

Extraterrestrial Hemorrhage Control: Terrestrial Developments in Technique, Technology, and Philosophy with Applicability to Traumatic Hemorrhage Control in Long-Duration Spaceflight

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It is likely humans will venture beyond the relative safety of low earth orbit (LEO) during the next century, in space-faring journeys termed exploration class missions (ECMs).^{1,2} These missions will include manned missions to the Moon and, ultimately, Mars. Such a mission to Mars could entail a period of years in which space travelers would be unable to quickly return to Earth in the event of a serious surgical condition.^{3,4} These medical care challenges are greater than the engineering ones.⁴⁻⁶ Space medicine will always be limited by logistical factors such as limitations in weight, volume, power, and crew training. It will be driven by a focus on conditions that are most likely to occur, or would have the most impact on the crewmembers and mission. A human surgical event has not yet occurred in space, though injury has been ranked at the highest level of concern regarding the probable incidence versus impact⁷ and is considered a critical problem for which no reliable countermeasures exist in the National Aeronautics and Space Administration (NASA) Bioastronautics Critical

Path Roadmap for long-duration, human space exploration.⁸

On earth, hemorrhage has been identified as the leading cause of potentially preventable injury-related death.⁹ Bleeding to death accounts for 80% of intraoperative trauma deaths,¹⁰ with more than one-half of these arising from abdominal injuries.¹¹ Although many deaths result from anatomically complex wounds, many are still relatively simple wounds in otherwise healthy victims in whom appropriate interventions were delayed.¹² Hemorrhage control must remain within the capabilities of space medicine. In this regard, exploration class space travel represents a unique paradigm.

Travel beyond low earth orbit will represent the ultimate remote medical setting, yet a traumatic event in space is very likely to occur within or adjacent to the space vehicle or surface habitat, greatly increasing the chances the injured astronaut will survive to "the hospital." In this case, advanced medical technology might be prepositioned. The health and safety of astronauts who venture beyond earth's orbit will depend on future advances in engineering, medicine, biology, informatics, and robotics.¹³ A previous article reviewed fluid resuscitation in weightlessness.² This article reviews basic approaches to hemorrhage control both within and exterior to the major body cavities, and focuses on the foreseeable challenges for future trauma care during space flight. With mission profiles that will include human activities or even habitation on extraterrestrial surfaces, future planners will also have to consider the possibility of injury and treatment in reduced gravity environments such as the Moon ($\frac{1}{6}g$) or Mars ($\frac{1}{3}g$).

Currently available hemorrhage control in space

A major traumatic hemorrhage in space on any of the current man-rated space vehicles would be catastrophic

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The views expressed herein are solely those of the authors and do not reflect the official policies of the Canadian Space Agency, the National Aeronautics and Space Administration, or other departments of the governments of Canada or the United States of America.

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Abbreviations and Acronyms

CMO	= crew medical officer
EVA	= extravehicular activity
IR	= interventional radiology
MIS	= minimally invasive surgery

because medical care systems are limited. Resuscitative procedures are limited by available supplies and equipment and training of the personnel involved. On the International Space Station, medical care has largely focused on stabilization and expeditious evacuation back to definitive care on earth.^{4,14-16} Medical specifications for the International Space Station mandate the ability to comply with standard advanced trauma life-support techniques.^{17,18} Initiating an intravenous infusion, performing endotracheal intubation, and placing a chest tube are technically and logistically within the skill level of the onboard crew medical officer (CMO), and have been found to be feasible during evaluations in the temporary weightlessness of parabolic flight.¹⁹ CMOs are not required to be surgeons, or even physicians, and currently receive only 34 hours of medical training.²⁰ Even in low earth orbit, the International Space Station has only 50% to 70% real-time communication coverage. A Mars expedition would confront the issue of communication delays requiring 8 to 40 minutes for a round-trip,^{14,20} making real-time contact with surgical consultants impossible.

Cardiovascular physiology in prolonged weightlessness

In weightlessness, a multitude of physiologic changes occur that are likely to impair the ability to withstand injury.^{4,14} These include reductions in circulating blood volume, reduced red cell mass, cardiac atrophy and reduced cardiac outputs, alterations in vascular tone and neuroendocrine function, loss of the protective bony mass, and possible immune suppression.^{4,13,14,21-23} What degree of partial gravity, if any, would ameliorate these changes is also unknown.²⁰

Astronauts lose 10% to 23% of their circulating blood volume during space flight, resulting in an earth-equivalent hypovolemic state.²⁴⁻²⁷ A further "anemia of space flight," with a decreased red cell mass, is consistently seen after long-duration space flight and would aggravate the effects of blood loss. Mean decreases in red cell mass approximate 10% to 20% of preflight.²⁸⁻³⁰

During space flight, the working parameters of the neurohumoral and cardiovascular system are reset. Research suggests that there may be a global resetting of the autonomic nervous system with either a beta compared with alpha receptor bias, or impaired receptor sensitivities, resulting in an overall attenuation of the cardiac chronotropic response.^{7,23,31-34} The resultant attenuation of aortic, cardiopulmonary, and carotid baroreflex responses to hypotension would presumably decrease the ability of astronauts to respond appropriately to hypovolemic stress.^{30,35}

Trauma in space

The majority of trauma in space is likely to be blunt in nature.^{4,14} Extravehicular activity (EVA or "space-walk") is believed to be one of the riskiest activities. There are potential risks of penetrating space injuries during EVA from micrometeorites,²⁰ the lethality of which would depend on the body area of impact, impact size and integrity of the suit pressure seal, and proximity to airlock ingress. Blunt trauma may differ from the typical decelerative injuries seen after terrestrial vehicular crashes, with crushing injuries more likely.²⁰ This is from the movement of high mass structures during EVA performed for space flight construction.¹⁴ In such settings, astronauts might be dehydrated, losing an additional 0.7 to 2.2 kg of fluid in the Russian EVA experience.²³ In animal models, premonitory dehydration markedly compromises the ability to survive hemorrhage.^{36,37} Severe head injuries, which typically occur in 60% of severe terrestrial blunt trauma,³⁸ might also be less frequent because of the protection offered by the rigid space helmet. If death and disability from serious head injury are reduced, this will magnify the importance of providing effective hemorrhage control in space.

Bleeding characteristics will differ in weightlessness. The majority of surgical bleeding results in fluid domes that remain at the site of bleeding or adhere to adjacent objects such as gloves and instruments, rather than free bleeding.^{25,39,40} The force and volume of venous bleeding increase in space as compared with 1g, possibly because of the lack of venous wall compression.^{4,41,42} Russian reports of increased parenchymal congestion and blood pooling in the abdominal viscera during the year-long MIR mission⁴³ suggest that intraabdominal hemorrhage might be increased as well.

Conceptual approach to hemorrhage control in space

Hemorrhagic shock resulting from blood loss can occur either externally from open wounds, including those that communicate with the gastrointestinal, respiratory, or genitourinary tracts, or internally from bleeding into closed anatomic spaces. In adults, these spaces are the thoracic cavities, intra- and retroperitoneal spaces, and the soft tissues of multiple extremities.⁴⁴ Unfortunately, multisystem trauma can involve combinations of all sites. External blood loss should be readily detected by careful observation and palpation. In operational settings, many physically robust individuals have exsanguinated from wounds that could have been quite readily treated had simple first aid been available.^{12,45,46} Truncal hemorrhage presents challenges of a new magnitude. Intracavitary bleeding occurring inside the thoracic and abdominal cavities will be more difficult to detect and will require greater skill and resources to control. A classification of potential technical measures for hemorrhage control in space is given in Table 1.

Extracavitary hemorrhage control

Both advanced and prehospital trauma life-support courses currently recommend direct pressure as the most effective means of controlling life-threatening external hemorrhage.⁴⁷⁻⁴⁹ Although this conceptual approach has changed little in 2000 years, recent developments in wound dressings have improved the effectiveness of direct pressure. The United States Army has evaluated a number of hemostatic dressings for testing in complex models of active hemorrhage. Candidate hemostatic dressings that have all shown efficacy in specific circumstances include microfibrillar collagen, oxidized cellulose, thrombin, fibrinogen, propyl gallate, aluminum sulfate, fully acetylated poly-N-acetyl glucosamine, and chitosan.⁵⁰ Overall, stringent testing in these challenging models has confirmed statistical superiority in hemorrhage control for a dry fibrin dressing comprised of “fibrin glue” components.^{50,51} In a porcine aortic injury model, such a dressing appeared as effective as suture repair in hemorrhage control.⁵¹ These dressings have shown decreased blood loss even in settings in which distal arterial flow can be preserved.⁵²

Other novel, externally applied hemostatic agents are becoming available. QuickClot (Z-Medica) is a granular zeolite with an extremely long shelf life that exothermically adsorbs water to promote clotting. It can simply be

Table 1. Classification of Potential Technical Measures for Hemorrhage Control in Space

Extracavitary
Direct pressure
Tourniquet
Direct tissue clamping
Air splint
Fibrin bandage
Quick Clot
Chitosan dressing
Intracavitary (performed by on-board surgeon, telementored or decision-supported novice, or robotics)
Open surgery
Traditional definitive
Abbreviated
Cavitary endoscopy
Internal tamponade
Minimally invasive surgery
Angiographic
Vasoactive manipulation
Angioembolization
High-frequency ultrasound
Open
Percutaneous
Cavitary endoscopy
Adjunctive
Intracorporeal
Optimize
Temperature
pH
Platelets
Clotting factors
Fibrinogen
Circulating volume and blood pressure
Pharmacologic
Recombinant factor VII
Transexaminic acid
Aminocaproic acid
DD arginine vasopresin (DDAVP)
Vasopressor agents
Inotropic agents
Extracorporeal
Cardiovascular support
Controlled exsanguination
Suspended animation

poured into a wound by an untrained responder,^{53,54} noting that nothing “pours” in weightlessness. This agent significantly reduced mortality in a complex groin wound model compared with both control and standard dressings,⁵³ although there are concerns regarding sec-

ondary thermal effects. Chitosan is a complex carbohydrate that demonstrates mucoadhesive activity.⁵⁵ Lightweight and flexible chitosan dressings have markedly reduced hemorrhage and improved survival compared with gauze packing in a severe swine liver injury model.⁵⁵ Additional comparative studies in space conditions are required, but if equivalent, logistics would favor the lightest, safest, and most compact choice.

"Tactical tourniquets" are appropriate in operational settings when necessitated for life-threatening bleeding,⁴⁸⁻⁵⁶ but carry risks if left in place beyond 2 hours.⁵⁷ Pneumatic tourniquets apply pressure in a more evenly distributed fashion around a limb, reducing tourniquet edge stresses that can damage nerves.^{58,59} Recognizing this safety aspect, an expert panel has recommended the greater availability of this type of tourniquet in the combat casualty setting (personal communication, JB Holcomb, April 21, 2004). So the trauma pod of a space vehicle or habitat might be equipped with this capability as an initial response to serious extremity hemorrhage.

Intracavitary hemorrhage control

Ninety-nine percent of civilian hemorrhagic deaths are from truncal injuries not amenable to manual compression.⁶⁰ Early recognition of such serious injury might be aided by biophysical monitoring devices that would be worn during EVA activity, providing an early indication of vital sign irregularity.²⁰ Besides standard measurements, noninvasive candidates for early detection of physiologic distress include near infrared spectroscopic or transcutaneous monitoring of tissue oxygen or sublingual capnography.⁶¹⁻⁶⁵ After serious injury, standard life-support measures such as airway protection and drainage of hemopneumothoraces would be required and would be followed by an intravenous infusion, all demonstrated to be feasible in weightlessness.^{4,14,17} Fluid resuscitation in space has been previously reviewed,² but will be of secondary importance compared with the need to rapidly localize and address major internal hemorrhage.

Diagnostic imaging for localizing sites of hemorrhage

On earth, CT is the most accurate and expeditious means of imaging an injured patient. The use of multi-detector CT scanners in trauma applications is expanding.⁶⁶ Functional magnetic resonance (MR) is another

aspect of imaging that also assesses physiologic functions including blood flow, oxygenation, and metabolic activity.⁶⁷ MR imaging can now be performed intraoperatively, with many terrestrial operating rooms currently equipped with this technology.^{68,69} A lightweight MR could be constructed given current technology. In this way, real-time three-dimensional imaging of a sick or injured astronaut could be provided on board a spacecraft. Satava⁷⁰ stressed the information systems integration benefits of total body scans (holomers). Imaging of the human body is also recognized as an important research opportunity for space flight.⁶

At present, none of these imaging technologies is in orbit, but diagnostic ultrasonography is.^{22,71,72} On earth, early use of ultrasound to screen the traumatized victim is an important resuscitative measure with a Level I recommendation.⁷³ The diagnostic utility of focused ultrasound is maintained in weightlessness.^{72,74-76} The Focused Assessment with Sonography for Trauma (FAST) imaging protocol was validated during expedition five of the International Space Station (personal communication, J Jones, July 14, 2004). Hemothoraces after blunt injury can also be rapidly detected with ultrasound both on earth⁷⁷ and potentially in space.⁷⁶

As a further refinement of two-dimensional ultrasound, three-dimensional ultrasound appears to be a reliable and reproducible method of measuring irregular fluid and blood collections.⁷⁸⁻⁸⁰ Fully automated volume calculations, combined with transducers that automatically perform fast real-time sweeps of a predefined area (four-dimensional technology),^{79,81} offer the potential for generating continuous real-time assessment of visceral hemorrhage. The ideal posttraumatic imaging technology would create the astronauts' holomer, identify areas of intracavitary fluid accumulation, and evaluate the rate of accumulation. Terrestrial bleeding rates of 25 mL per minute have been estimated to allow a 2-hour window before death; a blood loss of 100 mL per minute would be fatal on earth in 30 minutes.⁸² Decision-support software accounting for individual and space acclimatized physiology might then determine when an alarming rate of bleeding was occurring despite treatment measures to conclude that high-risk but necessary invasive operative control was required.

Surgical procedures in space

Conventionally, when ongoing intracavitary hemorrhage with hemodynamic instability is identified, defin-

itive surgery should be performed promptly to control the hemorrhage.^{44,47} The technical performance of open surgery in space should be no more difficult than in a terrestrial environment with proper restraint of the patient, operators, and equipment, assuming there is an appropriately trained CMO.^{4,83-86} To date, no human surgical procedure has ever been required or performed in space,⁴ although operation with full recovery of animals was performed on STS-90 during the Neurolab mission.⁸⁷ As early as 1983, a council of trauma surgeons, space physicians, and biomedical engineers concluded that the capability of performing laparotomy on board a space station before transfer to earth could be lifesaving.⁸⁸ Any discussion of surgical requirements for space exploration must include the limitations in terms of personnel, material, and human physiology involved in longterm space habitation.^{4,14} The original plans for the Space Station *Freedom* mandated a Level III trauma capability, supporting the ability to perform a laparotomy. Currently, the International Space Station has only minor surgical capabilities and local anesthetics.^{4,18,89} With great commitments to CMO surgical training and medical care system resources, surgical capability could be provided aboard a new class of space exploration vehicle. It would represent the most tested intracavitary hemorrhage control technique.

Minimally invasive surgery

Besides the obligatory surgical trauma inevitable in open surgery, there are concerns regarding environmental contamination of the closed circuit environment of the spacecraft atmosphere with biologic contaminants, and with protecting the patient from this same environment and heat loss.^{20,90} Microorganisms in space appear to have greater virulence and resistance to common antibiotics, and will not settle out of the environment, as in gravity.²⁰ Opening closed body cavities under operating room lights is believed to be one of the greatest thermal stresses to which an injured patient may be subjected.⁹¹ Minimally invasive surgical (MIS) techniques use the general principles of minimizing access incisions and completing the operative procedure within the patient's closed internal cavities.⁹² MIS for trauma in space has initial appeal and has been found to be feasible in weightlessness during parabolic flight.^{85,86} Benefits would include minimizing postoperative morbidity, shielding the cabin environment from biologic components, protecting the patient from environmental partic-

ulates, maintaining thermal stability, and facilitating blood collection and autotransfusion. Surgical endoscopy can be used to diagnose the presence and source of hemorrhage, to evaluate the degree of organ injury, to aspirate and collect shed blood for autotransfusion, and to perform some therapeutic procedures.^{93,94} Instilled fibrin sealant foam (FSF) has been shown to significantly decrease hepatic bleeding in animal models compared with no treatment or placebo foam.⁹⁵ Fibrin sealant foam is believed to bond only to damaged intraperitoneal surfaces,⁹⁵ so it could conceivably be injected into the body cavities through an MIS technique.

Despite these theoretic advantages in MIS, there are safety concerns. Because of the vascular volume contraction and cardiac deconditioning, astronauts would be at a greater risk of hemodynamic compromise with raised thoracoabdominal pressure. In addition, even on earth, the exact role of MIS in evaluation and treatment of traumatic injury remains uncertain.⁹⁶

The damage control approach

If experienced surgeons will not be available in space, then the goals of any intervention must be focused and simplified. "Damage control" describes a constellation of approaches to surgical problems beyond immediate local capabilities or patient physiology, constituting a staged approach to surgical problems.^{97,98} A "damage control" or "abbreviated" laparotomy constitutes hemorrhage control, prevention of enteric spillage, and a ready acceptance of planned secondary or tertiary reoperations.⁹⁷⁻⁹⁹ The procedure must be accomplished quickly without exhausting the patient's physiologic reserve by minimizing blood and heat loss. On earth, this approach has generally been associated with severely injured patients. In space, limitations in resources or abilities of on-board medical care may warrant the same conceptual approach to injuries of lesser magnitude. Any procedures beyond the capabilities of the CMO could be managed in a staged or minimalist approach, allowing for temporizing measures to be instituted rather than committing irreversible anatomic alterations. Many of the technical requirements to abbreviate a laparotomy are conceptually and functionally much simpler than the more complex procedures required for elective surgery.⁹⁸⁻¹⁰¹ Even traditionally simple surgical tasks might be completed in a staged approach, allowing "just-in-time learning" and virtual reality-based rehearsals.

Although it would be daunting for a nonsurgeon to perform a laparotomy, the actual technique of opening a standard midline incision is technically quite simple, and has been performed successfully by specially trained paramedics in dire circumstances.¹⁰² It is what to do after opening that constitutes the real challenge. Prompt surgical use of gauze packing to arrest otherwise uncontrollable hemorrhage is believed to be a major advance in trauma care in the last several decades.⁹⁸ European authors favor pelvic packing as the initial approach to patients in extremis from severe pelvic fractures.¹⁰³ Both fibrin sealant and dry fibrin sealant bandages have been effective in reducing blood loss compared with either no intervention or standard gauze packing in swine models.¹⁰⁴⁻¹⁰⁶ Neither of these materials mandates reoperation for removal.¹⁰⁴⁻¹⁰⁶ In a worst-case scenario, when the on-board imaging system recognized ongoing intracavitary bleeding commensurate with death, the CMO would quickly open the cavity, pack with both fibrin bandages, or foam, and subsequently leave the abdomen open to assist with ventilatory management.

Potential percutaneous interventions for space

Although the previous approach might be initially life saving, it would raise a host of secondary medical, nursing, psychologic, and mission-specific concerns related to caring for an open abdomen in space. Even on earth, this management remains fraught with opinion and controversy with little controlled data. It is thought to be a major conceptual advance in trauma care, but results in a postoperative condition that is extremely intensive in terms of human labor. Any means of hemorrhage control applied through an otherwise intact body wall is inherently desirable.

Pneumatic compression

The application of increased intrathoracic airway pressure in the form of positive end-expiratory pressure to create a tamponade effect has been described in cardiac surgery.¹⁰⁷ Controlled studies of this approach did not confirm a hemostatic benefit,^{108,109} and the excessive pressure impeded the venous return, worsening hemodynamics.¹⁰⁸ A similar approach has been suggested in the peritoneal cavity, where the degree of increased pneumoperitoneum pressure inversely correlated with reduced splenic bleeding in a standardized injury.¹¹⁰ But major hemorrhage reduces the safe and tolerable level of

intraperitoneal pressure,¹¹¹ even without considering the circulatory volume contraction of space.

Pneumatic counter-pressurization is an aerospace medical countermeasure used for many years to prevent adverse pulmonary and cardiovascular effects of hypergravity and positive pressure breathing,¹¹²⁻¹¹⁴ and is currently a standard countermeasure worn by pilots during the critical shuttle landing phase.²³ A novel method of preserving cardiac performance, rather than embarrassing it through reduced preload, is electrocardiographic-synchronized, high-frequency jet ventilation. Cardiac output and oxygen delivery are increased with this ventilatory mode compared with ventilatory and unsynchronized jet ventilatory modes, especially with ventricular failure.^{115,116} Although terrestrially, these benefits may not be marked in patients with augmented circulatory volume and preserved ventricular function,¹¹⁷⁻¹¹⁸ an astronaut will be comparatively hypovolemic and subjected to cardiac atrophy as discussed. Earlier work with phasic intrathoracic pressure used abdominal and chest wall counter-pressurization to significantly increase cardiac output.¹¹⁹ If G-suits are manifested for space use, consideration might then be given to exploring their full potential in a "smart" configuration to provide partial hemodynamic support in the presence of raised intracavitary pressures.¹¹⁴ This would allow a time window for other nonoperative hemostatic measures to assist in arresting hemorrhage.

High-intensity focused ultrasound

High-intensity focused ultrasonography uses ultrasound energy focused into an effective volume about the size of a grain of sand.¹²⁰ Potential advantages for space include its use in visceral hemorrhage control within the substance of an injured organ, without charring or burning. This suggests the potential for percutaneous use.¹²⁰⁻¹²³ Through acoustic streaming and cavitation resulting in blood coagulation and tissue homogenization, the technique has been used to provide an effective hemorrhage control method for injured organs with active "wet" bleeding in controlled animal models.^{121,122}

Percutaneous interventional capabilities

The ability to introduce a catheter into a major blood vessel is a basic skill that a CMO should possess. This would allow introduction of a guidewire over which cannulae could be placed into the central circulation. Simple needles with an integrated ultrasound transducer at

the tip have been available for some time, with mixed results.¹²⁴⁻¹²⁶ Newer generations of smart catheters would continue to use portable ultrasound, but would envision a fully automated vascular target identification.¹²⁷ Future development of robotic capabilities could potentially use three-dimensional ultrasound, CT, or MR imaging to complete the catheter insertion autonomously. This would then facilitate pharmacologic manipulation of the cardiovascular system, extracorporeal hemodynamic support, thermal control, therapeutic intraluminal interventions, and potentially facilitate either suspended animation or euthanasia, if coupled to “smart” autonomous systems. Initial work has suggested that closed-loop resuscitation using fluid administration proportional to the measured value of a predefined end point may achieve favorable outcomes with less overall fluid administration and avoidance of over-resuscitation.⁶³ Although skilled human performance of these interventions would be desirable, all are potential areas of robotic research.

After prolonged weightlessness, the vasopressor response will likely be attenuated and the vasculature inherently vasodilated.^{2,14,23} There may be vasodilatory mediators induced by either traumatic¹²⁸ or septic pathways.^{20,129,130} Vasodilatory cardiovascular decompensation could be profound and requires carefully titrated vasopressor infusion, which should only be given into the central circulation to prevent tissue injury.

Systemic hypothermia is common after serious injury and is associated with death in multisystem trauma.¹³¹⁻¹³³ It has been stated that standard rewarming measures cannot sustain the necessary heat transfer levels required to prevent acquired hypothermia in the seriously injured.¹³⁴ For this reason, extracorporeal rewarming methods have been developed that rewarm hypothermic trauma patients significantly faster, using either the patient's own perfusion pressure^{135,136} or centrifugal blood pumps¹³⁷ to perfuse heparin-bonded circuitry. Simple heat-exchanging catheters using endovascular saline-perfused balloons with closed-loop computer feedback have been shown to be remarkably effective in prophylactically controlling the body temperature of patients with severe traumatic and nontraumatic head injuries who are hemodynamically stable.^{138,139} These devices have the capability to warm to 42°C, and might be used early to prevent hypothermia-induced coagulopathies.

Potentially, the greatest benefit of vascular access might be to facilitate therapeutic occlusion, emboliza-

tion, or stenting of damaged blood vessels. General anesthesia is not necessary and sterile fields are much reduced. Interventional radiology (IR) procedures are regularly used as adjunctive techniques to augment attempts at hemorrhage control after serious injury.¹⁴⁰⁻¹⁴² Primary uses of IR procedures also obviate the need for formal operations in some situations.¹⁴³⁻¹⁴⁶ Some groups believe IR is a superior approach when feasible, because it can potentially spare intraoperative hypotension in the severely head-injured group,¹⁴⁴ a known independent cause of secondary brain injury.¹⁴⁷ Combined CT and angiography suites capable of providing immediate IR after CT have been used for the critically injured.¹⁴³ The extension of this concept to a combined resuscitative/critical care pod with CT, IR, operative capabilities, and critical care is intuitive.

Blood and blood product administration

The rationale for administration of blood and the development of a space-specific hemoglobin-based oxygen carrier has been previously reviewed.² More than 20 years ago, consensus opinion regarding trauma acknowledged blood transfusion as a rate-limiting step in managing severe trauma in space. It was suggested that fresh blood transfusions could be taken from a crew selected on the basis of blood type compatibility to facilitate “warm” transfusions.¹⁴⁸ Although there are a number of reasons why astronauts would not wish to either donate or receive a complex biologic product such as blood,^{107,149} uncross-matched, untested, fresh whole blood has often been required in contemporary military operations.⁴⁶ Fresh whole blood was required in Somalia and, subjectively, the surgeons were impressed with its ability to ameliorate acquired coagulopathies.⁴⁶ It is extremely unlikely any blood product replacements could be available other than lyophilized platelet products, which although promising, are still in the very early stages of development.^{150,151} In the future, autologous products might be stored for individual or general crew use, but currently it is necessary to consider adjuncts that might ameliorate posttraumatic coagulopathies.

Adjunctive and pharmacologic measures for hemorrhagic shock

The most basic adjunctive methods for maintaining hemostasis involve preserving or correcting normal physiologic parameters of temperature, pH, platelets, clotting factors, and fibrinogen, and avoiding hyper-

resuscitation and hypertension.^{107,152} Given the immense challenges of addressing hemorrhagic shock in space, those measures may be impossible or insufficient. Even in the best equipped terrestrial trauma centers, coagulopathies are common in the most severely injured patients.¹⁵³ In anticipation of this, drugs might be given either individually, or as a “trauma cocktail,” to complement physical therapies on gaining vascular access. Such a cocktail might contain oxygen-carrying, vasoactive, antiinflammatory, and procoagulant agents.

The fibrinolytic system is immediately activated after trauma and remains elevated in patients with major injuries,¹⁵⁴ so systemic antifibrinolytics might enhance hemostasis after trauma. A number of commercial preparations are available, including aprotinin, tranexamic acid, and ϵ -aminocaproic acid,¹⁵⁴⁻¹⁵⁶ although most of the evidence is from elective cardiac surgery.¹⁵⁷ Aprotinin is a general inhibitor of proteases involved in fibrinolysis, inflammation, complement activation, and the kinin pathway, and may stabilize platelet membrane binding functions.^{107,155,158,159} Aprotinin has been consistently shown to reduce blood transfusions during cardiac and hepatic surgery,^{156,157,159-161} and has been associated with almost twofold decreases in mortality in certain circumstances.^{162,163} These agents have also been effective in controlling bleeding, even in the absence of documented hyperfibrinolysis.¹⁵⁸ Other antifibrinolytic agents such as tranexamic acid and ϵ -aminocaproic acid have shown promise^{157,160} and have reduced blood requirements in off-pump cardiac surgery, in which coagulopathies caused by the extracorporeal circulation cannot be implicated.^{158,164} Tranexamic acid specifically reduces blood transfusions in orthopaedic operations using exsanguinating tourniquets.^{165,166} Even the short-term application of a tourniquet greatly raises fibrinolytic activity,¹⁶⁷ which might further justify the use of tranexamic acid if such physical compression were required. Desmopressin is a vasopressin analogue that immediately raises factors VIII, XII, and von Willebrand factors after administration.^{107,156,158} Although there were enthusiastic early reports of desmopressin use, more recent studies of potential hemostatic benefits in previously normal individuals undergoing major surgery do not suggest a benefit.^{158,160,168,169}

Recombinant factor VIIa specifically acts at the local site of injury where tissue factor and phospholipids are exposed, potentially leading to a 1 million-fold ampli-

fication of localized coagulation.^{60,155,158} It facilitates hemostasis by activating the tissue factor-dependent pathway.¹⁵⁴ Despite theoretic concern, no increased incidence of prothrombotic complications has occurred.¹⁵⁸ Early use of rFVIIa in the field has been suggested as a potential means of promoting stable hematoma formation in soft tissue and visceral injuries and to protect patients from renewed bleeding after fluid resuscitation.^{82,170} Remarkable, but anecdotal cases of rescue from refractory coagulopathic bleeding when all other measures have failed have been recently reported.¹⁷¹⁻¹⁷⁴ Whether these spectacular successes can be confirmed in a prospectively randomized multinational trauma trial is yet to be determined.

Extracorporeal support and suspended animation

If the wounds sustained are beyond the capabilities of the medical resources on board, exsanguination might be inevitable. A high-flow heparin-bonded extracorporeal circulation might offer potential “heroic last-ditch” options: one to ameliorate the vascular failure of end-stage shock in an attempt to maintain perfusion of vital organs, the other to accept vascular collapse and to attempt to induce tolerance to such collapse.¹⁰² A centrifugal vortex blood pump with an oxygenator has been previously used for cardiopulmonary support in the critically injured.¹⁷⁵ This technology might bridge a period of extreme hemodynamic instability, or allow oxygenation of a patient suffering from a severe respiratory insult such as a massive toxic inhalation, but would be unsatisfactory for anything but a quick extraction from low earth’s orbit.

Suspended animation comprises treatment to preserve the viability of the entire organism from ischemia during no flow or very low (shock) states.^{176,177} This time window is intended to allow transport to definitive care and repair in a bloodless field, followed by controlled rewarming. The goal is to induce such a state with either hypothermia, pharmacologic agents, or special fluids. At present, the main modality for inducing such tolerance has been ultraprofound hypothermia, which allows for up to 2 hours of pulseless viability in large animal models.¹⁷⁷⁻¹⁷⁹ Current efforts in this field include development of fully synthetic solutions that completely replace the circulating blood volume after total body washout.¹⁷⁸ Whether directed pharmacologically engineered resuscitative solutions containing buffers, antioxidants, inhibitors of the ATP-sensitive potassium

channels, and oxygen-carrying solutions might be of benefit in these situations is speculative. During an exploration class mission, this window might allow for "just-in-time" learning, virtual reality rehearsal, and damage control in a bloodless field, rather than definitive evacuation. Although isolated supercooled (not frozen) cat brains have maintained elements of viability for more than 200 days,¹⁸⁰ many future advances to allow longterm suspended animation remain to be discovered. Any increase in the viable windows though, will be of immense benefit.

In conclusion, long-duration space flight presents a unique paradigm, being the ultimate remote medical care setting, but one where advanced technologies might be available to aid in hemorrhage control. No single method would be expected to be sufficient for all possible scenarios, yet logistics will require selection of only certain capabilities. Experienced surgeons offering traditional interventions would be highly desirable, but mission requirements may preclude this. Novel strategies and technologies using advanced imaging technologies, decision-support software, modified damage control algorithms, semi or fully autonomous vascular access, circulatory support and manipulation, and development of physical and pharmacologic adjuncts to hemostasis may all have potential utility. The International Space Station represents the most complicated multinational project in history that could provide a unique medical research platform to address surgical issues related to long-duration space flight. When fully operational, the station should support the centrifuge accommodation module, which would allow performance of detailed technology objectives in both weightlessness and specific reduced gravity environments. An organized effort to validate or refute, and ultimately improve upon the concepts discussed here, is recommended.

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