Abnormal Uterine Bleeding Cliff

Branch Baseline

Abnormal uterine bleeding (AUB) is a common clinical presentation. In women of childbearing age, AUB is diagnosed by exclusion of pregnancy, iatrogenic, systemic or other genital tract pathology. (Albers, 2004)

The menstrual cycle has three phases. During the follicular phase, follicle-stimulating hormone levels increase, causing a dominant follicle to mature and produce estrogen in the granulosa cells. With estrogen elevation, menstrual flow ceases, the endometrium proliferates, and positive feedback is exerted on luteinizing hormone (LH), resulting in the ovulatory phase. During the luteal phase, progesterone elevation halts proliferation of the endometrium and promotes its differentiation; progesterone production by the corpus luteum diminishes, causing endometrial shedding, or menstruation (Albers, 2004).

Disturbances of menstrual bleeding manifest in a wide range of presentations. Abnormal uterine bleeding is the overarching term used to describe any departure from normal menstruation or from a normal menstrual cycle pattern including heavy menstrual bleeding (HMB), heavy and prolonged menstrual bleeding (HPMB), intermenstrual bleeding (IMB), and postmenopausal bleeding (PMB) (Fraser, 2011)

The International Federation of Gynecology and Obstetrics (FIGO) Menstrual Disorders Working Group recommended standardizing terminology and suggested “normal” limits, 5 to 95th percentiles, for menstrual parameters in the mid-reproductive years: frequency of 24 to 38 days, regularity of menses over 12 months, with cycle to cycle variation (days) +/- 2 to 20 days, duration of flow 4.5 to 8 days, and monthly volume of blood loss 5-80 milliliters (Fraser, 2011)

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:	Fixed
Space Adaptation:	No
Incidence Type:	Rate

Distribution Data	
Incidence:	Fixed
Occurrence:	Poisson

Female Data Characteristics	
Fixed Rate:	0.052

Incidence Comments

No cases have occurred in flight. Terrestrially, there are few studies of the incidence of abnormal uterine bleeding, most describe prevalence.

A Dutch study revealed that incidence of abnormal vaginal bleeding (AVB) is 52 per 1000 women per year (0.052 person-years). Information was obtained from a database for consultations between January 2000 and January 2002. Median age was 41 years, age range 36-46. In this group excessive bleeding (43%) and irregular bleeding (42%) were almost equally often recorded as reason for consultation (de Vries, 2008). Confidence intervals or standard deviation were not published in this article.

Information Regarding Prevention

Selection criteria

Disqualifying conditions in the Obstetrics and Gynecology category include: Any disabling disorder of the genitourinary system or associated anatomical structures that interferes with performance of duties; dysmenorrhea and other irregularities of the menstrual cycle such as premenstrual syndrome that interfere with performance of duties; history of recurrent, abnormal uterine bleeding or menorrhagia unless definitively treated; history of recurrent symptomatic ovarian cysts or history of recurrent corpora hemorrhagica unless definitively resolved; pregnancy until complete post-partum recovery. (International Space Station Program, 2009)

Any menstrual abnormality caused by polycystic ovarian conditions, anovulation, or disorders of the hypothalamic-pituitary-ovarian axis requires further investigation and Special Consideration by the MSMB. (International Space Station Program, 2009)

Vehicle requirements

Sanitary products and maximum absorbency garments are available on board (Jennings RT, 2008)

Other

Ten days before flight, female crewmembers are tested for pregnancy during preflight examinations. Pregnancy is disqualifying for space flight. For short duration flights, oral contraceptives offer the opportunity to reduce the menstrual efflux and to shift the menstrual cycle. For long duration missions, continuous menstrual suppression is often used. No incidences or complications related to method have been reported. (Jennings RT, 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
de Vries, 2008	4	Incidence

Alternative Incidence Data

Analog Populations

Persian Gulf War and surface fleet literature indicate that gynecological problems accounted for 20-25% of women's visits. These studies indicate that the six most common categories are menstrual disorders, dysfunctional uterine bleeding, sexually transmitted diseases, pelvic pain, cervical disease and incontinence. About 3% of cases needed referral to a gynecologist.(Kane, 2001)

Navy studies reveal a rate of 7-10% for spontaneous abortion (SAB) and 1.4-2.7% for ectopics. Both these conditions may require life saving surgery. Modeling calculation of risk for Ectopic pregnancy among officers in 1999, based on data from the Defense Medical Surveillance System (DMSS) resulted in a rate of ectopic pregnancy 1.17/1000 person years (0.00117). Assuming 4 female officers for each of 17 Trident submarines spending average of 6 months at sea, 68 person years. The calculated ectopic rate was 0.08 per year. Any complaint of abdominal pain or non-menstrual vaginal bleeding by a female crewmember should prompt a consideration of ectopic pregnancy and a pregnancy test. A positive could well indicate a spontaneous abortion with uncontrolled bleeding or an ectopic pregnancy, both of which will require immediate MEDEVAC. (Kane, 2001)

In the Royal Australian Navy ships, up to 20% of some crews are female. The fitness of sailors at sea is assured by high pre-deployment standards of health (including a requirement that female sailors are not pregnant), but such checks cannot prevent unforeseen accidents and unpredictable acute surgical emergencies from arising at sea. These include complications of early pregnancy and a range of gynecological emergencies. Medical illnesses from 1991-2000 and evacuations from 2001-2003 were studied. As a general principle, surgical procedures at sea in units not equipped with operating theatres should only be undertaken as a last resort. For the 14 ships, there were 65 medical evacuations recorded, spanning some 54 ship sea years, or about 1.2 evacuations per sea year for the whole study group. Obstetric and gynecological morbidity rate was 0.3338 (n 6) per 100,000 man sea days (O'Connor, 2004) (0.3338/100,000 x 365) or 0.0012 person-years.

A descriptive study of sick visits over a 12 month period, between March 1, 1999, and February 29, 2000, aboard 15 San Diego, CA Navy ships reported that there were 5,378 qualified encounters recorded in the 12-month study period. Women were seen at 18% and men at 82% of these visits; officers at 4% and enlisted (including warrant officers) at 96% of visits. The most frequent major categorical complaints were respiratory (31%), injury and musculoskeletal (29%), dermatologic (9%), and infectious or parasitic illnesses (8%). Frequency of diagnosis was largely unrelated to gender, although men were more apt to be seen for sprains and strains and women for genitourinary conditions and reproductive services. Visits for genitourinary category among officers amounted to 2% (n=4). The proportion of visits for genitourinary and reproductive services appears low compared with the body of literature and may indicate that for certain aspects of their care, women aboard ships studied in this sample sought treatment off ship. No information is available to explain this disparity; however the tendency to seek care off ship is plausible given the sensitive nature of reproductive, genitourinary, and family planning-related needs; sexually transmitted disease; and inherent confidentiality issues. (Freeman, 2012)

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 %: 96 - 100)	100	0.3 - 0.5	0 - 15	216 - 216 - 216	0	0	0
ISS-based Treatment (worst case scenario %: 0 - 4)	100	0.5 - 1	1 - 24	240 - 372 - 504	0 - 15	0	0
Untreated Best Case	N/A	N/A	1 - 24	216 - 216 - 216	0 - 15	0	0
Untreated Worst Case	N/A	N/A	9 - 27	240 - 372 - 504	1 - 27	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 a mild or moderate abnormal uterine bleeding, requiring only minimal treatment.

The worst case scenario is defined as severe abnormal uterine bleeding which does not respond to treatment and may require surgical management

Shock is addressed in the Hypovolemic Shock Clinical Findings form.

Percentages of how often best versus worst case scenarios occur were estimated based on de Vries' study, (de Vries, 2008) where of 270 women with abnormal vaginal bleeding 62% (n 167) received no medication, 34% (n 92) received medication, and 4% (n 11) were referred to a gynecologist. The worst cases were estimated at 0-4%, thus the best cases are 96-100%

Best Case Comments

Abnormal Uterine Bleeding's functional impairments (FI) calculation follows the IMM mild non-space adaptation template for cervical and uterine disease. For bleeding disorders the maximum class used is 1. Cervical and uterine disease ratings are based on Table 2-11, p. 152 (American Medical Association, 2008). Bleeding Disorders are based on Table 9-11, p 205 (American Medical Association, 2008). Combined FI ratings are calculated combining the mentioned tables using the Combined Values Chart as indicated in Appendix A, pp 604-606 (American Medical Association, 2008).

The majority of cases of Abnormal uterine bleeding occurring during spaceflight will be treated early and resolve without functional impairment. Clinical Phase I: 100% Functional impairment, for 20 to 30minutes (0.3 to 0.5 hours) based on the time required for initial evaluation and treatment of mild AUB using the ISS Medical (Mission Operations Directorate (MOD), 2011). During Clinical Phase II Functional Impairment is 0 to 15 %. Duration is estimated to be 216 hours or 9 days (Fraser, 2011). Clinical Phase III: Class 0 or 0% FI is based on complete resolution of AUB. No hospitalizations have occurred among the astronaut corps for AUB (Johnston, 2008)EVAC or LOCL are not expected.

Worst Case Comments

Abnormal Uterine Bleeding's functional impairments (FI) calculation follows the IMM mild non-space adaptation template for cervical and uterine disease. For bleeding disorders the maximum class used is 1. Cervical and uterine disease ratings are based on Table 2-11, p. 152 (American Medical Association, 2008). Bleeding Disorders are based on Table 9-11, p 205 (American Medical Association, 2008). Combined FI ratings are calculated combining the mentioned tables using the Combined Values Chart as indicated in Appendix A, pp 604-606 (American Medical Association, 2008).

By definition during **Clinical Phase I**, FI is 100% and duration is estimated to be 30 to 60 minutes (0.5 to 1 hour). Including physical exam, PMC and ruling out other causes of bleeding. During **Clinical Phase II**, Functional Impairment is estimated at 1-24%. IMM estimated duration at 240-504 hours, 10 to 21 days, based on FIGO definitions for the minimum duration plus 2 days (Fraser, 2011) and hormonal treatment cycle for the maximum. During **Clinical Phase III**, FI is estimated at 0-15%. No hospitalizations have ocurred among the astronaut corps for AUB (Johnston, 2008). EVAC or LOCL are unlikely.

Untreated Best Case Comments

Abnormal Uterine Bleeding's functional impairments (FI) calculation follows the IMM mild non-space adaptation template for cervical and uterine disease. For bleeding disorders the maximum class used is 1. Cervical and uterine disease ratings are based on Table 2-11, p. 152 (American Medical Association, 2008). Bleeding Disorders are based on Table 9-11, p 205 (American Medical Association, 2008). Combined FI ratings are calculated combining the mentioned tables using the Combined Values Chart as indicated in Appendix A, pp 604-606 (American Medical Association, 2008).

During **Clinical Phase II**, Functional Impairment is estimated at 1-24%. IMM estimated duration at 240-504 hours, 10 to 21 days, similar to the treated worst case scenario. However, there is no treatment available on this scenario. During **Clinical Phase III**, FI is estimated at 0-15%. No hospitalizations have occurred among the astronaut corps for AUB (Johnston, 2008) EVAC or LOCL are not expected.

Untreated Worst Case Comments

Abnormal Uterine Bleeding's functional impairments (FI) calculation follows the IMM mild non-space adaptation template for cervical and uterine disease. For bleeding disorders the maximum class used is 1. Cervical and uterine disease ratings are based on Table 2-11, p. 152 (American Medical Association, 2008). Bleeding Disorders are based on Table 9-11, p 205 (American Medical Association, 2008). Combined FI ratings are calculated combining the mentioned tables using the Combined Values Chart as indicated in Appendix A, pp 604-606 (American Medical Association, 2008).

During **Clinical Phase II**, Functional Impairment is estimated at 1-24%. IMM estimated duration at 240-504 hours, 10 to 21 days, similar to the treated worst case scenario. However, there is no treatment available on this scenario. During **Clinical Phase III**, FI is estimated at 0-15%. No hospitalizations have occurred among the astronaut corps for AUB (Johnston, 2008) EVAC or LOCL are unlikely.

Treatment and Options Level of Evidence (LOE)

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Citation	LOE Value	LOE Category
de Vries, 2008	4	BCWC
American Medical Association, 2008	3	FI
American Medical Association, 2008	3	FI
American Medical Association, 2008	3	FI
Johnston, 2008	2	EVAC

Additional Comments

Recent international discussion aimed to reach an agreement on the terminology used to describe normal limits and abnormalities related to uterine bleeding. It was recommended that the term dysfunctional uterine bleeding be abandoned (Fraser, 2011)

The Resource Table (RT)

Resource	Units Required Best Case	Units Required Worst Case	Units Available At Start Of Mission	Consumable	Essential	Rationale
Blood Oximeter	1	1	1	No	Yes	For VS monitoring
Blood Pressure Cuff (regular, large)	0	1	2	No	Yes	Measure blood pressure
Blood Pressure Monitor	0	1	1	No	Yes	Measure blood pressure
EPT	1	1	2	Yes	Yes	To determine pregnancy status
Medroxyprogesterone (Provera) 10 mg	7	14	100	Yes	Yes	To control uterine bleeding
Motrin (Ibuprofen) 400mg	42	84	400	Yes	Yes	Anti-inflammatory
Norethindrone and Ethinyl Estradiol (OrthoNovum)	0	21	105	Yes	Yes	To control uterine bleeding
Stethoscope	1	1	2	No	Yes	For VS monitoring
Thermometer	1	1	1	No	No	For VS monitoring
Ultrasound gel (2 packets)	2	2	17	Yes	Yes	For diagnostic purposes
Ultrasound machine	1	1	1	No	Yes	For diagnostic purposes

Resource Comments

Abnormal uterine bleeding is not addressed in the medical checklist (Mission Operations Directorate (MOD), 2011) however, resources included in the table are available on board.

Resources are based on terrestrial standards of care (Albers, 2004)and clinical practice guidelines (Lumsdem, 2007).

Based on Schrager's article (Schrager, 2002) describing best practices for treatment of abnormal uterine bleeding, Estrogen and an anti-inflammatory are for females who are already taking hormonal contraceptives. For IMM purposes, it is assumed that all female crew are taking hormonal contraceptives.

Required Resources Level of Evidence (LOE)

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Citation	LOE Value	LOE Category
Albers, 2004	3	Resources
Lumsdem, 2007	3	Resources

Level Of Evidence

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

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

Reference List

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