

CRYONICS

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EDITORIAL MATTERS

Many of you noticed--and told us so--that Michael Darwin's answering letter to Laurie Mann was left out of the November issue. We apologize for the editing error and have included Michael's letter in this issue, on page 6. This is one of the hazards of having one co-editor (Michael) in California and the other (Stephen) in Indianapolis.

It has also been noted that current IABS officers have not been listed. They are: Michael Darwin (Federowicz), President; Stephen Bridge, Vice-President; and Allen Lopp, Secretary-Treasurer.

CONSTRUCTION AT CRYOVITA NEARING COMPLETION

The first of three phases of construction at Cryovita Laboratories is nearing completion. The operating room has largely been finished, with only some ceiling work, painting and molding left to be put in place. The O.R. is a spacious 16'x21' and is capped by a loft already loaded with thousands of pounds of stored equipment and supplies. The loft, which is supported by standard second story construction, adds over 300 square feet of space to currently limited resources. A vivarium and an electron microscope room are slated for completion sometime next year.

DEPRESSURIZED AND DEPRESSED

The final chapter in the high pressure chamber saga appears to have been written. The chamber is an exotic super-pressure unit capable of subjecting a dog heart or kidney to 20,000 psi--a pressure high enough to allow vitrification in the absence of any ice formation under the right circumstances. The chamber was damaged during shipment to Los Angeles from Atlanta, Georgia. It is now apparent that the trucking company is unwilling to settle for more than a few hundred dollars, while the damages exceed \$15,000! What is worse, Cryovita incurred a \$1,500 bill just in having the chamber evaluated for repair by its original manufacturer! Fortunately, Steve Ruddel of the Life Extension Foundation in South Florida was kind enough to come to the rescue and pay for shipping and evaluation charges. We are deeply grateful to Steve for this tremendous show of generosity. We hope that someday we will be able to raise enough money to get the chamber properly overhauled so that it can once again serve its intended purpose. In the meantime, all 600 pounds of it will be used as a paperweight to maintain order on Mike Darwin's desktop.

THE SOCIETY FOR CRYOBIOLOGY -- A CLARIFICATION

In the November, 1981 issue of The Immortalist, Dr. E. Wesley Walton stated that "The Board of Governors of the Society for Cryobiology on September 4, 1981 issued a recommendation that "membership be denied to organizations or individuals actively engaged in this practice," i.e., cryonics. Several other cryonicists, apparently including Dr. Thomas Donaldson ("On Cooperating with Cryobiologists" in the November, 1981 issue of CRYONICS), also seem to be under this mistaken impression. We wish to make it clear that this was only a policy draft, submitted for consideration to the Society's Board. We have information that the Board is not likely to pass this recommendation, since several Board Members believe it to be indefensible or unnecessary. Even if the Board were to approve the measure, any limitation of the Society's membership must be voted on by the Society as a whole, which is also unlikely to pass such a strong denial of the scientist's freedom to pursue knowledge.

ECONOMICS AND NEUROPRESERVATION

The November, 1981 issue of CRYONICS contained a case study of suspension via neuropreservation (suspending only the patient's head or brain). There are several logistic and economic advantages to neuropreservation over whole-body suspension, including less storage expense, ease of handling--including rapid movement if necessary, and the use of standard-line containers without the long lead time required for order and manufacture of the special-order whole-body units. Unfortunately, due to the lack of available high-efficiency storage units, most of the neuro-patients currently in storage are being maintained in the bottom of large MVE dual-patient whole-body dewars. This means that in order to access the neuro-patients, the whole-body donors usually have to be removed--a major and costly undertaking fraught with technical difficulties and risks. In addition, neuro-storage in these almost impossible-to-move units prevents the neuro-patients from being quickly moved in case of legal, natural or other emergencies. One of the major advantages of neuropreservation is thus lost.

This problem now appears to have been solved, at least for those in California. Recently, the relative of a neuropatient now in suspension purchased for use by Trans Time a Minnesota Valley Engineering A-2542 long-term storage dewar. The container is the first truly workable human multiple storage unit, with a capacity of approximately 14 neuro-patients when full.

The dewar features incredibly low boil-off rates, in the range of 3.2 to 3.8 liters per day, as contrasted with 8 liters per day for the current dual-patient whole-body tanks, and 2.5 liters per day for the Linde LR-40 single-patient neuropreservation dewar. The A-2542 also has a nice safety feature in the form of a 120 day holding time (the length of time the dewar will still contain LN₂ after a complete fill.) The dewar also has good relative portability with an empty weight of 350 pounds, an outside diameter of 42 inches, and a

height of 41 inches. Because the dewar is wider than it is high, it is extremely resistant to tipping over in the event of an earthquake or mishandling--a feature which whole-body dewars, unhappily, do not have. The really exciting thing about the A-2542 is what it does to storage COSTS. With 14 patients in storage the yearly nitrogen cost (at 35¢ per liter) per patient is only \$36.50! If the \$5,000 cost of the container (including shipping and set-up charges) is amortized over 10 years (the expected container life), this means that total yearly costs for container and nitrogen per patient would be about \$70.00. Of course these figures do not take into account charges for items such as labor, storage space, and other overhead; but they do reflect a basic cost. The same costs on whole-body storage would be \$511 per patient per year in LN₂ costs and approximately \$500 per year per patient in dewar expense, for a total of over \$1,000 per patient per year. Even this amount does not take into account the higher secondary costs of whole-body storage: its comparatively high labor intensiveness, the requirements for facilities with higher ceilings, and the need for very costly cranes and special handling equipment to move both patients and the dewars themselves around.

A WESTERN TRAGEDY

by Michael Darwin

Not since I was a child have I found the notion of good guys in white hats and bad guys in black hats very believable. I realized fairly early in life that good is rarely pure white and evil almost never unadulterated darkness. Both are usually a mix of good intentions, limited insight, and honest difference of opinion. It was thus something of a surprise when I found myself at odds with a man who exhibited an absolute delight in torturing two innocent people and possibly costing a third his life. It is not possible for me to communicate the subtle shades of phrasing or tones of voice which convinced me this man enjoyed what he was doing, but I remain convinced that he did.

On the 18th of October, 1981, I received a phone call from a young man and woman who found themselves in an ugly predicament. Several months before, they had written to Bay Area Cryonics Society for information on cryonics. Before they could complete their plans, the young man's father suffered a cerebral hemorrhage and was lying in an Arizona hospital on a respirator, in a coma. What could be done? Such cases are never easy and most frequently, for one practical reason or another, nothing can be done. But this case was to take on a new twist and frustration which we had not previously encountered.

After a number of tentative calls, the young couple decided they wished to proceed. We were asked to speak to the neurologist in charge of the case to get more medical information about the father and to give instructions concerning any preparations that would be necessary. This was urgent, since the neurologist had informed the son and his wife that the patient was "brain dead" and should be disconnected from the respirator as soon as possible.

A call was placed to the neurologist's answering service. He was paged and we were told to expect a call shortly. Several hours went by and still we had not heard from the neurologist. Another call

was placed. Was the doctor in surgery? we asked. Had he received our message. Yes, he had received our message. After several similar calls, the neurologist, apparently tiring of our inquiries, returned our call. To say that he was hostile is less than accurate. Vituperative, bitter, and spiteful are more to the point. After a brief show of irritation he informed us that the patient was DEAD, absolutely and completely BRAIN DEAD, and that he could not see the point of cryonics or in wasting his time talking to us about it. Finally, after it was pointed out that it was the next of kins' wishes that he speak to us, he calmed down enough to provide some useful and relevant information. Yes, the patient had suffered a hemorrhage, an intracerebral bleed in fact; yes, he did have a flat EEG; and yes, his brain had been in essentially a no-flow condition for at least 48 hours. After a more detailed picture of the patient's medical history was given, one final question was asked of the doctor: had the patient been normothermic during the period of no-flow? The answer was yes. The physician was then told that we agreed that it was unlikely that any cortical ultrastructure was left, and that it would probably be pointless to proceed. But, we pointed out that a final decision on the matter must be made by the next of kin and that sometimes, even in such unfavorable circumstances, they decide to proceed.

We then contacted the son and his wife, explained the situation to them, and urged them to talk with the neurologist about the probable state of the patient's brain. This they did. Nevertheless, they were determined to proceed with the suspension. Both of them understood quite well the probable extent of the injury. On the other hand, they felt there was at least an outside chance that things might not be as bad as they seemed. We agreed on a middle ground of proceeding with the suspension on a neuropreservation basis in the absence of perfusion, and we agreed on invasive sampling of the brain tissue via multiple cranial burr holes for evaluation by light and electron microscopy. If no ultrastructure were found, the suspension would be terminated shortly thereafter, and they would be spared the expense of a long-term trust fund.

With this set of plans in place, the order was given to remove the patient from the respirator and pack him in ice for shipment to Los Angeles. To our surprise and horror, the neurologist refused the order and stated that he intended to keep the patient on the respirator indefinitely, or at least until the patient's usual physician returned from a weekend trip on Monday! The young couple were puzzled and shocked. Had the neurologist been mistaken? Was there still some hope? No, quite the contrary. The neurologist informed them that not only wasn't he going to take the patient off of the respirator, he was going to turn the case over to the coroner and invite an autopsy. He felt that should neatly settle their nasty plans for having his patient frozen. There wasn't going to be any of that nonsense in HIS hospital. Furthermore, he said, the hospital would not cooperate to the slightest extent in packing the patient in ice or in expediting his release to the coroner. As an aside, despite the fact that the patient met all criteria for brain death, the physician refused to write a death certificate, thus preventing the relatives from appealing to any higher source.

The Catholic hospital where the neurologist worked naturally backed him up and refused requests that he be removed from the case. "The matter will wait until Monday morning. The family is not qualified to make a medical judgement."

By this time, the horror of the case was beginning to sink in. Here this man was, lying around at near body temperature (I had been granted a request to have him placed on a cooling blanket and his temperature reduced to 90°F) and, because of the obstinance and religious convictions of a physician, he was going to stay that way for possibly another 48 hours.

After consulting with the son, it was decided that the family still wanted to proceed and we agreed to wait until Monday morning while trying a number of maneuvers in the meantime. When Monday arrived, it was apparent that the attending physician was going to be little more cooperative than the neurologist. The patient would stay on the respirator pending a court order, and it would be at least 3-4 days until the matter was settled. Emotionally exhausted, deeply hurt, and filled with frustration, the son and his wife decided not to proceed. It was a decision which is completely understandable, and they are to be commended for the extraordinary effort they put forth.

The good guys and the bad guys are not hard to find in this story. Indeed, it is a cast of characters right out of a Grimm Brothers' fairy tale. Unfortunately, there is no happy ending. What there is, is a lesson for all of us. As has been said before, if you don't have prior arrangements, you don't stand much of a chance of being frozen. But even with prior arrangements, it seems unlikely that this case would have been handled very differently by this particular hospital. Just as important as arrangements may be to have at least your personal physician on your side. In this case, it was clear from the outset that the neurologist felt it was his duty and responsibility to make the decision for the next of kin. After all, he was in possession of all the relevant information. He knew that patient was dead. He knew he wasn't coming back.

Now, this man also knew that he had no legal or medical right to force his opinions or certainties on others. There are limits to a physician's authority and responsibility. The relatives of a patient employ him to restore health and to prevent death, if that is possible. If it is not possible, the physician's responsibility ends there. It does not extend to making decisions of a personal nature about the disposition of human remains, where public health is not involved. The physician of a dying patient does not somehow become the legal guardian of the patient's next of kin. It is his freedom and even responsibility to offer what he considers to be reasonable advice; but if the family disagrees, it is not his prerogative, either as a doctor or as a human being, to ram it down their throats.

All of us in California are deeply disturbed by this case. We are very, very angry that this unethical disregard for human feelings was allowed to occur. If the circumstances are a little different the next time, we will not give up this quietly. Those who would play god with human emotions should be aware that there is frequently the devil to pay.

MICHAEL DARWIN'S REPLY TO LAURIE MANN

(This letter was sent to Lan's Lantern, a science fiction fan magazine. We inadvertently left it out of last month's CRYONICS.)

Dear Lan,

I read with something of a chuckle the article by Laurie Mann entitled "How the Cryonics Movement Thawed Out." Granted, there wasn't anything intrinsically funny in what Ms. Mann had to say, but I just couldn't help being struck by the irony of her remark: "By 1973 it was generally acknowledged that the cryonics movement was dying." I find that a bit humorous because as I read that line I sat surrounded by upwards of a million dollars worth of equipment in a nice, modern industrial bay in Fullerton, California which is dedicated totally to human cryonic suspensions and suspended animation research.

Far from being dead, cryonics has probably never been in better health. We just recently purchased our own electron microscope and we have several vigorous research programs underway. There are ten people in storage in the Bay Area (one of whom is awaiting transfer to liquid nitrogen and is currently on dry ice), all of whom are being well cared for and properly maintained. Most importantly there are several vigorous organizations in California with upwards of 200 people signed up, with all arrangements made in advance to be placed in suspension at the time they deanimate.

Since Ms. Mann obviously took a lot of time to write her article and to research it, I am puzzled that she didn't have the presence of mind to spend 18¢ and write us. She would have found a frank discussion of many of the problems she raises in our literature and she would surely have realized that we are neither pie-in-the-sky dreamers or simply naive.

If Ms. Mann has not seen numerous articles about us in the popular press, she should not conclude that we do not exist. Indeed, what we may conclude from reading Ms. Mann's comments on lack of press coverage being equal to lack of legitimacy is that she is another of the many victims of the "if it isn't on TV it isn't real" syndrome. We can only hope that she doesn't suffer from the associated syndrome of "if it IS on TV it MUST be real." Ms. Mann should learn that things can exist outside the media, and that in the Institute's case we by and large consider such an existence desirable. This is particularly true in view of the warped and distorted coverage the media has given cryonics in the past.

No one is pretending that cryonics represents anything other than extreme risk of one's time and money. We understand, perhaps far better than our critics, that the chances for survival of anyone being frozen today are very, very small. We also understand that no progress is made without a beginning and that a position of optimism is preferable to a position of pessimism. We KNOW we are dying. We are not afraid of "worms or mold"--we are unwilling to DIE. Contrary to Ms. Mann there is nothing more wrong with being afraid to die than there is of being afraid of any other catastrophe from being blinded to being paralyzed. Death just like any other personal catastrophe reduces our freedom to do what we choose and to be what we choose to be. It just so happens that death is the ultimate reduction in freedom.

Cryonicists reject the notion that death is something to be accepted. We are very thankful that men like Semmelweis, Lister, Morton, and Pasteur had the good sense and moral courage to reject the notion that disease and agony were normal consequences of being alive, simply to be accepted preferably with a wan smile.

Finally, I must comment on Ms. Mann's quoting of Fred Pohl's arguments against cryonics. Fred Pohl wrote a wonderful novel about cryonics entitled The Age of The Pussyfoot. It was a very positive piece about a man who was taken from his own time, place, and roots by death and thrust into an almost incomprehensible future. The take-home message of the book was that he adjusted, he was flexible, and he MADE IT. It is a sad commentary on Ms. Mann's and Mr. Pohl's states of mind and courage that they do not feel they have the mettle to make it. My condolences. Someday Laurie Mann and Fred Pohl may realize that they are more than the sum total of the parts of their lives, more than the continuity of daily activity, more even than their relationships with loved ones and friends. People have not merely survived with the complete loss of these things (i.e., refugees from primitive cultures and concentration camp survivors who lost EVERYONE and EVERYTHING right before their eyes), they have even managed to prosper. In any event we plan to make the journey in the company of our loved ones and friends. In the meantime we are not about to play shuffleboard while the ship goes down.

Sincerely,

Mike Darwin, President

Institute for Advanced
Biological Studies, Inc.

STROKES AND BLOOD SUBSTITUTES

In 1966 Dr. Leland Clark and his colleagues reported on the ability of emulsified fluorocarbon preparations to act as blood substitutes. Clark was able to successfully replace over 90% of the blood of experimental animals with fluorocarbon microcells and still have the animal continue functioning normally, with long-term survival as a routine outcome. One problem with Clark's artificial blood cells is that they were fairly unstable in solution: Small particles of the emulsion tended to clump together to form larger ones, making it impossible for the synthetic "cells" to pass through the capillaries. A more serious problem was that the fluorocarbon material itself had no natural route of elimination and tended to be retained in the liver.

Recently, all of these problems have been solved by the Japanese firm Green Cross. Green Cross is currently marketing a fluorocarbon blood substitute in Japan by the name of Flusol-DA. Flusol is about 35% fluorocarbon particles with an average size of $0.1 \mu^2$. The total surface area for gas exchange per unit of volume is about 170 times that of blood. Also, gas exchange occurs about twice as fast as with hemoglobin. The compounds are eliminated from the body primarily through the lungs where they are dumped to the atmosphere as a vapor.

A very excellent paper on the use of Flusol-DA in a stroke model middle cerebral artery occlusion appeared in the Sept-Oct. issue of

STROKE (Vol 12, #5, 1981, p.558). In this paper a group of Canadian investigators evaluated Flusol as a treatment for focal cerebral ischemia. It was felt that because of Flusol's incredibly small particle size and great oxygen carrying capacity, it would be able to reach vessels which were nearly occluded from edema. The animals subjected to MCA occlusion were divided into three groups: a control group which received no treatment, an experimental group which received Flusol (15ml/kg), and a conventionally treated control group which received mannitol. The animals were then evaluated both behaviorally and by histological techniques following sacrifice at the end of the experiment.

The Flusol-treated animals exhibited strikingly better performance in both behavior and histology. In the Flusol-treated group, 3 animals had recovered sufficiently to stand and walk at 6 hours, whereas in the control and mannitol groups only one animal had recovered to the same degree. Histological examination of the animals' brains revealed that the Flusol-treated animals experienced 50% less ischemic damage than either set of controls.

These results are very exciting, and they suggest a possibly large role for Flusol in treating other ischemic conditions such as anoxic encephalopathy and ischemia following extended periods of cardiac arrest, both conditions which are known to produce diffuse cerebral edema with resultant poor perfusion.

SPINAL CORDS REGENERATED?

Despite a variety of approaches and numerous attempts, up to this time no workable technique for regenerating spinal cords has been demonstrated. A number of factors appear to be responsible for the failure of the mammalian spinal cord to regenerate following transection. The most commonly mentioned cause is the formation of a dense scar at the point of the trauma to the cord. This scar formation acts as a barrier to the regenerating axons which sprout at the break in the cord. Other suggested causes are poor tissue perfusion at the injury site, free radical reactions, and cavity formation.

Now, researchers at the Department of Anatomy, Texas A & M University, report on an experimental technique which they claim has resulted in both functional and sensory recovery in rats with completely transected spinal cords. (Undersea Biomedical Research, Vol 7, #4, 1980, p.305).

The animals were subjected to complete transection of the spinal cord at the 5th thoracic vertebra by passing a scalpel through the cord a total of 4 times, maintaining contact with the floor of the vertebral canal with the scalpel at all times. The animals were then divided into three groups of ten each. Group I received normal post-operative care; Group II received hyperbaric oxygen (HBO); and Group III received HBO and DMSO. DMSO has already been demonstrated by a number of investigators to be profoundly effective in reducing neurological injury from trauma and ischemia. The animals in Group III were treated with 12 g/kg of DMSO every 12 hours for 3 days and 1 g/kg DMSO every 12 hours for 7 more days. Both Group II and Group III animals were treated with hyperbaric oxygen at 2.8 atmospheres for 90 minutes every day for 40 to 50 consecutive days.

None of the animals in the control group demonstrated either sensory or weight-bearing recovery. The animals which were treated with hyperbaric oxygen alone showed some recovery of hindlimb movement, with three of the ten animals showing good enough recovery to assist in walking with their hind legs. In the HBO + DMSO group, 6 of the 10 animals recovered coordinated hindlimb movement and 2 of these were able to support their own weight in the sixth post-operative week. The investigators also reported that the animals that recovered sufficiently to walk also demonstrated some return of sensory function in the affected limbs and would squeal and bite at the investigator when their tails or hindlimbs were pinched. No animals in the control or HBO groups demonstrated any return of sensory function.

Histological studies of the cord transection site showed reduced scar formation and cavitation in both the HBO and the HBO + DMSO groups. Many more axons were seen to have sprouted across the break in the cord in the treated groups than in the untreated groups.

This research has obvious implications for cryonics. At this time there are four neuropreservation patients who have gambled that just this kind of advance would be made. We will anxiously await confirmation of this work by other investigators. We understand that additional research is underway at Texas A & M to both confirm and extend the results of this work. Readers wishing an excellent survey of current research on spinal cord trauma and regeneration should refer to "Spinal Cord Injury: Review of Basic and Applied Research" by J.C. de la Torre, MD, PhD. in Spine, Vol.6, #4, 1981, p. 315-335.

IMPORTANT NEW DMSO BOOK

Reviewed by Stephen Bridge

DMSO, The True Story of a Remarkable Pain-Killing Drug. By Barry Tarshis, from the exclusive files of Dr. Stanley Jacob and Robert Herschler. Morrow, 1981. \$10.95.

In the early 1960's, Herschler, a chemist for Crown-Zellerbach Corporation, and Jacob, a professor at the University of Oregon Medical School, discovered the unique and amazing medical qualities of dimethyl sulfoxide--DMSO. Until that time DMSO had been a common, mildly useful, by-product of wood pulp manufacturing processes. Today the chemical is the center of the most complicated and senseless bureaucratic tangle in the history of U.S. medicine. For over 15 years the U.S. Food and Drug Administration has refused to approve the use of DMSO, a drug with the most far-reaching medical possibilities of any chemical presently known. The FDA contends that DMSO has not been adequately studied and that the effectiveness and safety of the drug remain unproven.

Written for the layman, but with detailed use of scientific papers, this book presents the evidence for DMSO, effectively disproves all of the FDA's weak allegations, and generally shows the intolerable muddle in which the American drug industry now finds itself. Tarshis shows that the drug is in fact one of the most studied drugs in recent U.S. history. Effectiveness has been shown without doubt in a number of conditions, and it has fewer known side effects than any

major drug in current use--including aspirin. The FDA's old saw about DMSO causing eye damage in humans has been thoroughly disproven. Now you don't have to take Tarshis's word on all of this. Many physicians and researchers have allowed themselves to be quoted, and the book contains an excellent bibliography of 80 research papers and books. It is a quality list of sources, not padded with articles from popular magazines.

It would require a full book to fully detail the actions and uses of DMSO, and I will not try to do so here. Most of our readers will already know about the successful uses of DMSO for treating injuries, arthritis, and burns. Less well-known is that it is the only effective treatment for the painful skin problems of persons suffering from scleroderma.

Other uses vary from the treatment of cold sores to shingles to diseases of the retina. Of particular interest to cryonicists is the chapter "To Save a Life," dealing with the uses of DMSO to protect the brain and spine after injury. Clinical results on human and animal tests have shown DMSO to be better than mannitol, steroids, or barbiturates in reducing intracranial pressure and ischemic injury. In addition, early tests have shown positive results in improving the conditions and capabilities of some previously paralyzed individuals. As reported in the preceding article in this issue, spinal cord regeneration may become a reality in the near future, partially through the use of DMSO. Finally, DMSO's ability to penetrate the blood-brain barrier and to carry other chemicals with it appears to be a key in dramatically increasing the IQ's of children with Down's Syndrome (mongolism). DMSO is able to carry into the brain the neurotransmitters (chemicals that activate nerve function) that Down's Syndrome children lack.

Readers would be well advised to purchase this book, read it, and then send it to their local U.S. Representative or Senator, along with a letter asking them to force the FDA to release DMSO from its bureaucratic prison. Your life and health may well depend on it someday, as may your future reanimation possibilities.

BRIEF UPDATE: LEGISLATION TO CHANGE CALIFORNIA VERSION OF UAGA

Many thanks to all of you who were concerned enough to write a letter to California State Senator John Holmdahl, requesting revisions of the California Uniform Anatomical Gift Act (UAGA), to include cryonic suspension under its provisions. I just spoke with Senator Holmdahl's aide George Stanos, who stated twice that they were receiving a lot of mail supporting this proposed legislation, from across the United States, and even from Australia and England. (Isn't it impressive that our small ranks can generate "a lot of mail" to a legislator?) Copies I have received of these letters have all been very well done, as one would expect from persons with intelligence enough to want to live forever.

Mr. Stanos also stated that unexpected developments, such as the Legislature being called into a one week special session, had changed their time schedule. When Senator Holmdahl's office does get ready to consider what legislation they will introduce in 1982, Mr. Stanos assured me that our proposed change to the UAGA would be one of the top two or three on their list for consideration. I will keep in touch with the Senator's office, and report on further progress.

TREATMENTS FOR HEART ARRHYTHMIAS: A PROBLEM OF INTEREST TO CRYONICISTS

Few outsiders, but many cryonicists, know that death usually happens with a good deal of warning. If there has been warning, of course, we or others on our behalf can easily make all the necessary preparations for our suspension. We can get agreement from hospital authorities and move to another area where conditions are more favorable if there arise any problems about our suspension in the locale at which our problem first develops. However to most noncryonicists it comes as a surprise, and one which they find difficult to grasp emotionally, that their death is unlikely to be sudden. Even for people of age less than 45, only 20% of deaths turn out to be unexpected (it is true that younger people are less likely to die, but heart or kidney disease or cancer take a high toll among those who do). When we examine the figures on rates of death from different conditions, we find a fact which contradicts prevailing belief even more forcefully. Among the total of all deaths, fully 78% of unexpected deaths were from circulatory conditions, and only 12% were from accidents. (As a matter of interest, only HALF the accidental deaths count as unexpected). All these figures come from the book LIFE BEFORE DEATH, by A Cartwright et al, which even now repays very close study by cryonicists and cryonics societies which may wish to plan out their services.

If fully 78% of all unexpected deaths come from circulatory conditions it follows that we ought to be able to make tremendous advances in the logistics of our suspensions if only we find ways to predict or to prevent these unexpected deaths. The matter has an importance out of proportion to the actual increase of lifespan these measures would obtain: if for instance we could turn all of these unexpected deaths into expected deaths with a warning time of 6 months, it would mean that suspension firms could afford far less preparations in advance, patients living far from a suspension center would have much security, and even the costs to others who already die expectedly will go down due to the lesser expense of readiness.

Of course the problem of making all deaths expected is too hard. However for the major proportion of these deaths, deaths from circulatory conditions, we have excellent prospects of seeing a reduction in the near future. Even though the public at large is oblivious to this problem, doctors do work on it and more recently a good deal of progress has happened. In this article I shall survey some of the advances which have been made.

When we examine this problem, of course, it breaks apart into a large number of different subproblems. The causes of unexpected deaths are manifold; even psychology enters into the question, because deaths which a bystander might reasonably expect might of course be a source of self-delusion on the part of the patient and his or her relatives. I won't discuss these other problems in detail, but concentrate my attention on one very major cause of heart disease deaths, sudden heart stoppage, or ventricular fibrillation. This condition is one in which the rhythmic motion of the ventricles of the heart is disturbed so that it ceases to pump blood; it appears to be the root cause of most if not all sudden heart failure. If doctors or paramedics can reach such a patient within 3 minutes of its occurrence, of course, they can revive the patient, but otherwise the patient will be declared dead and a suspension must begin on very short notice.

Right now, there are a large number of drugs under study for this problem. A recent review (Zipes, DP; NEW ENGL JOUR MED 304(8) (1981) 475) lists 5 different drugs particularly effective against ventricular arrhythmias. Amiodarone is one of these drugs, which Zipes mentions especially as being highly successful. It has a high therapeutic index (the therapeutic index is the ratio of the dose of a drug which causes toxic side effects over the dose of the drug needed to produce the therapeutic effect) and patients tolerate it relatively well. It causes only a small incidence of nausea or vomiting. On the other hand, it does have some side effects which might be seen as minor, but distressing to a patient. It may sometimes cause a slate-grey or blue color to the skin and a high rate of deposition of lipofuscin in the cornea of the eye. On the other hand, the drug seems very effective in suppressing ventricular arrhythmias: one doctor reported total cessation and control in 119 out of 145 patients, or 82 percent. The drug has been used clinically in Europe and South America for some year (Rosenbaum, MB et al AM J CARDIOL 38(1976) 934). A second drug which has shown quite considerable promise is encainide. Encainide first appeared in 1970, but was rejected for use in humans because it significantly slowed heart rhythm. When doctors overcame their inhibitions to testing it on humans, they found that it showed considerable effectiveness against ventricular arrhythmias and no measurable harmful effects due to the slower heart rhythm. DM Roden et al (NEW ENGL JOUR MED 302(1980) 877) who seem to have first realised its usefulness on human patients, report that on a test of encainide 10 patients out of 11 showed total suppression of their ventricular arrhythmias on a wide range of doses. They also showed that the slower heart rhythm was not harmful, both by prolonged monitoring with the electrocardiogram and by exercise testing. Like amiodarone, encainide has a high therapeutic ratio and appears to cause few side effects, even fewer than amiodarone in fact.

It appears from the work in this field that we need a wide variety of drugs for ventricular arrhythmias, since not all patients respond to them in the same way. Older drugs, such as practolol, procainamide, or propranolol, still have a use despite the fact that they tend to be less effective and show more side effects. As readers might guess, neither of the two drugs amiodarone and encainide is without problems, but both represent considerable advances over what has gone before.

A second major area of advance consists of the possibility of a miniaturized automatic and surgically implantable defibrillator. When a patient's heart stops and doctors can reach him or her in time, they use such a device to restart the heart. The main difference here is that an implantable defibrillator will be small enough to implant in the chest and smart enough to know when to act even without the doctor's advice. A recent paper in NEW ENGLAND JOUR MED 7 August 1980, 322-324) by M. Mirowski et al reports the development of such a device and trials of it on 3 patients all of whom had previously failed to respond to any drug treatment of their condition. It successfully prevented these patients from going into ventricular fibrillation with little discomfort to the patient, and while the patients themselves were even walking about as if they were well. In fact, in one patient, a 16 year old boy, the device prevented his heart from stopping no less than 5 separate times. The authors feel that their device should only be used on patients who fail to respond to any less drastic treatments; the likelihood, of course, is that quite soon such devices will become as routine as the ordinary pacemakers and no longer count as drastic treatments. For cryonicists this is very hopeful.

LEVODOPA AND AGING

As most cryonicists probably know, in 1977 Cotzias and others published an article in SCIENCE (196 (1977) 549) describing how longterm feeding with L-dopa will increase the lifespans of rats receiving it by 50%. Cryonicists will also recognize, of course, that a 50% increase is quite large. Somewhat later, Marshall and Berriosa published a second article (SCIENCE 206 (1979) 477) describing experiments in which the usual movement defects of aged rats (similar to the slow movement and uncoordination of the old people) would disappear after administration of L-dopa in their food. To anyone interested in aging these observations are very cogent and deserve close attention, confirmation, and rapid clinical application. In fact, some longevists have commenced to take L-dopa (cf. Mann, SECRETS OF LIFE EXTENSION), although to my knowledge not in the quantities likely needed for aging.

A recent article in LIFE SCIENCES (28(1981) 2945) has just appeared confirming these earlier results and presenting further information too. Papavasiliou, Miller, and others report that in yet again another experiment, L-dopa would produce a 50% increase in lifespans, and confirm that it will abolish the slow movement characteristic of old rats. They fed their animals a dose of 40 mg of L-dopa gram of lab chow (which is a high dose of 4% of body weight). The animals received doses of about 50 mg per day for the first 3 weeks, rising to 150 mg/day after 8 weeks. Besides verifying the previous observations about longevity of treated rats and the fact that they showed the same levels of activity and coordination when old as did young rats, Papavasiliou et al also measured the levels of various neurotransmitter substances and/or enzymes (such as dopamine or MAO) in their brain as they aged. Treated animals show distinctive changes different from those of controls; for instance, the level of dopamine in brains of treated animals increased by 50% over that of controls. I will not discuss these changes in detail, except to say that they seem to confirm theories that dopamine and MAO levels play a critical role in at least some of the derangements of normal aging.

Confirmation of the effect of L-dopa on lifespan is particularly interesting because at least one previous report found no increase, although the dose used was far less than that used by Cotzias or Papavasiliou et al. I plan to produce a longer article on L-dopa and its toxicology; good reasons exist why any cryonicist might seriously consider obtaining and using this drug. In fairness, however, one negative point needs making, which is that L-dopa is a costly drug and would cost over \$1000/year in the high doses needed for aging. Besides toxicological studies, we need close attention to means of obtaining it more cheaply.

MORE EVIDENCE FOR THE COMMITMENT THEORY OF CELL AGING

Some time ago Holliday and Kirkwood published an article in SCIENCE (198 (1977) 366) presenting a new explanation of the phenomenon of the limited lifespan of cells in culture. They called this theory the commitment theory; basically it consisted of the suggestion that most normal cell cultures contained two different populations of cells, the committed cells and the uncommitted cells. Committed cells had only a finite number of possible doublings, while uncommitted cells could divide indefinitely. Because of the fact that virtually all cell cultures in the laboratory had to be

periodically "culled", a cell culture would end up consisting, by chance loss of the uncommitted cells, entirely of committed cells and therefore would show a finite number of population doublings.

In their latest article Holliday and Kirkwood present some cogent arguments against an earlier suggestion that their theory did not conform with observation (basically the observation that the experiments of Harley and Goldstein purporting to show this (SCIENCE 207 (1980) 82) depended on an oversimplified version of the theory and did not conflict with it). They furthermore present additional observations giving further support for their theory.

If cells become committed over time, we would expect cell cultures to contain an increasing percentage of nondividing cells at about the same time as their growth rate falls off. Holliday and Kirkwood labelled their cells using thymidine containing the tritium isotope of hydrogen. When a cell divides, it will take up thymidine; by this means Holliday and Kirkwood could show that exactly the right percentage of nondividing cells existed at the right time in the culture. Secondly they verified the "bottleneck" phenomenon: that by vigorously culling a cell population at an early time in its life, the variation in lifespans of cultures derived from it would increase. This variation is expected under their theory and comes from the fact that such culls would contain widely varying proportions of committed to uncommitted cells, and this variation would depend in a characteristic way upon the time at which culling took place. This variation was exactly what they observed in their experiments.

Holliday and Kirkwood point out that their theory does not so much prove the irrelevance of cell lifespan studies to aging as change the direction of interest in their relations. For instance, we would like to know how the uncommitted cells behave with aging, and the reasons why cells may become committed might have a lot to do with aging.

EVOLUTION OF SPECIFIC LIFESPAN

As readers know, considerable work on the problem of how limited lifespans could evolve has already gone on. The famous early paper of Williams (EVOLUTION 11 (1957) 398-411) had already presented some incisive explanations for the evolution of senescence, even though these were not quantitative. (Incidentally, GC Williams is a theorist of evolution whom many nonbiologists could read with profit, even though he seems very little known except among his own circle of scientists). Williams' theory of the evolution of senescence was fundamentally that selection pressure for longevity would, because of the decreasing probability of survival to high ages even without aging, tend to produce animals and plants whose viability would decrease as they grew older: in other words, animals and plants which aged. Subsequent mathematical treatments of this phenomenon by Hamilton (J THEORETICAL BIOLOGY 12(1966) 12-45) bore out these conclusions and made them more quantitative.

Arnold R. Miller, of the University of Illinois at Urbana, has recently devised a computer model of evolution which still further supports the work of Williams. The essential point of Williams' theory is that the selection pressure involved has nothing whatever to do with any "group" or species benefit due to aging. It is simply false that a species is the way it is because that is the "best" design for the species. Specific age evolves because in the normal conditions of the species, no members of that species

live long enough to show it. The force of evolution has simply never acted on that characteristic. In the case of human beings, of course, our longevity increased recently (on evolutionary time scales) and now we grow old and die from old age because selection has not yet had time to create people who lived on longer.

Of course, medical means to achieve the same effect (rejuvenation) will succeed MUCH faster than selection!

Arnold Miller's model behaves much as the earlier work by Hamilton had predicted, although there are some fine differences in detail. In summary, the specific maximum lifespan always tends to increase, but toward a finite limiting value; this finite limiting value will decrease both if the deathrate due to accidental events increases, and if the fecundity of the species increases. One interesting difference with previous work is that Miller's work suggests that random genetic drift would alone be sufficient to degrade longevity of a species whose lifespan is normally limited by accidents: no special genes which give advantages in younger life at the expense of disadvantages later are needed. A much less technical conclusion from Miller's model is that it shows quite conclusively that no form of "group" or species selection is needed to explain evolution of senescence. It follows from this that the mere fact that we age definitely does not imply that any group of which we are a member, or our species, receive any benefit from our aging.

Almost every cryonicist will remember times in which some complainant has alleged that we injure "society" or the human race by living longer than our so-called allotted span. Their claim derives from an outmoded theory of evolution by now almost 100 years out of date.

WHAT IS AMYLOID NORMALLY?

One of the characteristic changes of aging is the deposition of plaques of amyloid in the tissues. Up until quite recently the nature of this substance, whether it was only formed in the tissues of the old as an instance of aging pathology, or whether it had some function in normal tissues, wasn't known. Some recent work reported in NATURE (293 (1981) 652) by SM Breathnach et al has told us an answer to this problem: the real nature of amyloid in normal tissues.

Using immunological techniques (the manufacture of antibodies to amyloid, then using these antibodies and immunofluorescence to locate the amyloid in normal tissues) Breathnach et al have worked out that amyloid is a normal component of elastic fibers in the skin and blood vessels of all normal adults. The amyloid is contained as part of microfibrils in these tissues; they appear also in association with but different from fibers of collagen, and both appear in all connective tissue. Amyloid also appears in the plasma: there is a normal plasma protein, serum amyloid P component, to which the antibodies to amyloid will also bind.

Although Breathnach et al can't give any ideas about the physiological role of amyloid in healthy individuals, they do point out that another protein, fibronectin, is also a constituent of serum blood serum and at the same time of connective tissues. Moreover, fibronectin also seems associated with amyloid.

These observations are rather far from a full explanation of why amyloid plaques often form in the old and what their significance may be. However the knowledge of normal role for amyloid does give us a better understanding of what these plaques may be.

BRAIN TISSUE PROTECTED BY DMSO

Cryonicists all know very well the small amount of research going on about the freezing of brains or brain tissue, and the critical importance of this problem to cryonics. A recent article in JOURNAL OF NEUROCHEMISTRY (37(2) (1981) 243) adds one more to a very short list of articles in which scientists report their studies of this problem. As many such articles have been, this one aims at finding better ways to preserve neurological specimens for study, rather than to preserve brains for eventual revival.

EA Haan and DM Bowen, of Department of Neurochemistry, Institute of Neurology, London, present work on the use of Farrant's two-step freezing technique, combined with DMSO, in the freezing of slices from brains of both rats and humans. They harvested the rat tissue immediately after decapitation of the rat, and human tissue from brain operations. They froze their protected brain tissue to -196C, liquid nitrogen temperature. DMSO concentration was 10%. They did not test the electrical activity of their frozen brain tissue, but did test for its biochemical activity. Tissue frozen with DMSO showed 89% of the normal ability of control, unfrozen, tissue to incorporate glucose into acetylcholine, the nerve transmitter substance, and 86% of the control ability to metabolize glucose. The uptake of noradrenalin from frozen brain tissue was nearly normal. In another series, they studied the effects of freezing without cryoprotection, and found a drastic loss of these same metabolic capabilities. For instance, only 15% of the ability of frozen cells to make acetylcholine was preserved by freezing without DMSO and the two-step procedure.

This article will probably repay close attention by cryonicists directly concerned with carrying out cryonic suspensions. One interesting point is that their two-step procedure was quite insensitive to the exact periods of holding time at high but subzero temperatures and the levels of DMSO above 10%. The article is also interesting for cryonicists in general, in that it documents the fact that even though glycerol may improve over DMSO as a brain cryoprotectant, nevertheless considerable functional survival remains after DMSO. A case might be made for using it still, particularly in cases where problems of perfusion exist.

BOOK REVIEW

Arlene Sheskin CRYONICS: A SOCIOLOGY OF DEATH AND BEREAVEMENT Irvington Publishers, Inc, New York 1979.

This book will be interesting to all cryonicists, though as history rather than as a sociological treatise. It tells the story of the breakup of the Cryonics Society of New York (alias, in Sheskin's book, the "Eastern Cryonics Society"). The history is interesting and (so far as it is told) contained much of which I had not previously heard. It is a sad tale, of course, though much of the failure came from faults in the actors themselves, overwhelmingly most important the emotional inability to give the subject the seriousness it deserves. Their consequent failure would be fully expected, perhaps even it is what they themselves secretly wished. Curtis Henderson, the President of CSNY, comes through this history even more vindicated than before (if that is possible!).

Ignoring all of the nonsensical sociology, the collapse of CSNY seems to have been the story of how a group of dreamers met very brutally the facts that reality and dream differ tremendously, that most important of all dreams are free while REALITY COSTS MONEY. Not only does reality cost money, it costs time, work, effort, heartbreak, even long periods of BOREDOM. It is one thing to dream about the wonderful world of the future, quite another to spend thousands of dollars of one's own hard-earned money on legal fees, painfully rudimentary suspension equipment, and all the rest needed to ACTUALLY suspend someone, and then afterwards to actually KEEP THEM SUSPENDED. Most of the cryonicists reading this review, of course, will have been through this sieve. They are the ones who made it: we all know many many people who haven't even reached the stage where they meet this test, much less pass it; they spend their lives in dreams, dreams, dreams till human voices wake them and they drown.

What happened? CSNY actually suspended some people, and actually had to pay for it. And so, all in kinds of cryonical dreamers commenced frantic attempts to avoid the central issue, which was that they would have to put out both money and time. (DO YOU MEAN I ACTUALLY HAVE TO PAY FOR THIS?) Relatives of the suspendees, apparently thinking that suspension would cost only a few thousand dollars, decided that Henderson and CSNY were frauds because they asked for much more. They learned that there wasn't any such thing as a free cryonics. Or perhaps more correctly, they did not learn this, but rather spent inordinate amounts of time attempting to avoid the obvious conclusion. Mostly they succeeded, and now with the Nelson case some of them have even found out how to turn their avoidance into a profit-making activity. Who remained frozen? Nobody remained frozen.

Sheskin of course lumps all levels of commitment, from the gaseous dreamer to the solid cryonicist who is willing to pay in whatever coin they can manage for as long as they can do so, all into the same pot as "cryonicists". Among other things her book made me realize just how little I considered all of the many people, the fellow travellers and hangers on who have never made suspension arrangements and never will, who cluster around every cryonics group: how little I had come to think of them as cryonicists at all. Of course, some small number of these may be potential cryonicists, and we don't yet know how to distinguish. It is that only which prevents us from booting them out the door.

Sheskin also reveals, through interviews, how often these quasicryonicists and semicryonicists had adopted what was frankly a religious attitude to cryonics. By this I mean that they had dissociated their cryonics beliefs from any kind of serious action other than the dissemination of opinions. It is religious to pray for safety on the sea; it is reality to check the lifeboats carefully and have lifeboat drill every Friday, to keep and maintain up-to-date plans of action on what to do if the ship sinks or founders. Some of the things she says about cryonicists, as interpretation, ring true if only for those she interviews. We can say, ourselves, that most new ideas and ways of acting have a painful birth, that these people hadn't yet figured out how to act about suspension, and that simply because it was new those who find themselves doing it would look silly, awkward, and half-formed.

As sociology I found the book quite painfully flawed. I've had a problem with sociologists and psychologists for a long time. Bluntly, far too many of them seem to me LESS percipient than the average about their society or their fellow men, and Sheskin's book confirms this. The most glaring fault stems from the fact that her conclusions are quite simply not supported by her evidence. She set out to study cryonicists because she thought that their practices might throw some light on American customs and behavior in death, bereavement, and grief. She was never able to understand cryonics or cryonicists well enough, she never managed to grasp the essential point that cryonicists don't believe that their frozen relatives are dead anyway, so therefore they cannot be said to grieve for them or to be bereaved. It is a logical consequence of the belief; Sheskin may disagree with that belief but that is irrelevant. A study of cryonicists has about as much to do with bereavement in America as would, say, the study of a population of people who had not learned of the death of a close relative during the period prior to their learning: we see them go about their affairs, sending their (unknown to them, dead) mother a birthday card, sending her letters, planning to visit her....only a VERY DENSE person would claim that this conduct had anything at all to do with bereavement. So, too, with cryonics.

She also makes a large number of other foolish or even sometimes quite vicious comments. She seems to believe that cryonicists keep their beliefs secret. It is true that we don't TALK about them, but their reality is different from talk (does she know this?). I wear glasses, hardly a secret, but rarely if at all do I talk about the fact. She comments about our insurance arrangements, our Medic-Alert bracelets, and all of the other preparations which serious cryonicists make, that they are uncertain (yes, they are) AND THEREFORE UNREAL. Visit men in combat, Arlene, who don't know even whether they will live to see tomorrow, and find out just how real uncertainty can be. She quotes with approval a sociologist (Toynbee) who makes perhaps one of the most outrageous statements in her book, that the survivors of a death are hurt even more than the one who dies, because the person dying doesn't have to live with his/her death, while their relatives DO! If such is really the standard of sociological morality and thought, a pogrom is very much in order.

I have wondered about reporters and interviewers for some time. They come round and we tell them about cryonicists and cryonics. They take it all down. In one sense, they are exploited, because quite clearly they are doing all this to avoid thinking about their own deaths and what it means to them. It's their arse we're talking about, nobody else's. Concentrating on the mechanics of the interview and the baggage of theoretical sociology, they never have to figure out whether or not what we're saying speaks to THEM. And so Sheskin never worked out that single premise that demolishes her entire study: her belief that "dead is dead" was so ingrained that she slipped back into it unthinkingly. The history her book tells will interest any cryonicist; the commentary and thought reminded me of nothing so much as a conversation between the computer program ELIZA and someone who had lost his baggage at the airport:

"I've lost my baggage. It didn't come out of the plane." "Do you often lose things?" "Not really, but I've lost my baggage. Can you help me?" "Who in your family helped you the most?" "My family has nothing to do with this. I've lost my baggage." "Why does your family have nothing to do with this?" "Because I want my baggage." "Sir, do you have any psychological problems?"

It never clicked for Arlene.

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