

# Patient Blood Management of the Gynecological Patient

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# Disclosure

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## □ Jeannie Callum

### ▣ Grant Support

- TEM International
- ORBCON
- CHS
- CIHR

### ▣ Clinical Trials

- Novartis (Ruxolitinib)

## □ Yulia Lin

### ▣ Grants/Research Support

- Sanquin
- Glaxo-Smith Kline
- ORBCON
- CHS
- CIHR

### ▣ Consulting

- Genzyme

# Objectives

Participants will further their understanding of PBM in obstetrical and gynecological surgery patients:


- Role of oral and IV iron in management of anemia
- Role of tranexamic acid in the management of bleeding
- Techniques to minimize blood loss in complex Ob/Gyn patients

# Case 1

- 32 year old G2P1
- At 12 wk GA: Hb 106 g/L, ferritin 8 ug/L
- At 24 wk GA: Hb 98 g/L, ferritin 5 ug/L
- Known placenta previa
- C-section planned at 38 weeks GA

# Case 2

- 32 F with 3 yr history of heavy menses
- Large uterine fibroids (no improvement with oral contraceptive pill or Mirena intrauterine system)
- Wishes myomectomy with fertility preservation
- Surgery is booked for 2 weeks from now
- Labs today: Hb 73, MCV 70



Preoperative PBM:  
Recognizing and treating  
Iron Deficiency Anemia

# Iron deficiency anemia is common

- US women (not pregnant)
  - ▣ 1988-1994: 4.9%
  - ▣ 1999-2002: 4.1%
  
- Even more common in pregnancy!
  - ▣ NHANES report 1999-2006
    - Trimester 1 – 7%
    - Trimester 2 – 14%
    - Trimester 3 – 30%
    - (Defined as ferritin < 12 ug/L)

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- But...

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- But...
- Women who are iron deficient
  - ▣ Cognition: worse attention, memory and speed
  - ▣ Exercise: slower run times
  - ▣ Mood: postpartum depression
- Babies of iron deficient, anemic women
  - ▣ Placental impact, neurodevelopment

# Diagnosis – Recognize IDA

- Who should be screened?
  - All pregnant women
  - Gyne patients with ongoing bleeding
  
- How?
  - Hemoglobin less than 120 g/L
    - Clue: microcytic anemia ( $MCV < 80$ ) when previously normal
  - Ferritin less than 30 ug/L
  - (Ferritin less than 100 ug/L and  $TSAT < 20\%$ )


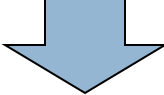
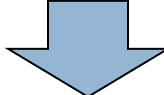
# Treatment – Iron Supplementation

- Prenatal vitamins are not sufficient
  - ▣ By 3<sup>rd</sup> trimester: 23.5% ID and 6.2% IDA on prenatal

Tablet	Iron	Elemental	Absorbed
Gluconate	300	35	1.4
Sulfate	300	60	2.4
Fumarate	300	100	4
Preg Vit	35	11	0.44
Materna	27	9 (4)	0.16

On empty stomach!

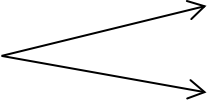
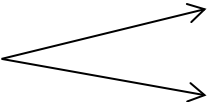
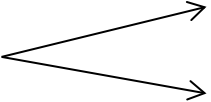
# Sunnybrook - stratify by ferritin at 12 weeks gestation

Ferritin < 15	Ferritin 15-70	Ferritin > 70
<ul style="list-style-type: none"><li><input type="checkbox"/> Rx Fe sulphate 300mg PO qhs or if Hb &lt;115 give bid</li><li><input type="checkbox"/> Inform patient to take at bedtime with orange juice</li></ul> <p style="text-align: center;"></p> <p>CBC and ferritin at 24 weeks</p>	<ul style="list-style-type: none"><li><input type="checkbox"/> Rx Fe gluconate 300mg PO qhs</li><li><input type="checkbox"/> Inform patient to take at bedtime with orange juice</li></ul> <p style="text-align: center;"></p> <p>CBC and ferritin at 24 weeks ONLY if Non compliant</p>	<ul style="list-style-type: none"><li><input type="checkbox"/> Continue prenatal</li></ul> <p style="text-align: center;"></p> <p>CBC and ferritin at 24 weeks</p>

# Case 1

- At 24 weeks, hemoglobin 98 g/L and ferritin 5
- She is only taking 1-2 tablets per week due to constipation
- She states she just can't take the oral iron
  
- What is the role for intravenous iron – is it safe? Is it effective?

# IV iron?

Anemic women		iv iron oral iron (with great compliance)	No difference
Anemic women		iv iron oral iron (with poor compliance)	iv iron better
Anemic women		iv + po iron oral iron	Combo better

# Data to support IV iron

- Switzerland: 500 pregnant women failing oral iron with Hb < 100 g/L treated with iv iron sucrose
  - ▣ Mean Hb increased from 92 g/L to 109 g/L (28 days)
- Reasonable when oral iron not tolerated and short time to delivery
  - ▣ Hb increase faster especially if poor oral tolerance



# Cases

## Case 1: Pregnancy

- 300mg of iv iron sucrose weekly x 2 doses
- At 32 weeks Hb 121 g/L and ferritin 65 ug/L
- Known placenta previa – at risk for post-partum hemorrhage

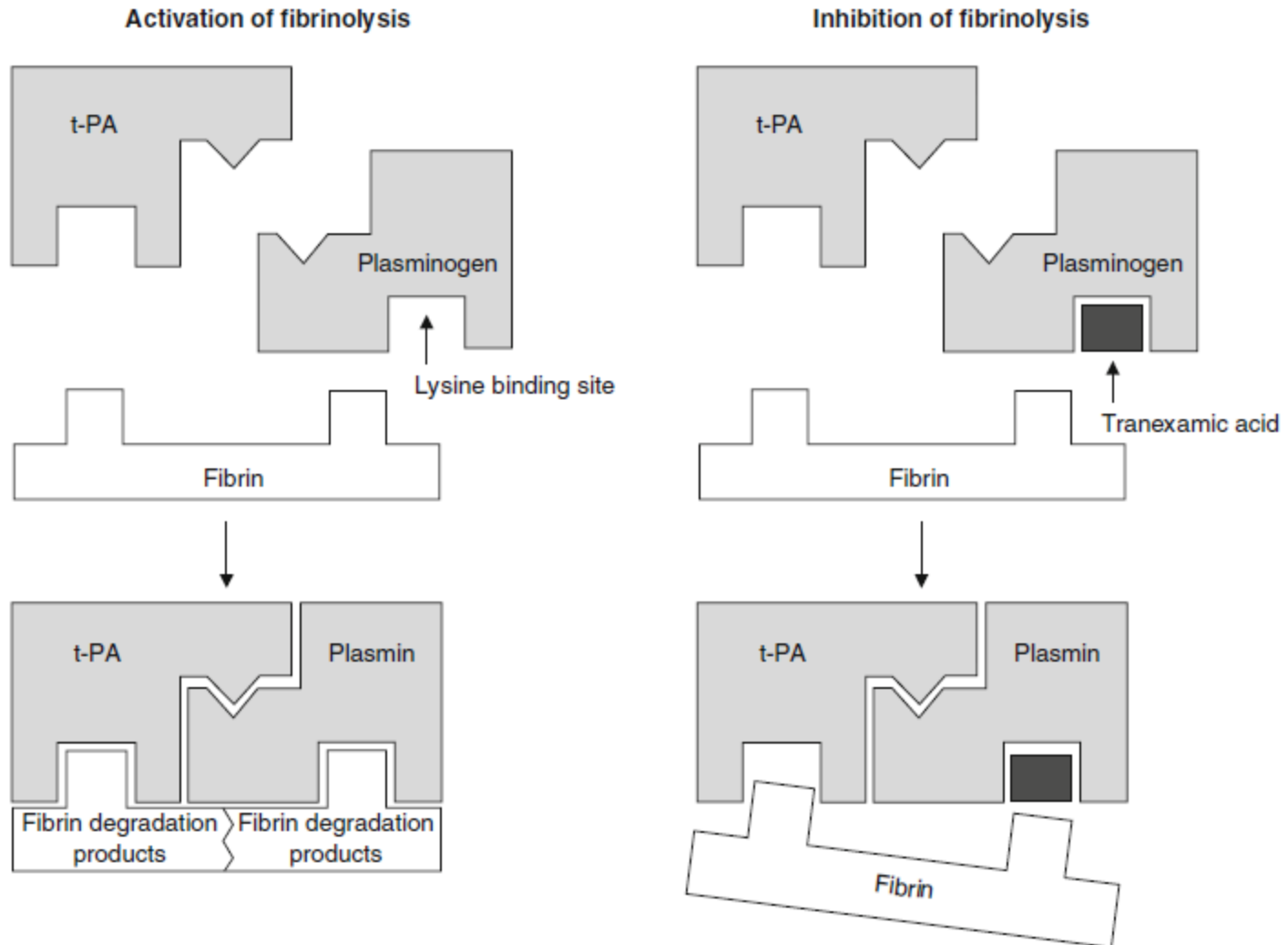
## Case 2: Fibroids / Myomectomy case

- Treat with IV iron due to short time to case



# Peripartum/Perioperative PBM: Tranexamic Acid

# Mechanism of Action: Tranexamic acid



# What's the evidence in Obstetrics?

Study	N	Dose	Outcome (*P<0.01)
Vaginal delivery Yang 2001	400	1g at delivery of shoulders	243 vs. 315mL*
Bouthors 2010	144	4g over 1h + 1g over 6h PP	46% reduction in blood loss*
C-section Gai 2004	180	1g iv over 10 min pre-CS	43 mL vs. 74 mL*
Gohel 2007	100	1g iv over 20 min pre-CS	75 mL vs. 133 mL*
Sekhavat 2009	90	1g iv over 10 min pre-CS	28 mL vs. 37 mL
Recur miscarriage Tetruashvili 2007	80	750 mg po x 7 d post-preg	2.1 vs. 5.6 bleeding days*

Since review, additional TXA RCTs in C section: Ahmed 2014; Abdel-Aleem 2013; Shahid 2013; Senturk 2013; Gungorduk 2011 totalling >1,700 pts – consistent ↓ blood loss

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# WOMAN Trial



- Patients: Women with clinically diagnosed postpartum hemorrhage
- Intervention: Tranexamic acid 1 g; repeat in 30 min if still bleeding
- Control: Placebo
- Outcome: Death or hysterectomy at 42 days
- Target 20,000 pts
  
- As of Mar 31, 2015: **15,584 pts** randomized

# Gynecologic Surgery

## □ 4 trials to date

Author	N	Patients	Outcome
Celebi 2006	105	Gyne CA surgery	↓ blood loss (100mL)
Caglar 2008	100	Myomectomy	no difference
Gupta 2012	60	Radical mastectomy and hysterectomy (30 pts)	↓ blood loss (250mL) ↓ transfusion
Lundin 2014	100	Ovarian CA surgery	↓ blood loss (200mL) ↓ transfusion

# What are the risks?

- No difference in thromboembolic events
  - ▣ Systematic review: TXA on surgical bleeding, orthopedics, obstetrics
  - ▣ CRASH-2: 20,000 trauma pts

Ker et al. *BMJ* 2012 May 17;344:e305

CRASH 2. *Lancet* 2010;376(9734):23-32

Peitsidis P, Kadir RA. *Expert Opin Pharmacother* 2011;12:503-16



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- Side effects? generally well tolerated
  - ▣ Nausea, vomiting, diarrhea, hypotension
  - ▣ Impaired colour vision, blurry vision (long term use)
  - ▣ Seizures described in cardiac surgery setting (not in OB/GYN)

Ker et al. BMJ 2012 May 17;344:e305

CRASH 2. Lancet 2010;376(9734):23-32

Peitsidis P, Kadir RA. Expert Opin Pharmacother 2011;12:503-16

# Adverse Effects

- Potential contraindications
  - ▣ History or risk of thrombosis, acute thrombotic event
  - ▣ Acquired disturbances of colour vision
  - ▣ Hematuria
  - ▣ Caution with DIC

# Obstetrical considerations

- Tranexamic acid does cross placenta
  - ▣ Animal reproduction studies have not demonstrated fetal risk
  - ▣ No reports of adverse effect on neonatal outcomes in RCTs
- Breastmilk concentration of TXA 1 hour after last dose is  $\sim 1\%$  of peak serum concentration
  
- Inexpensive \$4-6 per 1 g

# Cases

- Case 1: Placenta Previa
  - ▣ At time of C-section, if any concern of bleeding, administer TXA 1 g iv, can repeat in 30 min or run infusion
  - ▣ If PPH, give TXA early as above
- Case 2: Myomectomy
  - ▣ Given profound anemia, TXA 1 g iv pre-incision

# Summary

- PBM is a multimodal, multidisciplinary approach

## Learning Points for Today

- Preoperative PBM
  - ▣ Recognize iron deficiency anemia
  - ▣ Start treatment with oral iron
  - ▣ If not tolerated or short time: intravenous iron
- Perioperative PBM
  - ▣ Tranexamic acid = a key element of PBM toolbox