Appendix 2: Writing Case Reports

Introduction

The most important reasons for writing case reports are:

1. *To provide a transparent and detailed description of procedures and techniques for members of the cryonics organization and the general public.* Writing case reports "forces" cryonics organizations repeatedly to document its procedures and protocols in detail. A cryonics organization that never writes anything about its cases and procedures should be treated with more caution than an organization that does.

2. *To validate current protocol and procedures in general, and actual implementation in particular.* A case report should not only record what happened but should be used for guidance as to what should happen in the future. A detailed case report, especially when a variety of physiological data has been collected, contains a wealth of information that can be analyzed for the team members' and patients' benefit. Cryonics cases are relatively rare compared with other medical procedures, so we should try to learn as much as we can from the cases we perform. A series of case reports can be used for meta-analysis.

3. *To serve as a medical record to assist with future attempts to revive the patient.* Although advanced future medical technologies may make it possible to determine the physiological condition of the patient down to the molecular level, it is important to provide as much medical information as possible to help in efforts to revive patients. Having a detailed record of the patient's condition prior to pronouncement, subsequent stabilization, and cryoprotection, may also help the organization in establishing the desired sequence of revival attempts.

4. *To gain more scientific credibility.* If we want scientists and physicians to take us seriously, we need to convince them that we are attempting to cryopreserve our patients in a scientific manner. Professional case reports can provide this kind of credibility.

This article will mainly concern itself with the general question of how a case report can help a cryonics organization in improving protocol, techniques, and skills.

Protocol

To be able to assess the quality of patient care in a cryonics case, it is important to recognize what the intended protocol was prior to writing about the case. Only if we know what the organization was *supposed* to do will we be able to assess how successful the case was. For example, if there is no mention of collecting (and analyzing) blood gases during a case this may have been because it is currently not a part of the organization's protocol, but it may also be the result of a shortage of skilled personnel, defective equipment, or other problems and deficiencies. Unless the writer of the report specifies what should have happened, it is difficult to assess the quality of preparation and performance. If preparation for the case was limited and there was no (functional) extracorporeal perfusion equipment available, the case report should not simply state that the organization did a case without substituting the blood with an organ preservation

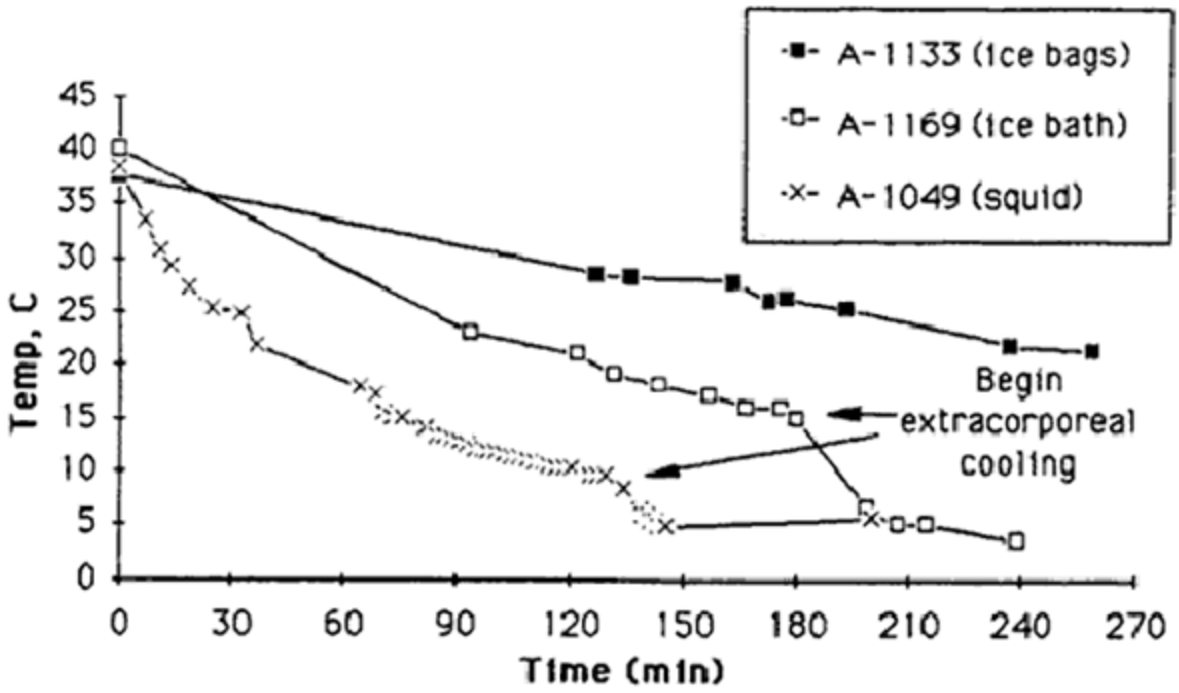
solution, but also identify and review the logistical factors or errors that were made that prevented a washout in the field. Since Alcor has a written protocol for all its major procedures, a case report can also refer to this instead of completely articulating it in the report. At a minimum, the case report writer(s) should check the performed procedures against the documented protocol (if available) and discuss changes or omissions in the report.

In practice there will be many deviations between the organization's protocol and what happens during a case. Human cryopreservation cases are not controlled laboratory experiments, and as many people who have extensive experience doing cases know, unique situations present themselves, including frustrating events that are beyond the control of even the most skilled medical professional. Nevertheless, the inherent unpredictability and uniqueness of cryonics cases is sometimes used as a reason for failing to follow established protocol, or for errors and omissions in patient care. Recognition of the intended protocol will help us to gain a more systematic understanding of what is possible (or essential) and within our control, versus that which is not.

Detail

The importance of writing detailed descriptions of the procedures and techniques employed during a case cannot be overestimated. This not only enables the reader to gain a comprehensive understanding of the techniques used, it also allows detailed analysis of the difficulties that were encountered during a case that would not have been noticed if there is only a brief mention of it. For example, instead of simply noting that medications were administered, providing comprehensive details and timelines is essential.

Case reports should be prepared with the possibility in mind that what may seem mysterious, or inexplicable, to the writer may be crystal clear to an expert or perceptive reader when provided with sufficient detail. Providing as much detail as possible also serves to allow for replication of the techniques used by others. This is a critical component of the scientific method. Other investigators or practitioners must be able to duplicate the procedures and obtain the same outcome. Yet another consideration is that factors currently not considered to be important may become so in the future. There are many examples of this in the history of cryonics that have proved essential to improving patient care. For example, in the early days of cryonics bags of ice were used to facilitate external cooling. It was not until comprehensive and consistent core cooling data were collected that it became apparent that this technique required 6-8 hours to cool a patient to approximately +20°C (room temperature) with the patient cooling at a rate of 0.064°C/min. Documentation of these very slow cooling rates provided powerful incentive to develop stirred water ice baths which increased cooling rates to between 0.15°C/min and 0.33°C /min, allowing cooling to about 15°C within 90 minutes to 2 hours after the start of cardiopulmonary support (CPS) (see graph below).



Comparison of Cooling Methods: Above are actual cooling curves for three adult human cryopreservation patients on Thumper support, using ice bags, the Portable Ice Bath (PIB), and the PIB augmented by SCCD (squid) cooling. Patient A-1133 weighed 56.8 kg, patient A-1169 weighed 57.3 kg, and patient A-1049 weighed 36.4 kg. As this data indicates, PIB cooling is approximately twice as efficient as ice bag cooling. The SCCD appears to increase the rate of cooling by an additional 50% over that of the PIB, (roughly adjusting for the difference in the patients' body masses). Source: Case Report Arlene Fried (A-1049).

This example is even more instructive because continued diligent and comprehensive monitoring of cooling in multiple patients made clear other factors that were critically important to good outcome or, conversely, prohibited it. A large-framed obese male with heavy fat cover and a large amount of thermal inertia will not cool at anywhere near the rate that an emaciated, petite woman will. Evaluating the patient for fat cover and body mass index before circulatory arrest allows reasonably accurate prediction of the cooling rate and may suggest the need for the addition of other cooling modalities such as "liquid ventilation" or peritoneal lavage with chilled fluid. Favorable results from application of peritoneal cooling in turn will suggest that even greater rates of cooling are possible for all patients and lead to the addition of the modality as a standard part of the protocol.

Failure to gather and promptly analyze data as basic as cooling rate precludes realization that problems exist as well as any possibility of solving them.

It is important to note that an incomplete case report doesn't necessarily indicate failure on the part of a cryonics organization. In a case where the number of team members is limited, all resources may have to be devoted to *doing* the case, instead of collecting data, or assigning an essential person to the job of taking notes. In the case of limited personnel, it is better to do a

good case without documentation than to document a bad case. To some degree this conflict between tasks can be avoided by having some of the team members (the team leader, paramedic, etc.) use a voice recorder with a clip-on microphone. But if the number of team members is insufficient, and data collection is not possible, this should be reported in the case report and recommendations should be made and implemented to prevent this situation from occurring again in the future. After all, deployment of insufficient team members it itself a breach of an organization's deployment protocol. Good data acquisition and scribe work are essential for a good case report and, if feasible, should be a full-time job during a case.

Analysis

Specifying the protocol and describing the case in detail is necessary but not sufficient. A critical review of the information and data culminating in a list of desired changes and specific plans to address them should complement this. Ideally every discrepancy between protocol and reality that has been observed during the case should be discussed. Even in a case where stabilization started promptly after pronouncement, and the protocol was followed to the letter, there is still a lot of (physiological) data that, once analyzed, may require a change in the protocol in future cases.

To assess skills, identify critical failures, formulate solutions, and compare cases in a meaningful and valid way, a consistent and systematic format of reporting cases is essential. A typical case report should be divided into sections describing protocol, patient assessment, preparation and deployment of standby assets, the details of the case (divided in sections such as airway management, cardiopulmonary support, external and other cooling methods, blood washout, cryoprotective perfusion, and cooling to storage temperature), analysis, recommendations, and a variety of (public or non-public) appendices. Such appendices should include time-lines and graphic presentation of data, medications, cryoprotectants, and statistical analysis and comparisons to other cases.

Each case report should not only present solutions, or suggest tests and experiments to identify solutions, but provide a plan of action as to how these things can be accomplished. One approach to ensure that research and tests to validate solutions are implemented, and appropriate remedial action is taken, is to appoint an officer in the organization who is responsible for quality assurance and quality control. This individual's job will be to ensure that case reports are written in a manner consistent with the guidelines as outlined by the organization, as well as to ensure implementation of required changes. It is important to ensure that any issues identified in a case are implemented in the next case (if feasible) and the following case report can then document the implementation of these measures.

Another critical role of case reports is to educate the organization's staff as well as consultants and, where appropriate, the patients' physicians and other health care providers about protocol, procedures and techniques. Although case reports are not and should not be a substitute for comprehensive written protocols, standard operating procedures (SOPs), and thorough training of personnel, sometimes solutions to problems can only be found in case reports where a team member was presented with an unusual problem. Consistent and systematic organization of case

reports will greatly enhance the utility of case reports for this purpose. For example, if a reader wants to know about surgical techniques, and problems encountered in gaining access to the circulatory system for blood washout, consulting a case report will be far easier if they're organized in a consistent and predictable manner.

Answering Objections

One objection to writing up a case report is that it is not a controlled experiment and at best provides only anecdotal evidence. This is not the case for the following reasons.

Not all the mistakes and issues identified are of a hypothesis testing nature. For example, if a patient presents team members with a problem that could not be managed with the equipment at hand, the cryonics organization doesn't necessarily need a larger number of cases to decide to make a change to their equipment and can start teaching employees the use the new equipment right away.

Similarly, what may be perceived as anecdotal evidence for the cryonics organization may be a consistent finding in nearly identical settings in mainstream medicine. For example, some issues during a human cryopreservation case may be well known in hemodynamic management of potential organ donors in hospitals, or, for example, a medication in the protocol that is undergoing trial as a stroke therapy may demonstrate the same adverse effects observed during transport of a cryonics patient.

Of course, such lessons are impossible to learn without broad and deep knowledge of medicine and the relevant research literature. Considering the ever-growing number of publications and hyper-specialization, case reports may increasingly become collaborations between numbers of people with expertise in diverse areas. The individuals with the most valuable input do not necessarily have to be the ones who did the case. A physician dealing with similar issues in a neuro-intensive care unit may identify problems and propose solutions not obvious to those delivering cryonics care to the patient. While the input of team members is necessary for a good report, it does not mean that they will be the most obvious writers of the report.

Monitoring

We don't know for sure how our patient is going to fare in the future but we can know a lot about how our patient fared up to the point of long term care if we monitor his condition continuously. This starts from collecting detailed pre-mortem medical data to monitoring fracturing events during cooldown and doing CT scans.

It is tempting to say that a case went very well if all the steps of the protocol were followed in a timely manner. This is not unreasonable because one would expect a strong correlation between an evidence-based protocol and optimal care. But it is important to keep in mind that the goal of stabilization and cryopreservation is to treat the patient and not the book (as a saying in emergency medicine goes).

Without comprehensive monitoring of the patient through all parts of the procedures a case report will only document a predictable series of mechanical steps and some crude visual

indicators of (relative) success at best. The things we are really interested in, like (quantitative) end-tidal CO2 measurements, cardiac output, pH, and cerebral oxygenation, cannot be observed without sophisticated equipment.

Not only do we want to know how the patient is doing after the fact, we would also like to be able to intervene *during* a case if we observe a trend that suggests (alternative) treatment. Only in-depth reporting and analysis combined with a sound understanding of the physiopathology and available treatments will enable us to do so.

Presentation

A comprehensive list of dos and don'ts in writing case reports is not something that can be explored in this article, but some things are worth mentioning. Stylistically, a human cryopreservation report should resemble a medical or research report rather than a sensationalized adventure for the patient or the standby team. This should apply to the organization of the material as well as the choosing of words. As a rule, mainstream medical terminology should be used instead of cryonics jargon or abbreviations that are only known and used within a particular facility. Editorializing should be limited, and if perceived necessary, be moved to the proper section of the report. For example, jumping from a technical description of procedures to quarrelling among relatives or complaining about government regulation doesn't look very professional. Adverse actions of individuals or organizations that must be reported because the actions materially impacted the case should be described objectively and dispassionately without speculation about motive.

Protocol, procedures, and techniques should be the subject of the report, not people. Cryonics preparation and procedures are very demanding and exhausting for all people involved and mistakes are made and will be made. Errors should be presented as dispassionately as possible to avoid a culture of blame and personal conflict. Experience also teaches that (potential) participants are more open to transparent reporting if a case report will not single out individuals by name in describing procedures. Issues that involve performance of specific people should be dealt with internally during case debriefings, not formal case reports.

No matter how competent the writer of the report is, each report should be proofread by most or all individuals who were involved in the case and, if possible, a variety of outsiders with appropriate technical and medical knowledge, before it is released to the public.

Confidentiality

If the patient of the case report selected in their membership paperwork to remain private after cryopreservation, then the public version of the case report must be stripped of all information that could be used to identify the patient. Pseudonyms may be used as appropriate, and identified as such. At least two people should independently confirm the public or private status of the patient by examining the most recent set of signup documents on file.

No non-staff members involved in the case, whether contract team members, volunteers, family members, medical personnel, funeral directors, or government officials should be identified by name in a public case report without permission of the individual. Similarly, company names,

such as funeral homes, hospices, or airlines should not be identified in public case reports without permission. Doing so might jeopardize cooperation in the future.

Public case reports should also exclude any medical history or case details that compromise the dignity or privacy of the cryopreserved person, whether the person is identified or not. Examples of such details include history of cosmetic surgery, substance abuse, sexual history, and mental health unless mental health was central to the cause of legal death. Writers and reviewers of case reports should edit the public version of case reports as though the report was describing their own cryopreservation. If there is doubt about whether a case detail is too personal, it should be excluded from the public report.

Patient Care

Writing case reports as presented in this article may be more demanding and time-consuming than generally has been done in human cryopreservation, but the results may improve patient care to a degree not previously seen. Ultimately, the most ambitious use of case reports will be one in which the case reports are analyzed as a series, measurements are compared, and patterns are established. Reading (and evaluating) a series of case reports in a systematic manner will even enable us to answer some very fundamental questions as to whether, or the degree to which, protocol, procedures, and techniques have improved over the years. A meta-analysis can also reveal what the typical expectations (cooling rate, duration of CPA, cryoprotective perfusion time, edema etc.) for a cryonics case should be given a certain protocol.

Providing the best patient care possible for current and future patients is the reason why cryonics organizations exist, and considering how powerful a tool a good case report can be, a responsible cryonics organization should devote considerable resources and time to writing them.

As our members and resources increase, and human cryopreservation gradually becomes a part of mainstream medicine, the successful transition from basic algorithmic, volunteer-driven care to evidence-based cryonics will be an important mandate.

Case reports and increasing caseload

One of the biggest challenges facing a growing cryonics organization is that it will also have more cases per year. This challenge is further amplified if all these cases need to be documented. Consequently, a cryonics organization will find itself allocating an increasing amount of time to writing case reports and falling behind publication schedule. One of the most unfortunate responses to such a development would be to try to keep writing case reports in the expected style but to lower standards and take short cuts.

An alternative approach is to develop a new format for case reports that allows for a shorter report but still captures the essential objectives of case reporting. One approach is to eliminate all the narrative that is not essential for following the mechanics of the case and evaluating the quality of care. In the past there have been several case reports with excessive narrative but little technical reporting or analysis. For a cryonics organization with a growing caseload the opposite approach should be followed. Another approach is to eliminate detail about procedures that were performed without deviations from past protocol and expectations, provided that this is made

explicit in the report. As a result, case reports will increasingly read as a description and commentary on events that diverged from protocol or new observations about existing procedures.

To establish a template for such case reports the following approach can be followed. First, it is established what kind of information is essential for doing a meta-analysis of all cryonics cases. Then these parameters are reverse-engineered to create a template for writing case reports that reconcile the need for economy of expression and documenting all the relevant aspects of a case. One important advantage of producing such case reports is they permit easier consultation of the technical details of the case and still meet the fundamental objectives of writing case reports.

Another attractive approach for writing case reports in an era of many cases is to identify one or more important issues or achievements in a case and build the report around this. This approach is consistent with the medical literature where case reports are often produced for patients with unusual outcomes, extraordinary interventions, or new medical developments. For example, a case could be published as "A-20xx: Extraordinary Cooling Rates Achieved During Stabilization" or "A-12xx: Patient with Fracture-Free Storage at Intermediate Temperatures". It should not be hard to find one or two important themes in the case data to justify such an approach. Writing case reports in this manner can be more rewarding for the writer and more engaging to read for the average reader.

The history of case report writing in cryonics shows an erratic potpourri of approaches and styles. One of the most unfortunate casualties has been the objective of using case reports to improve the practice of human cryopreservation and to formulate meaningful research questions for the sciences that inform cryonics. But if systematic thought is given to the objectives of case reporting outlined in this document, steps can be taken to leave this unsatisfactory situation behind while meeting the needs of a growing cryonics organization.

Who should write the case reports?

Historically, the tradition at Alcor was that a team member with the best writing skills and technical acumen wrote the case reports. As Alcor's caseload increased, this responsibility increasingly has shifted to the team leader and/or paramedic that was employed at Alcor. On the surface this does not appear to be an unreasonable choice but there can be complications. First, EMS personnel are not necessarily skilled writers or have the technical acumen to writes scientific evaluations of a case. Another problem is that there is a potential quality control conflict of interest issue when the person responsible for leading the case is also the writer. A possible solution is to recruit a quality control officer who is also responsible for writing the case report. This approach permits a more dispassionate analysis of the case and prevents skilled medical professionals being taken away from further education, training, and readiness responsibilities. A disadvantage of case reports prepared by persons not present is lack of direct knowledge of what transpired during the case. If different individuals write reports (which can happen when an organization tries to clear a long log of reports) it is still important to use a consistent template and style. Meta-analysis of large numbers of case reports becomes a lot more complicated when each case report is structured in a different manner.

A common flaw in case reports is high variability in procedure detail and data in a single report. Often this issue can be attributed to the practice of merging materials from various individuals and organizations without checking for (stylistic) consistency. A typical example of such a report is one with detailed stabilization report from the standby contract organization, an almost non-existent cryopreservation narrative from Alcor, followed by extensive unedited timelines.

Common flaws in case reports

The following list of recurring issues needs to be avoided in professional cryonics case reporting. In case of doubt, use mainstream medical case reports as a benchmark.

Inconsistent organization of the text from report to report

Improper use of team member names or cooperating people and institutions

Irrelevant anecdotical or biographical information

No reference to the protocol that should have been followed

Unedited, or excessively detailed, timelines

Detailed information about one procedure and little information about another

Imprecise nomenclature (such as the use of “suspension” or naming a section “perfusion” without specifying the type of perfusion)

No discussion of issues, recommendations, or follow-up actions

Notable Case Reports

1984

A-1056, A-1057 and unidentified patient

For all three patients fluid samples were obtained from the body of the patients after neuro conversion. The report specifies cryoprotectant osmolalities for all three patients in fluids obtained from different parts of the body. The author suggests that the low and variable distribution of cryoprotectant can be attributed to low volumes of the cryoprotectant and ischemia-induced perfusion impairment.

1985

A-1068 This case report contains an extensive discussion of blood, washout perfusate, and cryoprotectant perfusate samples.

1987

A-1133 This case report has an extensive appendix with graphs of blood gases, electrolytes, and enzymes data during cryoprotective perfusion.

1990

A-1049 One of the most comprehensive studies of a cryopreservation case ever written. This case also stands out for conducting a renal viability evaluation, which was possible because the patient was a neuro patient. The patient's kidney was subjected to renal slice intracellular/extracellular potassium/sodium ratio tests in a cryobiology lab and the average ratio of 3.5 corresponds to the expected value for such slices after a hypothermic storage time of approximately 2.5 days.

1995

A-1871 Detailed technical case report of the first cryopreservation by *CryoCare*, which was transferred to Alcor in 2001. Multiple external and internal cooling modalities are employed in this case.

2002

A-1876 Three boluses of perfluorocarbon, totaling more than 2 liters, were infused into the lungs of this Alcor patient to accelerate cooling, the first and only time basic "liquid ventilation" technologies have been used in cryonics.

2004

ACS 2004-1 Whole body field glycerol cryoprotection case by *Suspended Animation*.

2006

A-1097 The most extensive Alcor case report since the introduction of vitrification. This reports also includes the document "Advances in Cryonics Protocols, 1990-2006". Lowest first fracturing temperature recorded in an Alcor case (-134C)

2010

A-1712 Extensive documentation and discussion of Alcor's response to an autopsy case.