7. Patient Assessment

When a member of a cryonics organization is diagnosed with a potentially life threatening condition, the outcome of an eventual standby may be greatly improved if we can learn as much as possible about the condition, as early as possible before death is pronounced. This process of information gathering must be carefully distinguished from any active involvement in caregiving for a living person. A cryonics organization would face obvious potential conflicts of interest if it became actively involved in caregiving. While cryonics organization personnel or medical advisors are sometimes asked for and may offer advice regarding decisions relating to terminal care, actual care should be provided by and under the authority of independent medical personnel. Therefore, in this section we will deal only with the passive process of assessment, which may offer three significant benefits:

1. Standby is time-consuming, demanding, and costly. A cryonics organization must determine when it is sensible to deploy a standby team to the bed of the patient. More specifically, a cryonics organization needs to know when it is time to make some specific decisions such as drawing up medications and assembling the portable ice bath.

2. The pre-mortem condition should determine the nature and priorities for initial stabilization procedures. For example, a severely dehydrated patient requires a different protocol from an edematous patient. We may be better able to optimize our intervention after legal death is pronounced if we know as much as possible about the patient before pronouncement.

3. To facilitate future resuscitation, collection of patient data should be as comprehensive as possible.

Good patient assessment is a formidable challenge for a cryonics organization. Unlike the execution of basic stabilization protocols, where skills can be taught through repetition without understanding the underlying medical and technical intricacies, the task of patient assessment requires a detailed understanding of pathophysiology of the terminal and agonal phase.

This challenge is exacerbated by the fact that a lot of what is going on in the final hours of a patient's life has little clinical relevance in contemporary medicine. In fact, as cryonicists, we become most concerned precisely when medicine has "given up" on a patient. The last stages of the dying process receive relatively little attention in medical research because, by definition, the process has become irreversible and the condition has become incurable.

If a patient receives hospice care, we may hope and expect to receive informal bedside guidance from hospice staff based on their long experience with terminal patients. We may also feel more affinity with hospice caregivers than with nurses and physicians, because the processes of hospice and standby are likely to coincide. However, it is important to remember that hospice caregivers may only intervene to ameliorate pain and suffering, while we have an urgent mission to prevent cell death. The hospice and the cryonics organization have very different goals.

Consequently we may find limited guidance when we try to predict the time and circumstances of death, so that we may adjust the timing and protocol of our deployment appropriately. This unsatisfactory situation is unlikely to change until there is more widespread acceptance of the practice of human cryopreservation. Until that time, the best we can do is to document our experience to date and use on-site advice in conjunction with the little information that is available in the mainstream literature to the best of our capabilities.

Terminal Diagnosis and the Agonal Phase

As practiced today, cryonics interventions can only begin after pronouncement of legal death. This means that cryonics patients who do not die as a result of accidents or sudden death usually go through a prolonged terminal phase before cryonics procedures start. This terminal phase is likely to inflict

significant damage on the patient (as described below), and one of the most frustrating aspects of standby work is our inability to do much about this, beyond asking favors and reminding caregivers to honor the patient's wish to be cryopreserved with as little damage as possible.

A terminal illness can be defined as an active disease that cannot be cured or adequately treated with contemporary medical technologies. From a biological perspective this means that the patient is losing his battle to sustain himself as an integrated organism; ultimately his biochemical elements will decompose and return to the biochemical cycle of nature.

As a general rule, during terminal illness the probability of death increases until a point where the patient enters the agonal phase. The agonal phase can be described as a state of general exhaustion, minutes or hours before cessation of pulse and respiration. Its symptoms can be characterized as a state of profound shock in which various parts of the body become hypoxic. From the perspective of patient care, it is important to recognize that injury to the brain may often occur before pronouncement of legal death. As a consequence, the objective of cryonics stabilization procedures to maintain viability of the brain by contemporary criteria is not always possible as a result of pre-mortem pathologies.

Terminal Iillness and Deployment

The challenge for a cryonics organization is to deploy a standby team at the right time between the point of determination of terminal illness and pronouncement of legal death. Premature deployment exposes the cryonics organization to financial and logistical challenges, but late deployment can compromise the care of the patient.

It should be noted that deployment challenges are greatly reduced when the patient is moved to a location close to the cryonics facility. In such cases, observation of the patient is possible without making travel arrangements or relying on reports from medical staff or visitors. When there is an unexpected decline of the patient, the cryonics organization should be ready and able to limit the amount of time between circulatory arrest and start of stabilization procedures.

Patient assessment may begin when an applicant first completes the signup process and becomes a member of a cryonics organization. This is obviously of special importance if the new member has already been diagnosed with a terminal condition. The organization must be careful to comply with all provisions of HIPAA (the Health Insurance Portability and Accountability Act, which protects an individual's right to medical privacy), but may certainly explain the potential benefits of sharing data. For example, when a patient is diagnosed with an aggressive cancer, informing the organization of this fact will change the classification of this patient from green to yellow and local standby team members can be notified of the need to review and upgrade their equipment. When a patient becomes terminal or is admitted to a hospice for palliative care, the responsibility of the cryonics organization is changed to actual monitoring of the patient. The task of monitoring should be standardized through the use of data collection sheets which can be interpreted by medical professionals.

Psychological Aspects of Terminal Disease and Dying

A detailed discussion of this topic is beyond the scope of this book, but the cryonics organization can benefit from anticipating and recognizing the most common psychological responses from patients and relatives.

The *Kübler-Ross model* distinguishes five stages of grief for people who are diagnosed with a terminal disease:

1. **Denial:** The patient does not believe or is unwilling to accept the terminal prognosis.
2. **Anger:** The patient becomes agitated at life, with family, or medical professionals.
3. **Bargaining:** The patient is trying to negotiate with fate or a higher power.
4. **Depression:** The patient recognizes his fate and becomes depressed.
5. **Acceptance:** The patient comes to terms with his mortality.

These stages do not necessarily occur in all patients in this order, and some critics have questioned the model altogether. In the case of cryonics the model would have to be further refined because people with cryonics arrangements have a different understanding of what a terminal diagnosis means. There has not been a systematic study of how people with cryonics arrangements (and their loved ones) deal with terminal illness, but a good rule of thumb is to expect a combination of the various forms of grief and practical concerns about their cryopreservation and loved ones.

We should not assume that people who have made arrangements for cryopreservation have "dealt with" their fear of death. Cryonics may allow some hope for eventual revival, and the presence of a standby team can be a source of reassurance, but most cryonicists share a very strong attachment to life which may induce equal and opposite fear at the prospect of life being interrupted.

For the same reason, cryonicists may be as likely as anyone else to experience denial or anger when death is imminent. This state of mind may cause the patient to act in ways which are counter-productive or even self-destructive. A person who refuses to accept the reality of his condition may refuse to relocate to an optimal location for a standby, or may become unwilling to cooperate with cryonics personnel. We know of one case where the patient was in the last stages of cancer but was so deeply in denial, it was his wife who insisted that he relocate nearer to his cryonics organization—even though she had no personal interest in cryonics. She simply recognized his lifelong desire to be cryopreserved after legal death, while his state of denial convinced him that he wasn't going to die and therefore would have no need for cryonics. Such singular cases suggest that in standby situations, the only clear rule is to expect the unexpected.

More commonly, close relatives who are unconvinced by arguments in favor of cryonics may become actively obstructive. To them, a cryonics organization is an intrusion on the final intimate moments between them and the dying person. A cryonics organization needs to strike a delicate balance between respecting such feelings and ensuring that the wishes of the patient are being carried out.

As the patient's condition deteriorates, agitation, heavy sedation, depression, delirium, or coma may make communication impossible. If the patient has an active interest in optimizing stabilization and cryopreservation procedures, these issues need to be addressed when the patient is still clear and alert, preferably in the presence of relatives and medical professionals to encourage their cooperation.

The Agonal Phase

With the exception of people who die of sudden death or extreme trauma, most people will go through an agonal period prior to circulatory arrest. But the fact that the agonal phase is such a widespread phenomenon does not mean that there are a lot of systematic and scientific studies of the agonal phase. This should not be surprising because, per definition, the agonal phase is characterized as being a state for which there is no effective therapeutic treatment.

As in discussions about the signs and symptoms of approaching death, the characterization of the agonal phase is holistic in nature. It is the combination of signs and symptoms that characterize the transition from terminal illness to general exhaustion of the patient.

A distinction has been made between the "pre-active" phase of dying and the "active" phase of dying. In the "pre-active" phase the patient shows increased restlessness, confusion and agitation. He is aware and announces his impending death. There are increased periods of sleep and apnea. In the "active" phase the patient becomes unresponsive to most stimuli and can suffer from severe agitation and hallucinations. Physiological indications that the patient is losing the struggle for survival become evident; cyclic changes in breathing (such as Cheyne-Stokes respiration, which is characterized by progressively deeper and sometimes faster breathing, which then falls off rapidly, resulting in apnea or no breathing at all), the "death rattle," inability to swallow, incontinence, a significant drop in blood pressure, peripheral ischemia, cyanosis and a rigid unchanging position are all indicators of imminent death.

In his 1903 book *Om Doden og de Dose* (the title can be translated as "On Death and the Dead," but the book is not published in English), Oscar Bloch gives the following description of the agonal state:

"The dying person often lies still. Only a few involuntary movements of the extremities, mostly the hands, reveal that the flaccid muscles have not lost their power altogether. His facial features, anxiously observed by his nearest relatives, reveal no sign of concern, they have changed and he no longer looks himself. The glance of the eye, which indeed expresses the personality is dulled; the eye has lost its lustre; the entire surroundings of the eye which largely are decisive of the expression are flabby, the muscles are no longer capable of contraction and the eyelids are flabby too, contributing further to the dullness of the features. The face looks as is if has become longer, the nose more pointed. The dry lips hang flatly over the jaws. The mouth is half open. The complexion pale, with a yellowish or bluish hue. The brow is studded with droplets of sweat, but the person who wipes his forehead notices that it has become cool. The fumbling hands do not respond to the grasp with which his relative tries once more to communicate with him, from whom he is soon to depart. The breathing is audible, rattling mucus bubbles are heard to run up and down the windpipe, but the dying patient does not notices this and he makes no effort to bring up the mucus. Then the breathing becomes more shallow and weaker, the mucus rattling is heard no more and the patient draws his breath at long intervals. Does he still breathe? Often it is impossible to say when the breathing ceased, at other times the last breath is like a sigh. At the same time the pulse becomes weaker and weaker; it is irregular—and finally one does not know whether or not it can be felt. But yet the heart can be heard to beat, then the heart beat ceases—he dies."

Acidosis

Under everyday physiological conditions the human body regulates pH within a very tight range. This is known as acid base homeostasis. If pH drops below or rises above the normal range (7.35 – 7.45), endogenous extra-cellular and intracellular buffers and changes in respiration can bring pH back to the

physiological range. During terminal illness and the agonal phase these mechanisms are impaired or overwhelmed by extreme alternations in pH.

Different pathologies during the terminal phase can alter the ability of the body to maintain acid-base homeostasis. Because terminal disease ultimately will give way to the agonal phase, the emphasis in this review will be on agonal acidosis. Unless a patient is suffering from a rare disease that raises the pH prior to death, as a general rule, it should be assumed that the patient will be acidic shortly before and after death.

Blood samples taken from patients hours before death or just after death give pH values that are lower than the physiological range, or incompatible with life (lower than 7.0). Little relationship has been found between pH values and specific terminal diseases. This finding indicates that the general exhaustion that accompanies the agonal phase is characterized by peripheral ischemia-induced acidosis – which is further evidenced by high lactic acid values. These low pH values can be a direct cause of death or an important contributory factor. It has further been observed that the fall in pH is proportional to the duration of the agonal phase.

Acidosis in the cryopatient is detrimental for a number of reasons. A lowered pH increases sodium concentrations in the cell by activation of the Na+/H+ exchanger, releases iron and increases free radical formation through the Fenton reaction, suppresses neurotrophin synthesis, and decreases the ability to lower intracellular calcium accumulation. Acidosis may also impair cerebral vascular autoregulation. An acidic environment may further reduce or eliminate the effectiveness of drugs that are pH sensitive such as heparin and epinephrine. A low pH can also accelerate decomposition as hydrolytic enzymes are released from damaged lysosomes.

As a general rule, acidosis should be assumed after pronouncement of legal death. To counter acidosis two interventions are employed: prompt restoration of ventilation, and administration of the buffering agent THAM (Tromethamine). The use of sodium bicarbonate is discouraged because it can cause a paradoxical rise in intracellular pH as a result of diffusion of the carbon dioxide constituent into the cells. Blood gases and fluid samples can be taken during cardiopulmonary support, blood substitution, and cryoprotective perfusion.

Microcirculatory Disturbances

Before the patient's compensatory mechanisms are overwhelmed and inevitable decline sets in, the body tries to protect the essential organs by redirecting blood flow to the core. As a consequence, peripheral circulation is compromised. In the critically ill patient such a response is not followed by a return to healthy homeostasis, but by progressive disintegration.

If cardiac output falls, blood flow can bypass peripheral capillaries, which increases blood return to the heart but can produce regional hypoxia and endothelial injury. Endothelial hypoxia and inflammatory responses enlarge pores between vessels, which leads to increased permeability and edema. Microcirculatory stasis inhibits flow of red blood cells and other blood elements. The aggregation of formed elements and red blood cell hypoxia aggravate stasis of blood flow. As the deterioration of the patient increases, more and more parts of the body are affected and the central circulation will become progressively involved as well.

Also reduced is intestinal blood flow. Low splanchnic blood flow can lead to increased mucosal permeability, endotoxemia and multiple organ failure. Low gastric mucosal pH has been found to have a high specificity for predicting patient survival in critically ill patients. As such, the gastrointestinal system has been called 'the motor of multiorgan failure.' Cryonics patients experience many of the conditions associated with gastrointestinal dysfunction (e.g. , trauma, shock, hypovolemia) and are exposed to a number of cryonics procedures that can worsen these complications (e.g. , prolonged low flow CPR, vasoconstriction, hypothermia, CPB). Gastrointestinal complications such as hyperpermeability and abdominal swelling are not limited to stabilization and transport, but can also have profound effects on the ability to cryoprotect whole body patients. Gastrointestinal ischemia and its effects during the terminal and agonal phase should therefore be closely monitored because abnormalities observed prior to pronouncement of legal death are a good indicator of what can be expected during CPS, blood washout, and cryoprotective perfusion. When severe abdominal edema is observed prior to circulatory arrest a determination needs to be made regarding how this

condition can affect other parts of cryonics procedures and how to deal with them.

The No-Reflow Phenomenon

One of the most harmful events during terminal illness and the agonal phase is the development of perfusion abnormalities. Perfusion impairment of the (micro) circulation, and that of the brain in particular, has a number of adverse consequences. Pre-mortem, it can lead to energy depletion of neurons and initiate the beginning of the biochemical cascade ending in decomposition. Post-mortem, it can interfere with effective cardiopulmonary support, circulation of neuroprotective medications, and the efficiency of cooling.

Most research into the no-reflow phenomenon since the 1960s has studied the effects of various durations and forms of ischemia on flow. It is now increasingly recognized that perfusion impairment manifests itself in the critically ill patient as well. The causes of such disturbances in normal flow remain a matter of debate, but contributing factors include local and systemic inflammation, metabolic exhaustion and rheological abnormalities.

In the terminal patient a distinction needs to be made between alterations in blood flow as a defensive response of the organism to protect the brain and the vital organs and alterations in blood flow that reflect a general failure of the patient to maintain homeostasis. This difference becomes most clear during the agonal phase when the brain is no longer exempted from pathological events and metabolic and microcirculatory failure produce pronounced effects on the awareness and consciousness of the patient.

Aside from conveying this issue to the attention of medical caregivers and those that can make medical decisions for the patient, cryonics organizations can do little to prevent perfusion impairment during the agonal phase. The recognition that no-reflow is not just a potential risk of delayed intervention after circulatory arrest but should be assumed to exist in most patients has important consequences for standby and stabilization protocols. Unless otherwise indicated, aggressive protocols to reverse no-reflow such as hypertension, administration of (hypertonic) volume expanders, and rapid

induction of hypothermia should be given great priority. Minimizing the time between pronouncement of legal death and blood washout is also beneficial.

Dehydration

Most cryonics patients who present for stabilization are dehydrated. In rare cases this can be the consequence of the patient refusing food and water. In other cases the inability to process fluids without assistance can contribute to fluid imbalances. An important contributing factor is the decision to stop any kind of medical treatment, including palliative care, in the final phase of dying.

Severe dehydration (>9%) manifests itself through various symptoms including reduced blood pressure, alterations in pulse, increased heart rate (bradycardia in very severe cases), dry mucous membranes, sunken eyes, cool and mottled extremities, lethargic or comatose mental status, decreased urine output and severe thirst.

Most symptoms of dehydration (or the agonal phase in general) constitute no object for reversal during cryonics stabilization protocol. The fundamental reason why cryonics should be aware of dehydration is because rehydration with suitable volume expanders can increase blood pressure during stabilization. Extreme dehydration can also be a concern because a severe lack of water can reduce metabolism of neuroprotective drugs.

In the medical literature various forms of dehydration are distinguished. One distinction that is important for cryonics patient assessment is that among loss of water with equal electrolytes (isotonic dehydration), loss of water that exceeds loss of electrolytes (hypertonic dehydration), and loss of water that is less than the loss of electrolytes (hypotonic dehydration). When hypotonicity is expected, it is important not to aggravate this condition by the administration of isotonic or, worse, hypotonic solutions. As a general rule, hypertonic solutions are recommended for cryonics patients because these agents can recruit water from edematous tissue, including the brain.

Neurological Damage

Securing viability of the brain by contemporary criteria is the most important objective of cryonics standby and stabilization. Recognition of the mechanisms through which pathological events in the central nervous system can defeat this objective is of great importance. As a general rule, the risk for increased brain damage is higher during slow dying. For example, when the ventilator is removed from the patient who is not able to breathe on his own, the time between this action and circulatory arrest can be short. Conversely, when a patient is going through a prolonged terminal and agonal phase, (regional) injury to the brain can occur while the body itself is still fighting for survival.

The human brain has little storage of excess energy. As a result, hypoxia causes the brain to deplete its oxygen reserves within 30 seconds. The energy depletion that follows cerebral hypoxia during the dying phase has a number of distinct effects:

1. Excitation or depression of certain processes in the brain.
2. Alteration in the maintenance of structural integrity of tissues and cells.
3. Alteration of neuromediator synthesis and release.

The depletion of oxygen leads to a switch from aerobic to anaerobic energy production. As a consequence, there is an increase in the metabolic end-products of glycolysis such as lactic acid, which decreases pH in the brain. After five minutes, no useful energy sources remain in the brain, which can explain why the limit for conventional resuscitation with no neurological deficits is put at five minutes as well. Because the dying phase leads to progressively worse hypotension and hypoxia, the metabolic state of the brain after the agonal phase is worse than if there would have been sudden cardiac arrest.

Light microscopic changes have been observed in brain cells after five minutes of ischemia. Prolonged hypotension, as can occur in the agonal patient, can lead to the appearance of “ghost cells” and disappearance of nerve

cells. Such observations provide evidence that structural changes, including cell death, can occur prior to clinical death. Another manifestation of hypoxia (or hypotension) is the progressive development of cerebral edema. The resulting narrowing of vessels and decrease of the intercellular space can, in turn, aggravate energy delivery to tissues. Of particular importance for cryonics stabilization procedures is the development of no-reflow (see above), which can prevent complete restoration of perfusion to parts of the brain during cardiopulmonary support. There is no consensus whether no-reflow can occur as a result of prolonged hypotension (as opposed to complete cessation of blood flow) but an extended dying phase can set the stage for cerebral perfusion impairment after circulatory arrest.

The central nervous system does not shut down at once. Throughout the terminal and agonal phase, alternations in the brain progress from minor changes in awareness and perception to deep coma. As a general rule, more recent and complex functions of the brain disappear earlier than the most basic functions of the brain. The uneven brain response to hypoxia may reflect different energy requirements, biochemical and structural differences, and/or the activation of protective mechanisms to preserve the "core" functions of the brain. The CA1 region of the hippocampus is uniquely vulnerable to ischemia. This presents a problem for contemporary cryonics since the objective of human cryopreservation is to preserve the identity-relevant information in the brain.

The "Death Rattle"

One specific symptom that is often encountered in the dying is the so called "death rattle." This is a "choking" sound which occurs when air moves through mucus that has accumulated in the throat of a dying person who can no longer remove the secretions by swallowing.

In the technical literature a distinction has been made between the "real" death rattle that is a consequence of salivary and bronchial secretions, and a death rattle that is produced by pulmonary pathologies.

The death rattle is often associated with removal of mechanical ventilation in the patient. It is more commonly found in patients dying from brain trauma and brain tumors.

In the dying patient the death rattle is perceived as a good indicator of death, with studies predicting a median time of 16 hours until dead. In the specific case of removal of mechanical ventilation (or any other withdrawals of life support) these times can be much shorter. If the symptoms of the death rattle present during the agonal phase treatment is often confined to administration of drugs that reduce excretions to comfort the family. As a general rule, symptoms of the death rattle indicate that a cryonics standby team should be prepared for the initiation of stabilization procedures. If no such team is deployed yet, development of the death rattle, in combination with other symptoms, should be considered a reason to deploy.

Predicting Death

We would derive obvious benefits if we were able to predict a patient's time of death with reasonable accuracy. The time between circulatory arrest and start of cryonics procedures would be minimized. Time-consuming and costly standby deployments would be avoided, and team members would be less prone to sleep deprivation and fatigue. While it is true that a patient's prognosis tends to become more definite with the passage of time, unfortunately the prediction of death remains as much an art as a science. We have known hospice personnel who believe they have an instinctual predictive ability, and we have known doctors who make predictions based on data. In both groups, predictions have been wrong by as much as a week. In some instances, a patient recovers and returns to everyday life.

Still, the indicators listed below may provide valuable guidance, so long as they are used in conjunction with advice from experienced caregivers. As a general rule, none of these signs can be relied upon for precisely predicting the time of death and need to be interpreted in context. Establishing a trend is often more meaningful than relying on abnormally low or high values. Generally speaking, the probability of dying increases when an increased number of these signs are observed. It should be remembered that there is

often no comparison to discussing the terminal course of the patient with a practiced medical caregiver, in particular, those with extensive experience in palliative care. Hospice personnel can often predict death within about five hours of the event.

Signs of Impending Death

Blood gases and chemistry

- Acidosis
- Elevated lactic acid content
- High concentration of ions in the blood
- Reduced bicarbonate levels

Physiological

- Fever
- Hypotension
- Peripheral venous stasis
- Involuntary evacuation of urine and feces
- Irregular and weak pulse

Respiratory

- Death rattle
- Irregular breathing (Cheyne-Stokes breathing)
- Low end tidal CO values

Visual and tactile observations:

- Cyanosis
- Decrease in skin turgor
- Dilated pupils
- Dry tongue
- Extreme weight loss
- Edema of the lower extremities
- Jaundice
- No corneal reflexes

Pale skin color
Sweating

Neurological
Delirium
Dullness
Unconsciousness

We must emphasize that the absence of one or more of these indicators should not be used as justification for delaying deployment of team members. If many of these signs are observed, and follow a deteriorating trend, a standby team should be present at all times. Observing these indicators can be helpful for making practical and logistical decisions such as the changing of team members, drawing up medications and deploying equipment and other decisions that need to be made to provide prompt stabilization.

Many of these signs of impending death can be observed without invasive or complicated medical procedures. A pulse oximeter, for instance, merely makes external contact with the skin at the tip of a finger, while providing very valuable data. At the same time, the use of any medical device may constitute treatment, especially in the eyes of hospital staff, and cryonics personnel must be extremely careful to avoid crossing the strict line between passive observation and active involvement. Ideally, personnel should establish their right to share data obtained by caregivers on a cooperative basis, long before a patient becomes agonal; but in a less-than-ideal situation, diplomatic negotiation will be necessary.

At the end of this section we include four “pre-mortem” data collection sheets. Also you will find an information sheet with normal values for blood gases and chemistry, and the methodology to calculate the Glasgow Coma Score.

Notable Patient Conditions

In ideal circumstances the cryonics organization’s standby protocol would be tailored to the individual pathophysiology of the patient prior to circulatory

arrest. In the real world the best a cryonics organization can do is to strike a balance between providing basic stabilization procedures that are effective for all (such as rapid cooling) and recognizing special conditions of the patient that mandate a change in procedures. It is impossible to provide a comprehensive list of items that the cryonics organization needs to look for, but what follows is a basic discussion of such conditions. In some cases, information about conditions can be solicited when the member is still healthy. A cryonics organization should encourage their members to voluntarily submit such information to minimize the need for last-minute improvisation.

Logistical and Legal

Logistical and legal considerations fall outside of the scope of this chapter but it should be emphasized that the benefits of doing a thorough assessment of the condition of the patient are highly dependent on the location of the patient, securing cooperation from hospital or hospice staff and ensuring the legal and medico-legal elements are in place for a prompt stabilization of the patient.

Anatomical

The cryonics organization needs to be aware if a patient is extraordinary tall or heavy. In such circumstances additional logistical challenges should be expected. In rare circumstances custom-designed equipment needs to be built. Another scenario where conventional equipment (such as the portable ice bath) may be inadequate is when the patient suffers from a bone disease that does not allow the legs to be folded to fit the width of the ice bath. Extreme obesity or certain bone diseases may present challenges for mechanical cardiopulmonary support.

Cardio-Respiratory

There are so many physiological and pathological conditions of a patient that could induce the cryonics organizations to alter protocol that we can only list a number of them that impact basic stabilization procedures.

One of the biggest obstacles for vigorous cardiopulmonary support are fragile or broken chest bones. Such a condition can be due to diseases like

cancer or prior resuscitation efforts. If there are concerns about the wisdom of using aggressive mechanical chest compression due to a fragile chest, the Chief Medical Advisor should be consulted.

Many patients will have pulmonary edema at the time of arrest, or will develop fulminating edema during closed chest compressions. To counter the effects of large amounts of fluids in the lungs and alveolar flooding, conventional ventilation cannot be relied upon and needs to be replaced with continuous high pressure ventilation and PEEP.

Hemodynamics and Blood Abnormalities

Depending on the terminal course of the patient, the patient can be either severely dehydrated or very edematous. To complicate matters, edema and hypovolemia can co-exist in the terminal patient. Correctly assessing the fluid balance of the patient is important to choose the right course of action: either administration of large volume fluids to restore blood and cerebral pressure, or limiting large volume fluids to prevent increased edema in the patient.

Development of hyperviscosity, hyper-coagulation, and platelet aggregation during the terminal phase can present formidable obstacles to restoring blood flow as it will result in areas of the circulation being excluded from perfusion. In general, such a state should be expected in cryonics patients but if this condition exists to a more extreme degree, additional pharmacological strategies should be considered. Conversely, if the patient has recently experienced brain hemorrhage, administration of fibrinolytics, anti-coagulants and anti-platelet agents should be approached with caution.

A special case presents itself when the patient is suffering from cold agglutinin disease. In such cases, red blood cells will have a tendency to aggregate during induction of hypothermia. Because rapid induction of hypothermia is the most effective general neuroprotective intervention in cryonics the most effective response would be to minimize the time between pronouncement of legal death and blood washout.

As a general rule, energy depletion by cardiac arrest will initiate a cascade of events that produce microcirculatory pathologies and regional obstructions to cerebral blood flow. These events should be countered with a protocol of hypertension, hemodilution, and anti-coagulation. It cannot be

emphasized enough that the large volume medications are not intended to be administered as an afterthought but are meant to be used at the start of stabilization procedures concurrent with the neuroprotective agents.

Neurological

The fundamental objective of stabilization is to prevent (further) deterioration of the brain. If the patient presents with cerebral edema or elevated intracranial pressure (for example, as a consequence of brain cancer) the perfusion pressures generated by cardiopulmonary support may not be adequate and oxygenation and distribution of medications will be compromised. In such cases, the high volume medications should be given priority to restore pressure and hemodilute the blood. In particular, the anti-edema agent mannitol should be administered promptly to reduce swelling of the brain. Further reduction of cerebral edema can be achieved by substitution of the blood with the hyper-osmotic MHP-2 solution.

In patients who have experienced multiple episodes of stroke or suffer from prolonged neurodegenerative diseases the ratio of cerebral spinal fluid (CSF) to brain tissue may be elevated. As a consequence, equilibration of the brain with the vitrification solution will require longer perfusion times. A more radical intervention would be to evacuate the CSF from the brain to eliminate vast amounts of fluid with low glass forming tendencies.

Allergies

The sheer volume of medications used in Alcor's stabilization protocol excludes a detailed review of all the indications and contra-indications for their use, and the reader is referred to the documentation that is supplied with the drugs. Of notable interest is to determine whether there is a risk of anaphylactic shock, in which case the administration of large volume medications like Dextran 40 and hydroxyethyl starch (HES) should be reconsidered and replacements should be sought.

Infections and Transmittable Diseases

In some cases, the patient's condition can present a danger for the team members. As a general rule, special precautions should always be taken. In

cases such as AIDS or any highly dangerous diseases that can be transferred by blood or air, no stabilization procedures should be initiated without extensive consultation of Alcor's medical staff and advisors and the patient's caregivers.

A Special Case: Self-Denial of Food and Drink

One course of events that leads inevitably to circulatory arrest within a matter of weeks is the conscious decision to refuse all food and drink. Such a decision to hasten death should be distinguished from terminal states characterized by a decreasing appetite, such as seen in cancer.

Self-denial of food and drink is often the last resort for people who want to end their life in a dignified manner when physician-assisted dying is not available in their country or state, or when they do not meet the criteria for these procedures. Self-denial of food and drink is of special interest to cryonicists because it is the only form of self-directed termination of life that normally eliminates the risk of an autopsy. It is usually not employed to hasten death but as means to induce circulatory arrest to prevent a brain-threatening disease running to completion. Because self-denial of food and drink requires a resilient and committed patient to continue the decision made, there cannot be any doubt about the voluntary nature of this act.

There has been at least one well-documented case of self-denial of food and drink in cryonics and there is good reason to believe that this strategy to prevent progressive destruction of the identity of the person may be chosen by individuals in the future. As such, cryonics providers need basic knowledge about what this decision entails in terms of medical care and deployment.

If the decision to deny food and drink is respected by medical caregivers, the unfolding course of events is not necessarily harder on a patient than that observed in other irreversible terminal states. Although a doctor can refuse to participate in palliative care for a patient who has chosen this course of action, such a doctor is expected to release himself from the patient's care to make place for a physician without such objections.

The course of events for a person who has chosen to refuse food and drink depends on a number of things such as the medical condition of the

patient and the specific implementation of the decision. If a patient categorically denies any food and drink the time to circulatory arrest is shorter than if the patient gradually reduces his intake of food and fluids. Most patients who follow such a regime are expected to die between 7 and 15 days. The time course for patients who follow a more gradual approach is less predictable and can last for more than a month.

The ensuing course of events does not necessarily need to involve a lot of suffering if adequate attention to mouth care, pain management and prevention of delirium is given. In his publication 'A Hastened Death by Self-Denial of Food and Drink,' Boudewijn Chabot outlines a number of important points:

- The patient should express his wishes in his legal paperwork and, preferably, also in a signed and dated letter for his doctor.
- The bowel should be cleared prior to the start of fasting to avoid accumulation of food remnants in the large intestine which can facilitate a confused and anxious state.
- Adequate mouth care should be available to prevent drying out of the mouth and to relieve extreme thirst.
- As in conventional palliative care, medications should be provided throughout the course of events to relief pain, discomfort and anxiety.

Because hastening death by self-denial of food and drink is not a routine elective medical procedure, pathophysiological data about it are limited and confined to information gathered from medical caregivers, relatives, and data from related phenomena such as abstention for religious or political reasons.

When the intake of sugars or other carbohydrates ceases, the body will switch to other sources of nutrients such as fat and protein reserves. Increasingly, urea can no longer be excreted by the kidneys because of a lack of fluids. The generation of endorphins and the increase of urea levels in the blood can contribute to a pleasant state of drowsiness. As the hydration of the patient keeps declining, the concentration of ions in the blood keeps

increasing, eventually leading to cardiac arrest. Because the amount of fluid that is sufficient to moisten and hydrate the mucous membranes in the mouth falls short of the hydration that is required to sustain life, the adversity of effects of refusing fluid on the mouth, and the extreme thirst this produces, can be alleviated without reversing the course of events that the patient has chosen.

Unless the cryonics organization believes that the patient's medical condition would trigger a sudden acceleration of events leading to early cardiac arrest, the expected time-course after such a decision is announced should allow for a gradual deployment of standby equipment and a protocol of stepping up monitoring efforts. Because a decision to refuse all food and drink will often be made to avert destruction of the brain and facilitate a better cryopreservation, it is of great importance that officials of the cryonics organization abstain from involvement in the execution of this decision and care during the terminal phase.

Data Collection

Patient data during the terminal and agonal phase are usually collected by medical staff as a routine part of patient care. If there is good cooperation with the hospital and hospice staff, the most important job for the cryonics organization is to interpret the data and make sensible deployment, standby and stabilization decisions. After completion of the case, the cryonics organization should request all medical data that were collected during the terminal care to produce a detailed case report.

A meta-analysis of all available pre-mortem data will allow the cryonics organization to have better quantitative and qualitative understanding of its patients, which can contribute to better readiness, standby and stabilization policies. In particular, cryonics organizations have strong interest in knowing basic information about cryonics patients as a group such as the distribution of causes of death, location of death (hospital / hospice / out-of-hospital location) and duration of standby.

PATIENT TREND SHEET A

Client Name:______________________________ **Client Number:**____________________ **Page**_____**of**_____

Location:__________________________________ **Team Members Present:**____

Date	Military Time	Resp	Pulse	O_2 Sat	Cap Refill	Blood Pressure	Temp	Skin	L	Pupils	R	GCS	Init
		Rate: /min ☐ Regular ☐ Shallow ☐ Labored	Rate: bpm ☐ Regular ☐ Irregular		Hands: Feet: (seconds)	Sys: Dias: ☐ Central ☐ Peripheral	° ☐ C ☐ F	☐ Unremarkable ☐ Cool ☐ Pale ☐ Warm ☐ Cyanotic ☐ Moist ☐ Flushed ☐ Dry ☐ Jaundiced	☐ ☐ ☐ ☐	Size (mm) Round Reactive Sluggish Fixed	☐ ☐ ☐ ☐		
		Rate: /min ☐ Regular ☐ Shallow ☐ Labored	Rate: bpm ☐ Regular ☐ Irregular		Hands: Feet: (seconds)	Sys: Dias: ☐ Central ☐ Peripheral	° ☐ C ☐ F	☐ Unremarkable ☐ Cool ☐ Pale ☐ Warm ☐ Cyanotic ☐ Moist ☐ Flushed ☐ Dry ☐ Jaundiced	☐ ☐ ☐ ☐	Size (mm) Round Reactive Sluggish Fixed	☐ ☐ ☐ ☐		
		Rate: /min ☐ Regular ☐ Shallow ☐ Labored	Rate: bpm ☐ Regular ☐ Irregular		Hands: Feet: (seconds)	Sys: Dias: ☐ Central ☐ Peripheral	° ☐ C ☐ F	☐ Unremarkable ☐ Cool ☐ Pale ☐ Warm ☐ Cyanotic ☐ Moist ☐ Flushed ☐ Dry ☐ Jaundiced	☐ ☐ ☐ ☐	Size (mm) Round Reactive Sluggish Fixed	☐ ☐ ☐ ☐		
		Rate: /min ☐ Regular ☐ Shallow ☐ Labored	Rate: bpm ☐ Regular ☐ Irregular		Hands: Feet: (seconds)	Sys: Dias: ☐ Central ☐ Peripheral	° ☐ C ☐ F	☐ Unremarkable ☐ Cool ☐ Pale ☐ Warm ☐ Cyanotic ☐ Moist ☐ Flushed ☐ Dry ☐ Jaundiced	☐ ☐ ☐ ☐	Size (mm) Round Reactive Sluggish Fixed	☐ ☐ ☐ ☐		
		Rate: /min ☐ Regular ☐ Shallow ☐ Labored	Rate: bpm ☐ Regular ☐ Irregular		Hands: Feet: (seconds)	Sys: Dias: ☐ Central ☐ Peripheral	° ☐ C ☐ F	☐ Unremarkable ☐ Cool ☐ Pale ☐ Warm ☐ Cyanotic ☐ Moist ☐ Flushed ☐ Dry ☐ Jaundiced	☐ ☐ ☐ ☐	Size (mm) Round Reactive Sluggish Fixed	☐ ☐ ☐ ☐		
		Rate: /min ☐ Regular ☐ Shallow ☐ Labored	Rate: bpm ☐ Regular ☐ Irregular		Hands: Feet: (seconds)	Sys: Dias: ☐ Central ☐ Peripheral	° ☐ C ☐ F	☐ Unremarkable ☐ Cool ☐ Pale ☐ Warm ☐ Cyanotic ☐ Moist ☐ Flushed ☐ Dry ☐ Jaundiced	☐ ☐ ☐ ☐	Size (mm) Round Reactive Sluggish Fixed	☐ ☐ ☐ ☐		
		Rate: /min ☐ Regular ☐ Shallow ☐ Labored	Rate: bpm ☐ Regular ☐ Irregular		Hands: Feet: (seconds)	Sys: Dias: ☐ Central ☐ Peripheral	° ☐ C ☐ F	☐ Unremarkable ☐ Cool ☐ Pale ☐ Warm ☐ Cyanotic ☐ Moist ☐ Flushed ☐ Dry ☐ Jaundiced	☐ ☐ ☐ ☐	Size (mm) Round Reactive Sluggish Fixed	☐ ☐ ☐ ☐		

PATIENT TREND SHEET B
BLOOD GASES

Client Name:__________________________________**Client Number:**_____________________ **Page**_____**of**_____

Location:_______________________________________**Team Members Present:**____

Date	Military Time	pH	pO_2	pCO_2	TCO_2	HCO_3^-	O_2 Sat	BE	Lactate					Initials

PATIENT TREND SHEET C
CHEMISTRIES

Client Name:________________________________**Client Number:**____________________ **Page**_____**of**_____

Location:_____________________________________**Team Members Present:**____

Date	Military Time	Na	K	Cl	Ca	Mg	PO_4	BUN	Creat.	Hgb	Hct	Anion Gap	Osm.	Albumin	Total Protein	Initials

PATIENT TREND SHEET D
NOTES

Client Name:_____**Client Number:**_____ **Page**_____**of**_____

Location:_____**Team Members Present:**_____

Date	Military Time	Comments	Initials

APPENDIX 1

Glasgow Coma Score		
Eye Opening (E)	Verbal Response (V)	Motor Response (M)
4=Spontaneous 3=To voice 2=To pain 1=None	5=Normal conversation 4=Disoriented conversation 3=Words, but not coherent 2=No words.....only sounds 1=None	6=Normal 5=Localizes to pain 4=Withdraws to pain 3=Decorticate posture 2=Decerebrate 1=None
(Lowest possible score is 3 not 0.)		Total = E+V+M

(As an example, a Glasgow Coma Score would be recorded as follows: GCS 10 = E3 V3 M4 at 08:42.)

Scores are classified as: GCS ≤ 8 = Severe;
GCS 9 -12 = Moderate
GCS ≥ 13 = Mild

Normal Blood Gas and Chemistry Values:

		Arterial	Venous
pH	A measure of acidity or alkalinity	7.35 – 7.45	7.31 – 7.41
pO_2	Partial pressure of oxygen	75 – 100 mmHg	30 – 40 mmHg
pCO_2	Partial pressure of carbon dioxide	35 – 45 mmHg	41 – 51 mmHg
TCO_2	Total concentration of carbon dioxide	24 – 30	25 – 33
HCO_3^-	Bicarbonate	22 – 26 mEq/L	22 – 29 mEq/L
O_2 Sat	Saturation of oxygen	95 – 100% (sea level; room air)	60 – 85%
BE	Base Excess	-2 to +2 mmol/L	0 to 4mmol/L
Lactate		4.5 - 14.4 mg/dL	4.5 – 19.8 mg/dL
NA	Sodium	135 - 145 mEq/L	
K	Potassium	3.5 – 5.0 mEq/L	
Cl	Chloride	95 – 105 mEq/L	
Ca	Calcium (ionized)	2.2 – 2.5 mEq/L	
Mg	Magnesium	1.6 – 2.6 mEq/L	
PO_4	Phosphorus	2.5 – 4.5 mg/dL	
BUN	Blood Urea Nitrogen	5 – 25 mg/dL	
Creatinine		0.5 – 1.5 mg/dL	
Hgb	Hemoglobin	Male: 13 – 18 g/dL; Female: 12 – 16 g/dL	
Hct	Hematocrit	Male: 42 – 52 g/dL; Female: 37 – 47 g/dL	
Anion Gap		10 – 12 mEq/L	
Osmolality		280 – 300 mOsm/kg	
Albumin		3.5 – 5 g/dL	
Total Protein		6.0 – 8.0 g/dL	