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# Anesthesia and Critical Care Delivery in Weightlessness: A Challenge for Research in Parabolic Flight Analogue Space Surgery Studies

**Short Title**: Anesthesia and Critical Care in Weightlessness

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48 **ABSTRACT**
49
50
51
52 **Background**: Multiple nations are actively pursuing manned exploration of space beyond low-earth orbit.
53 The responsibility to improve surgical care for spaceflight is substantial. Although the use of parabolic
54 flight as a terrestrial analogue to study surgery in weightlessness (0g) is well described, minimal data is
55 available to guide the appropriate delivery of anesthesia. After studying anesthetized pigs in a 0g
56 parabolic flight environment, our group developed of a comprehensive protocol describing prolonged
57 anesthesia in a parabolic flight analogue space surgery study (PFASSS). Novel challenges included a
58 physically remote vivarium, prolonged (>10 hour) anesthetic requirements, and the provision of
59 veterinary operating room / intensive care unit (ICU) equivalency onboard an aircraft with physical
60 dimensions of <1.5 $m^2$ (Falcon 20). Identification of an effective anesthetic regime is particularly
61 important because inhalant anesthesia cannot be used in-flight.
62
63 **Methods:** After ethical approval, multiple ground laboratory sessions were conducted with combinations
64 of anesthetic, pre-medication, and induction protocols on Yorkshire-cross specific pathogen-free (SPF)
65 pigs. Several constant rate infusion (CRI) intravenous anesthetic combinations were tested. In each
66 regimen, opioids were administered to ensure analgesia. Ventilation was supported mechanically with
67 blended gradients of oxygen. The best performing terrestrial 1g regime was flight tested in parabolic
68 flight for its effectiveness in sustaining optimal and prolonged anesthesia, analgesia, and maintaining
69 hemodynamic stability. Each flight day, a fully anaesthetized, ventilated and surgically instrumented pig
70 was transported to the Flight Research Laboratory (FRL) in a temperature-controlled animal ambulance.
71 A modular on-board surgical / ICU suite with appropriate anesthesia / ICU and surgical support
72 capabilities was employed.
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74 **Results:** The mean duration of anesthesia (per flight day) was 10.28 hours over four consecutive days. A
75 barbiturate and ketamine-based CRI anesthetic regimen supplemented with narcotic analgesia by bolus
76 administration offered the greatest prolonged hemodynamic stability through an IV route (within multiple
77 transport vehicles and differing gravitational environments). Standardization and pre-packaging of
78 anesthesia, emergency pharmaceuticals and consumables was found to facilitate the interchange of the
79 veterinary anesthesia team members between flights. This operational process was extremely challenging.
80
81 **Conclusions**: With careful organization of caregivers, equipment and protocols, providing anesthesia and
82 life support in weightlessness is theoretically possible. Unfortunately, human resource costs are extensive
83 and likely overwhelming. Comprehensive algorithms for extended spaceflight must recognize these costs
84 prior to making assumptions or attempting to provide critical care in space.
85
86
87 **Keywords:** Weightlessness, Space-flight, Critical Care medicine, Anesthesia, Surgical Therapy, Animal
88 Studies
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91 ## 1.0 INTRODUCTION

92 The potential to regularly extend human spaceflight beyond low-earth orbit is current. Over the
93 coming years, both the White House and National Aeronautics and Space Administration (NASA) expect
94 to return to the Moon with an anticipation of lunar inhabitance, and move towards a human exploration of
95 Mars(1). Other nations, as well as private industry, are also developing space-faring technology and
96 hardware(2, 3). Exploration has always had a human cost though, and space exploration is no exception.
97 In 1994, Billica and colleagues (4) ranked traumatic injury at the highest level of concern regarding the
98 probable incidence versus impact on mission and health(5). When the extended duration of these missions
99 is coupled with the high risk of the occurrence of a traumatic event, it is possible that invasive surgical
100 and interventional procedures may be required(3). Furthermore, life-threatening emergency surgical
101 conditions may arise without prior warning in the healthiest and fittest of young crew members(6, 7).
102 Because of our difficulty in providing an optimal anesthetic in space, the humane provision of surgical
103 care necessitates a realistic review of peri-operative and anesthetic capabilities during spaceflight(4, 8, 9).
104 In addition to the inherent hostility of this environment, crew medical officers (CMO) and flight surgeons
105 must also consider mission objectives when assessing a flight crew's response to a sick crewmember.
106 Unlike the past strategy of a "scoop and run" concept that required only stabilization and rapid
107 evacuation, the current reality of a "stand and fight" scenario is much more involved(10). This will
108 undoubtedly describe the situation on remote outposts such as the Moon or Mars. As a result, this shift in
109 philosophy has forced a reassessment of our ability to provide appropriate medical care during spaceflight
110 and habitation.

111

112 While there has been a modest amount of attention paid to the challenges of providing surgical
113 care and support in space, study of anesthetic issues has been minimal(3, 9). These concepts are critical as
114 there is uncertainty regarding many aspects of both anesthesia delivery and maintenance, as well as the
115 altered molecular pharmacokinetics (11), pharmacodynamics (12) and bioavailability (13) of drugs in

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116 microgravity. Even if the issue of a lack of gravitational separation between liquids and vapors could be
117 addressed, gas scavenging equipment would still be required given the fragile atmosphere. During the
118 recently initiated Canadian parabolic flight analogue space surgery study (PFASSS)(15), a concurrent
119 evaluation of the appropriate anesthesia delivery techniques for the parabolic flight environment was
120 completed. The primary goal of this study was to evaluate the process of providing anesthesia and critical
121 care during all phases of a PFASSS, building towards the actual parabolic flight. We hoped that by
122 examining the anesthetic tools required to facilitate surgical research in an operational flight environment,
123 theoretical extrapolation to actual long duration human spaceflight might be possible. This was done
124 using hierarchal and translational testing from laboratory to flight.
125

126 ## 2.0 METHODS:

127 The study was approved by the Canadian Space Agency (CSA), the Institutional Animal Care
128 Committees of the Universities of Calgary (UofC) and the University of Ottawa (UofO), as well as
129 National Research Council of Canada's Central and Institute for Biodiagnostics Animal Care Committees.
130 Purpose-bred SPF Yorkshire-cross pigs composed the experimental subjects. The translational program
131 regarding operational delivery of anesthesia was divided into 3 phases. Phases 1 and 2 were experimental
132 readiness segments. More specifically, phase 1 was conducted entirely within the animal care laboratories
133 (UofO) vivarium, while phase 2 comprised all terrestrial care (1) during transport the animal from the
134 UofO vivarium to the NRC-FRL, (2) at the NRC-FRL itself and (3) onboard the aircraft prior to flight.
135 Phase 3 incorporated all in-flight experimental work (four consecutive flight days (one pig / day)). The
136 purpose of Phase I was to develop and rehearse the anesthetic protocols pre-flight that could adequately
137 be utilized in the analogue environment during Phases II and III. Phase II advanced this hierarchy to
138 study the chosen regimen both in 1g transport and onboard the research aircraft prior to flight. By flying a
139 parabolic or ballistic profile, the Falcon 20 research aircraft (14) generates up to 25 seconds of effective
140 weightlessness (0g). This constitutes the most realistic space research analogue environment available on

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141 the earth's surface. The 0g periods are preceded, and followed, by intervals of hypergravity (2g). Finally
142 Phase III consisted of studying and refining the regimen in a true PFASSS.

143

144 During Phase 1 (days 37 and 30 pre-flight), the experimental team developed the animal transport
145 and in-flight anesthetic regimen, as well as the surgical instrumentation methodology. The anesthetic
146 regimen accounted for both the surgical requirements of the study, as well as species-specific drug
147 pharmacology. Detailed medication information is provided (Tables 1 and 2).

148

## 149 2.1 Phase I - 1g Terrestrial Vivarial Surgical Laboratory Research Environment

150

151 The anesthetic drug regimen of each pig is described in Table 2. The animals were first sedated via
152 IM injection (tiletamine/zolazepam/xylazine) in their pens, and then transferred onto a surgical table for
153 an inhalational induction with isoflurane. Due to the species specific risk of laryngospasm, lidocaine spray
154 was applied directly to the vocal cords prior to intubation. Once the tube was secured, monitors were
155 applied. This included 2 peripheral intravenous lines in the marginal ear veins and 1 line in each external
156 jugular vein. Blood pressure was measured via cannulation of both the carotid arteries. Heart rate, EKG,
157 blood pressure, rectal core temperature, pulse oximetry, and end-tidal carbon dioxide was measured at all
158 times using a portable physiologic monitor (SurgiVet, Smith Medical PM Inc., WI). There was no central
159 venous monitoring, however the bladder was catheterized. Arterial blood gases were measured in
160 intervals during the anesthetic. Normothermia was maintained.

161

162 Anesthesia was maintained for this pre-flight groundwork with isoflurane during line placement,
163 urethral catheterization and placement of the surgical ports. Depth of anesthesia was judged based on
164 clinical assessment of physiologic variables (coronet – hoof pinch; anal sphincter pinch; corneal

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165 positioning; muscle relaxation of tongue and lower jaw; heart rate; blood pressure). Buprenorphine
166 intravenous was utilized for supplemental analgesia intermittently. Normothermia was maintained.
167

168 **2.2 Phase II – 1g Environment**

169 On flight days minus 14 and minus 1, the Phase I protocol was expanded to further refine the
170 anesthetic regimen. It facilitated the transfer of a fully anesthetized and ventilated animal with complete
171 physiological monitoring/support from the vivarium to the ambulance, and then to the Falcon 20 research
172 aircraft. This phase also had to account for a lack of surgical stimulation during transport (i.e.
173 hemodynamic stimulation). One of the two animals studied in phase II was carried on board the Falcon 20
174 research aircraft to fully simulate in-flight conditions (Figure 1).
175

176 The transition from an inhalational agent (isoflurane) to a continuous rate infusion (CRI) with a
177 steady-state drug level began immediately after completion of invasive monitoring and surgical
178 preparations. This was performed during preparation for transport (20-40 min). For the remainder of the
179 study including Phases II and III, sodium pentobarbital was employed as a basic anesthetic agent, which
180 was then supplemented with ketamine hydrochloride because of its cardio-stimulatory effects. Depth of
181 anesthesia was again judged based on clinical assessment of physiologic variables (coronet – hoof pinch;
182 anal sphincter pinch; corneal positioning; muscle relaxation of tongue and lower jaw; heart rate; blood
183 pressure). Intravenous buprenorphine was also utilized for intermittent supplemental analgesia (because of
184 the unpredictable swine-specific release of fentanyl skin patches which were administered 24 hours pre-
185 operatively). Neuromuscular blockade was not administered during this phase. Depth of anesthesia was
186 again clinically monitored. During ground transport from the vivarial laboratory to the FRL, the team was
187 also forced to adjust to an ambient temperature of -30$^0$C. Normothermia was maintained with warmed
188 fluids, foil blanket wraps, bubble wrap thermal blankets, chemical heat packs and/or hot water bottles.
189 The ambulance was also pre-heated to 12 $^0$C. None of the pigs experienced hypothermia.

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190

191 Transfer from the ambulance to the Falcon 20 research aircraft involved securing each pig to the
192 life-support surgical rack (LSSR). The LSSR is a modular, compact critical care / resuscitation / surgical
193 suite specifically designed and constructed to conform to the physical and electrical constraints of the
194 Falcon 20 aircraft (with the ability to withstand 7g gravitational forces). This compact platform provided
195 critical care physiologic monitoring of multiple vital signs, full CRI intravenous anesthesia and fluid
196 therapy with 3 constant infusion pumps, mechanical ventilation with blended gradients of oxygen (HT-50
197 Ventilator, Newport Medical, Costa Mesa, CA), laparoscopic visualization and surgical capabilities,
198 carbon dioxide insufflators, light source, and miniaturized camera with duplicative digital video disc
199 (DVC) recording capabilities (Figure 2). On-board, the anesthesia provider was positioned at the head of
200 the subject facing the LSSR physiologic monitors. The ventilators were positioned just below. The CRI
201 pumps were located on either side of the physiologic monitor with additional warmed fluids and
202 medications within reach (Figure 3.).

203

204 **2.3 Phase III - In flight Weightless Analogue Environment**

205 Phase III (onboard the Falcon 20) expanded upon the methods and protocols of Phases I and II by
206 adding in-flight laparoscopic surgical manipulation, pulmonary function parameter assessment, as well as
207 arterial blood gas sampling for terrestrial analysis using the i-STAT and i-STAT CG8+ cartridge (i-
208 STAT: Abbott Laboratories, Princeton, NJ). Given the use of sodium pentobarbital, arterial blood gases
209 were used to confirm relatively normal acid-base status. In- flight preparedness necessitated the pre-
210 packaging of resuscitative fluids and medications in anticipation of any physiological requirements
211 including resuscitation (Figure 4.). These materials were placed on board the research aircraft in personal
212 medical kits and/or in an on-board locker readily accessible to the veterinary team/anesthesia providers
213 (Table 1). Four animals were flown over four consecutive days (one per day). Each research day,
214 laparoscopy was performed during the taxis, level flight and parabolic flight periods. Fifty-nine separate

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215 parabolas were completed (total duration of anesthesia averaging 10.28 hours per day)(total flight time
216 was 81 to 106 minutes per day)(total microgravity time was approximately 30 minutes). Real-time
217 "lessons learned", and perceived effectiveness of interventions and pharmaceuticals were evaluated
218 through the compilation of daily flight logs. The in-flight anesthetic regimen is given in Table 2.
219 Intravenous pancuronium (0.06 mg/kg ) was administered at the onset of the daily flights only after
220 ensuring adequacy of anesthesia depth clinically. It should be noted that normothermia was maintained in
221 the same fashion as during phase II.
222
223 After all study phases were completed, the veterinary team reviewed all fluids and medications to
224 assess their relative importance for the space analogue environmental study, as well as to consider their
225 perceived applicability for future use. This ranking was completed using a simple assessment of "highly
226 and routinely useful" (Rank A), "highly but infrequently useful" (Rank B), "possibly useful" (Rank C), or
227 "not useful and/or not required" (Rank D) (Table 3).
228

## 229 3.0 RESULTS

### 230 3.1 1g Terrestrial Vivarial Surgical Laboratory and Transport Environment

231 Animals were surgically prepared for in-flight experiments on a standard surgical table with a
232 constant 1 g gravitational field. Inhalational anesthesia was preferred by the anesthesia providers due to
233 comfort and ease of titratability to the pigs' responses to various surgical procedures (including a
234 prolonged perineal dissection for urethral catherization in this species of animal). After trials of different
235 drug regimens including propofol, the final drug regimen of sodium pentobarbital and ketamine was
236 found to be most reliable and predictable for the prolonged duration of anesthesia and varying stimuli.
237

### 238 3.2 In-flight Weightless Space Analogue Environment

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239 The total duration of general anesthesia administered during the flight phases of the study was 9.0
240 hours on Flight Day 1, 10.1 hours on Flight Day 2, 10.7 hours on Flight Day 3, and 11.3 hours on Flight
241 Day 4 (average time = 10.28 hours per day). The in-flight weightless analogue environment proved to be
242 the most difficult environment of all settings because of the superimposed operational and anesthetic
243 challenges on an already technically complex animal model. Avoidance of hypothermia was also a
244 significant challenge during the on-board, in-flight segments of the experiments. More specifically, an air
245 draft under the LSSR promoted convectional heat loss. The parenteral fluid supply, which was warmed
246 pre-flight had often cooled to the ambient temperature.
247

248 ***3.2.1 Anesthetic Provider In-flight Space Analogue Environmental Issues***

249 The parabolic flight environment proved physically and psychologically challenging for the
250 veterinary team anesthetic providers. Motion sickness affected 25% (one if four) of the team. Engaging in
251 rapid head movements and reading multiple electronic monitors proved to be the most difficult activities.
252 This was particularly evident when the animal critical care support requirements necessitated these
253 activities during rapid turns and/or accelerations / decelerations. These positions are known to be the most
254 provocative for inciting neurovestibular distress.
255

256 ***3.2.2 Research Subject In-flight Space Analogue Environmental Issues***

257 The animals tolerated multiple transportation vehicles and the analogue environment with
258 provision of an effective anesthetic regimen. They did require ongoing fluid resuscitation to maintain
259 adequate blood pressure (systolic/diastolic pressure) however. The rate of crystalloid fluid administration
260 was 10 ml/kg/hour (from the time of sedation) unless hemodynamic complications arose. These scenarios
261 necessitated additional fluid support (e.g. blood loss; sepsis). Unexpected complications included a
262 cardiovascular arrest (ventricular tachycardia) during the third series of parabolic flights (approximately 9
263 hours after the induction of general anesthesia). The subject was successfully returned to spontaneous

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264 circulation using mechanical cardiopulmonary resuscitation (standard chest compressions for less than 1
265 minute performed in the 1g phase of flight), epinephrine (0.01-0.02 mg / kg, IV) and phenylephrine (1-3
266 ug/kg/min, IV). This pig subsequently developed a massive arrhythmia which was stabilized by
267 administration of lidocaine (1.1 mg / kg, IV) followed by a continuous infusion of 0.025 mg / kg / min.
268 The on-board care-providers assessment of medication effectiveness is provided (Table 3).
269

270 An additional complication occurred in the fourth flight (accidental bowel perforation early during
271 the first of four flights). The pig subsequently developed tachycardia, fever, and hypotension requiring the
272 ongoing infusion of large volumes of parenteral fluids (330 ml/kg/hour), phenylephrine infusion (1-3
273 ug/kg/min IV), as well as antibiotic (cephazolin, 25 mg / kg, IV) and steroid administration (prednisolone
274 sodium succinate, 100 mg, IV). This was consistent with a clinical diagnosis of septic shock. The animal
275 was supported for seven additional hours to complete three flights and 12 more parabolas. This critical
276 care support necessitated near constant care by a minimum of two veterinary team members, especially
277 during parabolic flight. During the alternating hyper / microgravity phase of flight, the animal required
278 repeated boluses of fluid in addition to crystalloid supplementation via a constant infusion. Pharmacologic
279 therapy was also needed. Although the team was reasonably “flight acclimatized” after a minimum of
280 three previous flight days, this level of work in a constrained and resource-limited flight-environment was
281 significantly challenging. It also exhausted the supply of parenteral fluid. While this effort rescued the
282 animal and research data, it was universally perceived to be non-sustainable with respect to human and
283 material resources on a long-term basis.
284

285 ## 4.0 DISCUSSION

286 In conjunction with resuscitation of a critically ill astronaut, anesthesia, post-anesthetic recovery,
287 and critical care life support will also be required if surgery is to be attempted in space. Although the

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288 ethical conduct of surgery for life-threatening conditions implies a need for these activities, there has been
289 little focus on the actual anesthetic and critical care requirements in either space, or space analogue
290 environments. Because our surgical research in a PFASSS environment incorporated a robust effort to
291 ensure the best possible veterinary care, we learned and documented a great deal regarding the challenges
292 and practicalities of delivering anesthesia and critical care in a microgravity environment.
293

294 A single previous report describing surgical procedures on rats in true space used intramuscular
295 and intra-peritoneal anesthesia injections to good effect(16). Although the procedures were intricate, they
296 did not require "prolonged" anesthesia of greater than 8 hours (17). All other modern literature describing
297 parabolic flight analogue environments has delivered anesthetics solely via an IV route(18-22). We found
298 the CRI approach provided the flexibility to deliver anesthesia "to effect." It also allowed providers to
299 respond quickly to both animal and surgical contingencies. Sodium pentobarbital, a veterinary anesthetic
300 agent with a long history, was utilized as the primary agent. Unfortunately, high doses of this drug are
301 required for provision of the appropriate in-flight surgical support. Because of the dose dependent
302 cardiovascular and respiratory depression, this medication was considered to be unacceptable as a sole
303 agent. Ketamine hydrochloride was therefore employed as a second agent (cardio-stimulatory via the
304 sympathetic nervous system)(23). The addition of ketamine permitted adjustments to the delivery of
305 sodium pentobarbital when blood pressure or heart rate was of concern to the veterinary team. More
306 specifically, during periods of decreased cardiac output, the rate of sodium pentobarbital infusion was
307 decreased (or withdrawn) until cardiac or physiologic parameters stabilized. The ability to deliver
308 increased inhaled fractions of oxygen (up to a $Fi0_2$ of 100%) was also critical given the utilization of a
309 sodium pentobarbital-based regimen. This protocol countervails not only the pharmaco-respiratory
310 depressive effects of the short-acting barbiturate and its derivative cardiovascular impact, but also the
311 effects of 2g gravitational forces experienced at the beginning and end of each flight parabola. It should
312 also be noted that the animal's positioning would likely have contributed to ventilation-perfusion

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313 disturbances because swine do not normally lie in dorsal recumbency. Furthermore, high pressure
314 abdominal insufflation may further compromise animal physiology(15).
315
316 It must be cautioned that while parabolic flight is currently the best available terrestrial weightless
317 analogue, it has numerous limitations. These are related to the short periods of true weightlessness (20 –
318 25 seconds), imprecision of the actual weightlessness (g-jitters), and requirement for hypergravity both
319 before and after weightlessness(6, 24-26). Additional study limitations related to the ability of our model
320 to act as a pure analogue for similar anesthesia issues during human spaceflight included a restriction to
321 IV sedation during flight (rather than inhaled gases) because: 1) the carrying capacity for oxygen would
322 have been limited if isoflurane had been employed, 2) the rules regarding anchoring of payloads in the
323 Falcon 20 were very strict, and 3) the operator risks would have been significant in an open cabin setting
324 in the event of a scavenging failure. These challenges are also present for humans in spaceflight where
325 intravenous agents (propofol, sodium thiopental, benzodiazepines, ketamine, opioids) using either a bolus
326 or continuous infusion technique are theoretically preferred (9). Other methodology fidelity included the
327 need to overcome a lack of gravity-dependent flow with IV pumps, as well as the use of filters to prevent
328 gas/air embolisms. The need for bilateral carotid artery cannulation is also unique to swine (who possess a
329 complete rete mirabilis and therefore receive significantly more cerebral perfusion from their vertebral
330 arteries) and not typically required for laparoscopy in human patients.
331
332 Our findings support many previous opinions regarding anesthesia in space. Pre-planning of
333 regimens and efficient packaging of pharmaceuticals is essential. Unlike the Neurolab mission which
334 administered pre-loaded syringes of anesthetic "cocktails" according to a tail-length nomogram, our
335 experience with larger animals suggests that local and IV anesthetic agents should be the preferred
336 method of delivering anesthesia for operative procedures. This could tentatively be extrapolated to
337 humans in true space-flight, assuming the issues of limited CMO training, insufficient supplies of

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338 consumables (IV catheters, tubing and needles), and the absence of multiple-line infusion pumps in
339 current spacecrafts are overcome (27, 28). Unfortunately these recommendations do not directly account
340 for the altered patient physiology, drug distributions or pharmaceutical responses found during true
341 spaceflight (i.e. compared to PFASS scenarios)(29-31). This also applies to many of the medications
342 utilized in our study including neuromuscular blockade agents, barbituates, dissociative anesthetic agents,
343 narcotics and vasopressors. Reviews of pharmaceutical behavior in microgravity have identified increased
344 animal sensitivities to drugs such as benzodiazepines and barbiturates(29). It is unclear if this is a result of
345 the decrease in plasma volume (decreased red cell mass, dehydration and increased fluid shifts to
346 extravascular locations) observed during space flight, or other factors such as alterations in the
347 neurovestibular, neuromuscular, renal or gastrointestinal systems(29).
348
349 Based on our three-tiered study of prolonged anesthesia in ground, transport, and flight phases, as
350 well as the greater risks of other potential anesthetic techniques, we recommend an IV anesthesia regimen
351 with blended gradient oxygenation for future PFASSSs. Not only are inhaled agents potentially dangerous
352 if leaked within a closed environment such as a spacecraft, but they also require a liquid-gas interface
353 based on Earth's gravitational field for adequate and predictable effects(9, 26, 28, 32). In the absence of
354 gravity, the ability to predict and precisely titrate pharmaceuticals remains unknown. This concept can be
355 extended to spinal anesthetics that depend on the relative baricity of drug in the spinal fluid (2, 9, 28).
356 The ability of a CMO with limited training to place a needle in the CSF is also suspect. The delivery of
357 pharmaceuticals is less concerning with IV anesthetics, as evidenced by the ability of trained personnel to
358 administer medications during operative interventions performed in microgravity(18, 33).
359
360 Similar to previous literature, we found that all complex anesthesia and critical care interventions
361 (in-flight re-intubation, mechanical ventilation, cardiopulmonary resuscitation, fluid and vasopressor
362 therapy) were feasible. The critical limitation appears to be one of sustainability. Critical illness or injury

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363 of any type will quickly consume a large proportion of consumable supplies on any spacecraft that cannot
364 be regenerated or produced(1). Both the Space Shuttle and International Space Station are provisioned
365 with a very limited supply of crystalloid fluids(2, 34). The requirements for maintenance and resuscitation
366 fluids that we experienced during our relatively brief PFASSS would have consumed all on-board fluids
367 early into any potential space exploration mission leaving none for any on-going postoperative or critical
368 care. Similar to the immense differences between terrestrial operating rooms and spacecraft surgical
369 environments, the capabilities of postoperative anesthesia recovery or intensive care units (ICU) are also
370 incomparable. In addition to subspecialty nursing, postoperative real-time physiologic monitoring
371 represents the true hallmark of a modern critical care unit. On a spacecraft, patient observation is currently
372 limited to a basic monitoring system with the ability to extract heart rate, blood pressure, respiratory rate
373 and body temperature metrics. Additional information such as abdominal compartment, central venous,
374 pericardiac, and intracranial pressures are not available. While these data points are not crucial to the
375 outcome of all patients, they do determine treatment plans and subsequent interventions in some.
376

377 More so than any equipment or supply limitation, potential human resource exhaustion is
378 particularly concerning. The ability of a non-medical CMO to place, interpret and maintain these
379 advanced monitoring systems is doubtful. The absence of comprehensive physiologic data (i.e. CVP, ICP,
380 pericardiac, IAP) question our ability to provide appropriate postoperative critical care during extended
381 duration space-flight missions where immediate evacuation to another facility is not possible. It should
382 also be noted that the need to perform a trauma-related damage control procedure to arrest acute
383 intracavity hemorrhage and control intestinal spillage aboard a spacecraft has been considered
384 important(35). In addition to repeated operative procedures and close physiologic monitoring, these
385 patients require adequate sedation and frequent paralyzation in their immediate post-operative course. The
386 challenges mentioned above would be amplified in such a context of advanced trauma care.
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388 Critical-care nursing is another medical commodity that may not be available in space missions.
389 Just as the skill and training of the surgeon and anesthesiologist are critical to determining which
390 procedures can be performed during spaceflight, so are the skill sets of the postoperative and critical care
391 nurses. Critical-care nursing is cognitively and procedurally demanding. In addition to interpreting the
392 most complicated monitoring systems available in medicine, nurses must prepare, calibrate and often
393 trouble-shoot these devices. This reality must be incorporated into future space mission training
394 assessments. The care of a critically ill patient is also incredibly taxing, often requiring near continuous
395 reassessment and intervention at the bedside. If a single on-board CMO were to administer an anesthetic
396 and provide postoperative critical care, there would be little distinction between the "operative" and
397 "ICU" phases. Independent of the increased stress in caring for a close associate akin to a family
398 member, the challenges of this scenario would likely extend beyond the mental or physical capabilities of
399 a single caregiver. In managing the case of septic shock from a bowel perforation during flight day four,
400 the provision of anesthesia, sedation, vasopressors, fluid resuscitation, and successful cardiopulmonary
401 resuscitation required the continuous service of a minimum of two veterinary physicians. This level of
402 care would not be sustainable, regardless of the dedication of a single crewmember. Furthermore, this
403 level of commitment would prevent that crewmember from completing any other duties. Such challenges
404 have led NASA to identify strategies that will provide autonomous critical care during Exploration
405 flights(1) using closed-loop algorithms for both ventilation and fluid resuscitation(36, 37).
406

407 Although the available "space-ready" surgical, medical, and critical care techniques might
408 contribute to overall success or failure, nursing and rehabilitation resources must also be considered. If
409 appropriate post-operative care cannot be offered, then perhaps it is unethical to offer initial surgical
410 intervention. In this scenario, palliation would be the only realistic solution. These questions must be
411 addressed through the development of protocols and decisional matrices in advance of a space mission, as
412 it would be nearly impossible for an emotionally involved crew-member to make them in isolation.

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413 Ultimately though the medical care limitations inherent in space missions will likely necessitate that as a
414 pre-condition of participation in the space mission, crew members be not only informed about but agree to
415 abide by these medical decisional matrices in advance of the mission (i.e. informed consent to non-
416 restorative medical treatment).
417
418 **5.0 SUMMARY**

419 Ethical experimental surgery in a PFASSS requires adequate general anesthesia. An IV anesthetic
420 regimen supported by multi-modal vital sign monitoring and a trained veterinary team ensured adequate
421 care throughout a period of prolonged surgical procedure and a moderate duration life-support. The
422 details of our regimen are thus presented to guide future investigators in planning similar investigations in
423 parabolic flight. The complicated logistics and pharmaceutical supplies required need to be appreciated
424 prior to initiating any surgical studies. The overall process was extremely intensive considering the
425 equipment, consumable, and even human resource costs. By extrapolating our experience to the projected
426 future delivery of care in a long duration space mission, we conclude that although a team of trained
427 providers could provide prolonged "routine" anesthesia and critical care support (and respond
428 successfully to many acute life-threatening emergencies), they could not sustain the high level of acute
429 care typically required in a terrestrial ICU for any significant length of time. As a result, one CMO would
430 not be able to provide anesthesia and surgical critical care support for an injured crew member. Additional
431 research is required in both microgravity research environments, and aboard a spacecraft to better define
432 the limitations of medical care delivery during a prolonged space mission.
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434 ## 6.0 Tables and Figures

435

436 ### 6.1 Tables

437 **Table 1.** **On-board Fluids and Medications for Parabolic Flight Space Analogue Surgery**

438 **Table 2.** **The Anesthetic Regimen**

439 **Table 3.** **Survey of Perceived Usefulness of In-flight Medications & Equipment for Future**
440 **Flights**
441
442

443 ### 6.2 Figures
444
445 **Figure 1.** **Phase II - Instrumentation and monitoring during in-flight simulation**

446 **Figure 2.** **Life-support surgical rack (LSSR) onboard the Falcon 20 aircraft**

447 **Figure 3.** **Phase III - Instrumentation and Ventilation onboard the Falcon 20**

448 **Figure 4.** **Pre-packaged pre-mixed pharmaceuticals for use during PFASSS**

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456 **Table 1 - On-board Fluids and Medications for Parabolic Flight Space Analogue Surgery**

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| MEDICATIONS | DOSE[1, 2] |
|---|---|
| Atropine sulfate, Bimeda MTC, Cambridge, ON, CDA | 0.02 mg/kg IV slowly up to 0.5 mg/kg |
| Buprenorphine, Buprenex®, Reckitt Benckiser Healthcare Ltd. Richmond, VA, USA | 0.025 mg/kg (up to 0.1 mg/kg) |
| Cefazolin®, NovoPharm Toronto, ON, CDA | 25.0 mg/kg |
| Dopamine HCl, Baxter Corp. Toronto, ON, CDA | 5µg/kg/min (range 0.5-10µg/kg/min) |
| Epinephrine, Epiclor®, Rafter Products, Calgary, AB, CDA | 0.01- 0.02mg/kg IV slowly |
| Fentanyl, Duragesic®, Janssen-Ortho, Markham, ON, CDA | 50 µg/hr skin patch |
| Furosemide, Lasix®, Sandoz, CDA | 2-4 mg/kg IV or IM |
| Isoflurane, AErrane®, Baxter Corp. Mississauga, ON, CDA | 5.0% to 1.0%.; maintenance 2.5% |
| Ketamine HCl, Vetalar®, Bioniche, Belleville, ON, CDA | 11.0-16.0 mg/kg/hr |
| Lidocaine HCl, Lidocaine Neat®, Ayerst, Guelph, ON, CDA | 1.1 mg/kg iv, then CI of 0.025 mg/kg/min. |
| Lidocaine spray, Xylocaine Endotracheal®, AstraZeneca, ON, CDA | 1 sec.spray to larynx 5 min. prior to intubation |
| Naloxone HCl, Sandoz, CDA | 0.03 mg/kg IV |
| Neostigmine methylsulfate, Sandoz, CDA | 50µg/kg IM dose with atropine at 0.04 mg/kg IV |
| Normosol-R, Hospira Healthcare Corp, Montreal, PQ, CDA | 10mls/kg/hr or as required |
| Pancuronium bromide, Sandoz, CDA | 0.06 mg/kg IV |
| Pentobarbital sodium , Euthansol®, Schering Plough Inc, Pointe Claire, QC. CDA | 10-20 mg/kg |
| Phenylephrine HCl, Sandoz, CDA | 1-3 µg/kg/min CRI IV |
| Prednisolone sodium succinate, Solu-Delta-Cortef ®, Pharmacia, Orangeville, ON, CDA | 100 mg IV |
| Propofol, Diprivan®, AstraZeneca, Mississauga, ON, CDA | 4mg/kg/hr – 7.7mg/kg/hr as required |
| Simethicone, OVOL® 180 mg , Church+Dwight Cda Corp. Mississauga, ON, CDA | 180 mg PO once |
| Tiletamine HCl –zolazepam HCl, Telazol®, Fort Dodge, Iowa, USA | 4.4mg/kg IM (used in combination with Xylazine) |
| Xylazine, Rompun®, Bayer, Toronto, ON | 2.2 mg/kg IM ( used in combination with Telazol) |

458 [1] Plumb, D.C., *Plumb's Veterinary Drug Handbook, 5th Ed.,* Stockholm, Wis: Blackwell Publishing, 2005: 1311 pp.
459 [2] Hawk, C.T., Morris, T.H., *Formulary for Laboratory Animals, 3rd Ed.,* Ames, Io, Blackwell Publishing, 2005: 203 pp.
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461 **Table 2 – The Anesthetic Regimen –**
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| PRE-SURGERY | | ANESTHETIC REGIMEN | | |
|---|---|---|---|---|
| | | Induction | Maintenance | |
| *24 Hours* | *8 Hours* | | *Inhalation* | *Constant Rate Infusion* |
| Fentanyl S-(50 ug/ Skin Patch) | Simethicone (180 mg PO) | Telazol-xylazine, IM (4.4 mg/kg & 2.2 mg/kg) | Isoflurane (2.5%) | Na Pentobarbital & Ketamine HCl (2 IV lines, 1 ear, 1 jugular) (10-20 mg/kg/hour and 11-16 mg/kg/hour, respectively) |
| | | Lidocaine: (Laryngeal Spray) | | Pancuronium , IV (0.06 mg/kg, IV) |
| | | Atropine, IM (0.05 mg/kg) | | Atropine, IV (0.04 mg/kg) |
| | | Buprenorphine, IV (0.025 mg/kg) | | Neostigmine, IM (50 ug/kg) |
| | | Fluids - Normosol®, IV (10 ml/kg/hour) | | Buprenorphine, IV (0.02 mg/kg to 1 mg/kg) |
| | | | | Fluids - Resuscitation- (Normosol® & Saline) |

463
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467 Using an HT 50 Transport Ventilator (Newport Medical, Costa Mesa, CA), mechanical ventilation was performed
468 after endotracheal intubation using a pressure-control mode set to 15cm $H_2O$; a 2 cm $H_2O$ end-expiratory pressure;
469 in inspiratory / expiratory ration of 1: 2; and a respiratory rate of 12 breaths / minute.
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474 **Table 3 – Survey of Perceived Usefulness of In-flight Medications & Equipment for Future Flights:**
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476

| FLUIDS | Volume | Location | Ranking |
|---|---|---|---|
| Saline 0.9% | As required for flushing | In-flight kit | A |
| Saline 0.9% | As required for rapid fluid resuscitation | Hangar | A |
| Normosol-R | 10mls/kg/hr | In-flight kit | A |

477

| MEDICATION | Volume Per Flight | Location | Ranking |
|---|---|---|---|
| Atropine sulfate | 1.4 cc x 2 syringes | In-flight kit | B |
| Buprenorphine | 3.0 cc x 3 syringes | In-flight kit | A |
| Cefazolin (diluted to 167 mg/ml) | 6.0 cc x 1 syringe into IV bag | In-flight kit | B |
| Dopamine HCl (diluted to 400µg/ml) | 3.0 cc x 3 syringes | In-flight kit | B |
| Epinephrine (diluted to 1:10,000) | 3.0 cc x 6 syringes | In-flight kit | B |
| Fentanyl | 50 µg/hr skin patch | Skin patch 24 hours prior to commencement | A |
| Furosemide | 3.0 cc x 3 syringes | In-flight kit | B |
| Isoflurane | 1.0% - 5.0% | Terrestrial vivarium only | A |
| Ketamine HCl (diluted to 10 mg/ml) | 25 cc x 3 syringes | In-flight kit | A |
| Lidocaine HCl | 3.0 cc x 3 syringes | In-flight kit | A |
| Lidocaine spray | 1 second spray once | Terrestrial vivarium only | A |
| Naloxone HCl | 2.6 cc x 1 syringe | In-flight kit | C |
| Neostigmine | 3.5 cc x 1 syringe | In-flight kit | C |
| Pancuronium | 1.0 cc x 2 syringes | In-flight kit | A |
| Pentobarbital Na | 20.0 cc x 3 syringes | In-flight kit | A |
| Phenylephrine HCl (diluted to 17µg/ml) | 6.0 mls x 6 syringes | In-flight kit | A |
| Prednisolone | 1 x 10 cc ampoule | In-flight kit | B |
| Propofol | 10 cc x 3 syringes | In-flight kit | C |
| Simethicone | 180 mg capsule | 8 hours prior to preparation | B |
| Tiletamine HCl & zolazepam HCl, with xylazine | Pre-flight only prepared to deliver 0.044 ml/kg total | Terrestrial vivarium only | A |
| | | | |

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| EQUIPMENT | Ranking | EQUIPMENT | Ranking |
|---|---|---|---|
| Endotracheal Tube | A | Increased oxygenation | A |
| Assisted Ventilation | A | Direct Blood Pressure Monitoring | A |
| End-tidal $CO_2$ Monitoring | A | Body Temperature | A |

479
480 Rank A* (high + routine); Rank B ( (high but infrequently used); Rank C* (possibly useful); Rank D* (not useful)
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483 **Figure 1.**

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486 **Phase II - Instrumentation and monitoring during in-flight simulation**

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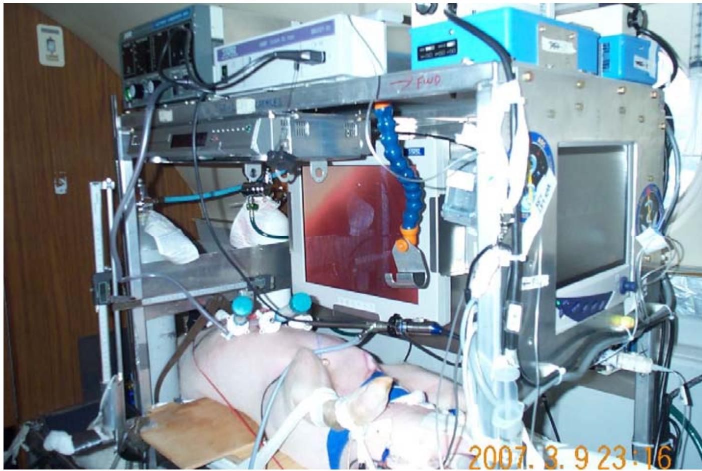
489 **Figure 2.**

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492 **Life-support surgical rack (LSSR) onboard the Falcon 20 aircraft**

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**Figure 3.**

**Phase III - Instrumentation and Ventilation onboard the Falcon 20**

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502 **Figure 4**

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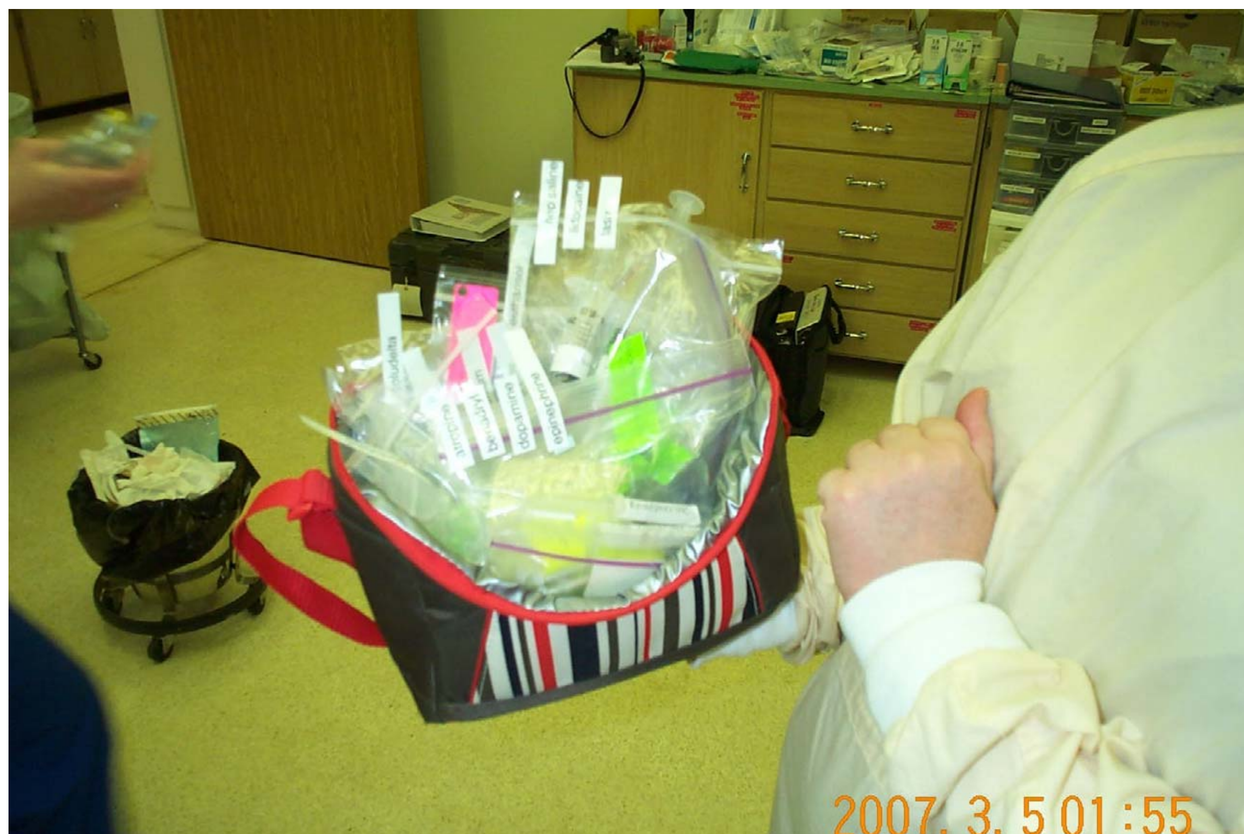
507 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509 **Pre-packaged pre-mixed pharmaceuticals for use during PFASSS**

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Figure 1

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Figure 2

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Figure 3

Figure 4

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