Vaginal Yeast Infection Cliff

Branch Baseline

Vaginitis is infectious or noninfectious inflammation of the vaginal mucosa, sometimes with inflammation of the vulva. Symptoms include vaginal discharge, irritation, pruritus, and erythema. The most common types of yeast vaginitis is candidal. Non-yeast vaginitis is commonly caused by bacteria such as coccobacilli or the protozoan trichomonas. Noninfectious inflammation may be due to foreign body and is rare. (Merck Manual, 2009)

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:	Raw Data
Space Adaptation:	No
Incidence Type:	Rate

Distribution Data	
Incidence:	Gamma
Occurrence:	Poisson

Female Data Characteristics	
Events:	129
Person Years:	334
Space Flight Incidence Rate (Events / Person Years):	0.38622754491018

Incidence Comments

Foxman surveyed (random dialing survey) 2,000 US women. 129 or 6.5 percent (95% CI, 5.4-7.5%) of women older than 18 years

reported a least one episode of presumed C vaginitis, defined as vaginal yeast infection, yeast vaginitis, candidiasis, during the

previous 2 months. Person Years is derived by taking the 2000 US women reporting previous 2 months (2000*0.167) (Standard error is 1.25%. 8% reported 4 or more episodes; standard error 9.33%. Overall, 55.7% of women will

experience at least one episode of C vaginitis in their lifetime (95% CI 49.6-62.6%) (Foxman, 2000)

Information Regarding Prevention

Disqualifying genitourinary conditions include: disease, injury, or other disorders of the kidneys or GU tract that could require emergency medical treatment or interfere with successful mission completion; diseases interfering with micturition and potentially requiring emergency medical treatment, any disabling disorders of the reproductive system or associated anatomical structures that could potentially require emergency medical care [International Space Station Program, 2009].

Other: Vulvovaginal candidiasis is listed as side effect of several antibiotics: Amoxicillin [AHFS, 2008], Cipro, [AHFS, 2009], Levaquin [AHFS, 2009], and Rocephin (Ceftriaxone) [Roche Laboratories, 2009].

Altemberg reported enhanced pathogenicity in Candida albicans in simulated microgravity. [Altenburg, 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
Foxman, 2000	4	Incidence

Alternative Incidence Data

Our search yielded numerous results, but very sparse epidemiologic information. The statement "*Approximately 75 percent of all women will experience at least one symptomatic yeast infection during their lifetime"* was quoted in several articles, but none presented a source for it. We tracked it to a study by Hurley, in Britain. (Hurley, 1979), (Sobel, 2007), (Eschenbach, 1994), (Mashburn, 2006), (Owen, 2004), (Workowski, 2006). Same difficulties were reported by Sobel in 1996 during the Consensus Conference on Vulvovaginal Candidiasis – A Contemporary Approach to Recognition and Management (Sobel, 1998).

The primary literature indicates that there is a wide variation in the normal vagina and that some of the symptoms associated with vaginal abnormality are found in well women (Anderson, 2004).

Information on the incidence of vulvovaginal candidosis is incomplete, since the disease is not a reportable entity and data collection is hampered by inaccuracies of diagnosis and the use of non-representative study populations. The infection—caused by Candida spp—affects 70–75% of women at least once during their lives, most frequently young women of childbearing age. It was found that 40–50% of women will experience a recurrence and 5–8% of adult women have recurrent vulvovaginal candidosis, defined as four or more episodes every year (Sobel, 2007).

Vulvovaginal candidiasis affects approximately 20% of women annually, but it is not well characterized epidemiologically (Geiger, 1995).

Geiger studied vaginal yeast infection incidence among university students, over a two years period, 1992-1993. The sample size was 1027; age range 17 to 52, median age 21 years, and 37.5% had a prior clinical diagnosis. The proportion of women ever diagnosed increased rapidly after age 17, with an estimated 54.7% of women diagnosed by age 25. The incidence is not reported per year (Geiger, 1995).

Botash (Botash, 2010) reported that vaginitis is common in adult women and uncommon in pre-pubertal girls. Vaginitis is one of the most common reasons for gynecologic consultation consisting of approximately 3 million office visits annually. Bacterial vaginosis accounts for 40-50% of vaginitis cases; candidiasis, 20-25%; and trichomoniasis, 15-20%. The source for this information is not reported in the article and we are unable to verify if the office visits were for initial diagnoses or recurrences. It was reported that 20-25% of 3 million office visits for candidiasis result in 600,000 to 750,000 visits. The total female population in the US for 2009 was estimated in 155,557,060 (U.S.Census Bureau, 2009). From the age ranges provided, we calculated the female population in the age range of 15 to 54 as 84,567,256 which served as the denominator. Our incidence is calculated as 0.0071 to 0.0089.

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 %: 80 - 90)	100	0.33	0 - 7	24 - 48 - 72	0	0	0
ISS-based Treatment (worst case scenario %: 10 - 20)	100	0.5	1 - 17	72 - 120 - 168	0 - 7	0	0
Untreated Best Case	0	0	1 - 17	24 - 48 - 72	0 - 7	0	0
Untreated Worst Case	0	0	17 - 20	72 - 120 - 168	1 - 20	0	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

The **best case scenario** is defined as uncomplicated vulvovaginal candidiasis (VVC), with mild to moderate, sporadic, or infrequent vulvar irritation, including itching and discomfort of the vulvar skin and vaginal epithelium, vaginal discharge, and discomfort with voiding which responds to all azole treatment regimens including short (3-day) and single-dose oral and vaginal therapy. The **worst case scenario is defined** as complicated, severe or recurrent vulvovaginal candidiasis. (RVVC) treated with oral dose of Fluconazole every third day for a total of 3 doses (day 1, 4, 7). (Workowski, 2006)

Percentages of how often best versus worst case scenarios occur: Approximately 10% to 20% of women will have complicated VVC (Workowski, 2006) which is our estimated worst case scenario.

Best Case Comments

Best case scenario: includes description of the medical conditions under the best case scenario. Along with explanation of how 1] the FI in all 3 Clinical Phases was derived 2] the duration in Clinical Phases I & II , and 3] the mission end states and their percentages

The majority of cases of Vaginal Yeast Infection occurring during spaceflight will be treated early and result in complete resolution without functional impairment. Clinical Phase I: 100% Functional impairment, for 20 minutes (0.33 hours) based on the time required for initial evaluation and treatment of mild vaginal yeast infection using the ISS Medical Checklist (International Space Station Integrated Medical Group, 2006). During Clinical Phase II Functional Impairment is assigned based on Table 7-10, Vulval and Vaginal Disease (American Medical Association, 2008). There was 0 to 7 % FI Class 0, or 0%, includes no symptoms of vulvar or vaginal disease, Class 1, 1 to 7% FI, includes symptoms or signs of vulvar or vaginal disease that do not require continuous treatment. Duration is estimated to be 24 to 72 hours (Sobel, 2007). Clinical Phase III: Class 0 or 0% FI is based on complete resolution of vaginal yeast infection. EVAC or LOCL are unlikely to occur. (Sobel, 2007)

Worst Case Comments

The **worst case scenario**: During **Clinical Phase I** 100% FI is assigned, similar to the best case scenario. Duration is estimated in 30 minutes assuming the worst case scenario would require longer time consultation with the CMO or the flight surgeon (International Space Station Integrated Medical Group, 2006). During **Clinical Phase II**: FI is estimated in 1 to 17%. Class 1, 1 to 7%, is when symptoms or signs do not require continuous treatment. Class 2, 9 to 17% FI, is when symptoms or signs require continuous treatment. Duration is estimated to be 72 to 168 hours to complete the treatment (Sobel, 2007). During **Clinical Phase III**: FI is estimated to be 0 to 7 %, Class 0 to Class 1. 0% FI is assigned considering vaginal yeast infection may resolve or 1 to 7% or mild signs and symptoms may continue (American Medical Association, 2008). Unresolved vaginal yeast infection will cause discomfort but does not require EVAC and it will not result in LOCL (Sobel, 2007).

Untreated Best Case Comments

During **Clinical Phase II**: FI is estimated to be 1 to 17%. Class1, 1 to 7% FI comprises symptoms or signs of vulvar or vaginal disease not requiring continuous treatment. Class 2, 9 to 17% FI, presents symptoms or signs requiring continuous treatment. However, treatment is not available in this scenario. The infection may resolve spontaneously. Estimated time is 1 to 72 days (Sobel, 2007). During **Clinical Phase III**, FI is estimated to be 0 to 7 %, Class 0 to Class , similar to the treated worst case (American Medical Association, 2008). Unresolved vaginal yeast infection will cause discomfort but does not require EVAC and it will not result in LOCL (Sobel, 2007).

Untreated Worst Case Comments

During **Clinical Phase II**: FI is estimated to be Class 2 to 3, or 9 to 20% with uncontrolled symptoms or signs and no treatment available in this scenario. The unresolved infection may cause possible performance decrement secondary to discomfort. Estimated time is 3 to 7 days. During **Clinical Phase III**, FI is estimated to be Class 1 to Class 3, 1 to 20% (American Medical Association, 2008). Unresolved vaginal yeast infection will cause discomfort but does not require EVAC and it will not result in LOCL (Sobel, 2007)

Treatment and Options Level of Evidence (LOE)

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Citation	LOE Value	LOE Category
American Medical Association, 2008	3	FI
Sobel, 2007	4	EVAC
Workowski, 2006	3	BCWC

Additional Comments

We searched PubMed using the terms vaginal yeast infections and incidence, vaginal candidiasis and incidence, vaginal candidiasis and epidemiology, candidiasis and aerospace medicine, and candidiasis and astronauts. Our search yielded numerous results, but very sparse epidemiologic information.

The Resource Table (RT)

Resource	Units Required Best Case	Units Required Worst Case	Units Available At Start Of Mission	Consumable	Essential	Rationale
Diflucan (Fluconazole) 150 mg	1	3	150	Yes	Yes	Antifungal infective medication

Resource Comments

The source of the resource table data was derived from the ISS Medical Checklist (International Space Station Integrated Medical Group, 2008).

Required Resources Level of Evidence (LOE)

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Citation	LOE Value	LOE Category
International Space Station Integrated Medical Group, 2008	2	Resources

Level Of Evidence

Input Data	LOE Average
Incidence	4
Functional Impairment	3
Best Case / Worst Case	3
EVAC / LOCL	4
Resources	2
QUALITY OF EVIDENCE	**3.2**

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

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