along with Harry, a study of the Audrey Smith approach to suspended animation in the hamster.

Unfortunately, the small salary I was getting as a college lecturer did not match the cost of paying a mortgage, supporting a laboratory, paying off student loans, and surviving, and soon I began accumulating debts and became unable to meet my bills. Nevertheless, it was still possible to study the effects of the diet, which was constantly being improved, for six months. More importantly, I convinced myself that the low tryptophan diet could reversibly arrest the process of maturation and aging in rodents. It is significant here that the first financial assistance that I received for this project was a \$50 grant from the Cryonics Society of New York (CSNY) which, at that time, was directed by Curt Henderson and Saul Kent. Ultimately the project grew from its meager beginning to a five year, \$226,000 study at the University of California at Berkeley and sponsored by the National Institute On Aging. More than 20 separate reports of these experiments appeared at various scientific meetings and symposia, or on the pages of journals and biomedical texts. Furthermore, the experimental results were carried to tens of millions of people around the world who viewed one or more of the many local, national, and international television shows which featured the results of these studies. Prior to our studies, gerontologists showed only a limited interest in the effects of severe nutritional restriction on aging. I believe that these low tryptophan experiments helped to stimulate the more recent nutritional restriction and aging studies in the laboratories of such eminent researchers as Dr. Roy Walford of UCLA, Dr. Ed Masoro of the University of Texas, Dr. David Harrison of Bar Harbor, Maine, and Dr. Robert Good of

Sloan-Kettering.

The \$50 grant from CSNY allowed me to buy cages which I needed to start the experiment. It also told me that I was not alone in attempting to do what the University of Pittsburgh (and earlier the National Institute of Health, which had denied me a fellowship to do this same work at the Brookhaven National Laboratory under the direction of the well known gerontologist Dr. Edgar A. Tonna) was unwilling to try.

By 1971 I realized that if I was to do this experiment right, and

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if I was to get my doctorate, I would have to find a center that had a specific program in gerontology. Such a program existed at U.C. Berkeley under the direction of Dr. P. S. Timirias, then Professor and now also Chairperson of the Department of Physiology-Anatomy. Dr. Timirias agreed to sponsor the project as part of my doctoral studies. During the last ten years we have been able to learning many interesting things about delayed aging. I mention all these details so that our readers, many of whom are unfamiliar with the day to day problems of doing research in academically "unpopular" subject such as gerontology was -- but no longer is -- may understand some of the problems facing the researcher.

Unfortunately, although support is growing for investigative gerontology, there is still little support in this country for empirical interventive gerontology -- studies aimed at developing "geroprotective" drugs and therapies designed to increase lifespan and delay and reverse senescence. And there is even less support available in the areas of whole mammal reversible solid state suspended animation.

The tryptophan deficiency studies have produced a number of interesting results. We have found that if the diet is started early in life, we can dramatically arrest reproductive aging, so that rats which normally cease to reproduce at 15 months of age can have offspring at 34 months, an age at which more than ninety percent of the control animals in the present study have died of aging and age-related diseases. We have also established that the low tryptophan diets, when fed early in life, can increase lifespan. We have perfected a diet and have been able to examine some results of raising and lowering tryptophan content within its confines. Exactly what kind of life extension we can achieve is still under analysis, but the work is ongoing. We expect to be able to identify some of the characteristics which distinguish the long-lived animals without our study from the short-lived. We have had a chance to see what aging and age-retarded animals look like, and to make hundreds of slides using tissues taken from these animals. Along with Dr. Judie Walton, we have also been able to obtain tissue samples from these animals for electron microscopy.

Most significantly, we have already had a chance to observe the characteristics of some animals whose aging process has been retarded extensively and so compare them to those whom the diet has not affected as much (each animal is affected somewhat differently by the same diet). We have learned, for instance, that those animals which have a history of convulsions during our study, grow more slowly than average, do not show tumors, and have coats which look good are those which will reproduce at 30 months and beyond. We have found that if the diet is started at 3 months (after puberty) instead of 3 weeks of age (before puberty) the degree of retardation of reproductive aging is greatly

diminished. We therefore think now that some critical events involving alterations such as neuronal loss and/or even some types of nerve cell maturation with an accompanying loss of plasticity may occur in specific areas of the rat brain between 3 weeks and 3 months of age which set the stage for aging. We think that the low tryptophan diet as well as some other kinds of restricted diets may delay this phenomenon, and therefore postpone aging. With additional funding, we may be able to introduce radioactive tryptophan into animals placed on the diet at 3 weeks and at 3 months of age and find out if there are any important differences between these two groups as to where, why, and how their brains react to this tracer. Then we may be a lot closer to understanding what exactly causes aging, and therefore how specifically to deal with it. Unfortunately, we have no immediate funding prospects for these experiments.

On this note I would like to turn to cryonics. As problematic as life is for a research gerontologist, life as a research cryonicist is many times more difficult. Many establishment scientists have no understanding of, and will even show open contempt for those of us who dare to delve into such dark subjects. There is absolutely no hope of currently getting a government grant to freeze and thaw whole mammals (I might mention here that it took about 5 years and 4 separate submissions to obtain the previously mentioned gerontology grant and this was with a principal investigator who was a widely published, world renowned professor and chairperson at one of our country's most prestigious scientific institutions.)

In fact, most cryonics researchers use pseudonyms or just keep quiet about their interests for fear of professional retribution. Others simply work outside the pale of established science in their own laboratories, and understandably do not bother with the academic flak. I am one of the very few scientific researchers within the academic community who can openly discuss his or her interest and research in cryonics. Therefore, in order to pursue research in this area, I was forced to: (1) group up with friends and buy a house, in order to create a suitable and convenient work space; (2) raise money independently and initiate a research project in cryonics; (3) work long hours with no compensation and make enough progress so that money could be raised to go a little further.

Recently, thanks to several generous and courageous donors and the financial, moral, and material support of BACS, Trans Time, and Cryovita Laboratories, we were able to reversibly place a hamster in a state of cardiac arrest at the ice point, remove its blood and replace the blood with a 6% Dextran 40 solution in Ringer's Lactate balanced to pH 8.4. This was followed first by the administration of a 50\50 Ringer's-Dextran-whole blood solution, and then by whole blood. When we brought the animal's body temperature up to 18°C, it began breathing on its own.

Unfortunately, the animal hemorrhaged when the carotid cannula was accidentally dislodged. The hamster stopped breathing and died somewhat later. From examining the EKG we are convinced that the animal had had a reasonable chance of total revival had the accident not occurred.

These results allow us to feel confident that our experimental approach is at least to some degree correct. The benefits of this approach can be

extensive. A technique which allows us to recover small animals from asanguineous perfusion at the ice point will allow us to examine several kinds of blood substitutes and perfusion techniques. We can search for those which will maximize survival at the ice point. Such kinds of perfusates may allow for "long term hibernation" in cases of medical distress, extensive surgery, or even for special purposes such as long-term human space travel or the transport of livestock to extraterrestrial colonies. Preliminary experiments of these kinds have been done with dogs, but dogs are very expensive to work with -- one weekend of dog perfusion experiments at Trans Time cost \$3000 and much more in donated labor. Hamsters can be obtained and raised very cheaply, and use hundreds of times lower amounts of expensive chemicals and solutions in each perfusion. Space requirements are much more modest as well. Experiments can be done on a small table, and 50 animals can be kept in easy cleaned cages on an average sized book shelf. Hamsters can be quickly heated and cooled, and since they are hibernators, they can stand relatively longer periods of longer temperatures than dogs. Also, since we have studied them in respect to deep hypothermia for many years, we know how to induce suspended animation and how to revive them from these states much more expertly than with other animals. As they are very resistant to infection, sterile technique is not essential during surgery. This aves enormous amounts of money, effort, and time.

There is an even more important harvest to be expected from the hamster perfusion model. This model will allow us to being to accumulate whole animal toxicity data with regard to various cryoprotective chemicals. We can at last begin to evaluate the toxicity of such agents as DMSO, glycerol, propylene glycol, dextran, HES, PVP, and many others. We can begin to develop systems of delivering increasing concentrations of cryoprotective agents as temperature is allowed to drop. We can explore whole animal applications of the gaseous perfusion techniques pioneered by Dr. Frank Guttman on the dog kidney. We can also experiment with techniques aimed at producing optimum ways of extracting cryoprotective agents from whole animals, possibly a very significant aspect of freeze-thaw damage. We can perhaps find asanguineous perfusates with cryoprotectant additives that will allow survival to temperatures below the ice-point but not in the cryogenic range.

There is evidence that by using glycerol, and other additives, it

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is possible to preserve tissues for periods of months and even years. Possibly, techniques will emerge that will allow for the suspension of individuals for months or even years at a time employing short-term intermittent revival every several weeks or months, followed by re-suspension. (Recent evidence has surfaced that some frogs over-winter in this way.)

I think the above examples suffice to make the point. We have reached a milestone in cryonics research. The difficult microsurgery necessary to cannulate a hamster carotid artery has been mastered to some degree. Basic elements, such as cannula design and implantation have progressed substantially. Asanguineous perfusates that permit the survival and functioning of the cardiovascular system and at least part of the nervous system (illustrated by the hamsters ability to breathe following warming and perfusion) have been developed. It now remains to improve our technique to the point of allowing full revival and long term survival, to perfect our approach so that extensive instrumentation and data acquisition

and analysis are possible, and to set up the experimental system in such a way as to make it reliable, convenient and easy to work with. In order to accomplish this, I would like to appeal to the cryonics community to help raise funds to continue this program. The following research proposal has been submitted to the Bay Area Cryonics Society:

Reversible Suspended Animation with Asanguineous Perfusion in the Syrian Hamster

- I. Development of fully vented and heated facility for rodents. \$1,000.00
- II. Animal positioning table allowing full instrumentation and accident-proof cannulation. \$500.00
- III. Physiological instrumentation of the experimental animal including:
 - EKG
 - Venous pressure
 - Arterial pressure
 - EEG
 - Respiration
 - Temperatureand permitting venous and arterial effluent analysis of:
 - pH
 - Oxygen
 - Carbon dioxide
 - Specific gravity
 - Chemical composition \$2,000.00

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- IV. Exploration of small animal anaesthetic techniques which allow reversible induction of deep hypothermia without severe cardiac and respiratory depression. Initial development to be in the hamster, then in the rat. \$1,500.00
- V. Hamster suspended animation and asanguineous perfusion experimentation leading to preparation of publishable manuscript, and submission of manuscript to scientific journal. \$3,000.00
- VI. Preparation and delivery of presentation at scientific conference (not including travel expenses). \$1,000.00
- VII. Preparation of a videotape describing reversible suspended animation in the hamster following asanguineous perfusion. \$1,000.00

There are a few points of explanation which I would like to offer concerning the above budget. During the last 20 years during which I have been engaged in life extension research, I have become allergic to the rodents on which I experiment. When I am in a room with a large number of rats, mice, or hamsters, I become uncomfortable and experience many of the difficulties encountered by mild hay fever victims and other allergic individuals. It is therefore necessary for me to keep animals in quarters separate from my work space. There is also the factor of climate control

which is important if the animals are to remain healthy. Therefore I plan to erect a small prefabricated shed in my backyard in order to house them.

I would like to close this article with another plea for help within the cryonics community. In a recent grant application to NASA, I requested funding for a similar set of experiments. The experiments were to be conducted under the auspices of the University of California with the supervision of one of its most accomplished and respected Professors. In a phone call by the chairperson of the Awards Committee, I was told that although my proposal was well designed and interesting, it was not a NASA priority that suspended animation research be funded. He advised that I seek funding from the Cryobiology Society. Of course, we all know where we stand with this august group! As I previously have stated, there is little likelihood of any research in cryonics being funded by the United States Government or any of its agencies. This leaves the ball in our court. Although I currently hold the position of Visiting Research Scientist at the University of California at Berkeley, I am not committed to any regular teaching or research schedule. My gerontology research studies do not at this time demand long hours daily. However I

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may not be able to keep this independent situation viable indefinitely. I feel it is urgent that a complete cryonics research program, based on the above described principles be funded and begun at once. Anyone interested in helping should contact me at the following address:

Dr. Paul Segall
Department of Physiology-Anatomy
University of California at Berkeley
Berkeley, California 94720
(415) 642-8235 or 642-4002

UPDATE ON REMOTE STANDBY INSURANCE

Art Quaife

In the February 1982 issue of CRYONICS, I reported on the availability of Remote Standby Insurance, covering the cost of flying a suspension team to a remote location if the insured Suspension Member is in imminent danger of death. A number of readers returned the accompanying questionnaire for forwarding to Crawley Warren, requesting this insurance.

In further correspondence with Crawley Warren to clear up remaining fine points, it has emerged that they have a major misunderstanding concerning the purpose of the insurance. A letter from them stated their understanding that the insurance would only pay off in the event of the death of the insured. This is not what we want or what we specified to them -- the insurance must pay off even in the hoped-for even that the insured survives!

In March I sent a further letter to Crawley Warren pointing out this discrepancy between what we had requested and what they were now quoting, but have not yet received a reply. I have just sent them a follow-up letter. In the meantime, Dr. Thomas Donaldson has reapproached Lloyds of London, and started correspondence with a different Lloyds broker to obtain the same insurance.

Dr. Donaldson has invested an incredible amount of time and energy in pursuing the possibility of remote standby insurance. It is a shame that it is so difficult to get it specified just as we want it, but then the ultimate cryonics purposes to which we will put it are somewhat unusual. I will retain all of the questionnaires sent to me until either (A) Crawley Warren sends us a draft Certificate of Insurance that meets the requirements we spelled out to them, or (B) Dr. Donaldson obtains an agreement from another Lloyd's broker to do so.