Massive Hemorrhage in the Obstetrical Patient: What's Unique?

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Conflicts of Interest

Widad Abdulwahab:

No COI

Heather VanderMeulen:

CSL-Vifor: consulting

Canadian Drug Agency: consulting

Learning Objectives

Understand the most **common causes** of massive hemorrhage in the obstetrical patient

Know the **unique considerations** of transfusing a massively bleeding pregnant patient, including blood product selection and transfusion thresholds

List the **negative consequences** of transfusion unique to obstetrical patients

Every year…

- 14 million women experience PPH
- 70 000 maternal deaths
- Surviving women experience morbidity, ‘lifelong reproductive disability’
- 2.9% USA deliveries are complicated by PPH

WHO 2023; Batesman et al., Anesth Analg., 2010

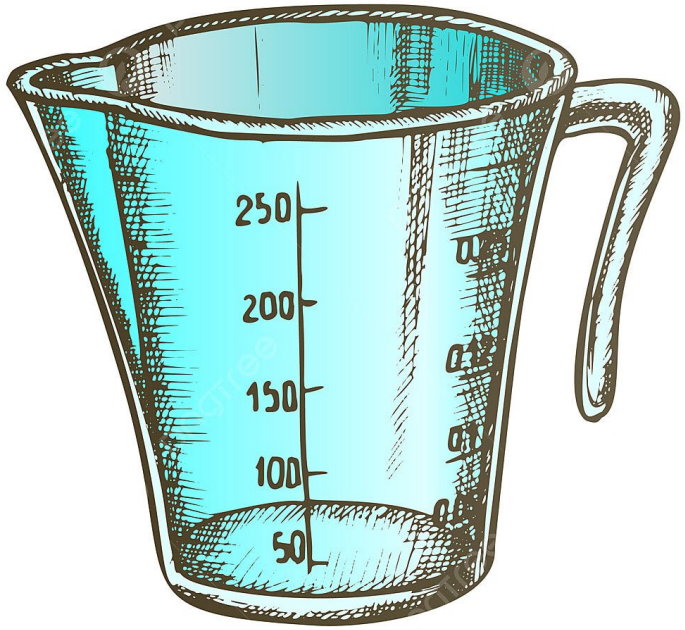
POLL: How comfortable are you with defining postpartum hemorrhage?

1) No clue

2) I could identify it if I saw it (how hard could it be?!)

3) I know when to ask for help

4) I have clear definitions of primary and secondary post partum hemorrhage



Identifying and Measuring PPH

Postpartum Hemorrhage (PPH):

Primary PPH: blood loss greater than 1000 mL within 24 hours of birth (regardless of mode of delivery)

Secondary PPH: ???

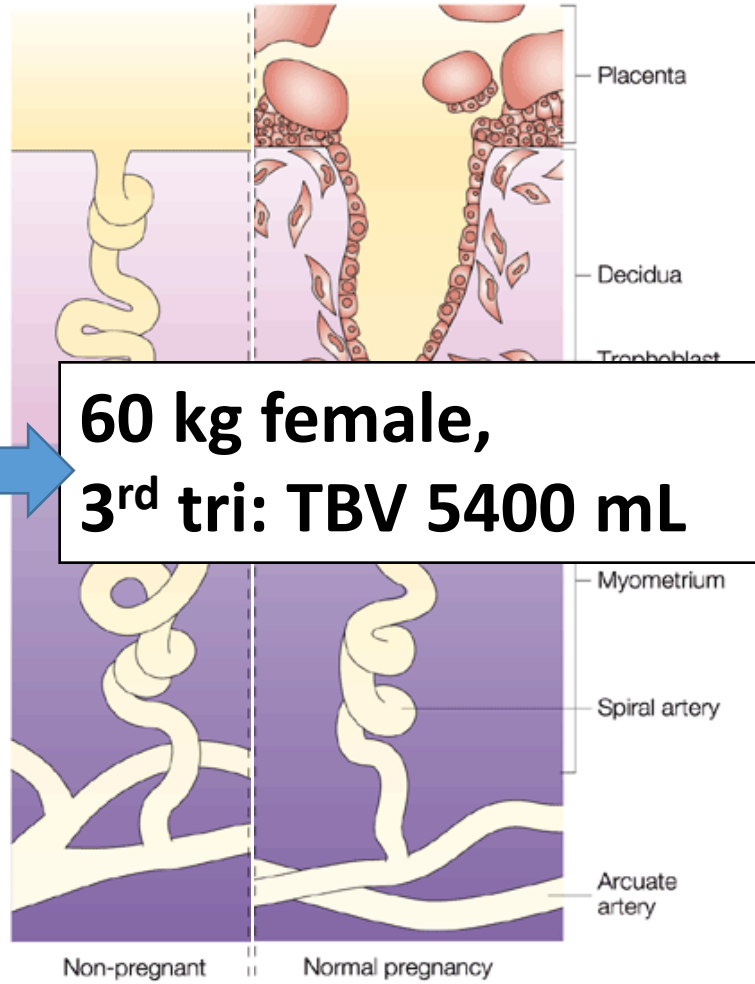
ACOG Practice Bulletin 183, 2017

Uterine Blood Flow in Pregnancy

At term:
>800 mL/min

60 kg female,
3rd tri: TBV 5400 mL

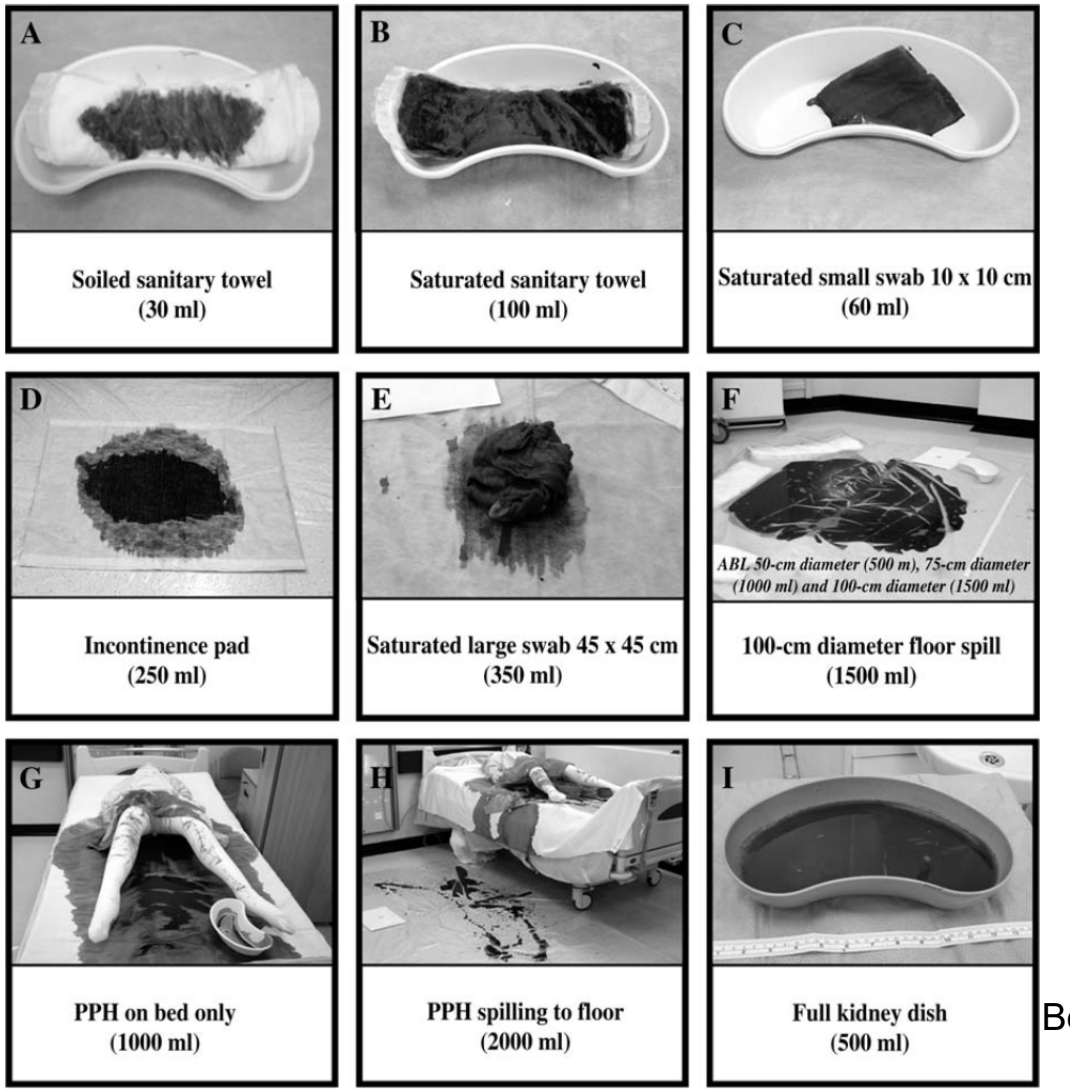
7 min



Nature Reviews | Immunology

Bell, E. A bad combination. *Nat Rev Immunol* **4**, 927 (2004). https://doi.org/10.1038/nri1514

Estimating Blood Loss is Hard…



Bose et al., BJOG, 2006

Blood loss	Clinical Features	Level of Shock
10% blood loss ~500mL if 50 kg ~800 mL if 80 kg	Mild tachycardia Normal blood pressure	Compensated
15% blood loss ~750mL if 50 kg ~1200mL if 80 kg	Tachycardia (more than 100 bpm) Hypotension (systolic 90-80 mmHg) Tachypnoea (21-30 breaths/minute)	Mild
30% blood loss ~1500mL if 50 kg ~2400 mL if 80 kg	Rapid, weak pulse (more than 120 bpm) Moderate hypotension (systolic 80-60 mmHg) Tachypnoea (more than 30 breaths/minute) Pallor, cold clammy skin Poor urinary output (less than 30 mL/hour) Restlessness, anxiety, confusion	Moderate
40% blood loss ~2000mL if 50 kg ~3200mL if 80 kg	Rapid, weak pulse (more than 140bpm) or bradycardia (less than 60 bpm) Severe hypotension (less than 70 mmHG) Pallor, cold clammy skin, peripheral cyanosis Air hunger Anuria Confusion or unconsciousness, collapse	Severe

Sunnynet postpartum hemorrhage policy, 2022

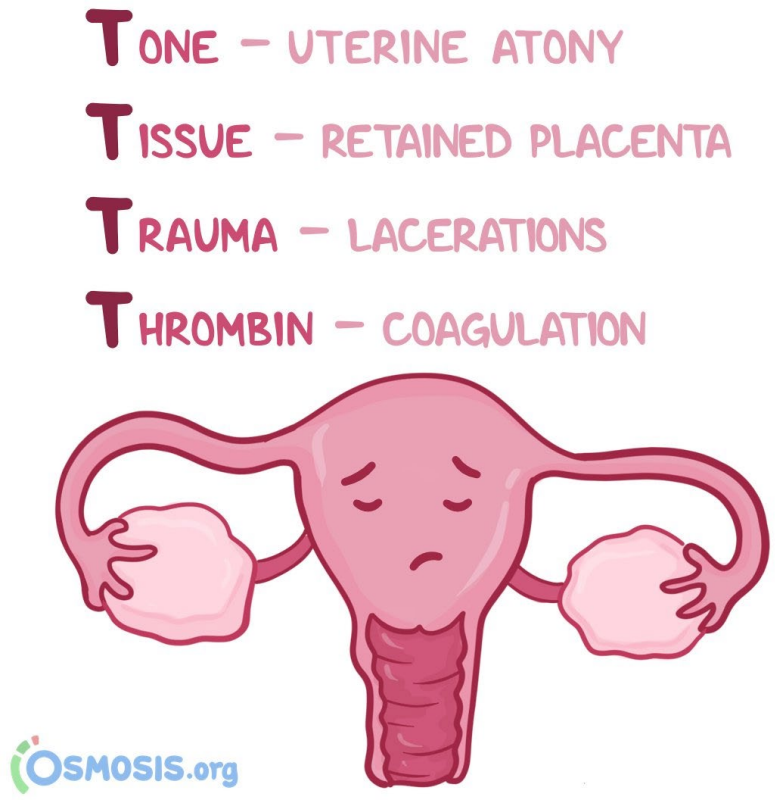
Calibrated Drapes

Image: Amornpetchakul et al., 2018

The Etiologies of PPH

Etiology of Postpartum Hemorrhage

Four T's	Cause	Incidence
Tone	Atonic uterus	70%
Trauma	Lacerations, hematomas, uterine rupture	20%
Tissue	Retained products, invasive placenta	10%
Thrombin	Coagulopathy	1%



Sunnynet postpartum hemorrhage policy, 2022

The Management of PPH (From a Blood Bank Lens)

POLL: A pregnant patient is experiencing massive hemorrhage. Which of the following is true?

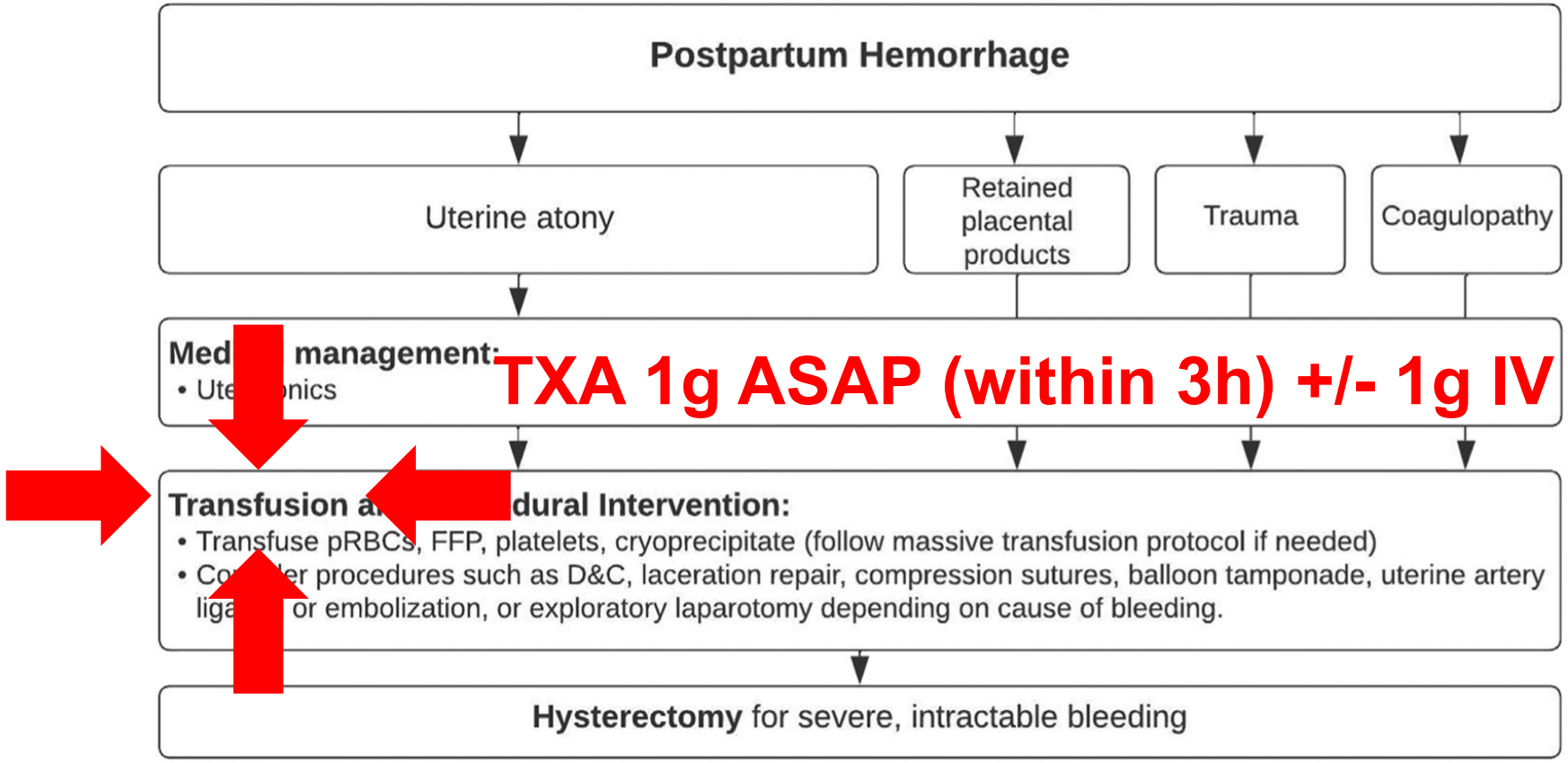
1. Do not prioritize sending a group and screen, the blood bank will issue ONEG anyways

2. Only give tranexamic acid if the fibrinogen level is <2.0

3. Hemorrhaging pregnant patients rarely required red blood cells

4. Hemorrhaging pregnant patients rarely require platelet transfusions

Managing PPH



ACOG Practice Bulletin No 183, 2017
Guan et al., AJOG 2023

WOMAN TRIAL:

- An international, randomized, double blind, placebo-controlled trial
- **N=20,060** women with PPH after vaginal birth or c-section
  (>500 mL or any blood loss within 24h associated with hemodynamic instability)
- **TXA** (1g +/- 1g for ongoing bleeding at 30 min or re-bleed within 24h) **vs placebo**
- Composite outcome: **mortality or hysterectomy**

WOMAN Trial Collaborators, Lancet 2017

WOMAN TRIAL:

- 21 countries, mostly in Africa (12,343) and Asia (6,030)

- Primary outcome:
  - TXA (n=10,051): 5.3%
  - Placebo (n=9,985): 5.5%

RR 0.97 (95% CI 0.97-1.09), p=0.65

- Death due to hemorrhage:
  - TXA: 1.5%
  - Placebo: 1.9%

RR 0.81 (95% CI 0.65-1.00), **p=0.045**

Death due to hemorrhage with EARLY TREATMENT (<3h)

RR 0.69 (95% CI 0.52-0.91)

WOMAN Trial Collaborators, Lancet 2017

Bottom line from WOMAN:

TXA reduces **death due to bleeding** when you give it early (**ASAP, always <3h**)

WOMAN Trial Collaborators, Lancet 2017
Callum et al., CMAJ, 2019

Blood Products and PPH: Where's the money?!

What's in the Coolers?

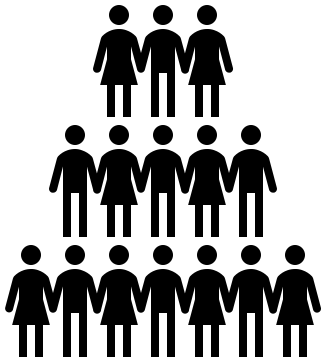
Pack number	Contents
1	4 Red cells
2	4 Red cells and 4 Plasma
All subsequent packs	4 Red cells and 2 Plasma

- **RBCs**
  - Emergency issue: ONEG, K negative in OB
  - Target Hb >80
- **Frozen Plasma**
  - Plasma provides additional clotting factors
  - Additional plasma guided by INR:
    - Target INR <1.8
- **Platelets**
  - Target Platelets > 50
  - Ordered on an as needed basis based on lab results
- **Fibrinogen Concentrate**
  - Target Fibrinogen > 2.0
  - Ordered on an as needed basis based on lab results

Transfusion Targets in Obstetrical MHP

- ☐ Hemoglobin greater than 80 g/L
- ☐ Platelets greater than 50 x 10^9/L
- ☐ INR less than 1.8
- ☐ **Fibrinogen greater than 2 g/L**

Trauma patient ≠ OB patient



≠

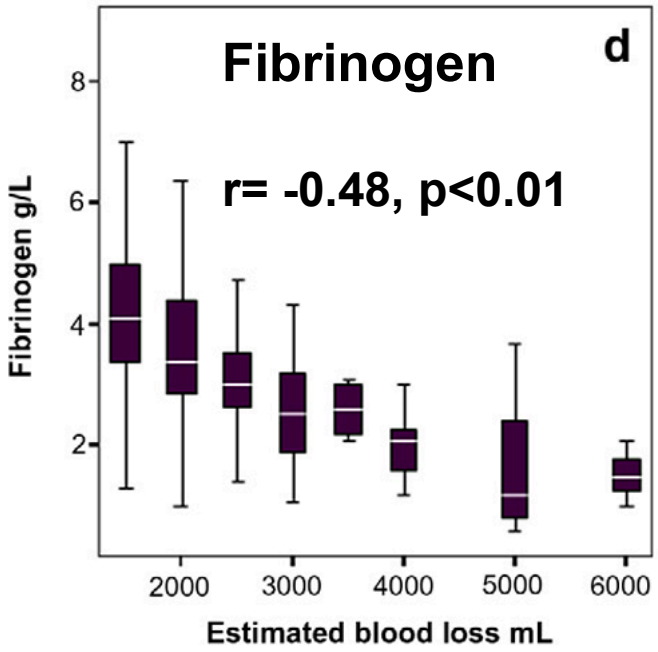
Fibrinogen in general population: 1.5-4 g/L

Fibrinogen at term: 4-6 g/L

↑ VWF, ↑ clotting factors
↓ protein S

Collins, Blood, 2014

Fibrinogen is the best predictor of EBL in PPH



de Lloyd et al., Int Journal of Obs Anesth, 2011

Fibrinogen Concentrate

- **4g for fibrinogen <2.0 g/L**

PTT and INR are RARELY abnormal in PPH

	<=2500 mL EBL (n=297)
PTT normal	296 (99.7%)
PTT abnormal	1 (0.3%)
INR normal	296 (99.7%)
INR abnormal	1 (0.3%)

Overall: 98.8% had normal PTT and 98.2% had normal PT/INR

Collins et al., Blood, 2014

Platelets in PPH

- Platelets rarely required for PPH

- 12/347 (3%) moderate to severe PPH required platelets

- All those transfused plt had 1 of:
  - Antenatal thrombocytopenia
  - Consumptive coagulopathy (abruption, amniotic fluid embolism)
  - >5000 mL hemorrhage

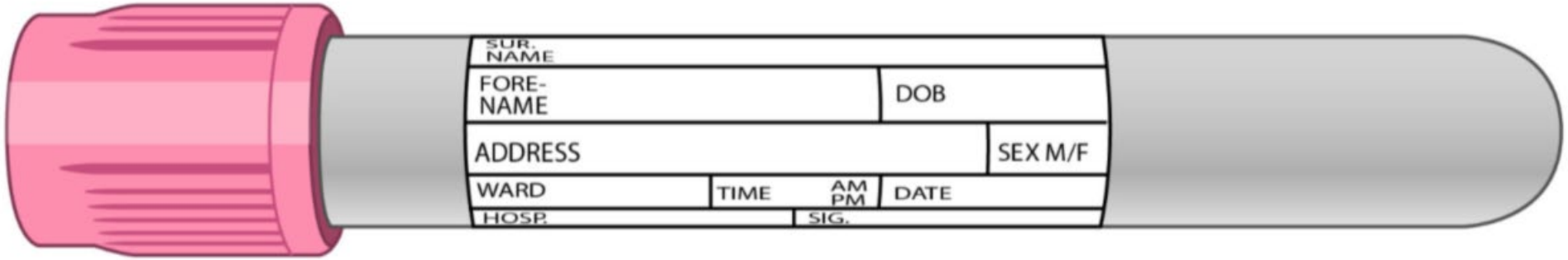
Jones et al., Aaesthesia, 2016

Red Cells

- Transfusion rate:
  - 0.49% emergency C-section
  - 0.28% vaginal delivery

- Emergency issue red cells:
  - ONEG, K negative (7% of Canadian donors)

A Group and Screen is required to switch to group specific red cells



Unique Consequences of Peripartum Transfusion

POLL: Which of the following is **NOT** a consequence of massive transfusion?

1. Hypocalcemia
2. Hyperthermia
3. Blood clotting proteins may be diluted
4. Future pregnancies may experience complications

Consequences of Massive Transfusion in OB Patients

Hypothermia

- Why does it happen?
  - Resuscitation fluids (crystalloids, blood products)
  - Opening of body cavities, **exposure**
  - Decreased heat production

- Consequences
  - ↓ liver metabolism
  - ↓ production of clotting factors
  - ↓ function of hemostasis

Preventing Hypothermia

- Keep patient warm > 36°
  - Their survival depends on it!
  - Bear hugger, warm blankets, room
- Warm blood and/or fluids
- Options: Level 1 infuser and fluid warmer
  - Rapid infuser can infuse up to 80 U/hr
  - Tubing is supposed to be changed q3h
  - Record Level 1 temperature hourly when infusing blood

Consequences of Massive Transfusion in OB Patients

Coagulopathy

- Why does it happen?
  - Dilution
  - Consumption
  - Acute coagulopathy: Abruption, pre-eclampsia, amniotic fluid embolism

- Consequences
  - ↓ Platelets
  - ↓ Clotting factors
  - ↓ Fibrinogen

Consequences of Massive Transfusion in OB Patients

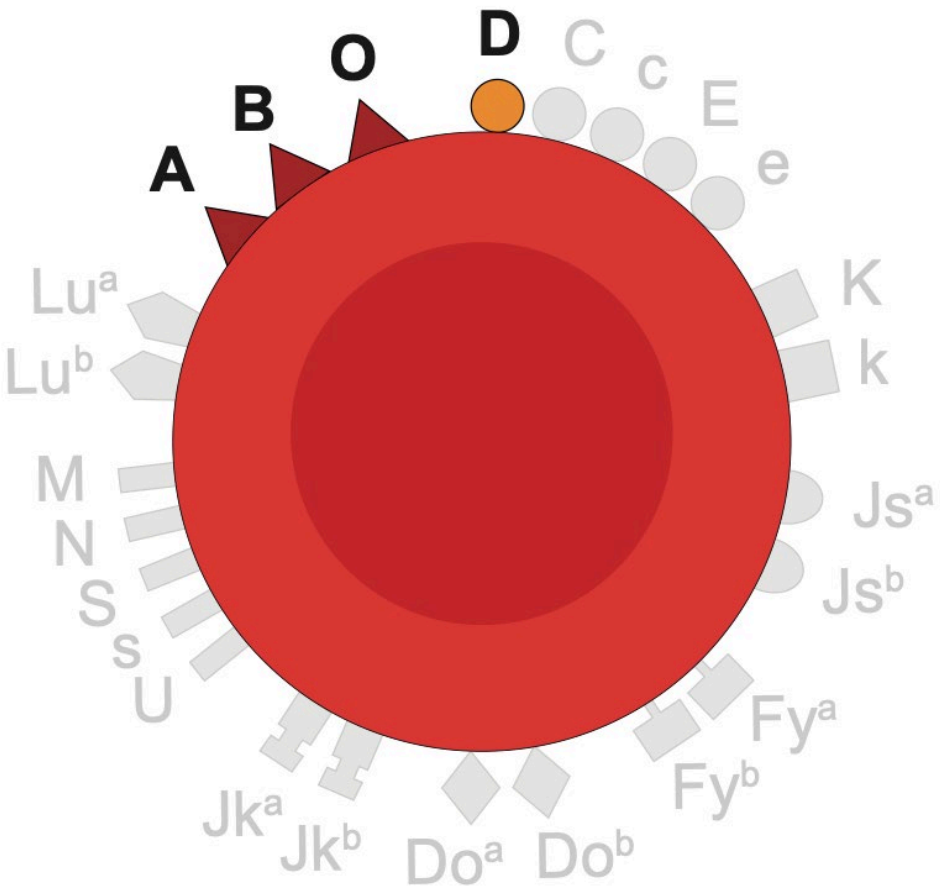
Electrolyte Abnormalities

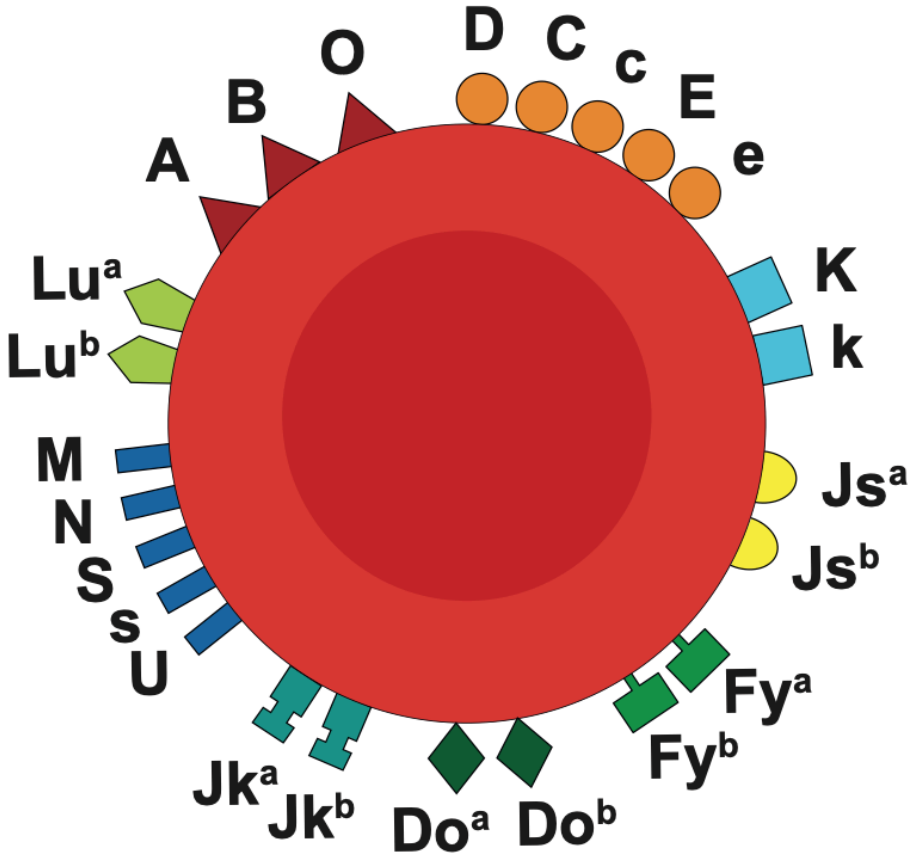
- Hypocalcemia
  - Citrate (anticoagulant in blood) - binds Ca^{2+}
  - Citrate can accumulate at high transfusion rates
  - Hypocalcemia: tetany, prolonged QT interval, decreased myocardial contractility, hypotension, coagulopathy

- Hyperkalemia
  - RBC transfusion: K^+ ↑

CAUTION: Patients on Magnesium infusions (e.g. for pre-eclampsia) can also have ↓Ca/ ↑ K

Red Cell Antigens



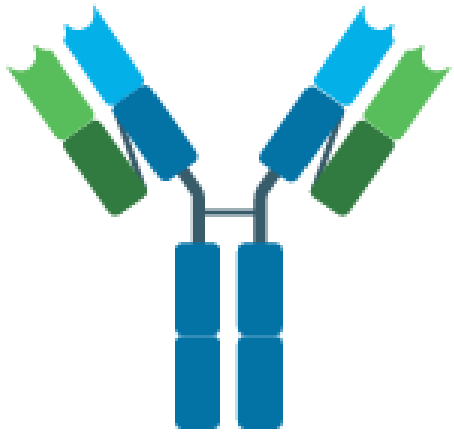


https://www.bgc.io/research/learning

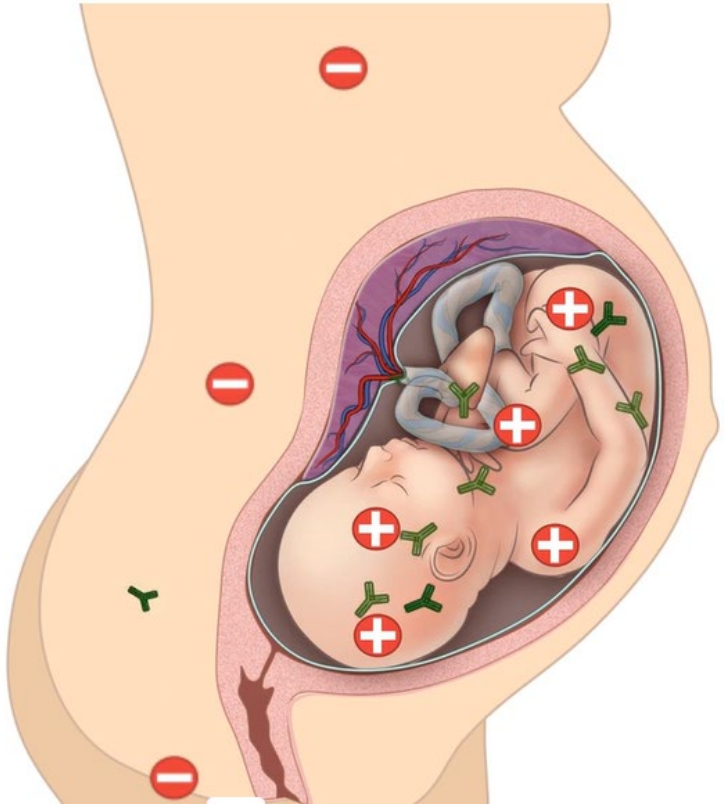
What is Alloimmunization?

Exposure to Foreign RBC Antigen

- Transfusion
- Pregnancy
- IVDU
- Transplant



Hemolytic Disease of the Fetus and Newborn (HDFN)



Antibodies cross the placenta and destroy fetal RBCs

The Spectrum of HDFN

No disease

- No fetal destruction of RBCs

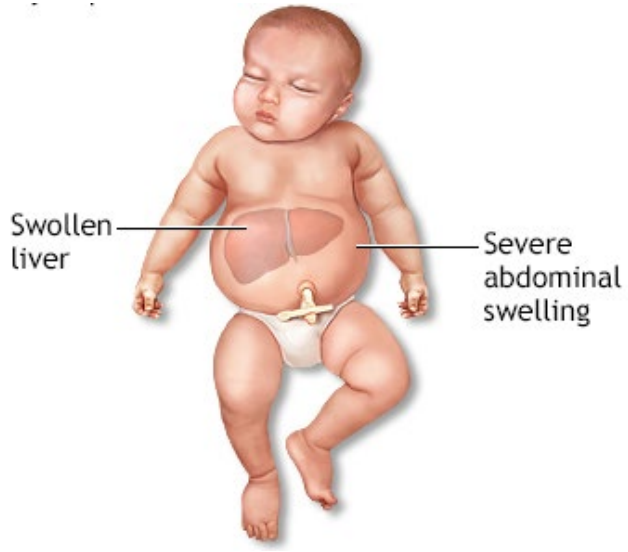
Mild disease

- Hemolytic disease of the newborn

Severe disease

- Hemolytic disease of the fetus requiring intrauterine transfusion

Fetal hydrops



Slide adapted from Dr. Nadine Shehata

What can we do?

- ONEG, K negative RBCs:
  - Avoid anti-D formation in D negative patients
  - Avoid anti-K formation in K negative patients

- Women of child-bearing potential should be informed of the **risk of red blood cell alloimmunization,** which may result in hemolytic disease of the fetus and newborn, and should be counselled to undergo red blood cell **antibody screening 6 weeks and/or 6 months after transfusion** (many antibodies are evanescent, and there is a brief window for detection)

Callum et al., CMAJ, 2019

Key Points

- Pregnant patients can lose a lot of blood, fast and still look “well”
- Quantification of obstetrical blood loss is flawed
- TXA reduces risk of death due to hemorrhage → give ASAP
- Send the G&S ASAP to help save precious ONEG units
- Red cells are life saving → only a minority of OB patients need plasma/platelets
- Fibrinogen levels predict severe PPH → replace if <2.0 g/L
- Alloimmunization is particularly important to pregnant patients
  → check G&S 6 weeks to 6 months after transfusion

Questions & Comments

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