CRYONICS

Volume 9(3) March, 1988 Issue #92

CRYONICS is the newsletter of the ALCOR Life Extension Foundation, Inc. Mike Darwin (Federowicz) and Hugh Hixon, Editors. Published monthly. Individual subscriptions: $20.00 per year in the U.S.; $30.00 per year in Canada and Mexico; $35.00 per year all others. Group rates available upon request. Please address all editorial correspondence to ALCOR, 12327 Doherty St., Riverside, CA 92503 or phone (800) 367-2228 (in California: (714) 736-1703). The price of back issues is $2.00 each in the U.S., Canada, and Mexico, and $3.00 for all others.

EDITORIAL MATTERS

Each month for over a year, producing CRYONICS has been more difficult. During the early part of last year it was due to the tremendous workload associated with relocating, then there was a suspension, and then another one -- and now the coroner's investigation. Each month the Editors of CRYONICS sigh and say, well, it can't get any worse than this. . . . We have been consistently wrong. On February 23, the Riverside County Coroner's Office filed a death certificate on Alcor Suspension Member Dora Kent listing the causes of death (in order) as: 1) Pneumonia; 2) Arteriosclerosis, and; 3) Barbiturate poisoning. The mode of death was listed as Homicide.

A corollary of such a death certificate being filed with the Public Health Service by the Coroner's office is an investigation by the District Attorney's office to determine if charges should be filed and who specifically should be charged.

At the time of this writing we do not know when or if a decision to bring charges will be made or who will be named. Nevertheless, it seems possible that one or more members of the Alcor Suspension Team may be charged with some sort of homicide: anything from 1st degree murder to involuntary manslaughter. Not a pleasant prospect.

Much of our uncertainty stems from the fact that we are innocent. (If we were guilty, at least we'd know who did it!) The national press has covered the accusations of homicide by the Riverside Coroner's Office in a sketchy and incomplete way. There was a brief article in TIME magazine and considerably longer articles in a fair number of major metropolitan newspapers on both coasts.

We have received many calls and questions regarding this case, and of course, it goes without saying we can discuss the case only in the "broadest brush strokes." Nevertheless, there are many practical questions about the case and about the future of Alcor which we can and will answer, and we make an effort to do so in an article entitled Some Questions and Answers, elsewhere in this issue.

More For Your Money

Despite the fact that we've been running behind with getting CRYONICS out to you, we've been putting out longer issues. While this issue and the previous issue may not look any bulkier in terms of pages than usual, we have gone to a smaller type size (via the wonders of laser printing) and are now running about 10% more copy per page. We can't promise to keep this up indefinitely, but at least it's some compensation for our

tardiness in the meantime.

* *

SOME QUESTIONS AND ANSWERS

Q. Outsiders and those on the periphery of cryonics sometimes ask if there is any substance to charges that barbiturates were administered before legal death occurred? In other words, "Did you do it?"

A. We ask this question here so that we can clearly and unequivocally answer it. No, we did not admin-

ister any barbiturates to Mrs. Kent before her legal death. There was no reason to do so -- and in fact a considerable effort had to be made to maintain her vital functions (i.e., keep her alive) until preparations for suspension were complete.

Q. What is the status of the UCLA stolen property investigation?

A. With all but a few exceptions, our property has been cleared for release, but it has not been returned to us. The major item UCLA police are contending was stolen is a large item of furniture (an $1,800 stainless steel medical cart) which was purchased by Alcor at UCLA Surplus and Excess Property. Witnesses to this purchase exist, as well as receipts. Despite early news reports to the contrary, UCLA has declined to file theft charges. We are confident that if they do, we will win.

There was no stolen property from in the Alcor facility from UCLA or anywhere else.

Q. What has been said by the District Attorney's Office about the Coroner's finding of homicide?

A. Statements have been mixed. Initially very radical statements were made to the effect that crimes in the form of stolen property and homicide were known to have occurred. Later, more moderate statements were made. But one thing seems clear: any trial of Alcor Suspension Team Members will be highly technical, attract enormous international press attention, and hinge on issues of fundamental importance to cryonics.

By way of example we quote from an article in the February 24th Riverside Press Enterprise, wherein Deputy District Attorney Curt Hinman made a statement that, "even if the people at the Alcor laboratory determined Kent was dead when the drugs were administered, the question is why barbiturates, which are sedatives, were given. If the reason is to keep her from reviving, then is she really dead? If they keep her from waking up, that's murder."

Needless to say they haven't asked why we give barbiturates (they reduce cerebral metabolic demands during poor tissue perfusion -- ischemia -- enormously) and the statement about preventing her from reviving only goes to illustrate the profound

---

ignorance and lack of even basic medical understanding which has surrounded this case from the start.

If a person is a "no code" (i.e., not to be resuscitated in the event of respiratory and/or cardiac arrest) such as Dora Kent, and dies, and you restore circulation and breathing artificially (i.e., via CPR) and you give them medications in the course of the procedure that would prevent them from resuming spontaneous respiration and breathing (which they wouldn't have done anyway unless you started CPR) and then you place them in cryonic suspension, have you killed them? Or to sum it up as one wag put it: "Those people at Alcor are a dangerous bunch. They killed a little old lady who died of natural causes and if they aren't stopped they may kill

other people who die of natural causes!"

Q. If Alcor Suspension Team Member(s) are indicted, what will happen to Alcor?

A. Alcor will continue to function. The quality of service we offer will remain unchanged while we await trial providing we can make bail. We are planning aggressively right now to insure that everyone who might be charged makes bail. We did not commit a murder or engage in any other criminal wrongdoing and we have commitments and responsibilities to patients in suspension and to our members -- we are not going to run away. Apparently the DA knows that, and that is why we aren't all in jail with astronomical bails right now.

If we are charged, it may well be as long as a year before we come to trial. Alcor will go on operating. A good measure of our continued effectiveness will hinge on our ability to make bail. If you can help in this regard please contact Alcor. You may be able to help by pledging property as collateral or by contributing cash for bail.

In any event, Alcor will continue to operate to the best extent possible. Contingency plans covering a wide range of possible unfavorable outcomes are in place to provide for continued patient care and suspension services for members.

Q. What effect has this "investigation" had on the practical ability of Alcor and other cryonics organizations to make necessary arrangements to facilitate a member's suspension -- such as hospital and mortuary cooperation?

A. Frankly, we don't know, but we can't imagine it would be good. If you have a working relationship with a mortuary, ambulance company, or physician now would be a good time to touch bases with the individuals involved and make sure things are still solid.

Generally we have found the community at large and people in general to be surprisingly supportive once they get the full story. Our best advice is to pull no punches. Let people know what's going on

and the nature of the trouble. Don't be afraid to have them call us if they need additional information.

And, if you haven't made local arrangements for emergency transportation and use of mortuary facilities in your community (i.e., you don't live in the Los Angeles or Miami areas) now is the time to do so.

Also, consider contacting your local coroner or medical examiner and explaining your interest in cryonics and your concern over the possibility of autopsy. It is never too soon to start educating these officials. And if you find they can't be educated -- move. It's just that simple.

Q. Are the Alcor patients still protected by the restraining order in the face of criminal charges?

A. Yes, to the best of our knowledge they are. Additionally, the nature of the case against Alcor is such that autopsy of Dora Kent's head is not going to yield any relevant information.

Why is the Coroner pursuing this course of action against Alcor?

We wish we knew for sure. Our best guess is that it is a mixture of ignorance, misunderstanding, and fear. Yes, fear. We know from published interviews that carrying out a cryonic suspension under optimum circumstances as we did in the case of Mrs. Kent made some of the deputies very uncomfortable (this is an understatement). Deputy Coroner Rick Bogan has stated on numerous occasions that he felt cryonics needed to regulated and it was apparent to us from the start that no one in the Coroner's office seemed to understand what cryonics was about -- let alone care in the slightest about the well-being of the patient's in suspension. Patients are just debris, just pieces of meat to be buried or burned.

If the Coroner thought even remotely that cryonics might work they would no more want to autopsy Dora Kent than they would want to go into an ICU and autopsy a patient struggling for life with a bullet in his brain.

No doubt another part of the problem is political. The press conference on December 23 started a chain reaction which has resulted in enormous expense and grief on both sides. It becomes a game of "chicken." On their side their careers are potentially at stake, on our side our lives. Because they don't understand cryonics and because they are convinced it won't work, they can't fully appreciate our position.

Someone in Northern California summed up their perception of the situation nicely: "[The Coroner's staff] thought this was just some crap game in the back of a sleazy little pool parlor and that everyone would run for the door as soon as they shouted 'Police!'." They were wrong. There is nothing dirty or ugly about cryonics -- it is one of the most powerful and positive things in our lives and we will stand up and defend it.

And as to our perception of them? Al Roca, one of our Associate Members on the East Coast, summed it up beautifully: "An Aztec official, if taken into an operating room today where open-heart surgery was being performed, would probably imagine it was a new form of human sacrifice. Likewise, Deputy Coroner Cupido sees the headless corpse of Dora Kent and can see only

homicide, which his principles say must be prosecuted. As cryonicist Thomas Donaldson wrote several years ago:

'Ixlipotli the Aztec had a life founded upon firm

moral values, such as cannibalism and periodic scarification. His high ethical principles gave structure and meaning to his life, and his achievements gave him a sense of deep personal satisfaction. To be chosen to cut out the heart of a captive was a great personal honor, signaling the respect which he merited throughout all Tenochtitlan. It was the year 1492, though not on his calendar.'

"Welcome to the third millennium, Mr. Cupido. Try not to cause too much damage."

Q. What is the utility of various political maneuvers to aid Alcor, such as letter writing campaigns?

A. It is the opinion of our counsel that this not an effective or particularly desirable thing to do at this time. The District Attorney has the matter under consideration and the DA is not likely to be influenced by letter writing or other such actions (as properly he should not be). At this sensitive time, attempts at "politicking" can actually be counterproductive. Counsel has advised us to adopt a conservative stance in this respect.

Also, keep in mind that even though you do not speak or act for Alcor directly, your actions and behavior may speak for us indirectly. In all of your communications and actions, use the highest standards of integrity and style. We want to remain in this community and be taken seriously as thoughtful, rational people -- not emotional kooks and flakes. Cryonics isn't a cult anymore than a self-help legal clinic is a cult. Granted, we are all very hurt, angry, and above all, frightened and frustrated by what has happened, but we must not lose our cool. We must demonstrate courage, which has been defined quite aptly as grace under pressure.

All of the Directors and Officers of Alcor feel quite strongly that the image we should strive ceaselessly to project is the image which best reflects the reality of Alcor: one of thoughtful integrity. A man is respected a thousand times more for bottling his anger and channeling it to productive ends than by shouting and complaining in the night. Harsh and angry words about those who oppose us only serve to bring us down to a level where we don't belong. And besides, those kinds of things will do nothing to resolve the situation -- only polarize and cloud the judgment of everyone involved. They may make us feel better in the short run, but in the long run they will only serve to hurt us.

Bear in mind also that any remarks you make about any of Alcor's operations or the individuals involved may end up in the newspaper and could powerfully affect the lives and well-being of suspension team members. And the press can be a very powerful tool -- for good or ill. It is so easy for remarks made out of context (or even in context, for that matter) to be misinterpreted or deliberately distorted. As has been said in other wars, "Loose Lips Sink Ships." It's probably best not to talk to the press about Alcor except in the most general way. On the other hand, it's perfectly fine to talk about personal

and overall impressions of Alcor and the people in it (hopefully these will be positive!).

Q. A reporter from the LOS ANGELES TIMES asked what would happen if key Alcor people went to jail over this affair? "Would-n't that be the end for Alcor and cryonics?" he asked.

A. The answer is "No and No." The quality of serv-ice may drop for a while, but as long as we are allowed to by the state, We will continue to oper-ate and care for the pat-ients we have in suspens-ion.

We intend to defend ourselves vigorously and we don't believe we will lose.

** TYPIST'S NOTE: THIS SPACE AND THE ENTIRE NEXT PAGE CONTAINED A NEWSPAPER CLIPPING FROM THE WEDNESDAY, FEBRUARY 24, 1988 "PRESS-ENTERPRISE":

CORONER SAYS LETHAL DOSE OF DRUGS KILLED CRYONICS CASE FIGURE

By DON BABWIN
The Press-Enterprise

Dora Kent, whose head was surgically removed in December at a cryonics laboratory in Riverside, was killed by a lethal dose of barbiturates, the Riverside County coroner's office said yesterday.

"We're saying this was an 83-year-old lady that was ill and pushed over the edge by the use of a drug," said Supervising Deputy Coroner Dan Cupido.

A death certificate amendment filed yesterday classifies Kent's death as a homicide. The case has been referred to the Riverside County district attorney's office, Cupido said.

Cupido said the findings by the coroner's office are based on the opinion of the pathologist contracted by the county, Dr. F. Rene Modglin, and those of toxologists who tested tissue samples and body fluids taken during Dora Kent's autopsy.

Deputy District Attorney Curt Hinman, said yesterday the case is still being investigated and that he is "fairly confident charges will be filed."

Hinman said he did not know when a decision on charges will be made. "One of the biggest questions is who committed it and who will be charged."

Dora Kent's death has been under investigation since the coroner's office learned of her Dec. 11 death at the Alcor Life Extension Foundation laboratory in Riverside. No doctor was present at

---

the time of her death, which was one of the factors that prompted the coroner's office to investigate whether she was alive when the procedure to remove her head was started.

The woman's son, Saul Kent, chose to freeze Dora Kent's head in the hopes that someday the rest of her body can be restored or replaced. Kent and other advocates of cryonics believe in storing bodies or heads at subfreezing temperatures in hopes of someday bringing them back to life through advances in science.

Yesterday, Saul Kent, who was present at the Alcor laboratory when his mother's head was removed, denied his mother was alive when the drugs were administered.

"I was there and she died of natural causes and then the procedure was started," said Kent.

Michael Federowicz, who was president of Alcor at the time and who was present during the operation, said finding barbiturates in Kent's system does not prove she was alive when the drugs were administered.

Cardiopulmonary resuscitation was begun after Kent died to intentionally distribute the drug throughout her system, Federowicz said.

Hinman said the tests showed levels of phenobarbital and secobarbital throughout Kent's system, including her liver, kidneys, and bone marrow, indicating Kent was alive when she was given the drugs.

Medical investigators found that Kent's body had metabolized the drugs, Hinman said,

"We think they gave it (the drugs) to her before she was dead," he said.

Hinman said, even if the people at the Alcor laboratory determined Kent was dead when the drugs were administered, the question is why barbiturates, which are sedatives, were given.

"If the reason is to keep her from reviving, then is she really dead?" he said.

"If they keep her from waking up, that's murder," he said.

Saul Kent said the barbiturates are given "after death," not to keep the patient from waking up, but to slow down the damage to the brain caused by the lack of oxygen.

The sooner the procedure is begun after death, Kent said, the better the chance of success.

The death certificate amendment lists the immediate cause of death as pneumonia and generalized severe arteriosclerosis. The death is, however,

classified as a homicide.

Kent said he did not understand why, if the coroner's office believes barbiturates killed his mother, they did not say the administration of the drugs was the immediate cause of death.

But Cupido said: "It's like you have a gunshot victim who develops pneumonia in the hospital and dies. It doesn't mean he wasn't shot."

The drugs, said Cupido, "expedited Dora Kent's death."

"A patient with that (the illnesses listed on the death certificate) given barbiturates will go over the edge," he said. The amendment to the death certificate says Dora Kent died between Dec. 9 and Dec. 11.

The investigation of Kent's death has spawned other inquiries.

The doctor who signed the death certificate, Dr. Steve Harris, a post-doctoral trainee in geriatrics and pathology at UCLA, was placed under formal review last month, according to a medical center spokesman.

Jerry Leaf, a research assistant at the university's School of Medicine and member of Alcor, was placed on investigatory leave at UCLA last month. Leaf, according to Alcor officials, performed the operation on Dora Kent.

UCLA has seized equipment from Alcor's Doherty Street laboratory to determine whether it was stolen from the university. That investigation has not been completed, school officials said.

DORA KENT CHRONOLOGY

Dec. 9, 1987: Dora Kent, 83, in failing health, is taken from the Care West-Mission Nursing Center in Riverside to Alcor Life Extension Foundation to die. The foundation, a non-profit organization, had moved to a Doherty Street industrial building in February from Fullerton.

Dec. 11: Alcor officials pronounce Dora Kent dead and remove her head to be frozen.

Dec. 23: The Riverside County Coroner's Office announces it is conducting an investigation to determine if the head of Dora Kent was removed before her death.

Jan. 7, 1988: Authorities serve a search warrant on the foundation's Doherty Street facility. Six people, including Alcor president Michael Federowicz, are taken into custody by the Riverside Police Department for questioning, then released. Boxes of documents and slides are seized and authorities discover Alcor has illegally dumped infectious body fluids into the city's sewer system. The head of Dora Kent is not found.

Jan. 12: Authorities serving additional search warrants at Alcor's laboratory find equipment and supplies suspected of being stolen from UCLA, and Dora Kent's hands. Also found are a gun, silencer, and armor-piercing bullets.

Jan. 13: Riverside Superior Court Judge Victor Miceli issues a temporary restraining order prohibiting the coroner's office from thawing the head of Dora Kent, should it be found, or any of the six heads and one body at Alcor.

Jan. 14: In a news conference, coroner's officials say Dora Kent was dead before her head was cut off. They also state she was in no immediate danger of dying when she was taken from her convalescent home to Alcor.

Jan. 19: Alcor officials at a news conference call the coroner's investigation a "vicious smear campaign."

Jan. 20: UCLA officials announce the man who surgically removed the head of Dora Kent has been placed on leave by the university, where he works as a technician in the medical center.

Feb. 1: Judge Miceli issues a permanent order barring coroner's investigators from thawing Dora Kent's head or any of the heads and body being stored at Alcor.

Feb. 23: Riverside County Coroner's Office files an amended death certificate reporting Dora Kent's death as a homicide. The coroner concludes Kent was administered a lethal dose of barbiturates.

ON BECOMING A COORDINATOR

We have received several letters recently from people asking about the possibility of becoming an Alcor Coordinator or working through Alcor to get a local cryonics group going. The Coordinator program has worked reasonably well for Alcor in the past, although somewhat disappointingly, it has not generated any viable new local groups. What it has done is provided a network of support people who can pass information on in a crisis and act as back-ups for Alcor in Southern California.

Need For More Flexibility

It has become clear since the Coordinator program was started that there needs to be a wider variety of types of Coordinators and that there needs to be some agreements in place defining what a Coordinator's rights and responsibilities are -- as well as what the limits of their authority are. Right now Alcor has two basic kinds of Coordinators: Rescue Coordinators; who are people with training and equipment to carry out initial stabilization and transport of Alcor cryonic suspension patients, and Information Coordinators, who do follow-ups on information requests and other leads in their territory and generally act as a clearinghouse for information among members and potential members.

Obviously both of these positions carry with them substantial

responsibility and liability for Alcor. Anyone acting to represent us either in a rescue/transport capacity or in terms of providing information about Alcor has to be someone we trust a great deal. Thus, a requirement for a Coordinator has been that we have a relatively long baseline of performance and interaction with that person to evaluate. It's a delicate position and one that can't be given out lightly.

Logistic Problems

On the other hand, it is difficult to establish such a baseline with people who are relatively new to cryonics and who still want to try to generate interest and action on a local level. Clearly, what is needed is a less formal "third alternative" for folks who just want to get the word out that they exist and want to hear from others in their area.

The first step in trying to form such a local group for mutual support and to provide a springboard for generating more interest in a given geographical area is to get together with others who are interested and "discuss things." Thus, we get a lot of requests for help in generating "cryonics discussion groups."

There are a few logistic problems with Alcor facilitating this, however. First is

the issue of confidentiality. We do not give out names, addresses, or phone numbers of members, or even of people who contact us for information, except to Coordinators. Members as well as people who make inquiries should be able to do so knowing that they will be handled discreetly and that their identity will be held in confidence.

After some thought on the matter we think we have a solution to the problems of maintaining confidentiality, not incurring liability, and encouraging the formation of discussion groups that can hopefully go on to develop into full-scale cryonics groups in the long run.

What we propose to do is to publish a list of people in each issue of CRYONICS and/or send with each information request a list of people who are interested in getting together with other cryonicists in their area. We've decided to call this class of person a Discussion Group Coordinator (DGC).

The Requirements

The requirements for a DGC will be fairly straightforward. First there will be a disclaimer from Alcor pointing out the DGC's "limits of authority and responsibility": i.e., they won't be representing Alcor in any formal way and Alcor makes no formal endorsement of them or their capabilities.

Second, the DGC must be a signed up Alcor Suspension Member. This requirement is in place for several reasons: First, no one will take cryonics seriously unless you take it seriously. That means being signed up. Second, since we are trying to broaden our base of support and we will be providing literature and information either for free or at very reduced cost, we want your loyalties to be with us. Third, we want to have a short baseline of contact with you so that we know that you at least understand the basics well enough not to be a

liability. (Even if A DCG doesn't formally represent Alcor, we still won't support someone who provides misinformation.)

We will provide support by releasing your phone number and address to people who are already members or who have requested information and are from your area. And of course we will provide you with support in the form of literature and information -- as well as one-to-one help (where we think it warranted) on the more practical matters of how to upgrade a discussion group to the level of a Rescue Coordinator or to a full-blown local cryonics organization.

If you think you might be interested in getting a discussion group going in your area, please contact Mike Darwin by calling Alcor (if he's not in, leave a message) at (714) 736-1703.

Good Luck!

THE FUTURE OF MEDICINE
Part 2 of 2

by Mike Darwin, with assistance from Steve Harris, M.D.

Anesthesia:

Expect "modular" anesthesia by the 1990's to the early 2000's. The development of potent anxieolytics (anxiety removers) which do not depress consciousness and the development of total pain inhibitors will allow for complicated surgical procedures on conscious patients. Expect to see major thoracic and limb surgery on high risk patients (i.e., patients unable to tolerate anesthesia) using such agents. Major abdominal surgery requiring deep muscle relaxation will continue to require skeletal muscle paralysis and general anesthesia. However, expect new drugs in the market place in the late 1990's which induce unconsciousness without respir-

atory or cardiac depression. Surgical and post surgical mortality will decrease sharply due to such anesthetics and the use of real-time physiological and biochemical monitoring during and after surgery using biosensors.

Surgery:

The biggest revolution in surgery will be in decreasing its use and its invasiveness. Less and less will a surgeon crack open a patient's entire abdomen or chest (or even make a large "gaping" wound) to effect repairs or treat disease. While tiny remote- or robot-controlled nanotechnological or microtechnological "submarines" cruising through the circulatory system are probably a long way off, their precursors in the form of catheter- and fiber-controlled instruments are here already. The next two decades will see an enormous shift towards minimally invasive surgical procedures. Catheters, laparascopes, and thorascopes with sensors, operating tools, and an impressive array of capabilities will be increasingly used.

Abdominal surgery will shift more and more towards the use of the fiberoptic laparascope, endoscope, and laser as miniaturization of tools occurs and disease is diagnosed earlier. Early diagnosis will create the need for less drastic procedures.

Fine-tuned repair of heart valves and blood vessels, and examination and biopsy of suspected abdominal and retroperitoneal lesions will be early candidates for application of this technology.

Surgery will also be used less for non-elective procedures because many of the conditions which require it will be amenable to diagnosis and treatment very early in their development, before they inflict major structural change. Also, a better understanding of the fundamental mechanisms of disease gradually will shift treatment away from destruction of tissue to meaningful changes or modifications in the biochemistry of the tissue in order to restore health. By way of example, expanding understanding of cancer, which is in reality a molecular disease, not a gross one, will shift treatment away from cutting and burning cells and towards learning how to turn them on and off appropriately.

In contrast to therapeutic surgery, the frequency of cosmetic surgery will probably increase dramatically as techniques are refined and prosthetics improve in quality and drop in cost. As people live longer, and stay productive longer as well, they will increasingly turn to medicine to maintain not only their health but their appearance. Cosmetic surgery will experience a boom until such time as the fundamental mechanisms underlying the aging process can be brought under

control.

Geriatrics:

Advances will be slow here, but significant. Expect increasing understanding and application of trophic factors and bioregulatory compounds. Early candidates for rejuvenation will be the immune system and other stem cell systems or systems with higher cell turnover. By the early decades of 2000, significant rejuvenation and geroprophylaxis of skin, bone, immune, and other "high turnover" tissues will be possible as the natural regulatory molecules which control these system are understood and applied. Expect several significant synthetic compounds to be discovered with these kinds of properties as well. There will be the possibility of profound improvement in personal appearance and general health as these agents enter the marketplace.

By the early years of the 21st century the first generation of compounds effective at "rejuvenating" (i.e., restoring some degree of normal maintenance and repair to existing brain cells) the central nervous system will be available. These drugs will work by turn-

ing on protein synthesis and stimulating natural repair mechanisms. However, pathologies of the brain and other nondividing tissues (renal, cardiac, and musculoskeletal system) will continue to be major sources of morbidity and mortality over the next two decades. As atherosclerosis and immune-related disorders are dealt with more effectively, expect an increasing shift of morbidity and mortality to central nervous system-related causes. Beyond 2000 this may be treated to a limited extent with fetal transplants, but a definitive solution will have to await a more sophisticated molecular-level medicine, capable of cell repair and regeneration.

Psychiatry and Behavior:

Diagnosis by brain scanning (metabolic MRI) and chemical analysis of cerebrospinal fluids will be commonplace in 20 years. As neuroregulatory compounds are better understood and as the biochemistry underlying mental disorders is elucidated there will be more effective treatments. Expect 2nd and 3rd generation drugs and combinations thereof for treatment of depression and psychosis by the late 1990's. There will probably be several very effective therapeutic agents for compulsive disorders in the marketplace by the early to mid 1990's.

One development likely within a decade is the creation of a new class of licit or semilicit drugs. Expect real aphrodisiacs and potentiators of sexual pleasure to be available by the late 1990's, if not before. It is already widely rumored that a certain peptide fraction of cholecystokinin (CCK) when taken by nasal administration is a potent aphrodisiac in both men and women. How potent? Potent enough to exceed even the wildest

dreams every teen-age boy had about spanish fly. A variety of molecules which regulate certain basic kinds of human behavior (rage, fear, and so on) will probably be filtering into the marketplace for both legitimate and illegitimate purposes. Developments in biochemistry will allow for the design of carrier molecules to move such agents across the blood-brain barrier. Such drugs will probably be used for both recreation and therapeutic purposes. Rejuvenation of the sexual system in the aged is one possible early, "legitimate" application of the CCK fraction.

Implants and Prosthetics:

Truly blood compatible surfaces and long term nonthrombogenic surfaces will be entering the marketplace in the mid to late 1990's. Initial application of these devices will be to heart valves, blood vessel grafts, and heart-lung machine and other extracorporeal tubing surfaces.

Early spectacular applications will be small vessel prostheses (wide use by the early to mid 1990's) for use in traumatized and atherosclerotic limbs and organs and venous prostheses (mid to late 1990's) for use in treating traumatic injuries and deep vein incompetence (which results in varicosities, chronic pain, and edema-related skin changes in the leg, often leading to nonhealing ulcers or limb loss). Another application of nonthrombogenic surfaces will be a practical artificial heart and more widespread use of extracorporeal support for infants, trauma and cardiac arrest victims, and others where anticoagulation provides a major barrier to the use of artificial circulation.

Good synthetic bone and skin should be available by the late 1990's to early 2000's. Good red cell and plasma substitutes (synthetic blood) should be seen increasing in clinical use throughout the early 1990's and in frequent use by the late 1990's to early 2000's.

There will be steady improvement in other synthetic materials such as hip, knee, and other joints, as well as in other less dramatic materials such as connective tissue replacements. Expect a slow replacement of prosthetic approaches to therapy as natural repair and regeneration processes are better understood and utilized. Expect to see synthetic connective tissue products for tendon repair which contain bioregulatory molecules (BRMs) that stimulate tendon regeneration. Artificial tendons made of both synthetic and/or natural materials will come into use in the late 1980's to early 1990's.

In short, expect stunning advances in tissue replacement technology for

all tissues that have primarily structural function and which are not complicated chemical processing plants, such as the liver or kidneys, or mechanically active such as the heart. In addition to connective tissue and bone, a candidate for early (late 1980's to early 1990's) replacement is the cornea. Expect evolution in biocompatible materials to allow for replacement of the cornea with an appropriate plastic, much like the lens of the eye is already replaced with polymer inserts.

Of course, no discussion of prosthetics can occur without reference to the artificial heart and to dialysis (the artificial kidney). Perhaps in no other area is an advance harder to predict. The artificial heart suffers from Space Program Factor more than just about any other medical technology that comes to mind.

The Jarvik Heart, which was the first so-called long term implant, actually has given a stellar performance so far! While the public perceives it as having killed and maimed every patient it has been chronically implanted in, it has in reality performed quite well. Several patients have done very well (including one Swiss businessman who was ambulatory, alert, and active with the device for over a year!) short term (weeks to months). Contrasted with the early days of dialysis or open heart surgery, this is a great success! Dialysis patients ALL died in the pioneering days of its development -- and they died of hideous, unthinkable complications of every imaginable sort -- bleeding, bone disease, nightmarish infections, depression. . . .

The difference, of course, was that there were no (or few) human experimental review committees and no public limelight. Most (but not all) of the early dialysis deaths were necessary. You don't learn about a brand-new technology unless you try it out -- and not just on animals. People are not the same as cows or goats or sheep. Particularly not sick people.

Expect slow progress in the artificial heart area because of the negative press. Progress may well come outside the US, in Japan or elsewhere, where failure is more acceptable and where transplantation is viewed as unacceptable (the Japanese in particular are opposed to transplants and do very few of them). Leaving aside the social factors and

concentrating solely on scientific and engineering ones, a good, fully implantable artificial heart (i.e., one capable of giving a patient a mean remaining life span of 3 to 5 years) should be on-line by the early to late 1990's. The only reason it isn't available now is Space Program Factor (SPF) and fear on the part of the government that they will end up picking up the tab for this expensive Band-Aid technology (see discussion at the end of this article).

Due to the current and projected shortfall in avail-

able organs for transplantation, the pressure will remain high for development of the artificial heart as at least a stopgap until an organ becomes available.

As opposed to total artificial hearts, small, chronically implanted balloon- or impeller-type intraortic pumps or left ventricular assist devices may increasingly be used until materials/blood compatibility problems can be solved.

Advances in hemodialysis will also be very incremental. There may be a gradual shift to peritoneal dialysis (PD) if good drugs to block glucosylation of proteins and inhibit cholesterol deposition are available. The major problem with PD today is that it raises blood sugars to astronomical levels, causing diabetic-like side effects. Inhibition of these side effects may lead to renewed application of this modality.

Direct changes in dialysis are likely to be along the lines of better membrane materials which allow for transport of wastes not currently removable by conventional dialysis and nonthrombogenic surfaces which will reduce the need for anticoagulation. The use of BRMs such as erythropoetin to treat anemia and bone growth factors to treat dialysis bone disease will help to improve the quality and quantity of patient's lives on dialysis. Perhaps the biggest advance in this area will be advances in immunology and infectious disease treatment. The ability to administer BRMs to stimulate immune function and improve general health should act to extend dialysis patients' lives considerably.

A corollary of better immune function and advances in biocompatible materials will be a revolution in "access site" technology for dialysis patients. Because dialysis requires repeated access to the patient's circulatory system in order to cleanse the blood (typically blood flow rates of 200 to 250 cc per minute are required) normal arteries and veins cannot be used.

Currently the best possible access site is a fistula -- a distended and "arterialized" vein created by the artificial cross-connection of an artery to a vein. The fistula can then be stuck with two large-bore needles for withdrawal and return of blood. However, many patients cannot develop adequate fistulas, and those that do often

lose them (the vein is often destroyed by repeated punctures). The next best thing to a fistula is a Goretex graft -- an artificial Teflon connection between artery and vein. Unfortunately Goretex grafts have many complications, including clotting and infection, and they have a very short lifespan.

Better materials will be developed which will allow for direct access to arterial and venous circulation and the use of ports which penetrate the skin and allow coupling to the dialysis machine without the use of needles. Improvements in blood access technology will also be used to treat cancer patients and provide total intravenous nutritional support for patients who are unable eat or unable to absorb food due to bowel loss.

Of course, the biggest improvement in the life expectancy and health of

dialysis patients will probably come in the form of the increasing use of transplantation and its application to a wider age range of patients with better long term results.

The most striking revolution in prosthetics will probably occur in dentistry. Expect a whole family of new materials to enter the dental operatory. A workable vaccine against streptococcus mutans should be available by the mid to late 1990's, greatly reducing the incidence of tooth decay by eliminating the major class of mouth organisms that cause it. Similar advances in prevention and in treatment of gum disease can be expected as well, although probably not as soon.

Repairing dental defects will also be revolutionized by the introduction of good, tough, and reliable polymers which will replace metallic amalgams. By the late 1990's to early 2000's biocompatible ceramics and coated polymers will be available that will allow for workable single tooth and multitooth gum-implanted prostheses.

Organ Preservation:

Perhaps no technology is dearer to cryonicists' hearts (and brains?) than organ preservation. It is linked to all our hopes and dreams for reversible suspended animation. What will progress be like here?

Several possibilities open up, and not all of them are rosy as far as cryonics is concerned. I'll start with the least favorable and go on the to most favorable.

Ever since the work of people like Mazur, Fahy, and Pegg was published, it has become pretty clear what the constraints are on long term viable cryopreservation of organs: don't form any significant amount of ice; it injures mechanically and it injures chemically. The problem is that water loves to turn into ice when it's cooled below 0øC. To circumvent this, a lot of very drastic changes have to be made in the system. Whenever you attempt to make a drastic change in a complicated, interdependent living system -- like replacing half the water in it with industrial chemicals -- you are in for trouble. The trouble will come in the form of a very tight or narrow window for success: everything will have to be "just right." This is where current vitrification technology is now. The existence of such a tight window means that vitrification of large masses will be a technological tour-de-force requiring very sophisticated computer controlled perfusion equipment and exotic and very costly high pressure chambers. Quality control and reliable storage and rewarming of organs will be very costly and difficult.

The future holds the possibility of developing better solute systems which vitrify more easily and which are less toxic (have a wider window for success). It is difficult to predict the pace of advance in this area since it will be arrived at by a mixture of empirical methods and theoretical insights. A big determining factor will be luck. Will

the NIH and the Red Cross continue to fund such efforts? And, more to the point, will technological advances in other areas of organ preservation obviate the need for them?

If we were betting men, we'd put our dollars on the latter rather than

on the former. Major advances in organ preservation (as opposed to cell and tissue preservation) over the next decade will probably be in three areas: 1) Extended hypothermic storage of organs in the 2 to 3 weeks range; 2) Extended normothermic or room temperature storage of organs in the weeks to months range and; 3) mixtures of the above two modalities which yield similar available time courses of storage.

By the late 1980's several systems should be in the medical marketplace which allow for storage of kidneys and hearts for 7 to 10 days using hypothermic techniques. Expect to see the debut of room temperature systems in the very late 80's or early 90's. These room temperature systems will employ a pump, lung, and tailor-made perfusate and will be designed to support the organ by meeting its metabolic requirements for vitamins, hormones, amino acids and so on. Expect metabolic wastes from the organ to be dealt with by frequent perfusate changes and the use of adsorber cartridges similar to those used in hemoperfusion (for treating liver failure and drug overdose) and hemodialysis.

Better networking for distribution of organs and rapidly escalating demand (as a consequence of better immunomodulation technology) will paradoxically decrease the need for organ storage. The development of techniques which allow for 5 to 7 day storage of major organs is probably adequate to meet the needs of the transplant community given the decreasing (indeed disappearing) need to carefully match donor with recipient.

The next 5 to 10 years should also see major advances in our understanding of the effects of deep hypothermia on the tissues and organs of nonhibernating mammals. These advances should be readily translatable into better flush and perfusion storage techniques for organs. A good understanding of lipid metabolism and mechanisms of cell swelling in deep hypothermia may allow for preservation of organs in the 2øC to 10øC temperature range for periods of several months -- thus definitively ending the need for long term solid state preservation of transplantable organs.

Unless a wild card breakthrough occurs in vitrification technology, such as a radical reduction in the toxicity of vitrification solutions, obviating a need for high pressure and exotic rewarming -- our bet is on hypothermic and room temperature support systems, not vitrification.

Unless Fahy and/or others can demonstrate real breakthroughs in vitrification (i.e., successful and routine long term recovery of transplantable mammalian organs in the laboratory) within the next several years, it seems unlikely that extensive Federal or private support will be forthcoming to pursue development of this option in the near future.

Indeed, assessing the picture objectively with reference to the other organ preservation technologies which are developing, it would seem that extended long term organ preservation in the solid state has serious application to only one area of medicine: medical time travel, i.e., cryonic suspension.

A good analogy here is blood banking. Despite the development of cryopreservation techniques for blood, very little blood is cryopreserved and that which is is confined to rare, hard to match types. This is so because the cost is high and the demand for blood is high -- so high that long term frozen inventories for major cell components are not really practical (ahh, would that only the supply be good enough and the preservation costs low enough that they were!!).

Repeated and careful assessments of this area of technology will thus be of great importance to cryonicists. Once again it is important to point out that we cannot count on cryobiologists to develop organ preservation techniques for cryonicists. Our needs are unique and are rather likely to remain so, given the rapid rate of advances in immunology and high temperature organ preservation.

However, in the areas of tissue and cell preservation there is likely to be far wider application of long term preservation techniques, including vitrification. Expect a shift away from freezing for blood components and embryos and toward vitrification, since vitrification solutions are relatively nontoxic to most cell systems and obviate the need for controlled rate freezing.

Other Approaches to Organ and Organism Preservation:

One possibility for a major advance over the next two decades is room temperature or hypothermic preservation of organs or organisms using metabolic inhibitors. There have been tantalizing clues in the examination of a wide variety of estivators (animals which go into states of profoundly reduced metabolism at normal temperatures, such as the African lungfish, which can shut off metabolism at temperatures in the range of 30øC to 40øC) that antimetabolite compounds exist which may be able to induce states of profoundly reduced metabolism at ambient (i.e., 70øF) temperatures. Purification and experimental (and perhaps even clinical) application of these compounds or synthetic derivatives to humans or human organs for transplant may occur sometime during the next decade or two.

Genetic Therapy:

Expect very gradual application of this technology. Early candidates for gene replacement will be in storage diseases such as Lesch-Nyhan, Tay-Sachs, and other "single enzyme missing" disorders.

Later applications will include treatments for hypercholesterolemia, some forms of hypertension, and other congenital missing enzyme syndromes. Very late applications (2000 or later) may be in the treatment of a wide range of mental illnesses and cancers.

Prevention:

Perhaps no other area of medicine will experience greater growth in capability -- and less success in application. Hopefully the next two decades will see more widespread application of the basic lessons of prevention learned during the last two.

And what are those lessons? The principal lesson is the lesson of the impact of

calorie restriction on overall health, well-being, and lifespan. The basic message here is "you are what you eat." In terms of treating atherosclerotic disease, the role of prevention is already clear. By reducing fat intake and decreasing serum cholesterol to below 150 mg/dl, most atherosclerotic disease can be avoided. Similarly, basic changes in nutrition such as trace element and vitamin supplementation can greatly reduce the number of late onset malignancies. Eliminating smoking will also be a major factor in achieving this end.

But it will take decades to do this. Making basic lifestyle changes will proceed slowly, and in the case of tobacco use may not be very amenable to widespread change. Nevertheless, the success of the American Heart Association and Nathan Pritikin in reducing the heart disease death rate by dietary manipulation and aggressive treatment of high blood pressure proves that it can be done.

Calorie restriction achieved by means of education and therapeutic agents seems the next big area of preventics to be explored by medicine. Expect the development of truly effective anorectics for treatment of gross obesity and eating disorders by the late 1980's and then secondary use of these for treatment of mild obesity and weight control in the normal middle aged. Products with reduced calories employing fat substitutes such as sucrose polyester should also be entering the marketplace in the early 1990's and these will help to reduce the calorie load further.

The Downside:

The vision painted above is not as rosy as nanotechnology, but is pretty exciting nevertheless. A relevant question becomes: what will be the drawbacks to all of this? Will there be any? The answer is: of course. A little information is a dangerous thing, and sometimes a lot of information can be an even more dangerous thing. The reason is that progress in therapeutics, which is relatively difficult, always lags far behind progress in diagnosis, which is relatively easy. This imbalance results in a tension which forces premature treatment which often does more harm than good. It is well to note that each new diagnostic modality brings with it a flood of new information which will at first be grossly misused before anyone understands what it means (Harris's Law of Diagnostics Advance).

A recent example of this sort of thing is the EKG machine, which for the first time showed that many seemingly normal people had strange cardiac rhythms, some of which were seen also around the time people died suddenly of heart problems. Because of this association, for the last 15 years, a number of very powerful drugs have been used to treat people with such rhythms. Many drug-induced fatalities resulted. Unfortunately, only now is it beginning to be understood that most people with good heart function are less in danger from such rhythms than they are from the drugs used to treat them -- a finding of little consolation to the people already killed by the drugs. When the reader considers the flood of new diagnostic information which will pour out of the advanced implantable sensors and fancy medical body imagers described above, he/she may well feel a chill run up the spine. How will we know what it all means? The answer is: at

first we won't, and only later will we find out through the use of that most potent tool for discerning truth: statistics. Computers will help with this, but will not obviate the problem completely because human mortality studies (by far the most important kind) take a certain minimum time to complete. Also, it is an unfortunate reality of life that every increase in computational power increases the number of new statistical questions which can be asked, faster than it answers the old ones. Eventually the answers will be forthcoming, but in the meantime, a lot of people are going to be killed by their doctors and by their doctor machines.

What can be done about this on a personal basis? It is not generally realized that the proper answer to new and powerful medicinal drugs is sometimes the same one coined by the Reagan Administration for recreational drugs: Just say "No." Each patient, when evaluating a new therapy which carries significant risk, is responsible for finding out the answer to one question and one question only: "What is the evidence that this intervention saves lives?" Not "What is the evidence that this intervention will fix the funny numbers coming out of that new diagnostic machine?" The patient (and the doctor) who remembers the difference will be ahead of the crowd.

There is a second downside to advanced medicine, of course, besides the danger, and that is the cost of "middlingly advanced technology" (such as what we'll see in the next fifty years) in a society which takes a socialistic view of health care. Such as ours. Non-molecular technology is expensive. It should be obvious to the reader, with a bit of thought, that in a world of non-molecular technology, the potential demand for medical care as technology advances, is (for all intents and purposes) infinite. In America, we have adopted the unfortunate policy of letting everyone pay for everyone else's medical care, which has had exactly the same result as if we had let everyone pool their money and pay for each other's lunch: everyone orders lobster. We have paid for the lobster only by spreading the costs around to places where they are not obvious. For

instance, when you buy an American car, you pay more money for the health care costs of the people who built it than you do the steel that goes into it. This kind of thing can continue very subtly and very insidiously until a very large fraction of the gross national product is eaten up by health care costs. (In our country, it is already 11% and rising). One day, you may find that you have had to forego your family vacation in order to buy Granny that new AUTODOC which measures 245 different chemicals in her blood every minute and transmits all of the results to Medical Multivac in Bethesda.

Of course you may not realize this: all you will know is that the vacation went because money is so tight, taxes are so high, and inflation is so bad. But your money went to Granny nevertheless. The only answer to this problem, short of nanotechnology, is rationing.

But rationing itself becomes the last great social cost of advanced medical technology under socialism, because history shows that it is never done on an individual (person by person) basis. When people do not pay for their own medical care, no one (not doctors, families, or the government) has ever been willing to make the decision of who should benefit from a given technology, and who should not. Therefore, all systems of rationing to control medical costs ultimately have come down in the past to rationing technology across the board.

To push the previous metaphor, this is equivalent to removing lobster from the menu entirely, so that it is not available even if you want to pay extra for it. The social cost of rationing at the technology level should be obvious. The indiscriminate use of existing technology by people who do not need it drains money from a national economy which should be going toward research. In addition, most new technologies pass initially through an "expensive" phase before they become generally available at an affordable price. If rationing cuts technologies off before they can pass through that phase, new technologies fail to be developed, and the pace of progress slows. That nearly happened to MRI (magnetic resonance imaging) in this country, and it is happening to the artificial heart. It will happen more and more.

So all of the rosy predictions made in this article must be tempered with the

"social" realities that medicine will have to deal with in the next 20 years. Many of the advances we have discussed may simply not materialize because we are not wealthy enough to afford them collectively. That will be a great tragedy.

A REVIEW: THE ENCYCLOPEDIA OF MEDICAL IGNORANCE
R. Duncan and M. Weston-Smith, Eds., Pergamon Press, 1984.

by Thomas Donaldson

Duncan and Weston-Smith have had a very happy idea, which is their series "The Encyclopedia of Ignorance." Rather than just put together an account of what we think we know about various subjects (physics, astronomy, biology, and so on) they approached a series of experts in particular fields, asking them to write about what we do NOT know. By now, some years after starting this effort, they have got round to discussing one variety of ignorance near to our hearts, medical ignorance.

As cryonicists we'll find the discussions in this book both interesting and frustrating. The editors did a "good" job. That means that they talked to all the right people. The right people, of course, are all the publicly acknowledged experts in medicine. This means that if they had written their encyclopedia of ignorance, say, in 1903, they would have missed the Wright Brothers. In 1959 they would have missed spaceflight.

And so, in 1987 they have missed several avenues of medical research (and therefore, several forms of ignorance) which someday should become very important. There is no discussion in this book at all about nervous tissue regrowth, repair, or transplantation. There is no discussion about recovering nerve tissue from strokes or ischemia. There is also no discussion of the whole issue of growth and development; control of growth and development will eventually affect medicine much more profoundly than antibiotics ever have. There is also no discussion of another mystery, the many causes of mental defectiveness.

They do present an article by T. Samorajski, "The hypothalamus as an aging clock," which discusses aging, and another by Sir Martin Roth on senile dementia. Of course, the discussion is quite "establishment." Among other lacks, Paul Segall's work on possible biochemical origins of the relation between the hypothalamus and aging is omitted from Samorajski's article. To be fair to Samorajski, he does mention the work on tryptophan (as done by Timiras, not by Segall) but does not discuss its biochemical motivation.

However, it's also true that if we forget (willing suspension of disbelief??) the fact that several issues which are very important, are neglected, and ought not to be, then this book is quite interesting.

N. Geschwind contributes an interesting article, really more history than a discussion of the unknown, pointing out that German neurologists at the turn of the century (1900) already knew about the importance of the callousal system which separates the two halves of the brain. They had described what happens if this connection is severed, even the phenomenon of two independent brains which it caused. Their work was neglected after

WW I by the victors, who had to rediscover the whole thing over again in the 1950s. (This is very similar to German work on development in the 1930s, which the victors, this time the US, independently rediscovered with much fanfare in Scientific American in the 1960s.)

It also contains an interesting article "Destiny and the genes: genetic pathology and the individual," by P. G. H. Gell. The article discusses how some conditions run in families, but with spotty inheritance which does not follow the gene exactly. Usually traits involve a complex interaction between genes and environment, which we need to trace out and understand (and we have not done this yet). The most interesting part of this article was its discussion of particular cases; everybody knows the general truth.

One very neglected area of medicine consists of the parasitical diseases. We neglect these because we live in areas of the world where (now) they present few problems. The article by Keith Vickerman begins with the sentence, "It is difficult for dwellers in temperate climes to realize the stranglehold that infectious disease still maintains on the lives of those living in the tropics." The point that Vickerson makes in his article is that most of the human race still suffers from infectious diseases. We haven't really left the period in which infectious disease is a major cause of death, and we don't understand (yet) how to deal with these diseases.

Finally the article by J. Dickinson ("Cardiovascular system") talks about what we don't about regulation of blood pressure. It turns out that we don't know a good deal, and that this knowledge would be important to understanding blood pressure diseases and cardiovascular diseases in general.

One striking commonality in many of these papers is that (to my interest) they did not actually discuss ignorance about matters of fact, but got involved in issues about moral behavior too. I have read the "Encyclopedia of Ignorance" on the physical sciences, which spends much more attention on matters of fact which we do not know than on the determinants of human behavior. The medical version spends much more time on issues such as why people smoke, why they visit doctors in the first place, and so on. This probably has to do with the secret role of doctors, which is as moral arbiters for the community.

If you can suspend your disbelief at omission of such elementary unknowns as those of nerve tissue repair, this isn't a bad book. Someday it may even prove very interesting, when historians of 2187 read it to see just what doctors of 1987 thought were the leading questions of their day.

* * * * * * * * * * * * * * * * * * * *

Trudy

by Dave Pizer

Oh, what I'd give to live again
To walk this world where I ain't been
While my mind's forever advancin'

Oh, what I'd give to live again

Oh, what I'd give to be young again
In a body whose age has been locked in
To an eternal stage of ten plus ten
Oh, what I'd give to be young again

Oh, what I'd give to love you again
To hold your hand on the day we win
As our timeless loves once again begin
Oh, what I'd give to love you again

We will come back someday to
Live again
Be young again
Love again
. . . Forever

The following article was generated in large measure from one of the depositions provided in support of Alcor's plea for a preliminary restraining order in the case of Dora Kent. It has been extensively edited and modified by Mike Darwin and the CRYONICS staff.

THE CRYOBIOLOGICAL CASE FOR CRYONICS

Contents

* * * * * * * * * * * * * * * * * * * *

Introduction

Any casual newspaper reader will have decided quite confidently by now that cryonics has no chance whatever of success, due to the systematic misinformation contained in all media coverage of this subject to date. Not only has the scientific evidence supportive supportive of cryonics not been presented, but the unchallenged, supposedly scientific criticisms of cryonics presented in the media have been as harsh as they have been vapid and without merit. In reality, it seems that no supposedly scientific criticism of cryonics has ever addressed the real issues involved or ever been based on a grasp of them. The purpose of this discussion is to provide a summary of the extensive cryobiological evidence which exists to support cryonicists' premise that existing freezing techniques preserve the

molecular basis of human memory and personality and thus offer a reasonable chance of allowing future restoration of cryonics patients to life.

Why has this evidence not been presented previously? The reasons are largely political. Also it should be appreciated that even a neutral position with respect to the emotionally charged subject of cryonics is hazardous for a cryobiologist because of hardened opposition on the part of many key scientists who control job availability and grant support. This opposition is generally based on a gut reaction and/or philosophical objections that do not invite further consideration. Unfortunately, almost no-one ever seriously asks whether anything as seemingly outrageous as cryonics could have any compelling scientific foundation, despite the fact that it does. The problem is that the relevant scientific facts are far from obvious or readily available, and that no well-established scientist has ever dared or even been able to enunciate them.

The result has been the suppression of discussion, the creation of anxiety, the propagation of gross misinformation among the general public, and the censorship of valid scientific observations: in short, the antithesis of what science is supposed to be all

---

about. It is time to consider the scientific facts and to show that what is really outrageous is not cryonics but the notion that there is no scientific basis for cryonics or that cryonics cannot possibly work.

A. Premises and their scientific evaluation

What are the cryobiological issues? Another way of asking this question is: what is the minimum cryobiological requirement for "success" with the cryonics endeavor? Since the one indispensable goal of cryonics is restoration of the brain, we can limit our attention to the cryobiological requirements for the achievement of this goal. Questions concerning maintenance of the brain after restoration are not cryobiological and can therefore be neglected here.

What then would be required for the brain to be restorable? First, the brain must be preserved well enough to repair, i.e., it must be possible today to preserve with some reasonable fidelity the basic biological components of the brains of humans shortly after these humans have clinically died. Second, repair technology must be available to carry out any repairs required.

The two indispensable premises of cryonics, then, are reasonable brain preservation and the development of advanced molecular scale (nanotechnological) biological repair devices. Both premises are fully open to scientific scrutiny and falsification by experiment or calculation and, in fact, both seem at present to withstand such scrutiny, as the experimental evidence which is presented in this paper as well as the work of others on the problems of biological repair (see K. Eric Drexler's book, "Engines of Creation," and his technical papers) should show. If both premises are valid (assuming cryonic suspension is done under reasonable conditions and nonscientific problems do not intervene), then in principle cryonics should work to at least some extent.

As noted above, this article is about the cryobiological basis of cryonics rather than the cell repair aspect. But because the cryobiological premise of cryonics loses significance without the

nanotechnological premise of cryonics, it is necessary to comment at least briefly on nanotechnology in order to clarify the relevance of the evidence to be presented about cryobiology. There appear to be no significant flaws in K. Eric Drexler's concepts of molecular scale cell repair devices, and this judgment is supported by the absence of even a single significant and coherent objection to his concepts. The concepts involved are powerful enough to make it easy to imagine the technology not only for repairing the fine structure of the brain but also the technology for transplanting a brain into a new body. It seems not only possible but inevitable that such technologies will be developed, and a person waiting in liquid nitrogen should remain changeless for centuries if need be while such technologies are developed.

B. Short introductory summary of general conclusions

It can be stated quite firmly that cell bodies, cell membranes, synapses, mitochondria, general axon and dendrite patterns, metabolites such as neurotransmitters, chemical constituents such as proteins and nucleic acids, and general brain architecture are preserved reasonably well or excellently with current techniques. The brain can withstand severe mechanical distortion by ice without impairment of subsequent cognition, and a glycerol concentration of less than 4M -- a concentration achieved in current cryonics procedures -- can be shown to limit ice formation to quantities currently thought to be consistent with good functional recovery of the intact brain.

Information is lacking about the ultrastructure of frozen-thawed brains, but much can be inferred from the customary observation of a high level of functional recovery of

frozen-thawed brains, brain tissue, or brain cells which depends on a high degree of both local and long-range ultrastructural integrity. Absolute proof is lacking about the quality of preservation in each and every brain region, since not all brain regions have been examined by neurobiologists to date. However, in the experience of those who have histologically examined entire cross sections through the frozen-thawed brain at many different levels, no clear differences in preservation quality from one brain region to another have ever been apparent.

A reasonable way of summarizing the world literature on this subject at present is to say that wherever either brain structure or brain function has been evaluated after freezing to low temperatures and thawing, robust preservation has almost always been demonstrable provided at least some minimal attention was paid to providing at least token cryoprotection, and in some cases good preservation has been documented in the complete absence of reasonable cryobiological technique. The implication of these findings is that structures and functions not examined to date will also respond in a favorable way to freezing and thawing.

C. Detailed review of relevant current cryobiological knowledge

1. General cryobiological background

Freezing is not a process of total destruction. It is well known that human embryos, sperm, skin, bone, red and white blood cells, bone marrow, and tissues such as parathyroid tissue survive deep freezing and thawing,

and the same is true for systems of animal origin. In 1980 a table was published listing three dozen mammalian organized tissues and even a few mammalian organs which had been shown to survive cooling to low temperatures (1), and this list could now be expanded due to additional experiments on other systems. Such survival could not occur if the molecules comprising biological systems were generally altered by freezing and thawing and, in general, freezing does not cause chemical changes or protein denaturation.

Contrary to popular imagination, cells never burst as a result of intracellular freezing. The expansion of water as it is converted to ice causes less than a 10% increase in volume, whereas cells can withstand far larger increases in volume, e.g., 50-100% increases. But the primary flaw in this concept is the idea that ice forms in cells at all under ordinary conditions of slow freezing: it does not. Instead, ice forms between cells and water actually travels from the interior of the cell to the ice outside the cell, causing shrinkage rather than bursting of the cell.

Cell death during slow freezing may be related to changes in the cell membrane produced by cell shrinkage, or to toxicity of cryoprotectants as they are progressively concentrated as a consequence of the formation of pure ice in initially dilute solutions. Both of these putative causes of death are relatively mild on the molecular level and are certainly not irreversible in principle. But whatever the cause of death, cells examined in the frozen state appear to be structurally intact even when they are known to be nonviable upon thawing (with very few exceptions on the part of nonmammalian systems not relevant to the brain). This is true both for single plant and animal cells and for cells that comprise animal tissue. Hence, lack of functional recovery after thawing is not proof of lack of structural preservation in the frozen state before thawing, and it is the latter that is relevant to cryonics.

A truism of cryobiology is that different types of cells require different protocols of cryoprotectant treatment, cooling and warming rate, and cryoprotectant washout in order to exhibit maximal survival. Some kinds of cells are particularly difficult to freeze

---

without killing them. All of these differences can be minimized greatly by using high concentrations of cryoprotectant, provided such concentrations are tolerated. Nevertheless, other than a few generalizations such as those described above, it is impossible to extrapolate from one biological system to another in terms of predicting the details of its cryobiological behavior.

For this reason, if we wish to understand what happens to the brain when it is frozen, we can't argue on the basis of results obtained with kidneys or plant cells or embryos or granulocytes, but must, instead, focus specifically on the brain. Herein lies one of the largest errors cryobiologists and other scientists have made in dismissing the prospects for cryonics: making sweeping negative statements without knowing anything about the cryobiology of the brain (or, for that matter, the primacy of the brain, or the concepts of nanotechnology).

In order to examine the scientific evidence bearing on the only indispensable cryobiological premise of cryonics, then, the balance of this article will be devoted to an extensive review of the contents of a large number of scientific papers on the freezing of brains, brain tissue, and/or

brain cells. As extensive as the following remarks are, it should be understood that they are not exhaustive. No attempt has been made to obtain the complete scientific literature describing the state of brains after freezing in ways which are relevant to the issue of cryonics. This review simply reflects all relevant information currently at hand.

2. Living adult animal brains

Dr. Robert J. White, the Chairman of the Dept. of Neurology at Case Western Reserve University's School of Medicine, has favorably discussed the prospects for the eventual successful cryopreservation of human brains (2,3,4). (Dr. White is also an expert on cephalic transplantation and hypothermic brain preservation and has published several scientific papers on these subjects.) However, it is clearly impossible to experiment with entire living human brains, so the closest we can come to evaluating the degree of total brain preservation achieved in best-case cryonics procedures is to review the results of freezing the brains of animals.

The earliest observations of this sort were made by Lovelock and Smith (5,6) in 1956. These investigators froze golden hamsters to colonic temperatures between -0.5øC and -1øC and quantitated the amount of ice formed in the brain, allowing them to determine how much ice formed in the brains of animals which made full neurological recoveries. They determined that at least 60% of the water in the brain could be converted into ice without damaging the ability of the hamsters to regain normal behavior after thawing. Considerably more ice was consistent with restoration of breathing, a complex neural function. However, the exact quantity of ice (above 60%) consistent with full neurological recovery could not be clearly determined, because of death due to intestinal, pulmonary, and renal bleeding. Nevertheless, tolerance of at least 60% ice by the brain shows that this organ is considerably more tolerant of freezing than is the kidney.

The prospects for successfully avoiding damage due to the formation of ice at much lower temperatures can be assessed to a first approximation based on this finding of Lovelock and Smith. The quantity of glycerol required in theory to prevent mechanical injury from ice (C_{gr}) can be calculated from the equation (derivable from reference 7)

$$C_{gr} = 9.3 - .093V_t$$

where V_t is the percentage of the liquid volume of the brain which can be converted into ice without causing injury. Assuming V_t = 60%, C_{gr} is 3.72M.

The work of Lovelock and Smith was followed up by Suda and his associates (8,9,10), who made a number of critical observations on frozen glycerolized cat brains. Their first publication, in 1966, demonstrated that cat brains gradually perfused with 15% v/v glycerol at 10øC and frozen very slowly for storage for 45-203 days at the very unfavorable temperature of -20øC regained normal histology, vigorous unit (individual cell) activity in the cerebral cortex, hypothalamus, and cerebellar cortex, and strong if somewhat slowed EEG activity (8) after very slow thawing.

These results are remarkable in a number of ways. First, it is clear that no other organ would be capable of the same degree of activity after such prolonged storage at such a high subfreezing temperature. Second, Suda et al. made no attempt to supplement their perfusion fluid (diluted cat blood) with dextrose, which must have become depleted fairly rapidly, worsening the EEG results. Third, Suda and colleagues did not wash the glycerol from the brain carefully, and this may have caused injury during brain reperfusion. Fourth, the presence of EEG activity implies preservation of long-range neural connections and synaptic transmission, and unit activity indicates preservation of cell membrane integrity, energy metabolism, and sodium and potassium pumping capability. In short, these brains appeared to be basically viable based both on function and on structure. Although "pial oozing" after about an hour of blood reperfusion was noted (but not described adequately), this defect seems minor.

Their second publication, in 1974 (9), went considerably farther. After 7.25 years of storage at -20øC, "well synchronized discharges of Purkinje cells were observed" (i.e., normal cerebellar unit activity) as well as "spontaneous electrical activity . . . from the thalamic nuclei and cerebellar cortex," and short-lived EEG activity from the cerebral cortex. Another brain stored for 777 days showed cortical EEG activity for 5 hours after reperfusion. In both cases, EEG activity was of lower quality than EEG activity of fresh brains, but the existence of any activity at all after such extraordinary conditions is amazing. Cell loss after 7.25 years and hemorrhage after reperfusion of brains stored for 5-7 years is not surprising.

More important was a comparison of the frequency distribution of EEG activity in a fresh brain before perfusion and then after storage at -20øC for 5 days. The EEG pattern before freezing and after thawing was very nearly the same (9). It should be noted that in a typical cryonics operation, the time spent near -20øC is measured in hours rather than days or years and, based on the work of Suda et al., should not therefore involve appreciable deterioration of the brain.

It is noteworthy that in both reports of Suda's group, the brains were successfully reperfused with diluted cat blood after thawing. The quality of reperfusion was not documented in detail, but the autocorrelogram comparing the EEG of the 5-day cryopreserved brain to the EEG of the same brain before freezing could not have been as good as it was without relatively complete restoration of cerebral circulation. This is an important question not only with respect to viability and functional recovery but also with respect to the accessibility of the brain to nanotechnological repair devices which might be administered via the vascular system.

Also relevant were unpublished results mentioned in passing (9) on storage at -60øC and -90øC and on the effectiveness of other cryoprotectants (dimethyl sulfoxide or polymers). Evidently, EEG activity could be obtained after freezing to -60øC and storage for weeks, but not after freezing to -90øC, and dimethyl sulfoxide was effective but not as effective as glycerol. This is confirmed in an unpublished manuscript by Suda (10), which reveals also that unit (single cell) activity can still be recorded in brains frozen to -90xC. This unpublished paper (written in Japanese) also shows that brain reperfusion was better after thawing when glycerol rather than DMSO was used.

These results can be evaluated with respect to the information obtained previously by Lovelock and Smith. For protection against mechanical injury at -90øC, as noted above, the results with hamsters suggest that 3.72 M glycerol, or 27.2% glycerol by volume, might be required, whereas Suda and colleagues used only 15% glycerol by volume. It can be calculated (11) that at Suda's storage temperature of -20øC, 62% of the liquid content of the brain was converted into ice, while at -60øC, 77% of the liquid volume of the brain was converted to ice, a quantity which equals or exceeds the tolerable degree of distortion by ice in the hamster brain. Therefore, the finding by Suda and his colleagues of no injury at -20øC for 5 days but of injury after freezing to -60øC and especially to -90øC is entirely consistent with predictions from the work of Lovelock and Smith and is also entirely consistent with an absence of any such mechanical injury in the brains of cryonic suspension patients perfused with more than 3.72M glycerol.

The work with hamsters and with cat brains demonstrates that extensive freezing of the brain at high temperatures is compatible with its full functional recovery and that at least partial functional recovery from low temperatures is a reasonable prospect, but these studies do not describe the histological effects of freezing brains to the low temperatures required for truly long term preservation. This information was provided by Fahy and colleagues (12-14a). They reported that with either 3M or 6M glycerol, excellent histological preservation of the cerebral cortex and the hippocampus was observed after slow freezing to dry ice temperature (-79øC). In fact, there was no difference in structure between brains which had been perfused with glycerol only or brains which had been perfused, frozen, and thawed. Although Fahy et al. did not report it formally, this finding was also true in every other region of the brain examined, such as the cerebellum and the area of the ventral brain containing giant neurons and well-organized axonal bundles. It is of interest that Fahy et al. observed brain shrinkage if the perfusion temperature was held constant below room temperature (14a). But Suda and his colleagues also observed the same degree of brain shrinkage (10), yet this did not prevent apparent survival of their frozen cat brains.

One report (14b) has appeared which briefly documented the ultrastructural effects of now-obsolete cryonics procedure on the brain. A single dog was perfused directly with 15% DMSO for 55 minutes at 10-17øC. The head was then cooled at 0.1øC/min to -14øC and then cooled at 0.5øC/min to lower temperatures. The brain was estimated to have reached -79øC after 3 hours, after which it was shipped cross-country for thawing, fixation, and examination by light and electron microscopy. Histochemical staining of undefined nature showed evidence for appreciable enzymatic activity and cellular retention of histochemical reaction product, i.e., intact cell membranes. Ultrastructure, as documented in a single electron micrograph, revealed intact cell bodies, an intact double nuclear membrane, intact myelin sheaths around small myelinated fibers, recognizable organelles (mitochondria and endoplasmic reticulum), and recognizable synapses. Extensive damage was also apparent, but it was not clear whether this was due to freezing and thawing, perfusion with DMSO in one step as opposed to gradual addition, or abrupt dilution of DMSO upon fixation. No details were provided as to DMSO washout and fixation procedures. Significantly, the concentration of DMSO employed was not sufficient to prevent mechanical damage according to "the Smith criterion" mentioned earlier. The presumption would be that current cryonics procedures, employing the preferred cryoprotectant glycerol in higher concentrations, better preserve ultrastructure. Nevertheless, it is not obvious from the published micrograph that the original brain structure could not be inferred.

3. Living adult human and animal brain tissue

In 1981, Haan and Bowen (15) reported that they had collected sections of cerebral cortex from living human patients (during brain operations requiring removal of cortex to allow access to deep tumors), and frozen them using 10% v/v dimethyl sulfoxide (DMSO) as

the cryoprotectant. The DMSO was added and removed essentially in one step each, with some agitation of tissue samples to promote equilibration in the short times allowed for equilibration at 4øC. Freezing was accomplished by a two-step method in which the tissue was placed at -30øC for 15 min (5 min required to reach -30øC, for a cooling rate of about 6øC/min, and 10 min of equilibration at -30øC) and then transferred directly to liquid nitrogen. Thawing was rapid. For comparison, rat brain tissue was obtained by decapitating rats and removing their brains (probably involving a warm ischemic insult of 5-10 min), and this rat brain tissue was equilibrated with dimethyl sulfoxide and frozen in the same way.

The results? Norepinephrine uptake was 94-95% of control uptake for both rats and humans. Incorporation of glucose-derived carbon into acetylcholine was 89-100% of control incorporation for rats and 85% of control for humans. Incorporation of glucose-derived carbon into CO2 was 86-100% of control for rats, 78% of control for humans.

Haan and Bowen noted that their tissue prisms are mostly synapses, so their results imply that synapses of both rats and humans survive freezing by their technique. This agrees with inferences noted above that synapses survive in whole brains frozen with completely different techniques. Although not strictly brain tissue, the superior cervical ganglion, considered part of the central nervous system, also demonstrated 100% recovery of synaptic function after freezing to dry ice temperature in 15% glycerol, according to Pascoe's report in 1957 (16). It was noteworthy that Pascoe's ganglia also showed 100% recovery of action potential amplitude and conduction velocity after thawing from dry ice temperature (16).

In 1983, Hardy et al. (17) confirmed the extreme survivability of synapses in human brain tissue beyond any doubt. Once again, normal living adult human cerebral cortex was removed during operations on deep brain structures and compared to viable rat forebrains in terms of freeze-thaw recovery. The best results were obtained by freezing 1-5 gram pieces of human brain (or 1 gram rat forebrains), as opposed to freezing homogenates. The cooling rate to -70øC was slow but was not measured or controlled; the thawing rate was fast but not measured or controlled; the sole cryoprotectant was 0.32 M sucrose (Far from an optimal regimen!). After thawing, synaptosomes were prepared from the tissue samples and tested for functional recovery. Here is a summary of the results:

Measurement	Percent recovery* human	rat
number of synaptosomes recovered	not done	80
number of mitochondria recovered	133**	67
increase in number of unidentifiable (damaged) structures	29	24

amount of protein recovered	91	70
oxygen uptake/100 mg of protein	78	59
stimulation of oxygen uptake by veratrine	86	86
potassium accumulated/100 mg protein	86	70
loss of potassium stimulated by veratrine	39	85
retention of neurotransmitters (aspartate, glutamate, GABA)	good	good
stimulated transmitter release (amount, selectivity, and drug modulation	good	good

* recovery compared to unfrozen control samples.
** suboptimal technique

As Hardy et al. stated, it is apparent that both human and rat brain tissue frozen to -70øC with almost no cryoprotection has synapses "closely comparable to (those from) . . . fresh tissue."

As if this were not demonstration enough, Walder (18) has shown that not even cryosurgery destroys synapses. He applied a -60øC cryoprobe to the brain of cats for 5 min and examined the resulting lesions in the electron microscope. Not only were well preserved synapses found, but also cell bodies, organelles, and neuronal processes could be identified, despite considerable damage to the organization of the neuropil and to astrocyte cell membranes.

4. Living fetal human and animal brain tissue

In 1986, Groscurth et al. reported the successful freezing of human fetal brain tissue (19). 1x2x2 mm brain fragments from a 9-14 week abortus were treated with 10% DMSO and 20% fetal calf serum and placed into a -30øC environment for 3 hours or overnight, then stored at -80øC for several weeks, then finally transferred to liquid nitrogen. After storage for 3-12 months, the samples were "thawed at room temperature," trypsinized, and seeded on glass cover slips for 2-4 weeks of tissue culture at 37øC. The brain cells were found to be alive and to grow in culture: "Twenty-four hours after trypsinization the cells formed clusters of variable size . . .. During further cultivation numerous fiber bundles were found to grow from the margin of the clusters. Single fibers showed varicosities as well as growth cones at the terminal projection. Bipolar spindle-shaped cells with a smooth surface were regularly apposed along the bundles."

The first reports of attempts to freeze fetal animal brain tissue seem to be those of Houle and Das in 1980 (20-22). These attempts were fully successful, the frozen-thawed transplanted cerebral cortex being indistinguishable from non-frozen brain tissue transplants in every way. Das et al. have more recently described their technique in finer detail (23). Briefly, they use 10% DMSO, a cooling rate of 1øC/min, storage at -90øC, and rapid thawing. Survival was best if the tissue was not dissociated or minced before freezing.

Although a variety of conditions allowed for 100% success rates for 16 and 17-day neocortex, brainstem tissue from 16-day fetuses showed at best a 50% survival rate, and Das et al. suggested that these more differentiated cells, which have a low transplant survival rate even in the absence of freezing and thawing, might be more damaged by freezing and thawing. On the other hand, it should be kept in mind that, as should be clear from the

earlier discussion of cryoprotectant concentrations necessary for protection at low temperatures, 10% DMSO is a rather low concentration of a possibly suboptimal cryoprotectant (Suda indicated that glycerol was superior to DMSO for brain), and better survival might well have been obtained using the more gentle freezing/thawing conditions employed in cryonics procedures.

Jensen and colleagues (24) reported their work on freezing fetal hippocampal tissue in 1984, again using 10% DMSO, a cooling rate of 1øC/min, storage in liquid nitrogen, and rapid thawing. Treatment with DMSO at 4øC was for 2 hr, with rapid washout at room temperature (not necessarily an innocuous approach; unfortunately, no DMSO controls were done). Although 21% of the cryopreserved hippocampi showed ideal structural preservation after development in oculo, in general there was some structural alteration compared to nonfrozen control hippocampal transplants. It was felt that this may have been due to the extra manipulations of the cryopreserved tissue (controls were not washed in DMSO solutions, etc.). Only half of the cryopreserved transplants at most were found to be present after 20-68 days in oculo, survival rate being dependent upon fetal age. It was

felt that this once again may have been due to loosening of the hippocampal structure by the experimental manipulations.

This tended to be confirmed by transplants into the brain rather than into the eye: the brain provides more confinement to transplanted hippocampi, helping to prevent disintegration of the grafts, and, in fact, 100% of hippocampi transplanted to the brain survived. (It should be obvious that the hippocampus of a frozen intact brain will of course receive support from all surrounding structures and will thus be more analogous to the intracerebral transplants noted by Jensen et al. than to the intraocular transplants, in addition to being spared from disruptive manipulations in vitro.)

Frozen-thawed hippocampi grown in oculo were smaller than control grafts, and frozen-thawed hippocampi transplanted either to the eye or to the brain showed a loss of dentate granule cells (a 35% loss was seen in oculo). In several other ways, this complex brain structure important for encoding and decoding memories appeared to be unaffected by freezing and thawing. Moreover, freezing in 10% DMSO, as noted above, might not be an ideal procedure. It should be noted that Fahy et al. were not impressed by any loss of dentate cells in whole adult rabbit brains after freezing and thawing (12-14a).

Jensen's group followed up this work with more extensive work on many different subregions of the fetal rat brain, i.e., the neocortex, habenula, septum and basal forebrain, cerebellum, and retina (25). All of these regions showed good survival and preservation of normal structural organization after transplantation into an adult recipient's cerebral cortex, despite wide, uncontrolled variations in cooling protocol from run to run. The only exception was the cerebellum: only 2 of 7 grafts were found at the time of sacrifice, although they were structurally normal. The numbers involved are too small for adequate statistical analysis, and no control cerebellar grafts were performed to determine if this rate of takes is normal for this tissue. All in all, then, this paper tends to confirm the impression from other studies that tissue from many quite different brain areas survives freezing and thawing quite well.

5. Living human and animal isolated brain cells

Silani et al. (26) dissociated human fetal cerebral cortex into cells and froze the cells at 1øC/min in 7% DMSO plus 20% fetal calf serum. After more than 12 months in liquid nitrogen, the cells were thawed rapidly. Immediately after thawing, the cell recovery was 96.5+/-2.1%, showing that brain cells are not physically destroyed by freezing even under rather severe conditions. After 72 hours of culture, 53% of the total cell population was alive, but only 24% of the neurons were alive. The surviving neurons were, however, morphologically and functionally normal, as were astrocytes. Silani et al. considered their yield of human neurons to be a high one. These results show unequivocally that human brain cells can survive freezing and thawing and imply that, as was the experience of Hardy et al. (17) and Das et al. (23) (and as is suggested by the experience of Jensen et al. (24)), it is best to use undissociated tissues (analogous to the intact brain in cryonics procedures) rather than dissociated cells to obtain optimal results.

Kim et al. (27) isolated living oligodendrocytes and astrocytes from the white matter of brains of human cadavers aged 62, 86, and 93 years after 5, 14, and 6 hours of clinical death, respectively. These cells were cultured for 2-28 days, then scraped from their substratum, exposed abruptly to 10% DMSO, frozen to -70øC at an unknown and uncontrolled, exponentially decreasing rate, immersed in liquid nitrogen for 1-3 weeks, thawed rapidly, and abruptly diluted to 1% DMSO, further washed, and recultured. The excellent morphology of the cultured cells after thawing and the robust presence of

---

membrane markers was not different from what existed before freezing. 70%, 60%, and 55% survival was obtained after 2, 7, and 28 days of culture before freezing, respectively.

Kim et al. (27) also reported informally the following. "Recently, we have frozen various types of neural tissue cultures and found that the recovery of frozen neurons and glial cells was excellent. The neural cultures tested were: (a) dissociated chick embryo spinal cord and dorsal root ganglia; (b) dissociated newborn mouse cerebellum and dorsal root ganglia; (c) dissociated adult mouse dorsal root ganglia, and; (d) dissociated or explant fetal human brain cultures."

Kawamoto and Barrett (28) froze rat fetus striatal (including overlying cortical) and spinal cord cells by dissociating these tissues in 5-10% DMSO and placing them into uninsulated boxes in a -90øC freezer and leaving them there for up to 88 days. They were then thawed rapidly and exposed immediately to DMSO-free solution, a procedure these scientists found to be damaging. Nevertheless, they observed "neuronal survival rates comparable to those of brain tissues plated immediately after dissection." Preliminary results indicated similar survival of neuroglia frozen in the same way. Survival was roughly independent of DMSO concentration above 5%. Increased sensitivity of the cells to mechanical forces was observed after thawing or after simple cold storage, but this was reduced by using cryoprotectant carrier solutions low in sodium. Beautiful morphology was seen after thawing, and vigorous regrowth of cellular processes occurred after thawing to give mature cultures indistinguishable from controls. Surprisingly, dissociated cells survived freezing and thawing better than

cells embedded in undissociated tissue.

Scott and Lew (29) gradually exposed undisturbed cultured adult mouse dorsal root ganglion cells to 10% DMSO, placed them in a -15øC environment for 30 min, then placed them in liquid nitrogen vapor. Thawing took 5 min, after which the DMSO was removed gradually. Other cultured neurons were dissociated and frozen and thawed similarly as a cell suspension. The relative number of surviving neurons was not quantitated in this study, although there was evidently considerable cell death (probably due to the high cooling rate below -15øC, which would be expected to induce intracellular freezing and cell death). Nevertheless, many neurons survived and were capable of basically normal electrical activity as well as regeneration of new nerve fibers.

6. Post-mortem human and animal brains

Human brain banks are now in existence for investigators interested in understanding human brain biochemistry and pathology (30-33). Sections or subregions of post-mortem human brains, frozen rapidly several hours after death, are sent to medical researchers who analyze these brains for neurotransmitters, proteins, enzyme activity, lipids, nucleic acids, and even histology. There would be no reason for such banks if no molecular or structural preservation were achieved by freezing.

Haberland et al. (34) isolated synaptosomes after freezing the nucleus accumbens of rats and of 72 (plus or minus 5) year old humans. The humans were dead 15 +/- 5 hours before this brain structure was removed and frozen. Previous studies indicated that dopamine uptake by synaptosomes could still achieve 55% of the values of fresh brains even 24 hours after death. In this study, the humans were not refrigerated until 3-5 hours after death. Freezing was done with varying concentrations up to 10% DMSO, 1.2øC/min to -25øC, and subsequent immersion in liquid nitrogen. Experiments on rat nucleus accumbens (NA) removed 5-10 min after decapitation of the rat indicated that freezing to -25øC caused no measurable reduction of dopamine uptake. When rat NA was frozen to -196øC, survival ranged from 96% of control using 0.07 M DMSO to 99.7% of control using 0.7 M DMSO. Human NA frozen to -196øC as described in the presence of 0.7 M DMSO (5% v/v)

yielded dopamine uptakes equaling 102.9+/-5.2% of unfrozen control uptakes.

Stahl and Swanson (35) looked at the fidelity of subcellular localization of 6 brain enzymes and total brain protein after guinea pig or post-mortem human brain tissues were frozen to -70øC without a cryoprotectant simply by being placed into a freezer. Their conclusion: "subcellular fractionation of brain material is possible even with post-mortem tissues removed from the cranial cavity some hours after death. Two other groups have subsequently fractionated human post-mortem brain and have come to a similar conclusion: "Our present study further shows that even after freezing and prolonged storage, human and guinea pig brains can be separated into biochemically distinguishable subcellular fractions . . . . Frozen storage for several months did not strikingly modify the fractionation characteristics of freshly homogenized cerebral cortex."

Schwarcz (36) subjected rat brains to post-mortem conditions comparable to those experienced generally by humans: 4 hours of storage in situ at

room temperature followed by 24 hours of storage in situ at 4øC followed by brain isolation and freezing of brain regions by placement in a -80øC freezer for 5 days. Glutamate uptake by striatal synaptosomes prepared from striata frozen in this way amounted to 26% of control uptake by fresh tissue synaptosomes, an amazing degree of preservation. (Schwarcz noted, however, that glutamate uptake processes may be more resistant than serotoninergic, dopaminergic, and cholinergic uptake mechanisms.)

Brammer and Ray (37) confirmed that it is possible to isolate intact, if not living, oligodendroglial cells from bovine brain white matter after freezing to -30øC without any cryoprotective agent, more than 1 hour after the slaughter of the cow. (The original paper describing isolation of human oligodendroglia under similar circumstances is that of Iqbal et al. (38)) If the white matter was treated with polyvinyl pyrollidone (PVP) before freezing, cytoplasmic enzyme activities were not different from enzyme activities in unfrozen cells (without PVP, enzyme activities were one half to one fourth of control values, which demonstrates significant preservation of enzyme structure and function even under these highly adverse circumstances.) Although no data were shown concerning the effects of glycerol or DMSO, it was stated that these agents did not improve enzyme activity. Nevertheless, it should be recalled that Kim (27) isolated the same cells from post-mortem human brains before freezing and found that pretreatment with 10% DMSO allowed them to survive freezing to liquid nitrogen temperature.

Morrison and Griffin (39) isolated undegraded messenger RNA from human brains after 4 or 16 hours of death, with or without freezing in liquid nitrogen. The mRNA was used to direct protein synthesis in vitro, which was then analyzed by 2-D O'Farrell gel electrophoresis. Normal protein populations were observed, causing them to conclude "that post-mortem storage for 4 and 16 hours at room temperature had little effect on the spectrum of isolated mRNAs" and "the profile of proteins synthesized . . . was not changed . . . when the tissues were stored in liquid nitrogen."

Many similar reports exist in the literature. Tower et al. showed preservation of oxygen consumption and enzyme activities in brains of many species, including whales subject to many hours of warm ischemia, after isolation from the dead animal and freezing (40-42). Hopefully, the point is clear that brain structure and even some brain functions and enzymatic activity survive freezing even when freezing is done after hours of unprotected clinical death and even with minimal or no cryoprotection.

7. Post-mortem human spinal cord and outflowing nerves

One report (43) is available documenting the effects of cryonics procedures on the

spinal cord, which is part of the central nervous system. A human cryopreserved by now-obsolete cryonics procedures was decapitated while frozen, the body thawed, and the spinal cord and spinal nerves examined histologically after aldehyde fixation and osmication. The basic finding was that myelin sheaths were intact and shrunken axoplasm could be seen within the myelin sheaths, conceivably indicating intact axolemmas. Large neuronal cell bodies were observed which appeared intact and normal in shape. In general, the histological preservation was impressive. Apparently intact blood vessels were observed within the spinal cord.

(Other, non-neuronal tissues were also examined and were found to be surprisingly intact, with the exception of the liver and, to a lesser extent, the kidney.)

Summary

The scientific literature allows no conclusion other than that brain structure and even many brain functions are likely to be reasonably well preserved by freezing in the presence of cryoprotective agents, especially glycerol in high concentrations. Thus, cryonics' premise of preservation would seem to be well supported by existing cryobiological knowledge. This is not to say that cryonics will inevitably work. But it is to say that cryonics may work and that it is a reasonable undertaking -- not the provenance of madmen or misguided fools.

List of references cited

General cryobiological background

1. Fahy, G. M., Analysis of "solution effects" injury: rabbit renal cortex frozen in the presence of dimethyl sulfoxide., Cryobiology, 17, 371-388 (1980).

Living adult animal brains

2. White, R. J., Brain, In: Organ Preservation for Transplantation, A. M. Karow, Jr., G. J. M. Abouna, and A. L. Humphries, Jr., Eds., Little, Brown, & Company, Boston, 1974. pp. 395-407.
3. White, R. J., Brain In: Organ Preservation for Transplantation, Second Edition, A. M. Karow, Jr. and D. E. Pegg, Eds., Marcel Dekker, New York, 1981. pp. 655-674.
4. White, R. J., Cryopreservation of the mammalian brain, Cryobiology, 16, 582 (1979).
5. Smith, A. U., Revival of mammals from body temperatures below zero. In: Biological Effects of Freezing and Supercooling, A. U. Smith, Ed. Edward Arnold, London, 1961. pp. 304-368.
6. Lovelock, J. E., and A. U. Smith, Studies on golden hamsters during cooling to and rewarming from body temperatures below 0øC. III. Biophysical aspects and general discussion, Proc. Roy. Soc. B,\145, 427 -442 (1956).
7. Fahy, G. M., D. I. Levy, and S. E. Ali, Some emerging principles underlying the physical properties, biological actions, and utility of vitrification solutions, Cryobiology, 24, 196-213 (1987).
8. Suda, I., K. Kito, and C. Adachi, Viability of long term frozen cat brain in vitro, Nature (London), 212, 268-270 (1966).
9. Suda, I., K. Kito, and C. Adachi, Bioelectric discharges of isolated cat brain after revival from years of frozen storage, Brain Res, 70, 527 -531 (1974).

10. Suda, I., Unpublished Japanese language manuscript (including figures) based on a talk given by Dr. Suda (President of Kobe University) in Japan and reportedly being prepared for publication in English.
11. Fahy, G. M., Analysis of "solution effects" injury: Equations for

calculating phase diagram information for the ternary systems NaCl -dimethylsulfoxide-water and NaCl-glycerol-water, Biophys J, 32, 837 -850 (1980).
12. Fahy, G. M., T. Takahashi, A. M. Crane, and L. Sokoloff, Cryoprotection of the mammalian brain, Cryobiology, 18, 618 (1981).
13. Fahy, G. M., T. Takahashi, and A. M. Crane, Histological cryoprotection of rat and rabbit brains, Cryo-Letters, 5, 33-46 (1984).
14a. Fahy, G. M., and A. M. Crane, Histological cryoprotection of rabbit brain with 3M glycerol, Cryobiology, 21, 704 (1984).
14b. Gale, L., Alcor experiment: Surviving the cold, Long Life Magazine, 2, 58-60 (1978).

Living adult human and animal brain tissue

15. Haan, E. A., and D. M. Bowen, Protection of neocortical tissue prisms from freeze-thaw injury by dimethyl sulphoxide, J Neurochem, 37, 243 -246 (1981).
16. Pascoe, J. E., The survival of the rat's superior cervical ganglion after cooling to - 76øC, Proc. Roy. Soc. (London) B, 147, 510-519 (1957).
17. Hardy, J. A., P. R. Dodd, A. E. Oakley, R. H. Perry, J. A. Edwardson, and A. M. Kidd, Metabolically active synaptosomes can be prepared from frozen rat and human brain, J Neurochem, 40, 608-614 (1983).
18. Walder, H. A. D., The effect of freezing and rewarming on feline brain tissue: an electron microscope study In: The Frozen Cell, G. E. W. Wolstenholme and M. O'Connor, Eds., J. & A. Churchill, London, 1970. pp. 251-266.

Living fetal human and animal brain tissue

19. Groscurth, P., M. Erni, M. Balzer, H.-J. Peter, and G. Haselbacher, Cryopreservation of human fetal organs, Anat Embryol, 174, 105-113 (1986).
20. Houle, J. D., and G. D. Das, Cryopreservation of embryonic neural tissue and its successful transplantation in the rat brain, Anat Rec, 196, 81A (1980).
21. Houle, J. D., and G. D. Das, Freezing of embryonic neural tissue and its transplantation in the rat brain, Brain Res, 192, 570-574 (1980).
22. Houle, J. D., and G. D. Das, Freezing and transplantation of brain tissue in rats, Experientia, 36, 1114-1115 (1980).
23. Das, G. D., J. D. Houle, J. Brasko, and K. G. Das, Freezing of neural tissues and their transplantation in the brain of rats: technical details and histological observations, J Neurosci Methods, 8, 1-15 (1983).
24. Jensen, S., T. Sorensen, A. G. Moller, and J. Zimmer, Intraocular grafts of fresh and freeze-stored rat hippocampal tissue: a comparison of survivability and histological and connective organization, J Comp Neurol, 227, 558-568 (1984).
25. Jensen, S., T. Sorensen, and J. Zimmer, Cryopreservation of fetal rat brain tissue later used for intracerebral transplantation, Cryobiology, 24, 120-134 (1987).

Living human and animal isolated brain cells

26. Silani, V., A. Pizzuti, O. Strada, A. Falini, et al, Human neuronal cell cryopreservation, (abstract from unidentified literature source)
27. Kim, S. U., G. Moretto, B. Ruff, and D. H. Shin, Culture and

cryopreservation of adult human oligodendrocytes and astrocytes, Acta Neuropathol (Berlin), 64, 172-175 (1984).

---

28. Kawamoto, J. C., and J. N. Barrett, Cryopreservation of primary neurons for tissue culture, Brain Res, 384, 84-93 (1986).
29. Scott, B., and L. Lew, Neurons in cell culture survive freezing, Exp Cell Res, 162, 566-573 (1986).

Post-mortem human and animal brains

30. Itabashi, H. H., W. W. Tourtellotte, B. Baral, and M. Dang, A freezing method for the preservation of nervous tissue for concomitant molecular biological research and histopathological evaluation, J Neuropath Exp Neurol, 35, 117-119 (1976).
31. Tourtellotte, W. W., R. C. Cohenour, J. Raj, A. Morgan, R. Warwick, J. Sweeder, et al, The NINCDS/NIMH human neurospecimen bank, Neuro -Psychopharmacol, 2, 1593-1595 (1978).
32. Bird, E. D., Brain tissue banks, Trends in Neurosci, 1(5), I-II (1978).
33. Tourtellotte, W. W., H. H. Itabashi, I. Rosario, and K. Berman, National neurological research bank: A collection of cryopreserved human neurological specimens for neuroscientists, Ann Neurol, 14, 154 (1983).
34. Haberland, N., L. Hetey, H. A. Hackensellner, and G. Matthes, Characterization of the synaptosomal dopamine uptake from rat and human brain tissue after low temperature preservation, Cryo-Letters, 6, 319 -328 (1985).
35. Stahl, W. L., and P. D. Swanson, Effects of freezing and storage on subcellular fractionation of guinea pig and human brain, Neurobiology, 5, 393-400 (1975).
36. Schwarcz, R., Effects of tissue storage and freezing on brain glutamate uptake, Life Sci, 28, 1147-1154 (1981).
37. Brammer, M. J., and P. Ray, Preservation of oligodendroglial cytoplasm in cryopreservative-pretreated frozen white matter, J Neurochem, 38, 1493-1497 (1982).
38. Iqbal, K., et al., Oligodendroglia from human autopsied brain. Bulk isolation and some chemical properties, J Neurochem, 28, 707-716 (1977).
39. Morrison, M. R., and W. S. T. Griffin, The isolation and in vitro translation of undegraded messenger RNAs from human post-mortem brain, Anal. Biochem, 113, 318-324 (1981).
40. Tower, D. B., S. S. Goldman, and O. M. Young, Oxygen consumption by frozen and thawed cerebrocortical slices from warm-adapted or hibernating hamsters: the protective effects of hibernation, J Neurochem, 27, 285-287 (1976).
41. Tower, D. B., and O. M. Young, The activities of butyrylcholinesterase and carbonic anhydrase, the rate of anaerobic glycolysis, and the question of a constant density of glial cells in cerebral cortices of various mammalian species from mouse to whale, J Neurochem, 20, 269-278 (1973).
42. Tower, D. B., and O. M. Young, Interspecies correlations of cerebral cortical oxygen consumption, acetylcholinesterase activity and chloride content: studies on the brains of the fin whale (Balaenoptera physalus) and the sperm whale (Physeter catodon), J Neurochem, 20, 253 -267 (1973).

Spinal cord and spinal nerves

43. Anonymous, Histological study of a temporarily cryopreserved human, Cryonics, #52, 13-32 (Nov, 1984).

Meeting Schedules

Alcor business meetings are usually held on the first Sunday of the month. Guests are welcome. Unless otherwise noted, meetings start at 1 PM. For meeting directions, or if you get lost, call Alcor at (714) 736-1703 and page the technician on call.

The APRIL meeting will be held at the home of:

(SUNDAY, 10 APR 1988) Virginia Jacobs
29224 Indian Valley Road
Palos Verdes, CA

The MAY meeting will be held at the home of:

(SUNDAY, 8 MAY 1988) Bill Seidel and Candy Nash
10627 Youngworth
Culver City, CA

The JUNE meeting will be held at the home of:

(SUNDAY, 12 JUN 1988) Paul Genteman
535 S. Alexandria, #325
Los Angeles, CA

---

* * *

The Alcor Cryonics Supper Club is an informal dinner get-together. These meetings are for newcomers and old-timers alike -- just an opportunity to get together and talk over what's happening in cryonics -- and the world!

If you've wanted an opportunity to ask lots of questions about cryonics, or if you just want a chance to spend some time with some interesting and nice people, pick a date and come! All dinners are scheduled for Sundays at 6:00 PM.

SUNDAY, APRIL 24
The Breakers (seafood)
400 Fisherman's Wharf*
Redondo Beach, CA

(213) 376-0428

*Take Torrance Blvd. all the way down to the ocean.

DUE TO THE LIFE AGAINST DEATH WEEKEND MAY 27-30,
NO SUPPER CLUB MEETING IS SCHEDULED FOR MAY