

Fetal Loss Update





Fetal Loss

- With the Letter of Amendment, fetal loss is NOT considered an adverse event
 - “Chemical pregnancy”
 - 7 week spontaneous loss
 - 22 week spontaneous loss
 - 34 week stillbirth
- The loss of the pregnancy is NOT an adverse event. Symptoms associated with that loss may be.



Fetal Loss

- Maternal complications or side effects associated with fetal loss that would otherwise be reported as an adverse event are considered adverse events



Is This an Adverse Event?

- 1st step: take out the fetal loss from consideration
- Would the symptoms or signs that are left be considered an adverse event if the status of the pregnancy hadn't changed or the woman was not pregnant?
 - NO-> no adverse event
 - YES-> adverse event



Female Genital Grading Table

- Some Pregnancy related AEs are listed on the last two pages of the Female Tox Table
- Examples:
 - Chorioamnionitis
 - Preterm rupture of membranes
 - Preterm contractions



Two Confusing Situations

- When is pain (contraction) an adverse event?
 - What do we call it?

- When is bleeding an adverse event?
 - What do we call it?

Pregnancy Related Pain

- Pain (with the exception of term contractions) is an adverse event
 - Cramping at 8 weeks gestation
 - AE
 - Preterm contractions at 25 weeks
 - AE
 - Contractions at 38 weeks
 - NO AE!!!!!!!!!!!!

What To Call This?????

- 20 weeks is traditionally the cut off between a “spontaneous abortion” and “preterm labor”
 - “Labor” is delivery of the baby after 20 weeks
- Uterine cramping or contractions
 - “Pelvic Pain” if < 20 weeks
 - Contractions if >20 week
- Preterm Uterine Contractions are graded as follows

	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Preterm Contractions	None	Preterm contractions which resolve without medical intervention	Preterm contractions with cervical change which result in medical intervention but not resulting in preterm delivery	Delivery at 33-36 weeks' gestation or 1501-2500 grams birth weight	Delivery < 33 weeks' gestation or \leq 1500 grams birth weight

Pregnancy Related Bleeding

- Bleeding prior to labor is an adverse event
 - Bleeding prior to the onset of labor is unexpected and an adverse event
 - Normal bleeding during labor is expected and not an adverse event
- Per LOA#1 Bleeding in pregnancy prior to labor:

PARAMETER	GRADE 0 NORMAL	GRADE 1 MILD	GRADE 2 MODERATE	GRADE 3 SEVERE	GRADE 4 POTENTIALLY LIFE-THREATENING
COMPLICATIONS OF PREGNANCY					
Bleeding during pregnancy prior to the onset of labor	None	Spotting or bleeding less than menses	Bleeding like menses or heavier, no intervention indicated	Profuse bleeding with dizziness or orthostatic hypotension, transfusion indicated	Potentially life-threatening profuse bleeding and/or shock

Excessive Bleeding

- Excessive bleeding during labor and delivery is an adverse event
- It is graded using the post partum hemorrhage row in the tox table

	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Postpartum hemorrhage	EBL < 500 cc for vaginal delivery or < 1000 cc after CS or reported as normal	EBL 500-1000 for vaginal delivery or 1000-1500 for CS or reported as slightly increased	EBL > 1000 for vaginal delivery or > 1500 for CS, with or without mild dizziness, no transfusion required	Hemorrhage at a level for which transfusion of 1-2 units of packed cells, but no other blood products indicated	Hemorrhage with shock or coagulopathy, for which transfusion of > 2 units of packed cells or any amount of other blood components is indicated

What To Call it?????

- 20 weeks is traditionally the cut off between a “spontaneous abortion” and “preterm labor”
 - Labor is delivery of the baby after 20 weeks
- For bleeding
 - Bleeding prior to labor is an AE
 - Bleeding at 7 weeks, ultimately delivers at term
 - Bleeding at 7 weeks associated with a spontaneous abortion at 7 weeks
 - Bleeding at 22 weeks, ultimately delivers at term
 - Bleeding at 36 weeks, ultimately delivers at 39 weeks
 - Bleeding associated with labor is not an AE
 - Bleeding at 40 weeks associated with delivery
 - Bleeding at 25 weeks associated with delivery*
 - Bleeding at 21 weeks associated with delivery*

*the adverse nature of this occurrence is captured elsewhere



Some Examples

- Positive pregnancy test at Month 5, negative pregnancy test at Month 6. No bleeding or cramping
 - No AEs

Some Examples

- Pregnant participant at 7 weeks experiences bleeding and cramping but goes on to deliver at term
 - AE for bleeding (not expected)
 - “Bleeding during pregnancy prior to the onset of labor”
 - AE for pelvic pain
 - “Pelvic Pain”



Some Examples

- Spontaneous miscarriage at 7 weeks associated with bleeding and cramping
 - AE for bleeding (not expected)
 - “Bleeding during pregnancy prior to the onset of labor”
 - AE for pelvic pain
 - “Pelvic pain”

Some Examples

- Pregnant participant at 21 weeks experiences bleeding and cramping but goes on to delivery full term
 - AE for bleeding (not expected)
 - “Bleeding during pregnancy prior to the onset of labor”
 - AE for preterm contractions (per tox table)
 - Grade based on the fact that she didn’t deliver
 - Not “pelvic pain” because >20 weeks

Some Examples

- Spontaneous miscarriage at 21 weeks associated with bleeding and cramping
 - Bleeding is part of labor therefore not an AE
 - >20 weeks gestation= labor
 - AE for preterm contractions (per tox table)
 - Delivery after 20 weeks = preterm delivery

Female Genital Grading Table

	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Preterm Contractions	None	Preterm contractions which resolve without medical intervention	Preterm contractions with cervical change which result in medical intervention but not resulting in preterm delivery	Delivery at 33-36 weeks' gestation or 1501-2500 grams birth weight	Delivery < 33 weeks' gestation or \leq 1500 grams birth weight



Some Examples

- 28 week delivery of live infant-contractions and normal bleeding
 - AE for preterm contractions

- 28 week delivery of still born baby-contractions and normal bleeding
 - AE for preterm contractions



Some Examples

- Term delivery of live infant associated with contractions and normal bleeding
 - No AEs
- Term delivery of still born baby associated with contractions and normal bleeding
 - No AEs



Some Examples

- Vaginal delivery of term infant complicated by hemorrhage
 - Postpartum hemorrhage= AE

- Vaginal delivery of term still born complicated by hemorrhage
 - Postpartum hemorrhage= AE

Some Examples

- Vaginal delivery of **live** preterm infant complicated by post partum endometritis
 - Preterm contractions= AE
 - Post partum endometritis= AE
- Vaginal delivery of **still born** preterm infant complicated by post partum endometritis
 - Preterm contractions= AE
 - Post partum endometritis= AE



Some Examples

- Miscarriage at 7 weeks associated with bleeding, cramping, and infection
 - Bleeding during pregnancy (not expected)= AE
 - Pelvic pain= AE
 - Post abortal endometritis= AE



Questions?