CRYONICS

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EDITORIAL MATTERS

This issue of CRYONICS represents a great deal of thought, effort and hard work—by writers and editors alike. As you may have noticed, this issue is almost double our regular length, and this is no accident. We have attempted to play catch-up and bring you a number of articles which bear on the stability of the brain and brain components during and after freezing. There is an ever growing body of indirect evidence which greatly encourages us that we are right. That our memories, personalities and identities can survive freezing. In order to spare those of you with a less technical bent from being overwhelmed by this presentation, we have included all of our regular features and tried to balance things out a bit with slightly longer than usual news notes and commentary. We think that this issue of CRYONICS is a good one, and we hope you'll agree that there is something in it for everyone.

CALIFORNIA PHYSICIANS AGAIN FACING TRIAL FOR MURDER

In the April 1983 issue of CRYONICS we reported on a rather amazing ruling by Los Angeles Municipal Judge Brian Crahan who refused to return murder indictments against two California physicians, Dr. Neil L. Barber and Dr. Robert J. Nejdl in the death of their comatose and brain damaged patient Clarence Herbert. The prosecution has appealed that decision and the ruling of Judge Crahan was overturned in Long Beach Superior Court. It now appears that unless Nejdl's and Barber's attorneys can successfully appeal this most recent ruling the two physicians will have to stand trial for murder. We will keep our readers posted on this case as it develops.

Our initial optimism about the significance of this case to cryonicists with regard to withdrawing life support in cases of severe brain damage so that cryonic suspension might begin is fading.

AND PEOPLE THINK WE'RE MACABRE

Several months ago a story appeared in the ORANGE COUNTY REGISTER and the LOS ANGELES TIMES which was right out of Dachau, DeSade or Chatsworth. It was reported that the Neptune Society and several other cremation organizations were disposing of deceased clients by stuffing three or four of them at a time into the cremation retort, and in some instances by dismembering them with power tools in order to completely fill the retort and thus cut fuel and labor bills. It was alleged that the Neptune Society in particular was aware that this practice was being used by the crematorium it employed for disposition of its member's remains.

This story has relevance to some cryonicists because Alcor and some BACS neuropreservation members have arrangements with the Omega Society, another low cost cremation service similar to the Neptune Society. We hope that by now all of our neuropreservation members have received the excellent mailing from the Omega Society decrying this practice and urging legislation prohibiting mass cremations and dismemberment without prior consent of the client or the next of kin.

At this point it is probably wise to tell our members and prospective members who are likely to join the Omega Society a little bit about the nature of their operation and how we came to arrive at an agreement with them. Approximately a year ago, Alcor began to look around for a way to solve the somewhat delicate problem of how to dispose of member's remains after neuropreservation. After many refusals by local morticians, we finally found a firm that was willing to do it—for the "slight" fee of $1,500! (Consider that

the actual cost of a cremation is about $70.00 at present.) Not wanting to expose our members to this kind of extortion we turned to the "cremation societies" and tried to pursue lower cost arrangements on a pre-need basis. One of the first organizations we contacted was the Neptune Society. To say that the treatment we received from the Neptune Society people was less than courteous would be an understatement. The upshot of our contact with them was the suggestion that large sums of money (similar to the arrangement we already had with a local firm) would be required. We were not impressed with their way of doing business.

Finally, we contacted the Omega Society. We found its proprietor, Mr. Jeremiah deMichaelis to be everything the Neptune Society people weren't. He was forthright, very direct, and the first thing he asked was to see our physical plant and records to verify that we were serious, credible and honest. We promptly obliged him on all counts, and after spending several hours together at Cryovita/Alcor we concluded an arrangement for cremation of our members' remains at no higher cost than any other Omega Society member pays. In turn, we looked into the Omega Society's operations and found them to be honest and the contractors they deal with to have good reputations. We wish to reassure our members who have made arrangements with the Omega Society that their remains will be handled with dignity and decorum and that there will be no co-mingling of ashes. While this may seem a trivial point to many cryonicists it is important to realize that we do not need any more public relations problems than we already have, and we certainly don't need additional grounds for the next of kin to complain. Please rest assured that we here at Alcor will continue to monitor the performance of our contractors and to select only the best available.

BIRTH OF FIRST HUMAN COOLED TO LIQUID NITROGEN TEMPERATURE EXPECTED

Recently the major wire services and science newsmagazines reported on the successful implantation of a human embryo which had been frozen to liquid nitrogen temperature for four months. Dr. Alan Trounson of the Monash University Medical School in Melbourne, Australia reportedly implanted the embryo in a woman with fertility problems approximately 14 weeks ago. The embryo was one of four which were successfully fertilized in vitro after the woman was superovulated. The first three embryos were placed in the woman's uterus shortly after fertilization with only one embryo implanting successfully. Unfortunately that pregnancy ended at eight weeks in a miscarriage. The fourth embryo was frozen at the time the other three were implanted and was maintained in liquid nitrogen storage for later use.

An article which appeared in SCIENCE NEWS (123 (19) 295, 7 May 1983) outlined a preparation prceodure similar to that now in use with cattle and other mammalian embryos for cryopreservation. The technical achievement of successfully freezing and thawing a humam embryo is not the significant event here. Rather, it is the tremendous ethical impact this experiment is likely to have. Already, some cryonicists are using this development to their advantage in dealing with fundamentalist, Catholic, or "right to life" skeptics who challenge us about the "problem of the soul." Any cryonicist who's been around for awhile has heard the question; "but where do their souls go when they're frozen?" Many, if not most of these people believe that the soul enters the body at the moment of conception. Hopefully very soon we will have the opportunity to point up that normal, healthy infants who were frozen for months, weeks or years as embryos can be born who are apparently not san souls. While this will not convince such skeptics that our approach is the right one, it will shut them up on this one point anyway, and further erode their position on

metaphysicial objections. We were able to quite effectively silence and/or embarass several dogmatic types we encountered at the Alcor booth during Future World Expo. In this battle every little victory counts.

ALCOR AND FUTURE WORLD EXPO

After a tremendous amount of work preparing for it, Alcor showed up at Future World Expo with more than a little doubt and trepidation about how we would be received and about how things would "go." At first, things did not appear to be going well. All of us staffing the booth were extremely nervous and unsure of ourselves; after all this was the first time any of us had ever done something like this. The initial reactions of passersbys was nothing to write home about either. As people walked over to look at our rescue mannequin hooked up to an HLR for transport there were more than a few gasps of incredulity when they found out what we were doing. But, thanks in great part to advice from Laurence Gale and Frank Rothacker, we rapidly learned the ropes. What did we learn? We learned that we should approach people walking by who glanced our way with good eye contact, an open smile and a flyer describing our activities. We learned that we should launch right into an explanation of what we are doing and why we think it is a good thing to do—don't give them the chance to say they're not interested, or to feel put on the spot by being asked if they want to hear about Alcor and cryonics. We also learned the importance of having an organized line of patter which covers all the points we wanted to make, and yet allows for enough variation to make it spontaneous and bearable for the person presenting it. These are all basic lessons in dealing with the public in an information-giving capacity. Old lessons perhaps, but without the good example and the good advice we were given we would not have learned them.

All of us at the Alcor booth felt tremendously positive about the weekend. We had a chance to meet and talk with personally about 2,000 people, and to put a copy of our flyer "Why We Are Cryonicists" into the hands of over 1,900 people. The two days following the Expo our answering machine was jammed with calls and we have several people who have made appointments to come visit the lab/storage facility in Fullerton. While it was an exhausting weekend for the staffers, we feel that we had an opportunity to reach an unprecedentedly large number of people on a personal basis with our message.

Perhaps just as important as what we learned about how to say what we have to say, was what we learned about the public's reaction to what we had to say. The issues of death occuring before the procedure takes place, brain damage and the lack of reversible freezing techniques seem to be uppermost in people's minds. We also discovered that a large percentage of people, as high as 80% by one informal count we did, were very concerned about long-term care and stability as a result of the Chatsworth debacle. Many people, perhaps as many as 15% to 20% thought that cryonics was no longer available and that the practice had died out with Chatsworth.

Several education areas seem urgently in need of work. We need to educate people about the nature of the dying process and to make them more aware that it is a process rather than a black or white, all or none event. We also badly need to offer more convincing evidence that the fine structure of the central nervous system is well preserved by freezing and that repair of injury that does occur will be possible. We are very weak on being able to provide believable scenarios for repair and reanimation. In short, a great deal of basic consciousness-raising remains to be done.

The final and perhaps the most important lesson to be learned is the one of human contact. Person to person contact with eye contact and an opportunity for visual scrutiny seemed to help build interest and kill hostility to cryonics.

People could see and evaluate us more intimately without the depersonalizing distance of radio, television and the printed page. We were also able to tailor our strategies based on feedback from the interested party. We could answer questions which were of interest to that person in particular, and we could back off on an approach which was giving a negative response. All in all it was a valuable weekend. We plan more such encounters in the future and we hope our objective of just one new person per such encounter or two can be realized. One thing's for sure, if we don't at least replace the people we have, we're going to fail in this endeavor. Perhaps the most basic thing we learned from Future World Expo was that people will be convinced of this idea or at least not be immediately turned off to it, only if we make a real effort to reach them with our message in a positive way; in as enthusiastic and articulate a manner as possible. That is lesson enough to have made the weekend more than worthwhile.

SIMON CARTER VISITS FROM CRYONICS ASSOCIATION OF AUSTRALIA

On May 14 Simon Carter, Secretary of the Cryonics Association of Australia visited the facilities of Cryovita and Alcor in Fullerton, California. Mr. Carter has been involved with CAA since its incorporation over three years ago, and has been involved in cryonics for over six years.

Mr. Carter reported that CAA, while small, is making definite progress. CAA's most important goal is to improve suspension capability in Australia. Mr. Carter emphasized that there are only six signed up cryonicists with a few "hangers on."

Mr. Carter stated he was very impressed with the facilities in Southern California and expressed the hope that CAA might move along the road toward complete capability if half a dozen or so more people can be involved in the coming years.

LETTERS TO THE EDITORS

Dear Editors,

About the joy of cryonics (see "Public Relations" in the February 1983 issue of CRYONICS). I read your piece and it woke some powerful memories in me, so much so that I wanted to comment.

I'll be blunt. Isolated as we are here, I just can't say that I've got much joy at all from being a cryonicist. It has been very slow, very frustrating, not only uphill, but almost VERTICAL work for years, and after all these years we've got a grand total of SIX cryonicists in Australia. Just before the February issue of CRYONICS which contained your comments arrived I had finished answering HONESTLY a letter from Western Australia from someone (I'm caricaturing a bit, but you can get the idea!) who seemed to believe that we were a large and prosperous organization. I most certainly do not find being a cryonicist a fun thing to do: not in any way or in any sense of the word "fun."

But what I would want to say to anyone who writes to us and asks about cryonics, young and old, is something that is really very hard to say but easy to show, that is if they will think about what is happening. I did not become a cryonicist because it is joyful or fun or any of those things, but because I became convinced it was my best, only, and even likely chance at immortality. To the 15-year-old who asked you, I would simply say that yes, he must have found a lot of people who seemed to feel that being a cryonicist was a terrible thing to happen. But then, IT MUST BE SOMETHING REALLY POWERFUL which convinces people to become a cryonicist even despite all those problems. It is not, after

all, as if we were born with the problem, like black skin or phocomelia. If we didn't want to be cryonicists all we have to do is to forget about the whole thing and go buy a videocassette recorder instead. But we're not going to do that.

I've often compared cryonics to a lifeboat, and I think the analogy is very close, so close it might not even be an analogy. Well, being in a lifeboat during a storm is not a very happy situation. It is incredibly grim, and anyone speaking to those people in the lifeboat should not be surprized that they fail to radiate happiness and optimism. But then, NOT being in a lifeboat would be FAR WORSE! If there is anything worse than being a cryonicist it is NOT being a cryonicist.

Long Life,
Thomas K. Donaldson, Ph.D.
Canberra, Australia

Dear Thomas,

Your letter woke powerful memories in me too. Memories of desperation and despair, of feeling helpless and defeated when I left Indiana and packed up Soma and IABS and moved to Los Angeles. I know so well what you are going through. One of the beauties of being here in Southern California is that for the first time I am dealing with and surrounded by cryonicists and I HAVE SOME HOPE THAT IF I DEANIMATE SOMEONE WILL EXERT A MAXIMUM EFFORT TO SUSPEND ME AND DO A COMPETENT JOB IN THE BARGAIN. The isolation is terrible. The insecurity of being the only one who will probably perform well in an emergency is almost unbearable. I know where you are coming from, but I cannot agree with the attitude of your letter and I stand by my original points.

You are wrong to some extent when you say we were not born with the problem. We were born with the problem. We did not choose to die just as we did not choose to be born. That ultimate insult to our freedom was imposed on us by biology, by nature, by the universe. It is just as much a curse of fate as being blinded or crippled. It is important to realize and to keep always in mind that cryonics is not the cause of our problems but in a very real, almost religious sense, is our only chance of salvation.

I didn't mean to imply that cryonics is fun in the sense of going to the movies or even adding a room to your home. Cryonics is not fun for most of us, but it is, it should be joyous. Without cryonics, we would be in total blackness, as hapless as poor Unamuno and as broken and bitter as all the other hopeless, devastated men and women who truly faced and realized the fact that they were going to die—and could do nothing about it. For that reason alone I think we should have some deeply positive feelings of warmth and joy that we are cryonicists. Even in my blackest moments I am comforted by the fact that cryonics exists, and my very blackest moments have been nothing but wrenching doubts or great concerns that cryonics might might not work for one reason or another.

From a purely selfish point of view surely you must realize that optimism and joy, even if we don't always feel them, are important things to project. I'd much rather climb into somebody's lifeboat (if I had a choice) who was good humored, patted its stern and said to me; listen friend, this going to be one hell of a trip, and we may well not make it but by god we've got this boat, and we've got guts, and we're going to give it one hell of a try!" than I would climb into a boat captained by a fellow who proceeded to tell me about how miserable a thing it is to be stuck in a storm, how inadequate lifeboats are and how we're all likely to starve to death and be eaten by sharks for our troubles

anyway. Many people do not become cryonicists all at once. They come to understand things slowly, and their first impression is an important one. Steve Bridge, the other editor of this magazine, was such an individual. I feel certain that if his first contacts were negative ones, he would probably not have become involved. We are not all born zealots or instantly transformed into them. For many of us it is a long, slow personal odyssey, precarious at first. Remember that many people are attracted to this idea at first because they are just beginning to deal with the unhappiness that accompanies the realization that they are really going to die. I think it is important that we don't give them the impression that cryonics is something worse.

I feel so much for you and your suffering. I and the other people in Alcor have tried to do what we can within our meager limits to be of help. We will continue to try and help. Nevertheless, I feel compelled to point out that if you reach the point where the day to day struggle leaves you angry, and bitter, and drained, you should think about cutting your load. Come to Los Angeles, or San Francisco and at least know that you won't have to worry about the most basic things. Know that such a move can be not a defeat but a profound opportunity to grow and make cryonics grow. I cannot describe the relief and the increased productivity I have experienced in making such a decision. Know also that such a decision carries with it sacrifices: lost employment opportunities, social disruptions, broken relationships. Only love of life and a personal determination of what that is worth can guide you in such a decision.

I hope you and your cohorts remain in Australia. I hope you grow strong and independant and that you can act to shelter us should adversity beset us here. I hope also that you can realize that finding some reason to feel hope and joy when you talk to others about cryonics will be essential to your success. Maybe cryonics is a pretty grim business. But then, so is birth, and even through the worst of it mother and child find some comfort in knowing that without it there can be no life. So, as we sit in this lifeboat and wait out the storm and darkness for rebirth, let's see if we can't manage a brave song or two and a little good cheer that we're in a lifeboat and not lost amongst the waves.— M.D.

Dear Editors,

For the record, your statement in CRYONICS that I first heard about cryonics when Bob Nelson came to my high school could not be further from the truth. I first heard about cryonics from Rosenfeld's control of life series in LIFE magazine, then I heard about it by finding Ettinger's books in a bookstore, and finally I heard about it by looking up "immortality" in the Reader's Guide to Periodic Literature. Your main point is correct: I was young throughout all of this, beginning it all around age 15. I would not have gotten involved without the influence of Curtis Henderson and Saul Kent, because they and they alone convinced me that they were serious about the idea so that I would not be taking on the world by myself. Nelson, by contrast, was the last person to get any information to me! And when he came to my high school to speak, it was because I invited him.

Corey Noble, Ph.D.
(Corey Noble is a pseudonym)

Dear Editors,

I wish to comment on two recent articles in CRYONICS, which I believe in some respects give a distorted picture of current cryonics activity and plans in Northern California. I recognize that it is natural and fitting that Alcor's publication will tend to represent the position of Alcor and their editor-members. I also realize that Northern California cryonicists are at fault for not sending down more articles describing our activities, in spite of the expressed urging and willingness of CRYONICS to publish such submissions. Perhaps this letter will help fill the information gap.

1. The article "A New Direction for BACS, TRANS TIME, and ALCOR?" (March 1983) states that "According to Lee Gabriel, BACS intends to chart a new course which includes decreased emphasis on cryonics and increased emphasis on the Life Extension Sciences such as gerontological counseling and products." This part of your article has been further over-interpreted by some readers to mean that we we are phasing out of the cryonics business.

I am unaware of any proposal to decrease emphasis on cryonics, by either BACS or Trans Time. We have considered the fact that in spite of the substantial publicity we have been able to generate for cryonics, the ranks of signed-up cryonicists remain small, and hence dues revenue and volunteer labor are barely able to cover the costs of keeping our doors open to provide the desired services. The broader program of Life Extension, including comparatively easy strategies such as nutritional and pill regimens, is much more acceptable to the public -- witness the tremendous success of Life Extension (Pearson and Shaw). We are actively considering broadening the scope of services we offer, by offering products such as vitamins and future-oriented books, and services such as connection with medical clinics promoting life extension. We hope that this increased scope will produce revenue and some additional members for our primary concern of cryonics. This is much the same strategy that Alcor adopted some years ago, at the time it changed its name from the "Alcor Society for Solid State Hypothermia" to the "Alcor Life Extension Foundation."

2. The article also states "BACS is apparently in the process of choosing to remove itself as a major interface between Trans Time and its members," and goes on to state why this is a bad idea.

But this is not the plan. Attorney Jim Bianchi has been preparing an extensive set of documents for use in arranging for cryonic suspension. Jim has recommended that Trans Time should contract directly with cryonics clients, for services rendered before death, such as enrollment and emergency responsibility. But the documents still provide that suspension funds available upon death go to a trustee, to invest and dole out to the service organization as services are rendered, and BACS is a leading candidate to be such a trustee. BACS would thus remain as a "major interface" between Trans Time and the deanimated member.

3. An earlier article "Unlocking the Directorates—BACS and TT Disagreement"

(July 1982) reported on problems experienced last year between the two organizations, particularly over fees for services and the establishment of a service contract. But most of the disagreement resulted from the positions of one or two BACS Governors, and since the January 1983 election of BACS Governors, neither of them are on the BACS Board. Since this election, former problems between the two organizations have been rapidly resolved. BACS has become current on its bills to Trans Time. And after a six year gestation period, BACS and Trans Time have just again signed a full cryonics service contract! The reasons for this long delay are various, but as a result we have one very thoroughly inputted and reviewed contract. And peace once again reigns in the valley.

One valuable part of the contract is a statement of Trans Time "Policy and Practice Concerning Suspension Services Rendered," which I have attached to this letter.

Evermore,
Art Quaife, President
Trans Time, Inc.

CRYONICS SCIENCE UPDATES by Thomas Donaldson and Corey Noble, Ph. D.

IS AIDS LINKED TO HEPATITIS?

A recent paper in the NEW ENGLAND JOUR MED (308 (1983) 125-9) reports that (for some reason unknown: perhaps God hates Haiti) normal heterosexual Haitians, who are not drug addicts, can also suffer from AIDS. Many popular publications have already reported this fact: the authors of the paper, J Vieira et al, found 10 Haitian men who suffered from AID at the Kings County Medical Center in Brooklyn during 1981-1982.

This paper is particularly interesting for several suggestive facts it reports about these 10 patients. They report that 86% of all Haitians show blood markers suggestive of present or past infection with hepatitis B. Of course this is an unproved connection, but homosexuals and drug addicts also often suffer from hepatitis. Five out of the 10 patients had also undergone treatment for tuberculosis at one time; some of the drugs used might depress the immune system and make them susceptible to AIDS.

So far, of course, all is confusion about AIDS. The closest analogy to AIDS in my mind is Legionnaire's disease. Certainly doctors first discovered it in members of the American Legion, but not long afterwards they were finding it in many people where before no one had recognized it. No one claimed that we could protect ourselves from the disease simply by not joining the American Legion.

EDITORIALS IN MECHANISMS OF AGING AND DEVELOPMENT

Many people eventually became cryonicists not in spite of, but BECAUSE, they came to understand the widespread apathy among outsiders about the problem of aging and death in general. True, the band of cryonicists is painfully small; but after some years of watching developments in the field eventually it dawns that CRYONICISTS ARE THE ONLY PEOPLE AROUND, and all the rest is gaseous blunder. I have myself noticed among people interested on longevity (but not yet cryonicists) a delusion that large numbers of scientists care about and are working on the problem of aging, and that of course this work will produce immortality without any need for them to make hard choices. They seem to live in a world of crash programs in which governments inject large amounts of money into aging research. Curiously they do nothing themselves, even for research on aging. They believe in progress, but haven't really noticed that progress happens only at the rate at which people come forward to make it happen. What they don't notice, of course, is that THEY ARE ON THEIR OWN COMPLETELY!

One of the oddest things about aging research is the quite fantastic double standard people, doctors, and scientists have on the question. Recently MECHANISMS OF AGING AND DEVELOPMENT published an editorial, "On aging research and the borders of the self", (20 (1982) 267), presumably by Strehler (although I don't know this for sure since the editorial was unsigned) discussing, of all things, the problem of identity and survival after death. Don't get me wrong: Strehler wasn't being mystical. Instead he decided that we could perhaps get some consolation from the fact that even after we die other people will have the same kind of sense of individuality and self as do we.

Perhaps his ideas make some kind of sense, IN THEIR PLACE. But if the journal publishing them were, say, CANCER or DIABETES most readers would feel Strehler needed a SANITY HEARING. "We might never be able to do anything about cancer", he might say, "but if you are dying of cancer it may be some consolation to know that other people in future will have the same sense of their selves as you have of YOUR self!" And this in a journal which claims to be published by and for scientists studying biological aging, we HOPE for its medical application.

The fundamental problem is that even gerontologists do not feel or react to this problem of aging as one which concerns them deeply. It's much more a <u>philosophical</u> problem than a medical one: an interesting puzzle, yes, on which we might even build a fruitful academic career. It's certainly not MY arse which is at stake. There does not now exist, and will not exist for many many years, the kind of consensus that produces a March of Dimes or a War on Cancer for aging research. By now there are a lot of drugs which MAY help aging: if someone suffers from cancer, doctors administer drugs which induce constant vomiting, make the hair fall out, and destroy the immune system. If the problem is aging,

they go all shivery at the thought of BHT which does none of these things, and they ask about the SIDE EFFECTS. To actually administer or take drugs for aging is a fringe activity. Given all of these attitudes and the way in which people's ideas change so slowly, how is it possible to really believe that antiaging research will make YOU immortal?

MEMORY AND CYCLIC AMP IN MICE

We have recently published several articles dealing with recent work on memory, particularly in the mollusc Aplysia, the sea hare. One of the more recent discoveries coming out of this work is the observation that a special chemical, cyclic AMP (adenosine monophosphate) plays a critical role in memory, at least in the sea hare.

Often in the action of drugs or hormones of many kinds the drug binds to a special chemical in the outer cell wall (the receptor), and the bound pairs of receptor-drug then cause increases in special internal messenger chemicals inside the cells. Cyclic AMP is one of these messengers, and many different drugs and hormones cause it to increase or decrease: insulin, ACTH, and glucagon among others. Exactly what happens within a cell once the level of cyclic AMP has changed of course depends on the cell type: liver cells respond very differently from brain cells, in that high insulin levels (and consequent decreases in cyclic AMP) cause them to cut down on release of glucose, while brain cells do not release glucose and so will not respond this way.

However brain cells, in a sense, store and release memories and these recent discoveries on cyclic AMP in Aplysia suggest that it is involved in this storage and release. However we are fundamentally less interested in release of memories in molluscs than we are in release of our own memories, and we would like corroboration of these discoveries on mammals.

An interesting paper by D Quartermain, CT Randt et al in PHARM BIOCHEM BEHAVIOR (17 (1982) 677-680) has just reported a new drug which can increase memory ability in mice and which improves the evidence that cyclic AMP plays an important role in memory. The drug is Rolipram, and these scientists have shown that Rolipram will actually reverse the amnesia caused by anisomycin, a drug which inhibits synthesis of proteins and therefore prevents longterm memory formation. They first gave anisomycin to their mice before training, then gave Rolipram immediately afterwards. They trained their mice not to lick water from a special dispenser; the dispenser not only dispensed water but also an electric shock. Control mice which did not receive Rolipram but did receive anisomycin would forget their previous bad experience with the water dispenser and lick it very soon after their next exposure to it, while experimental mice would take much longer.

Rolipram inhibits the special enzymes which break down cyclic AMP in the brain, and therefore it will keep levels of this chemical in brain cells higher for significantly longer. Other drugs will have a similar effect: papaverine and isobutylmethylxanthine (a drug related to caffeine) will inhibit the same enzymes, although less strongly, and other scientists have reported that these drugs will enhance the learning ability of animals receiving them (A Routtenberg, HJ Kim in CHOLINERGIC MONOAMINERGIC INTERACTIONS IN THE BRAIN, ed L Butcher 1978). This more recent report by Randt, Quartermain et al shows that a similar drug will not only improve memory but reverse an amnesia caused by another drug.

Randt, Quartermain et al also directly studied the levels of cyclic AMP both before and after giving their drug to mice. On testing the brains of treated mice they showed that Rolipram would raise the amounts of cyclic AMP in three different brain regions, the frontal cortex, the thalamus, and the hypothalamus. This provides additional evidence that cyclic AMP plays an important role in formation and storage of memories.

This work only indirectly tells us how memories get transferred to longterm storage. The role of cyclic AMP here is that higher levels of cyclic AMP occur just after learning and seem somehow to promote transfer of memories to longterm store. In a sense, Rolipram would act by increasing the length of time our short-term memories remain active. However the likelihood that cyclic AMP mediates this transfer to longterm storage does suggest something about how longterm storage takes place: cyclic AMP often acts by causing chemical modifications to proteins. It is also very suggestive about drugs which may improve memory: at least one report says that papaverine will improve memory (JA Yesavage et al ARCHS GEN PSYCHIAT 36 (1979) 220-227).

TEN BILLION TINY COMPUTERS

Few cryonicists would feel surprized to hear once more that we STILL don't know how longterm memory is stored, and therefore have no proof of its stability against the injuries attendant upon "death" and freezing. However three very important papers in the 28 January issue of SCIENCE (219 (1983) 397-408) describe some very significant inroads upon the problem. Indeed, given funding, we now have good reason to believe that the problem will not only be solvable in the near term, but that simple experiments possible on a relatively low budget would confirm or fail to confirm stability against normal injuries.

The papers concern conditioned learning in the mollusc Aplysia, the sea hare. Already many neurologists have studied the sea hare, so closely that they have actually worked out maps of circuits between individual neurons. In the first report, Kandel, Carew, and Hawkins describe their work on differential conditioning in the sea hare. Differential conditioning is a quite uncomplicated idea: in ordinary associative conditioning an animal learns that one stimulus (the conditioned stimulus, say the ringing of a bell) precedes another: the arrival of food. The animal will then salivate whenever a bell rings. In differential conditioning, the animal is presented with two different stimuli (say, two tones of bell) and learns that one bell precedes food while the other does not.

Everyone reading this will recognize that Pavlov first worked out associative conditioning in dogs many years ago, and since then scientists have shown that many different vertebrate species could learn these associations. But it was only in the 1970's that neurologists showed that many different kinds of invertebrates also show associative conditioning (GJ Mpitsos et al SCIENCE 180 (1973) 312 and others). This fact is important because associative conditioning is one of the simplest kinds of learning, and simple animals such as Aplysia or cockroaches have simple nervous systems whose actions are much easier to trace out in detail.

On the scale of "learning-like" behavior perhaps first would come habituation, in which an animal might learn not to respond to a stimulus to which it had formerly responded; next would come associative conditioning, in which the animal learns an association between one stimulus and another, and third would come differential conditioning. But the most important fact for memory studies in this work on Aplysia is that (as is very much not the case in mammals or vertebrates) because we have maps of the nervous system we can trace out EXACTLY which nerve cells change when the animal learns. Knowing this, we can go on to study the biochemistry of the process.

In their first experiments with Aplysia Kandel et al taught the animals to associate a very weak touch to their mantle shelf or their siphon with a subsequent strong electric shock to their tail. They divided their animals into two groups, one of which was shocked after a touch to their mantle shelf and the other of which was shocked after a touch to their siphon; each group was touched at both locations. The animals successfully learned the distinction and would contract their siphons and gills when touched at the right place. What is most interesting about this experiment is exactly that the neural circuitry involved is precisely understood: we know exactly which cells are involved. In fact, Kandel et al could even train the animals to differentiate their response depending on whether they were touched on the top or the bottom of their mantle: and touch to the top or bottom of the mantle activates precisely known nerves in one particular cluster (the LE cluster).

In itself this paper says little about the physiology of conditioned learning in Aplysia. However in their second paper, in the same issue of Science, Kandel et al described their work with the electrophysiology of this response, together with a theory of how conditioned learning happens.

To explain their theory and the experiments supporting it, we can look at the very simplest kind of learning, habituation or sensitization. If we shock Aplysia in their tails while stimulating their siphons the nerves in their siphons will produce a measurably stronger electric response to stimulating. In other words, because of one stimulus to one set of nerves, another set responds more strongly. The anatomical work on neural circuitry in Aplysia has already shown that tail shock will excite a particular group of facilitator neurons, the L29 cells; it is these neurons in their turn which make the sensory neurons (which actually receive the stimulation to the siphon) react more strongly.

Kandel, Carew et al therefore surmised that in conditioning what happens is that the previous stimulation of the sensory neurons would increase the effect of the facilitatory neurons. This process would explain how conditioning could happen in animals such as Aplysia with very small nervous systems. To test this hypothesis, they duplicated the previous experiments with conditioning, only this time working only will nerve cell preparations from the animals and measuring the nerve cells' responses electrically rather than by the behavior of the animal. Molluscs such as Aplysia, unlike mammals, have very large nerve cells which can be easily stimulated and measured on an individual basis with electrodes.

Their hypotheses about behavior of this neural circuit turned out to be correct. The effect of the L29 cells was greater upon sensory cells which had just been stimulated than upon unstimulated ones. They were also able to exclude several other hypotheses: for instance, by measuring impulses in the facilitator cells themselves, they could show that it was the activity of the sensory cells which affected facilitation, and not the fact that both sensory cells and withdrawal-reflex cells had been stimulated at the same time. They could also show that the facilitation took place in the strength of response of the sensory cells, rather than in any increased sensitivity of the cells involved in the withdrawal reflex.

The last kind of conditioning, intensively studied by Skinner, is operant conditioning, which happens when one kind of response increases whenever it subsequently receives a reward. Kandel, Carew et al point out that similar kinds of nervous circuits could lead to operant conditioning also, and thus give us an explanation in terms of neural circuits of how learning takes place.

Finally a paper by Byrne and Walters describes some additional work and theory on the same lines; Byrne and Walters appear to have achieved much the same results as Kandel, Carew et al at much the same time.

There is more to this matter than a simple account of the experiments might suggest. In particular, the actual biochemical processes by which sensitization happens in Aplysia are relatively well understood. What happens is that cyclic AMP increases in the stimulated cells; cyclic AMP is a common intracellular messenger involved in many cellular reactions to drugs and other stimuli. When conditioning happens, Ca++ ions also increase within the cell, and the combination causes an amplification of the response.

How this response later encodes into longterm store still needs an answer, since neither the increase in AMP nor the increase in Ca++ could be permanent. What probably happens is that these increases cause the production or change of some special proteins in the cell near the synapses (where the nerve cells connect). What is important about this work is not its direct answers about longterm memory but the simple fact that until we knew how short-term memory worked we had no chance of deciphering longterm memory.

Even despite this these experiments tell us a good deal about memory and how our brains must store our identity. First, the mechanisms described make it virtually certain that we will never find, say, a special chemical encoding differential calculus, nor ever be able to "read out" a personality or memory like a computer tape. The "memory" described in Aplysia is not the mass memory of facts or how to do something of which we are consciously aware and which we ordinarily refer to as "memory". Instead it is learning carried out by individual nerve cells, which learn simply to respond with more or less strength depending upon input from one of a finite number of other nerve cells to which they connect. Each individual nerve cell therefore acts as a small computer, with both a memory store (very limited in our terms) and an ability to integrate and process the impulses from other nerve cells. Complete knowledge of the memory of any single cell will tell us nothing about the content of total memory, which from these experiments seems quite clearly a mass effect, the result of billions of cells working together. To read out someone's personality or memory, we would have to read out the individual memories of a high percentage of their brain cells. In that sense our brains are NOT single computers, but rather a very large number of computers all linked together in a network.

Furthermore, this work makes it seem increasingly unlikely that memory has anything to do with growth of new physical connections between neurons. The anatomy of Aplysia has been well characterized and remains the same for many individuals of the same species. Conditioning in Aplysia does not involve any change in this anatomy: that is, the network linking all of these computers remains constant during learning and comes inborn in the animal. If this is true for Aplysia we have little reason to believe that mammals are different.

What do these experiments and ideas have to say about durability of memories? As yet we still don't know the chemical nature of longterm memory, although this work takes some big strides towards uncovering it. On this point we are left with the same simple observations (that lowered temperature decreases rate of chemical reactions, and that very many biological compounds are very stable at cryogenic temperatures) as before. On the other hand, as a mass effect of many neurons our "memories" in the sense of our conscious memories will certainly remain recoverable even if some high percentage of the memory chemicals in individual neurons might be destroyed. The point here is simply that the full collection of memories of any individual neuron carries almost no information about our total memory; highly redundant, it could be destroyed without any loss.

Furthermore, the fact that nervous anatomy in Aplysia does not change significantly from individual to individual, and certainly does not carry memory, means that our own nervous anatomy is unlikely to carry any information about our memory or identity. It therefore follows that our brains could undergo very gross physical disruption (dicing into small pieces) without any loss whatever of the information involved in our memory and personal identity. Since the circuit diagrams for human brains remain known whether or not our own particular brain has its circuits

disrupted, all that would be required to recover us is to reconnect our dismembered neurons according to the circuit diagrams supplied.

Finally one suggestion about how revival could happen needs extensive revision in the light of these experiments. Often the idea of cloning is put forward as a form of revival; it seems to me that as commonly put this idea assumes precisely that we are a single computer with a single memory store, which need only be "read out" and then "written" to another brain. But if we are instead a network of billions of computers, to read out the memory we would have to read out billions of individual memories, for each individual neuron. This is not at all inconceivable, but any medical means to do this would involve control and sensing at so precise a level that the "readout" would be hard to distinguish from direct reconstruction and repair of the individual brain. Cloning or some other form of forced growth could of course be used to provide this reconstructed brain with a BODY, but that is another story entirely.

UNDERSTANDING GROWS ABOUT BRAIN INJURY

Cryonicists will hardly have failed to notice the work on reviving brains (and people!) suffering the effects of prolonged lack of blood flow or oxygen. A recent review article by ME Raichle in ANNALS OF NEUROLOGY (13 (1983) 2-10) sets out clearly just what level of theoretical understanding scientists have attained on the problem. One of the more interesting general facts which it lets fall is that neurologists working on the problem now quite widely believe that brain cells are much more durable than previously thought. All of this past work, which we have already reported in the cryonics press, has developed several main ideas, which should be worth summarizing here.

First, the two main sources of injury to brain tissue when blood flow or oxygen cuts off are lactic acidosis, the development of high acidity due to the accumulation of lactic acid, and disturbance of normal ion content in the brain cells. Cryonicists probably already know about damage due to lactic acidosis; common methods of cryonic suspension involve vigorous attempts to keep down acidity in the tissues of the patient. Disturbances in normal ion content involve both potassium and calcium ions. Increased potassium ions in glial cells causes them to swell and increases their metabolic rate in the absence of oxygen. This causes more injury due to lactic acid produced. Increased calcium ions in the nerve cells causes breakdown of cell membranes (releasing free fatty acids to cause more damage) and blocking the ability of the mitochondria to respire and produce energy for cell functions.

To date the idea that free radicals themselves cause damage to brain tissue when it suffers a loss of circulation or oxygen hasn't found much support. Another much more common idea about the reasons for damage to nerve tissue is that injury occurs simply due to lack of energy; however when scrutinized closely, the degree of cell damage doesn't correlate to the amount of

energy deprivation the brain cells have suffered. For instance, low levels of blood sugar cause a loss of energy in the cerebellum (the brain region controlling coordination) without at the same time causing cell damage.

One of the more puzzling facts about brain damage due to lack of blood flow or lack of oxygen is that partial blood flow or low oxygen levels have seemed to cause more damage than a total cessation of blood or oxygen. Neurologists can now give a good account of why this happens: the difference comes from lactic acidosis. When blood flow continues, the brain cells can produce lactic acid much more than they could with no glucose at all. This lactic acid then causes more damage then would otherwise happen. This explanation also accounts for the well-known greater ability of infants to survive loss of blood flow to the brain: their brain produces just as much lactic acid, but their blood-brain barrier works less well, so that the actual brain concentration of lactic acid is less.

This work suggests that future perfusions use verapamil or some other calcium blocker to deal with the injury due to ion concentrations. Since calcium ions also play a role in damage to cell membranes, particularly important in freezing, a calcium blocker ought to improve patient status a lot. It also confirms that we should vigorously deal with blood acidity as we have already done.

BRAIN CELLS SURVIVE 14 HOURS WITHOUT OXYGEN, 21 HOURS OF CYANIDE POISONING

We are all aware of the importance of cerebral ischemia to cryonics and of recent advances in the prevention and reversal of this type of damage. A recent paper ("Synaptic Activity Mediates Death of Hypoxic Neurons", by Steven M. Rothman, appearing in Science, volume 220, pp. 536-537, April 29, 1983) helps to focus attention on a possible mechanism for anoxic (lack of oxygen) brain cell death and strongly supports current efforts to prevent it.

Brain cells were grown in culture (where all conditions can be precisely controlled) for several days and then subjected either to anoxia or to sodium cyanide poisoning and the integrity of the cells monitored under the microscope. (Cyanide prevents mitochondria from using oxygen to generate ATP for cellular energy needs.) Untreated cells swelled and developed vacuoles (intracellular cavities) within one hour and began to disintegrate after 4 hours. (This does not necessarily establish the upper limit on the length of ischemic damage that can be reversed in the intact brain, because, among other reasons, it may take cells in the brain, as opposed to cells in culture, either longer or shorter periods to begin disintegration.) Cells treated with 10 mM (millimolar) magnesium chloride ($MgCl_2$) before and during anoxia or cyanide poisoning were not affected by either insult! When normal conditions were restored and the magnesium washed away, the cells behaved normally, even after 14-21 hours of insult.

Rothman suggests that magnesium protects by blocking synaptic activity. Interestingly, cells could survive anoxia in culture without magnesium if the cells were cultured for a time too short to allow extensive synapse formation before the insult was applied. If Rothman is correct, there may be implications for brain cell death produced under other circumstances, for example, during brain aging. But it is also possible that magnesium is acting as a calcium channel blocker, as would be suggested by the work of Blaine C. White, which has been discussed in an earlier issue of CRYONICS. Rothman did not consider the possibility that magnesium is preventing cellular poisoning by calcium.

(Continued on page 18.)

SURVIVAL OF HUMAN BRAIN SYNAPSES AFTER FREEZING AND THAWING

A paper of great importance for cryonicists ("Metabolically Active Synaptosomes Can be Prepared from Frozen Rat and Human Brain") has just appeared in the Journal of Neurochemistry (volume 40, 608-614, 1983). A synaptosome is a structure which can be isolated from brains and consists of a synapse complete with the portions of the cells on each side of the synapse which give the synapse its structure and identity. Most cryonicists will know that the synapse is a gap between two nerve cells across which chemical messages pass (in the form of neurotransmitters) from one nerve cell to the other, causing the receiving cell to either increase or decrease its activity. The cell fragments which form the synaptosome consist of the nerve end (complete with packets of neurotransmitter, mitochondria, and other apparatus) and a post-synaptic vesicle or sac made of post-synaptic membrane (complete with neurotransmitter receptors and other apparatus). Synaptosomes are living structures, and it is possible to test them for viability after freezing and thawing, which is just what the authors of this report (John A. Hardy et al.) have done. Both human and rat synaptosomes were isolated after thawing and their activities compared. Histologically normal human cerebral cortex was removed from patients during surgery for brain tumors or aneurysms to allow access to these structures.

The following results were obtained by freezing 1-5 gram pieces of brain immersed in 0.32 M sucrose. (Freezing homogenates gave poorer results.) The cooling rate (not measured) was slow and the warming rate (not measured) was fast; other cooling rate/warming rate combinations gave poor results.

Measurement made	species	% recovery*
number of synaptosomes recovered (for homogenates, the results were rat 66%, man 64%)	rat	80
	man	not done
amount of protein recovered	rat	70
	man	91
oxygen uptake/100 mg of protein	rat	59
	man	78
stimulation of oxygen uptake by veratrine	rat	86
	man	86
potassium accumulated/100 mg protein	rat	70
	man	86
loss of potassium caused by veratrine	rat	85
	man	39
retention of neurotransmitters	rat	good
	man	good
stimulated transmitter release (amount, selectivity, and drug modulation)	rat	good
	man	good

*recovery compared to unfrozen control samples

It is apparent that rat and human brain tissue frozen to -70°C with essentially no cryoprotection has synapses "closely comparable to . . . fresh tissue", as the authors conclude. It is also apparent that human and rat synapses are about equally resistant to freezing damage (although the authors mentioned less uptake of glutamate by the human synaptosomes). These results are very similar to those of Haan and Bowen (J. Neurochem. 37: 243-246, 1981), who froze rat and human cerebral cortex with 10% DMSO and measured uptake of norepinephrine (94-95% recovery for both rat and man) and incorporation of glucose into acetylcholine (89-100% recovery for rat, 85% recovery for human) and into CO_2 (86-100% recovery for rat, 78% recovery for man), and attributed most of this activity to synapses. These two papers, together with others in which rat brain (Life Sci. 28: 1147-1154, 1981) or rat superior cervical ganglion (Proc. Roy. Soc., Ser. B, 510-519, 1957) was studied, clearly establish beyond much doubt that the synaptic connections in the human brain will substantially withstand cryonic suspension. If nerve ends also remain connected to their neurons of origin, then the brain's "wiring" pattern (the blueprint for identity?) will also survive. We will be awaiting the final word on that question with some anxiousness!

AIDS: ARE MEDICAL PERSONNEL NEXT?

Recently this journal carried correspondence on the problem of AID (Acquired Immune Deficiency). It's certainly true that AID at present seems to afflict mainly homosexuals, but it certainly doesn't follow that it might not spread in future to other groups nor that it ONLY afflicts homosexuals. I myself don't feel that AID is a major danger, although it is certainly a terrible thing to happen to anyone who acquires it.

In this vein, a recent article in NEW ENGLAND JOUR OF MED (20 Jan 1983, 156) by Masci and Nicholas describes the precautions one hospital has taken to prevent the hospital personnel themselves from catching AID. As yet we don't know how AID travels from person to person (this alone should really be enough to cause ANYONE some disquiet even if not panic). On the hypothesis that AID may resemble hepatitis in its mode of transmission, Masci and Nicholas recommend using gloves during all blood drawing and direct contact with secretions, labelling and bagging of blood specimens from patients with AID, and disposal of all needles and syringes used on them. Hospitals already have standard practices for isolation of patients with hepatitis B: for instance, dialysis machines used for them are separate. These procedures should be used.

Furthermore, it usually takes some time to diagnose AID; all these isolation procedures should be used for patients even if it is only strongly suspected that they suffer from AID. This includes all those under 60 who are strongly suspected to have Kaposi's sarcoma (a form of cancer typical in AID patients) or infections characteristic of immune deficiency, or Haitians, or hemophiliacs, or homosexuals with fevers which are not readily diagnosable.

A significant number of people on suspension teams are medical or paramedical personnel. This means that they too might be at risk, just as they are at risk for hepatitis B. They would then have to be frozen by other suspension team members; and these pointers may help prevent cryonicists from losing ALL their qualified suspension personnel.

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Regardless of the mechanism, there may be practical consequences of this paper. Rothman himself points out the difficulty of using magnesium clinically, but it is not certain that this is impossible or that magnesium in combination with other treatments would not help to prevent or reverse ischemic brain injury. Those of us taking magnesium supplements as an anti-aging modality may feel just a little bit safer! But the main implication may be in experimental or clinical cryostasis procedures. 10 mM $MgCl_2$ in the perfusate might be a good insurance policy in experiments and might even save some brain cells in clinical procedures. At the very least, Rothman's work should lead to a much better understanding of brain cell ischemic death, with all of the spinoffs that will come from that knowledge.

WHY PERSONALITY SURVIVES **by Thomas Donaldson**

One of the fundamental ideas of cryonics is that our SELVES, that is, our personality, memories, and everything which essentially makes us ourselves (and including and especially everything which gives us our own sense of consciousness and continuity) have far more durability than the commonalty believe: that our selves survive freezing even given present conditions, that they survive the so-called "death", and that we have every reason to believe that this survival can be demonstrated by actual REvival by sufficiently advanced techniques.

In essence the argument for this survival rests on simple, nonmystical observations no one could deny. Unfortunately at this time they don't definitively PROVE our case. Yet that misses the point: we can't PROVE that memory will survive, but still WE HAVE OUR REASONS. Many people would also think our reasons outrageous, but that also is not an argument. In bare form, our reasons consist of the observation that we are not only PHYSICAL beings, but very complex physical beings, even and especially in the structure of our brains; that "death" and even cryonic suspension cause comparatively few changes in this structure, and that therefore ONE WAY OR ANOTHER all of the information which specifies you or me as an individual, including all of the information which makes me, me, and you, you, is highly likely to survive in some form. To restate the proposition: our memories and selves are unlikely to be coded in only one form in our brains, and the survival of even only ONE of the forms of memory and self will be sufficient to allow an advanced medical science to resurrect us.

However put so barely the argument needs filling out. What would need to be discussed would be the many possible forms in which this memory and self might be encoded and their likely resistance to destruction. What is to keep ALL of the forms of the code from being destroyed? We are frozen because we think that freezing will preserve more; it must follow that SOME degree of destruction would mean our total destruction.

I shall begin by explicating some of the logic of our proposal. In fact, since right now we know so little about memory, a lot of what I'll have to say will consist of logical analysis. But to begin, what would be so important about our complexity?

To recover someone after their suspension is likely to be a form of inference and detection. In order for inference and detection to have the best chance, there must exist a trail of clues to the former state of our brains. Any incident, fact, or event is going to be more or less recoverable depending on whether or not it leaves traces; to be complex rather than simple means in this case that the fact or incident would have many consequences of many different kinds and so leave a correspondingly wide variety of traces from which inference could proceed.

Analysis of how such detection might actually proceed brings out

another point which badly needs saying. The survival of traces from which memory can be recovered is not at all the same as the survival of the "usual memory storage device" (whatever that may be) of a patient. We must expect that memories leave many traces, not merely traces on those devices in our heads which are specifically designed for memory storage. Here is an analogy: a detective may recover evidence of a murder by examining dog hairs found on the seat of a car. Someone might ask: but what have dog hairs, or cars, got to do with murder? They normally have nothing to do with murder, nor were they left there to provide clues; it merely happens that for THIS murder dog hairs and cars had a lot to do with the event. Nor does it have to be that such traces must be simple, or easy to find, or obvious as soon as we understand how memory is normally stored, or recoverable merely if the person who died is revived, no more than it is necessary for the detective for a relation between dog hairs and murder to be any of these things. It is sufficient for our purposes if evidence survive that a memory passed this way.

Given all this, what are the treatments that memory is KNOWN to survive? What are the treatments which memory will PROBABLY survive? And perhaps most important, what does this suggest about the variety of traces which memory and personality might leave on the brain?

Even at this time, with so little known about memory or personality, quite a few treatments will produce clear survival of memory. First, it is clear both from the clinical reports of people revived after as long as an hour of clinical death at room temperature (Medical World News, 18 Jan 1982) and the work of Audrey Smith in the 50's with hamsters and rats that MEMORY DOES NOT REQUIRE ONGOING ELECTRICAL OR CHEMICAL ACTIVITY FOR ITS SURVIVAL. This means in particular that survival of memory does not need continuous energy input to the brain, and strongly suggests that it is encoded in some form more like structure than like a pattern of activity; exactly WHAT structure of course remains to be found.

Second, Paul Pietsch and others have already carried out an extensive series of experiments in salamanders. These experiments document the survival of behavior patterns, including learned behavior patterns, in pieces of brain transplanted from one animal to another, even across species lines (in fact, even between FISH and salamanders). It is important to analyze exactly what these experiments show. They all depend on the ability of salamanders and fish to regenerate part of their central nervous system; we unfortunately lack that capability (it has never failed to amuse me how when an animal has a capability we lack, that is because it is PRIMITIVE, while when we have a capability which it lacks, that is because we are ADVANCED!). But the ability to regenerate a damaged nervous system would not be enough to allow a transfer of memory by a transplant, since the nervous system might have conceivably regenerated without ever showing signs of the memory. What these experiments suggest very strongly is that the NORMAL STORAGE OF MEMORY DOES NOT REQUIRE

ANY PARTICULAR AREA OF THE BRAIN FOR SURVIVAL OF A PARTICULAR MEMORY. The much earlier work of Lashley, in which he removed parts of rats brains to see if they still remembered how to do particular tasks, supports this conclusion: memory is normally stored in some fashion with a very high redundancy.

That survival of memory need not require survival of its NORMAL form of storage should be quite significant here: its survival is even more likely than the redundancy of normal storage would suggest.

Furthermore, Pietsch's experiments upon analysis suggest a good deal more. I have said that memory may be stored in some structural change in the brain. Since the brain has a complex structure, many possibilities exist for that structural change. To discuss and analyze these possibilities I shall first review the elementary structure of our brains.

Neurons are not simple entities, nor are the wiring connections, the axons and dendrites, simple undifferentiated wires. Described in very general terms, neurons contain a cell body (the SOMA) just like most cells, together with a large number of NEURITES which connect it electrically and chemically with other neurons. The term "neurite" is a general term for a "wire-like" part of the cell; often, however, neurites of particular cells easily fall into two classes, the DENDRITES and the AXONS. (One class of nerve cells lacks distinguishable axons, although they do have neurites: these cells are called AMACRINE CELLS). The dendrites are the principal parts of the cell specialized for reception of inputs (unfortunately for clean theories, however, they will sometimes also send impulses!). Dendrites as a recognizable type of extension from the nerve cells don't correspond to the extensions in the cells of invertebrates. Although dendrites can be quite long, they tend to be shorter than axons and much more highly branched; one of the characteristic properties of AXONS, absent in dendrites, is the presence of a SHEATH, which consists of the cell membrane of specialized glial cells (the oligodendroglia in the central nervous system and the Schwann cells in the nerves to the rest of the body). These sheaths act as insulation, apparently even in an electrical sense, and increase the conduction velocity of the axons, specializing them for long-distance conduction of impulses.

Perhaps for our purposes the most important structural characteristics of neurons consist of their INTERNAL arrangements. Like most cells, neurons contain a nucleus, mitochondria, and endoplasmic reticulum (internal membranes which are sites of cell metabolism). Besides these structures, however, neurons contain others: neurofibrils, fibers which under an electron microscope appear of two types, the neurofilaments and the microtubules. Neurofilaments are indefinitely long, unbranched, and extend as fine threads through the bodies of the neurites; microtubules are also of indefinite length, but have a different wall structure. Both structures appear to have a role in the TRANSPORT of substances within the neuron, in particular

in transport down the lengths of the neurites. A second distinguishing structure of neurons are the Nissl bodies; these contain ribonucleic acids and many ribosomes; they are sites of protein synthesis within the neuron, of which a great deal takes place as part of the normal workings of the neuron metabolism. Neurons contain both of these kinds of structure very densely in their cytoplasm. Finally, of course, neurons contain many SYNAPSES; these are the points where a neuron makes contact with another. Just as neurons are not undifferentiated wires, synapses are not undifferentiated connections, nor are they of only one type. The same neurons may connect at several different synapses and several different parts, synapses between the cell bodies, the dendrites, or the axons. A characteristic of synapses is that they conduct in one direction only, so that the anatomy of a synapse on one side of the circuit differs from that on the other. Cell surfaces at the synapse appear thickened, containing vesicles which enclose chemicals for transmission of impulses between the neurons (these vesicles are in their turn of at least four different types, depending on the chemicals contained); synapses also have characteristic chemical structures which link them very tightly to one another. The binding is an ionic chemical binding; it resists most treatments and will return if the ionic solvents which break it are removed. Indeed the binding is strong enough that the tightly bound membranes on both sides of a synapse can be dissociated from their cell bodies and studied as independent preparations. Finally, just as the "sending" side of the synapse is specialized with synaptic vesicles and special structure, the "receiving" side is also specialized, particularly with receptors for the different chemicals which carry a transmission.

We can now step back from this detail for a moment and draw some conclusions. Even at this level, we have many quite complex structures, of which some are certainly going to survive all reasonable (and some quite unreasonable!) treatments of the brain. What, then, are the likely ways in which our brains might store memories?

POSSIBLE FORMS OF MEMORY STORAGE

1. Memories might be stored in the topological connectivity of the neurons within the brain (that is, in the actual physical wiring diagram of the brain). Many writers about memory unfortunately use the term "connectivity" to describe almost any relation between neurons synapsing upon one another; by "topological connectivity" I mean the existence of a synapse between two neurons, with no prejudgement as to its properties or whether it may be unique or one among many.

2. Memories might be stored by means of differences in the number or type of synapses connecting two neurons. Neurons might connect in many ways; memories probably code in a much more precise way than simply in the existence or nonexistence

of a connection. However for this possibility I intend that synapses of a given (fixed) type respond identically; the coding of memory would not involve any chemical coding at the location of the synapses, but rather choices in the location and number of the synapses.

3. Memories might be stored in a propensity of the individual synapses to respond one way or another depending on stimulation. Here again, a lot of confusion persists. If there is more than one synapse between two neurons, different synapses may behave differently. The response of neither synapse need be simply "all or none"; in particular, a synapse may respond to one class of impulse and not to another.

We'll have to realize first that all of these kinds of storage must be linked together. If memory consisted SOLELY of the topological connectivity of the brain cells, then it is quite hard to see how any neuron could perform any integration or choice among its inputs: a single impulse would cause an all-or-nothing transmission; how then could NEW connections come to form? And if memory consisted of a change in propensity to respond, then to recover that memory in practice we would also have to know how the neurons containing it were topologically connected to one another (otherwise the incorrectly wired neurons would merely produce a mish-mash of response).

A second point which becomes very plain indeed is that "memory" in the sense of our personal memories and our personal sense of remembrance must involve the integrated action of BILLIONS of individual neurons. The memory is a mass effect of the action of many neurons, rather than the single effect of a few. In one sense, single neurons would "remember" and contain "memories", but these memories stand at a much lower level than our personal memories: the neuron remembers how to respond to a certain constellation of input from other neurons, while WE remember the smell of tea in our grandmother's kitchen.

This character of memory probably underlies the experiments of Pietsch. In order to transfer a memory by transplant of a PART of a brain, the recipient brain must be able to deduce from the activity pattern of the transplant what the proper activity pattern for a whole brain must be. It's particularly interesting that the neither individual neurons nor the parts of the brain need to be redundant for such a recovery to be possible: the activity pattern (which is the memory of which we are aware) occurs on a quite different level. For CRYONICS purposes, of course, we don't even require that our revived brain have any independent capability to recover this pattern of activity, it is enough that the information exist in some form.

Pietsch's experiments show us more. If our conscious memory depended upon a precise set of connections of some of our neurons with others, and would be disrupted if these connections were destroyed, then we would not expect that transplant of brain

parts could transfer memory, since it would be unlikely that the neurons of the donated part would form precisely the correct connections with those of the recipient. It may happen, of course, that underlying a particular connectivity there were other chemical markers on the cell membranes involved which would specify what these connections OUGHT TO BE, but if so that would mean precisely that memory consisted of more than the topological connectivity of the neurons.

I shall now analyze these three possibilities, "storage as topological connectivity", "storage as type of connectivity", and "storage as a propensity to respond" more closely, with special reference to cryonics.

For cryonics purposes it is not critical exactly how our memories are stored, so long as this storage leaves many traces. What, then, are the traces left by each of these three possible forms of storage?

If two neurons are connected in life, this connection may break after the injuries which caused deanimation or after suspension. To repair the patient we must somehow recover the connectivity which was lost. The anatomy of the brain is such that neurites, in many regions of the brain, form a mat of neuropile the exact connectivity can become very hard to trace visually. BUT we don't have to rely only on visual tracing: since neurons are not undifferentiated wires we would have to expect that even if a neurite is cut we will have more than simply the cut ends to give us clues to reconstruction. In the first place, we have already seen that neurites carry biochemicals of many kinds, enzymes and amino acids, between the cell body and the synapses; neurons themselves also differ from one another in many ways, each of which is likely to leave markers on the cell. Over forty different ways in which neurons can differ from one another have been distinguished; if two fragments of neurite belonged to the same cell originally (before the damage which caused death and the damage of suspension) then they would have to be IDENTICAL on all of these criteria. Once frozen, of course, the cells would retain whatever markers or biochemicals they carried indefinitely, and we can recall that whatever biochemical or marker does survive, it need have nothing intrinsic to do with memory, any more than dog hairs have to do with murder.

What then about the second possibility, differences in the number and type of synapses between neurons (where the existence of a connection between these neurons would not be in question)?

The most important point I can make here is that the SYNAPSE itself is quite durable, more durable than the actual cell walls. As an ionic binding, chemicals with similar ionic binding will tend to separate synapses; 1 molar solutions of NaCl will separate synaptic bindings, but even the separated cell membranes will retain thin connecting filaments (Pfenninger, KH J. ULTRASTRUCT. RES 34 (1971) 103-122; 35 (1971) 451-475). Furthermore, the membranes on both sides of a synapse have a

special structure: in the electron microscope the cell membranes at a synapse are thickened and chemical studies show that they have a characteristic composition different from that of the normal cell membranes; it therefore follows that BOTH THE CELLS OF ORIGIN OF THE SYNAPSES, AND THE FACT THAT A SYNAPSE EXISTED AT THAT LOCATION BETWEEN THESE CELLS, WILL SURVIVE FREEZING AND MOST LIKELY DAMAGE TO THE BRAIN. Finally, if synapses differ in type (whether because of differences in the neurotransmitting chemicals used, or in their structure) these differences are likely to survive also.

In addition to the class of synapse which might carry memory in connecting two neurons, some further possible ways in which synapses may differ need discussion. One event which often happens in development of the nervous system, and may also occur with learning and experience, is the formation of dendritic spines. These are stalklike bodies projecting from the cell membrane and containing synapses with other neurons. One form by which memory might code could be whether or not the synapses were located on dendritic spines or not. Whether or not a region of the cell surface forms a dendritic spine must be determined by some characteristic chemicals (as yet unknown) forming its structure; these are highly likely to survive both freezing and other cellular damage.

A further possibility by which the number and type of synapse connecting two neurons might affect memory may consist of controls over ongoing production of synapses. Some scientists have found evidence that synapses are continually forming and reforming in mammalian brains (cf Sotelo, C, Palay, SL; LABORATORY INVEST. 25(6) (1971) 653-671; Eccles, JC; 89-103 in Rockstein (ed) DEVELOPMENT AND AGING IN THE NERVOUS SYSTEM). It seems very unlikely that this constant change would affect topological connectivity, since neurons would have to have at least one connection in order to pass impulses. What it WOULD suggest is that other underlying biochemical events actively guided this formation and reformation of connections, and if this constant change related to memory, then these underlying events would likely survive both freezing and damage, and therefore remain to provide clues to memory.

Thirdly, we must consider survival of "propensities to respond". This point is the hardest to make specific for the simple reason that we almost totally lack specific data on how such propensities might act at a synapse. Nevertheless the problem permits some analysis. What we must have is an integrated SYSTEM capable of guiding the response of a synapse depending upon the type of stimulus received. If there were a single chemical or class of chemicals such as Ungar's memory polypeptides, then neurons would also have to contain systems to READ these chemicals and, once read, respond appropriately. This entire system would consist of chemicals such as ribonucleic acids, proteins, polypeptides, or others which are likely, as chemicals, to survive both freezing and considerable damage to the cell. It is almost certain that the "read-in, read-out" systems would

depend on exact structure and arrangement of their components in order to FUNCTION; but for survival of memory we do not at all need survival of FUNCTION, but only survival of INFORMATION, which is far more durable.

One last general point needs making. Storage of a "memory" in the sense of a conscious response must necessarily take a complex form, since such memories are very complex. But if we ask how an INDIVIDUAL NEURON might remember its own response, this neuronal memory needs very little complexity. The individual neurons do not have to carry a wide repertoire of possible responses in order for the whole brain to show great complexity.

Here are some possible forms for storage of memory within single neurons:

POSSIBLE FORMS FOR MEMORY STORAGE IN NEURONS

1. Memory might be coded in a variety of chemicals, whose presence or absence within the synapse determines response of the synapse to impulses.

2. Memory might be coded in changes in the structure or conformation of particular chemicals or chemical mechanisms. As readers probably know, enzymes, for instance, can sometimes change their structure in order to modulate their response; memory storage within a neuron might consist of such a change.

These are of course not mutually exclusive possibilities. Each one deserves some discussion about STABILITY OF INFORMATION carried by them.

The first leading point I can make about stability in both cases is that memory is very unlikely to depend on only one molecule, and even unlikely to depend on molecules of only one type. If there are either chemical or structural changes involved, then they will happen in a large number of molecules of the same kind.

The second leading point common to both types of storage is that they must be relatively insulated from any normal cellular destructive processes. In particular, we already know that memory will survive clinical death at normal temperatures for at least an hour. They will also survive for a lifetime in normally alive people. Whatever changes are involved must be highly stable.

I feel that the fact that memories ordinarily survive for years merits a lot more weight than many may think. Let's suppose that our "memory chemicals" are continually being broken down and rebuilt. If so, the process involved would have to involve steps

to recognize what a memory should be and construct a copy of it before its destruction. Simple enzymes such as cathepsins or trypsins which degrade proteins could not do this; the "copying" part of the process would have to be at least as complex as that involved in the copying of DNA or RNA. On simple efficiency grounds, ("why on Earth would our neurons go to all of that trouble?") this seems quite unlikely. THE MERE PERSISTENCE OF MEMORY FOR YEARS THEREFORE STRONGLY SUGGESTS THAT THE CHEMICALS INVOLVED ARE AT LEAST AS STABLE AS DNA.

Another point common to both forms of storage is that memories will probably leave traces other than in the "memory storage" chemicals themselves. To see this we might consider the analogy of protein synthesis. The "plans" for a protein are contained in the DNA, but that is not the only form in which the INFORMATION about the protein exists. A detective could recover the necessary information to describe proteins in a cell from the MESSENGER RNA which carries this plan from the DNA to the actual location of synthesis or from the ACTUAL PROTEINS THEMSELVES, all of which will exist in profusion in the cell. If a memory chemical is itself a protein, or even requires the synthesis of characteristic proteins or types of proteins, all of this apparatus could be used to recover what it was. I could hardly fail to mention here that many experiments show that extensive protein synthesis occurs in brains during and after learning.

For an argument depending less on analogy I can summarize the mechanism by which a nervous impulse is transmitted across a synapse. Transmission of impulses can happen purely electrically; scientists have found neurons from all major groups of animals in which electrical transmission occurs. However a much more widespread method is <u>chemical</u> transmission. Many different chemicals act as neurotransmitters, although acetylcholine is the best known. The transmitter chemical is held in special locations, the <u>vesicles</u> already mentioned. Arrival of an electrical impulse at the location of the synapse causes the release of the contents of many of these vesicles at the same time. The transmitter then diffuses to the other side of the synapse, where special <u>receptor molecules</u> detect it. The detection of this transmitter then causes changes in electrical properties of the receiving neuron; the neurotransmitter is then degraded after its reception by special enzymes (in the case of acetylcholine, the enzyme acetylcholinesterase).

If individual synapses carried memory, it would act by either controlling release of neurotransmitter from the synaptic vesicles or by controlling response of the receptor neuron to the impulse (or both!). Neither possibility allows a direct relation between any presumptive memory chemical and the control of response from a synapse; both possibilities will have to involve a long chain of events probably comparable in complexity to processes such as protein synthesis; IT STANDS TO REASON that formation and existence of a memory would have to leave traces other than those of a single memory chemical or conformational change.

In all of the above I have discussed the case for survival as it stands among all the various possibilities for memory. By adopting such an approach I understate, if anything, the likely durability of memory, since some of these possibilities are less likely than others. In particular, anyone considering the case for survival of memory and personality would have to bring out also the fact that Possibility 1 (that memory could be coded in the topological connectivity of neurons) has looked sicker and sicker as more and more information about nervous systems accumulates. At present, in many invertebrates such as the leech or many insects, and even for particular nerve cells and nervous circuits in vertebrates such as fish, neurobiologists have found FIXED, EXPLICIT WIRING DIAGRAMS identical for every member of the species. Furthermore, in no case has any new connection between neurons developed under experiments on learning, EVEN AND ESPECIALLY in nervous systems in which the number of neurons is small (such as the cockroach or planaria), and even in the case of preparations known to be capable of learning even in the absence of a brain (such as in leeches or earthworms)*.
If new topological connections don't form in invertebrates when they learn, why should we believe that they form in mammals?

If our "wiring diagram" IS genetically fixed then it would follow that that both memory and personality could be recovered from brains in which virtually the entire set of connections had been disrupted. Freezing without cryoprotectants will cause exactly such extensive disruption, extensively destroying structure while probably leaving chemistry intact. Unfortunately, of course, we don't actually KNOW that our wiring diagram is fixed in this way.

A complete discussion of memory would also describe the possible changes in dendritic structure with learning. For instance, rearing in enriched environments *may increase the number of dendritic spines* and cause other brain growth in glial cells. I should also point out, however, that in those neurons whose connections have been explored, a constancy exists in the area of the web of dendrites at which a given neuron connects to another; what may be affected is the number of synapses and the dendritic spines, not the existence of a connection or even its location on the cells. The suggestion here is that one sign of memory may be dendritic spines. This would give us some hold on the existence of a memory itself, since the former existence of such spines is very likely to survive freezing and other cellular damage.

For CRYONICS the essential enterprise depends on survival of information. We can prove that the information has survived by showing the survival of FUNCTION, but even if function does not survive that does not prove the loss of information, as we see already in the case of revival from clinical death. And indeed survival of information is far broader than the simple survival of memory; since the problem of cryonics, which is the problem of reviving people, is a problem of DETECTION, it will probably never receive final answer or proof. Even in 3000, how could we

(*) Learning without a brain is a good trick

know that we had not missed some critical clue?

TO LEARN MORE:

Much of the scientific basis of my argument depends on elementary neurology. A up-to-date textbook is:

Bullock, TH, Orkand, R, Grinnell, A; INTRODUCTION TO NERVOUS SYSTEMS, 1977. WH Freeman and Co.

A much more advanced symposium on the specific subject of synapses is:

Cottrell, GA, Usherwood, PN (ed);SYNAPSES, 1977. Blackie and Son, Ltd.

Paul Pietsch's book, apparently unnoticed by neurobiologists, is:

Pietsch, P; SHUFFLEBRAIN, 1981. Houghton-Mifflin Co.

A book with tantalizingly inconclusive information on possible biochemicals determining, in fetal and adult mammals, the wiring of their nervous system is:

Barondes, SH (ed); NEURONAL RECOGNITION, 1976. Plenum Press

A book by a neurobiologist who attempts to frame hypotheses on memory storage (despite its name, the nerve cell connections involved are propensities to respond rather than physical, topological connections) is:

Mark, R; MEMORY AND NERVE CELL CONNECTIONS, 1974. Clarendon Press, Oxford

None of this information proves a thing. It may however allow you to argue with more sophistication.

A Cryonicist

by Michael Darwin

Curtis warned me that the price was very high—
Too high for any mortal man to pay
But I was full of young adventure and could not hear
And went my way

No doubt Prometheus was warned
By others who were cast upon the rock—
Warned of loneliness and intimacies lost,
Of coming home to empty rooms
Still aching with the sting of lover's fresh remorse
At walking out
When love and need were strong
To spend my passions in the ranks of
Silent dead

I was warned of days and weekends lost
Spent not in laughter but in lust
To research and explore
Unreeling hours around high tables
Altars made of metal
Nothing more

Warned of losing touch with everyone
But others so inclined
To spend their days and nights
In wild pursuit of answers
That they cannot find

I was told of guarding thoughts from friends
And wrapping them in lies
To stop the cut of anger's ragged ends
Judged cowardly for my lack of will to die

Where is the youth who in innocence once set forth?
Was loss of innocence another price to pay?
Or merely forfeiture of trust to cynicism's way?

Now he's leaving
Or am I leaving him?
Walking down some long corridor of darkness
Will I turn to poisons for the mind
To kill the pain of vultures tearing at me
As others have who've walked along this way?

And are there answers from those whose care is mine?
If I turn to them and walk among their stoppered faces
And rage and shout the question of the hour
Will they answer through the haze and pain of dying
Stopped from death?

I have stood at midnight in the awesome quiet
Of the room where they are kept
Tear stained, through gritted teeth
The question has been wept
Is the chance of a tomorrow worth the agony and dread?
Is it worth the pain to end up something merely less than dead?

In the silence—
Amidst the eyes all glazed and frosted over
And naked soul with eyes no more to see—

None could answer me.

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