Pharyngitis Cliff

Branch Baseline

Sore throat is an extremely common presenting symptom. Acute pharyngitis accounts for 1.3% of outpatient visits to health care providers in the United States. Streptococcal pharyngitis occurs most frequently in children between 5 and 15 years old. Group A streptococcus is responsible for 5 to 15% of pharyngitis in adults. The onset of symptoms is abrupt. It may present with fever, chills, malaise and headache. Certain persons are asymptomatic carriers. Fever resolves in 3 to 5 days and throat pain resolves within 1 week, even without specific treatment. (Wessels, 2011)

The sore throat, malaise, and fever associated with acute pharyngitis are distressing, but, with few exceptions, this illness is both benign and self-limited. (Bisno, 2002)

Incidence Data Included in the Model

The model imports the following incidence information from the IMM database: incidence data category, space adaption status, incidence data, incidence and occurrence distribution data and incidence data characteristics. Data category defines the type of data available for incidence calculations (i.e. raw data vs. fixed data). Space adaptation identifies medical events that onset occurs in the first 5 days of flight and does not reoccur. Incidence values vary by data category and define the number of medical events per person-year or medical events per person-at-risk for each medical condition. Incidence values can be modified by crew characteristics such as gender. Modifying characteristics are noted below and incidence values are listed individually for each characteristic. Distributions are assigned to medical events incidence values and occurrences in the model. For each crew member in a given trial, the incidence and number of occurrences of each medical condition are randomly selected from these probability distributions. Detailed descriptions of the distributions are included in the IMM Technical Description Document.

Incidence	
Data Category:	In-flight
Space Adaptation:	No
Incidence Type:	Rate

Distribution Data	
Incidence:	Gamma
Occurrence:	Poisson

Data Characteristics	
Events:	11
Person Years:	45.49
Space Flight Incidence Rate (Events / Person Years):	11 / 45.49 = 0.241811387118048

Incidence Comments

In the US space program 11 events of pharyngitis have been reported in space flight. (Walton, 2010)

All events have been mild uncomplicated sore throat events. Duration for 4 events is unknown, one lasted less than 24 hours, two lasted 24 hours, three lasted 48 hours, and one lasted 144 hours, 6 days. (Walton, 2010)

Three viral and one beta-hemolytic events were detected in pre-flight exams. Post-flight, two events were found; one caused by Influenza B virus, one by non-type A beta hemolytic streptococcus. One event was described as mild pharyngitis which lasted 6 days with and managed with symptomatic therapy. (Hawkins, 1975)

Added 18.17 persons years based on the real world system's incidence data information (Saile, 2017)

Updated the Person-Years based on the revised real world system integrated incidence data. The integrated person years changed from 18.17 to 18.13 so the conditions person years changed from 45.53 to 45.49 (Saile L., 2017)

Information Regarding Prevention

Selection criteria

Disqualifying conditions in the nose, sinuses, mouth, and throat category include: Deformities, injuries, or destructive diseases of the mouth, nose, throat, pharynx, or larynx that interfere with breathing, speech, mastication, and/or the swallowing of ordinary food, unless surgically corrected with normal function restored; chronic enlargement of the tonsils, adenoids or redundant soft tissue of the oral pharynx that interferes with speech, swallowing, breathing, or is associated with recurrent otitis media. May be considered after surgical correction. In general, any medical condition that, in the judgment of the MSMB, may compromise mission operations, performance of duties, crew health or safety. In the infectious diseases category: Acute or chronic infectious diseases, until appropriately treated that might compromise mission operations, performance of duties, or crew health or safety. (International Space Station Program, 2009)

Other

Pre-flight quarantine program was established to limit viral or bacterial infection exposures to crewmembers. Breaches are possible and have been reported. Treatment of pharyngitis in the first days of flight is similar to that on the ground. Sore throat, cervical lymphadenopathy, and fever are more suggestive of bacterial pharyngitis. (Marshburn, 2008)

Incidence Level of Evidence (LOE)

The IMM level of evidence appropriate assessment of the quality of the IMM input data. Since IMM incorporates input data from a wide variety of sources including astronaut population, terrestrial or analog populations, and external models, an innovative approach to assess the quality of input data was required. Information obtained from the astronaut population and/or space flight is the more relevant so it is assigned the highest level of evidence and less relevant data sources are assigned a lower level of evidence.

Citation	LOE Value	LOE Category
Walton, 2010	1	Incidence
Saile L., 2017	1	Incidence

Alternative Incidence Data

Analog Populations

An analysis of 10 years of data collected on Polaris submarine patrols over the ten year period 1963-1973 reported a total of 1685 medical events treated. Illness rates are indicated as new/cases/1000 man-days. There were a total of 165 Ear, Nose and Throat (ENT) diseases during the 1963-73 period with an illness rate of 0.036 and 0.013; for the 1963-67 and 1968-73 periods respectively. There were a total of 96 events of pharyngitis; causing 249 sick days, mean duration 2.6 days, during the 1963-1973 period. (Table A8). (Tansey, 1979)

Incidence rates for the period 1963-1967 and 1968-1973 were 0.01314 (0.036 *365 / 1000) and 0.004745 (0.013 *365 / 1000) person years. The average of these two incidence rates is 0.0089425 per person-years. Pharyngitis (96/165) accounted for 58.2% of the ENT events, or a rate of 0.005204535. One EVAC occurred but there is no information by condition.

Thomas reported on health of US Navy submarine crews during periods of isolation. There were 55 events of upper respiratory infections among officers and 502 among enlisted men. The incidence rate for upper respiratory infections was 9.3 for officers and 9.4 for enlisted crew, per 100 person years. Effect of illness was minimal 0.75 (officers) to 1 day (enlisted men). Digestive was the second most common cause of limited or no duty. Only 4.2% of officers and 7% of enlisted men had greater than 2 days illnesses. Thomas concluded that officers are most analogous to current space program participants. Majority of medical events reported were minor, non life-threatening, with little or no impact on unit mission. (Thomas, 2003) The incidence rate per person-years is 0.093 (9.3/100). Pharyngitis ICD9 code is 462, but we cannot segregate the pharyngitis data, from the upper respiratory group.

Non Analog Populations

Incidence for the United States population is challenging to determine. Children experience more than 5 upper respiratory infections (URIs) per year and an average of one streptococcal infection every 4 years. The occurrence in adults is about one half that rate. Inpatient care usually is not indicated except in cases such as epiglottitis, severe dehydration, deep-space infection (i.e. peritonsillar abscess), or other airway compromise. Airway compromise secondary to pharyngitis is rare. (Acerra, 2010)

Treatment and Outcomes

Based on the best evidence available best and worst case percentage ranges are assigned. The medical condition is divided into three clinical phases in all three clinical phases a functional impairment is assigned. The clinical phase I and II's functional impairments remain for the duration for that respective clinical phase. The function impairment in clinical phase III represents final impairment for this medical condition and remains for the rest of the mission. Other mission end states include evacuation and loss of crew life.

The IMM checks medical resource availability once the number of medical events and scenarios has been established. If there is not sufficient essential resources called out in the CliFF, then the medical condition will go down an untreated best or worst case scenario pathway.

The table below summarizes the treated and untreated best and worst case scenarios.

	Clinical Phase I Diagnosis & Initial Treatment[1]		**Clinical Phase II On-going Treatment / Convalescence[2]**		**Clinical Phase III Recovered / Mission End State[3]**		
	FI* (%)	**Duration (hrs)**	**FI* (%)**	**Duration (hrs) (Min - ML - Max)**	**FI* (%)**	**EVAC** (%)**	**LOCL** (%)**
ISS-based Treatment (best case scenario %: 91 - 100)	100	0.25	0 - 9	48 - 84 - 120	0	0	0
ISS-based Treatment (worst case scenario %: 0 - 9)	100	0.25	1 - 27	120 - 144 - 168	0	0	0
Untreated Best Case	0	0	1 - 27	48 - 84 - 120	0	0	0
Untreated Worst Case	0	0	11 - 42	120 - 144 - 168	0 - 9	0 - 1	0

[1]Clinical Phase I: Clinical phase I covers only the initial assessment of the affected crew member to define his or her medical condition, and completion of appropriate initial treatment to stabilize the crew member. While the affected crew member is being assessed, he or she is not able to perform any assigned tasks, thus Functional Impairment during this phase is considered 100%. In the untreated case, there is no diagnosis performed or treatment given, therefore Functional Impairment and Duration will always be "not applicable".

[2]Clinical Phase II: On-going Treatment and Convalescence- During clinical phase II, the affected crew member is receiving any appropriate follow-on treatment for his or her medical condition to allow the crew member to recover as much as he or she is able to recover in the ISS environment. Clinical phase II also encompasses relapses or reoccurrences of the same original medical condition in clinical phase I necessitating additional treatment or recovery time due to unsuccessful primary treatment response. The duration in Clinical Phase II is expressed in minimum, most likely (ML) and maximum hours. This was updated for future capabilities in IMM but is currently not being used by the model.

[3]Clinical Phase III: Recovered/Mission End State- Clinical phase III is reached once the affected crew member has recovered from the medical condition as much as he or she is able to recover in the ISS environment. This may or may not be recovery from the given medical condition to the full extent possible. If this "recovered" state results in an evacuation or loss of the crew member, this will be noted in the mission end state results.

*Functional Impairment (FI) is a measure of the affected crew member's health and performance ability.

**Two mission end state results are addressed in the CliFF: 1) Evacuation (EVAC) - crew and patient are evacuated from the spacecraft due to the medical condition, and 2) Loss of crew (LOCL) - death of affected crew member due to medical condition. EVAC is considered as an end state result if any of the following criteria are met: 1) potential LOCL, 2) potential significant permanent impairment, or 3) potential intractable pain. Probability distributions are assigned for each range of values within the Table of Treatments and Outcomes.

Refer to the Integrated Medical Model Technical Document for more information on how risk is reported by the IMM, Crew Health Index (CHI) and Quality Adjusted Mission Time calculations.

Definition and Probability of Best and Worst Case Scenario: (includes definitions of best and worst case scenarios and identifies the probability of those scenarios.)

Scenario Comments

Best case scenario is defined as mild uncomplicated pharyngitis that resolves spontaneously or with symptomatic treatment.

Worst case scenario is defined as severe pharyngitis that may require antibiotic treatment.

The **percentages of how often best versus worst case scenario occur** are determined using space flight data. (Walton, 2010) We assume all cases have been best cases. If the next case is a worst case (1/11) 9% would be worst cases. If the next case is a best case 0% would be worst cases. Our estimate for worst case scenario is 0 to 9 %. Thus, the best case scenario is 91 to 100%

In the rare event of complications causing bacteremia or respiratory distress, these complications are addressed in the Sepsis Clinical Finding Form.

Best Case Comments

Pharyngitis functional impairments (FI) calculation follows the IMM mild non-space adaptation template, except in Clinical Phase III due to the self-limited course of pharyngitis. For the treated worst case and untreated best case scenarios, FI is estimated at 0%; for the untreated worst case FI is assigned class 0-1, or 0 to 9%. Air passage deficits are based on Table 11-6, p.267. (American Medical Association, 2008)

By definition in Clinical Phase I, FI is 100%. Duration of physical exam as described in ISS checklist for the best case scenario is estimated in 15 minutes. During Clinical Phase II, FI is estimated in 0 to 9%. Duration is estimated in 48 to 120 hours (2-5 days). (Wessels, 2011) In Clinical Phase III, by definition, full recovery is expected and FI is 0%; EVAC and LOCL are not expected for the best case scenario.

Worst Case Comments

Pharyngitis functional impairments (FI) calculation follows the IMM mild non-space adaptation template, except in Clinical Phase III due to the self-limited course of pharyngitis. For the treated worst case and untreated best case scenarios, FI is estimated at 0%; for the untreated worst case FI is assigned class 0-1, or 0 to 9%. Air passage deficits are based on Table 11-6, p.267. (American Medical Association, 2008)

By definition in Clinical Phase I, FI is 100%. Duration of physical exam and IV procedure as described in ISS checklist is estimated in 15 minutes. During Clinical Phase II, FI is estimated in 1 to 27%. Duration is estimated in 120 to 168 hours (5-7 days) based on terrestrial data. (Wessels, 2011) In Clinical Phase III, full recovery is expected and FI is estimated at 0%. By definition, EVAC and LOCL are not expected for this condition.

Untreated Best Case Comments

Pharyngitis functional impairments (FI) calculation follows the IMM mild non-space adaptation template, except in Clinical Phase III due to the self-limited course of pharyngitis. For the treated worst case and untreated best case scenarios, FI is estimated at 0%; for the untreated worst case FI is assigned class 0-1, or 0 to 9%. Air passage deficits are based on Table 11-6, p.267. (American Medical Association, 2008)

During Clinical Phase II, FI is estimated at 1 to 27%. Duration is 48 to 120 hours (2-5 days), similar to the treated best case scenario. In Clinical Phase III, by definition, full recovery is expected and FI is 0%; EVAC and LOCL are not expected for the best case scenario.

Untreated Worst Case Comments

Pharyngitis functional impairments (FI) calculation follows the IMM mild non-space adaptation template, except in Clinical Phase III due to the self-limited course of pharyngitis. For the treated worst case and untreated best case scenarios, FI is estimated at 0%; for the untreated worst case FI is assigned class 0-1, or 0 to 9%. Air passage deficits are based on Table 11-6, p.267. (American Medical Association, 2008)

During Clinical Phase II, FI is estimated at 11 to 42%. Duration is estimated in 120 to 168 hours (5-7 days), similar to the treated worst case scenario. In Clinical Phase III, by definition recovery may occur or be partial and FI is estimated at 0-9%. EVACS have not occurred in analog populations for respiratory conditions. (Thomas, 2003); (Nice, 1987) To allow for uncertainty EVAC is estimated at 0-1% for the untreated worst case. LOCL is not expected for this scenario.

Treatment and Options Level of Evidence (LOE)

The IMM level of evidence appropriate assessment of the quality of the IMM input data. Since IMM incorporates input data from a wide variety of sources including astronaut population, terrestrial or analog populations, and external models, an innovative approach to assess the quality of input data was required. Information obtained from the astronaut population and/or space flight is the more relevant so it is assigned the highest level of evidence and less relevant data sources are assigned a lower level of evidence.

Citation	LOE Value	LOE Category
American Medical Association, 2008	3	FI
Thomas, 2003	2	EVAC
Nice, 1987	2	EVAC
Walton, 2010	1	BCWC

The Resource Table (RT)

Resource	Units Required Best Case	Units Required Worst Case	Units Available At Start Of Mission	Consumable	Essential	Rationale
Amoxicillin 500 mg capsule	0	20	100	Yes	Yes	Antibiotic
Motrin (Ibuprofen) 400mg	6	14	400	Yes	Yes	For pain and inflammation.
Otoscope (Head, Handle, and USB cable)	1	1	1	No	Yes	Light source for exam of throat
Penlight	1	1	2	No	Yes	Illuminate a patient's throat
Thermometer	1	1	1	No	No	To measure temperature
Tongue depressor	1	1	20	Yes	No	To examine throat

Resource Comments

The table was revised on 8/18/2011. We added rationales.

The ISS medical checklist includes procedures for sore throat treatment. All resources included in the resource table are available on board (MOD, 2011).

Bacteremia or respiratory distress secondary to pharyngitis are rare; these complications are addressed in the Sepsis Clinical Finding Form.

Comparison of ISS Med Checklist procedures versus clinical guidelines

ISS medical checklist recommends symptomatic treatment and treatment with antibiotics after communication with a flight surgeon, similar to current guidelines. Strep test is not available on board.

Some articles, including 2001 American College of Physicians-American Society of Internal Medicine (ACP-ASIM) “Principles of Appropriate Antibiotic Use for Acute Pharyngitis in Adults” emphasize patient symptom relief while the others, including 2002 release of the Infectious Disease Society of America (IDSA) “Practice Guidelines for the Diagnosis and Management of Group A Streptococcal Pharyngitis,” give higher priority to preventing unnecessary antibiotic use. (Centor, 2007).

Of note, a recent study showed that immediate penicillin V, given for 7 days, decreased group A streptococcal symptoms in 2.5 days, and non-group A streptococcal symptoms, in 1 day in adult patients. The study focused on patients at the heart of the controversy: those with pharyngitis scores of 3 or 4. (Zwart, 2000)

Required Resources Level of Evidence (LOE)

The IMM level of evidence appropriate assessment of the quality of the IMM input data. Since IMM incorporates input data from a wide variety of sources including astronaut population, terrestrial or analog populations, and external models, an innovative approach to assess the quality of input data was required. Information obtained from the astronaut population and/or space flight is the more relevant so it is assigned the highest level of evidence and less relevant data sources are assigned a lower level of evidence.

Citation	LOE Value	LOE Category
NASA Mission Operations Directorate (MOD), 2011	2	Resources

Level Of Evidence

Input Data	LOE Average
Incidence	1
Functional Impairment	3
Best Case / Worst Case	1
EVAC / LOCL	2
Resources	2
QUALITY OF EVIDENCE	**1.8**

Description	Range
Excellent	1-2
Good	2.1-3
Fair	3.1-4
Poor	4.1-5

Reference List

Reference
Acerra J. Pharyngitis in Emergency Medicine . Dyne P, editor. WebMD - Medscape Reference . 5-6-2010. New York, WebMD. 8-18-2011.
American Medical Association. Ear, Nose, Throat, and Related Structures. Guides to the Evaluation of Permanent Impairment. 6th ed. Chicago: American Medical Association Press; 2008. p. 247-79.
Bisno AL, Peter GS, Kaplan EL. Diagnosis of strep throat in adults: are clinical criteria really good enough? Clin Infect Dis 2002 Jul 15;35(2):126-9.
Centor RM, Allison JJ, Cohen SJ. Pharyngitis management: defining the controversy. J Gen Intern Med 2007 Jan;22(1):127-30.
Hawkins WR, Zieglschmid JF. Clinical Aspects of Crew Health. In: Johnston RS, Dietlein LF, Berry CA, editors. Biomedical Results of Apollo. NASA SP-368 ed. Washington D.C.: NASA; 1975. p. 46-84.
International Space Station Program. Medical Standards for ISS Crewmembers - MED Vol A. 3.2 ed. NASA; 2011.
Marshburn TH. Acute Care. In: Barratt M, Pool S, editors. Principles of Clinical Medicine for Space Flight.New York: Springer; 2008. p. 101-22.
NASA Mission Operations Directorate (MOD). International Space Station Integrated Medical Group Medical Checklist. Mission Operations Directorate (MOD), Systems Operations Data File (SODF) . 6-24-2011. Houston, TX, National Aeronautics and Space Administration (NASA).
Nice DS. U.S. Navy medical communications and evacuations at sea. Mil Med 1987 Sep;152(9):446-51.
Saile L., Boley L, Kerstman E. Integration RWS ISS STS Observed Incidence V2. 2017.
Saile L, Boley L, Kerstman E. Integration RWS ISS STS Observed Incidence. 2017.
Tansey WA, Wilson JM, Schaefer KE. Analysis of health data from 10 years of Polaris submarine patrols. Undersea Biomed Res 1979;6 Suppl:S217-S246.
Thomas TL, Garland FC, Mole D, Cohen BA, Gudewicz TM, Spiro RT, et al. Health of U.S. Navy submarine crew during periods of isolation. Aviat Space Environ Med 2003 Mar;74(3):260-5.
Walton M, Kerstman E, IMM. In-flight Compilation v20100414_Incidence_calculation. 2010.
Wessels MR. Clinical practice. Streptococcal pharyngitis. N Engl J Med 2011 Feb 17;364(7):648-55.
Zwart S, Sachs AP, Ruijs GJ, Gubbels JW, Hoes AW, de Melker RA. Penicillin for acute sore throat: randomised double blind trial of seven days versus three days treatment or placebo in adults. BMJ 2000 Jan 15;320(7228):150-4.