

Acute Pancreatitis CLIFF Peer Review

1. *Strength of evidence presented in CLIFF in modeling the characteristics and mission impact of this medical condition within the spaceflight environment?*

Score: 2

Grading Scale:

4 - *Confident*

3 - *Somewhat confident*

2 – *Neutral*

1 – *Somewhat unconfident*

0 – *Not confident*

2. How confident are you that these data accurately represent the spaceflight environment?	Tables 1, 2 Composite Incidence and Level of Confidence	Table 3, 4 BC/WC Loss of Crew and probability	Table 4 - Clinical Phase 1, 2 durations Table 5 – CP 2 Loss of Crew	Table 4 – RTDC % Table 6 – RTDC Loss of Crew	Table 4 – Loss of Crew Life % Table 7 – Loss of Crew Life, Loss of Crew	Table 8 – TI
Score	2	3	3	2	2	2

Comments and limitations:

1. General comments. This CLIFF characterizes acute pancreatitis which is inflammation or infection of the pancreas. There are a number of etiologies of pancreatitis, but terrestrially alcohol and gallstones account for the large majority of cases. Since astronauts will presumably not have access to alcohol during the mission and have been extensively screened prior to launch, these causes are thought to be unlikely. Other less common causes to be considered include medications, toxins, infections, hypercalcemia, IgG4 disease (autoimmune pancreatitis), and hypertriglyceridemia. The latter can also be screened out prior to launch. Once pancreatitis occurs, it is more likely to recur. Complications include necrosis, pseudocyst formation and sepsis. Most mild cases respond well to aggressive IV fluids, bowel rest, and analgesia. Very large amounts of IVF's are usually required which might tax the onboard supply of crystalline solutions. A definitive diagnosis of pancreatitis can be made clinically if there is a typical history and supporting laboratory/radiographic findings. If lipase is not available on board and imaging is limited to ultrasound, it may be difficult to differentiate pancreatitis from other causes of mid-upper abdominal pain such as peptic ulcer disease, gastritis, GERD, biliary disease, or even myocardial infarction. The best case is considered to be an uncomplicated case of acute pancreatitis which resolves with minimal intervention

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(observation while NPO, IVF hydration, and minimal pain management). The worst case is complicated acute pancreatitis with severe systemic manifestations (i.e., acute renal failure, necrotizing pancreatitis) requiring standard (pain management and aggressive IV hydration) as well as more advanced interventions (e.g., IV antibiotics, parenteral nutrition). Acute cholelithiasis and biliary colic is covered in a separate CLIFF

2. Incidence. There have been no inflight reports of acute pancreatitis. The incidence calculation was based on a large multi-center study of hospitalizations for acute pancreatitis. The data from this study was broken down by etiology. When alcohol, biliary tract stones, and elevated triglycerides were excluded (which can be avoided by proper pre-flight screening), the incidence was 0.0003536 per person years. This could be an underestimate because it only represents hospitalizations and does not include patients who presented to the EC who were not admitted. However, it also could be an overestimate because the astronaut population is healthier and better screened than the general population, and some of the idiopathic causes such as toxins and medications (illegal and prescription) are less likely to occur in the spaceflight environment. The best case/worst case probabilities used data from terrestrial studies that showed that 10-24% of patients with pancreatitis will have severe disease. A midpoint of 15% was chosen as the worst case probability. The clinical phase durations, RTDC and Loss of crew life probabilities are supported by terrestrial evidence, and I am in agreement with their calculation. The probability density curve that was derived appears to be a reasonable representation of the data presented.

3. Clinical phase data. I am in agreement with the clinical phase 1 duration entered in this CLIFF. This data was compiled by a team of expert clinicians, and I was involved in the discussions leading to the calculation of the clinical phase duration. CP2 was supported by terrestrial evidence.

4. Task impairment. The analysis was performed and reviewed by a separate team of expert clinicians. I am aware of the methods that were used but did not directly participate in the discussions.

5. Dependence on mission phase or duration of mission. This medical condition is not dependent on mission phase as pancreatitis may occur during any time during the mission. However, pancreatitis is often recurrent, and the incidence would be expected to rise in individuals who have experienced their first case of pancreatitis.

6. Limitations

- Acute pancreatitis is primarily due to gallstones, alcoholism, and hypertriglyceridemia for which astronaut crew members are well-screened prior to flight. Alcohol is prohibited aboard US spacecraft. The assumption is that no biliary tract stones or elevation in triglycerides will occur de novo during flight. This assumption, while reasonable, could be in error.
- The term “idiopathic” is used to refer to any cause other than the most common 3 etiologies. However, many other causes of acute pancreatitis can be readily identified and are therefore not truly “idiopathic.”
- The best case scenario includes very mild disease and the worst case scenario includes severe disease; however, presentations of “intermediate” disease are common and not well represented in this CLIFF.
- Literature on pancreatitis includes primarily patients with comorbidities and advanced age. These patients skew the calculated rates of Loss of crew life and RTDC.

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- Incidence was calculated using data from hospitalized patients. This could lead to an underestimate because it only represents hospitalizations and does not include patients presenting to the EC who were not admitted. However, it also could be an overestimate because the astronaut population is healthier and better screened than the general population, and some of the idiopathic causes such as toxins and medications (illegal and prescription) are less likely to occur in the spaceflight environment.
- A definitive diagnosis of pancreatitis can be made clinically if there is a typical history and supporting laboratory/radiographic findings. If lipase is not available on board and imaging is limited to ultrasound, it may be difficult to differentiate pancreatitis from other causes of mid-upper abdominal pain such as peptic ulcer disease, gastritis, GERD, biliary disease, or even myocardial infarction.
- This medical condition is not dependent on mission phase as pancreatitis may occur during any time during the mission. However, pancreatitis is often recurrent, and the incidence would be expected to rise in individuals who have experienced their first case of pancreatitis.
- The standard deviation of the incidence distribution is fairly small as a result of the large number of subjects in the terrestrial study that was used to calculate incidence. This could lead to overconfidence in the accuracy of the incidence calculation.

Reviewed by:

David C. Hilmers