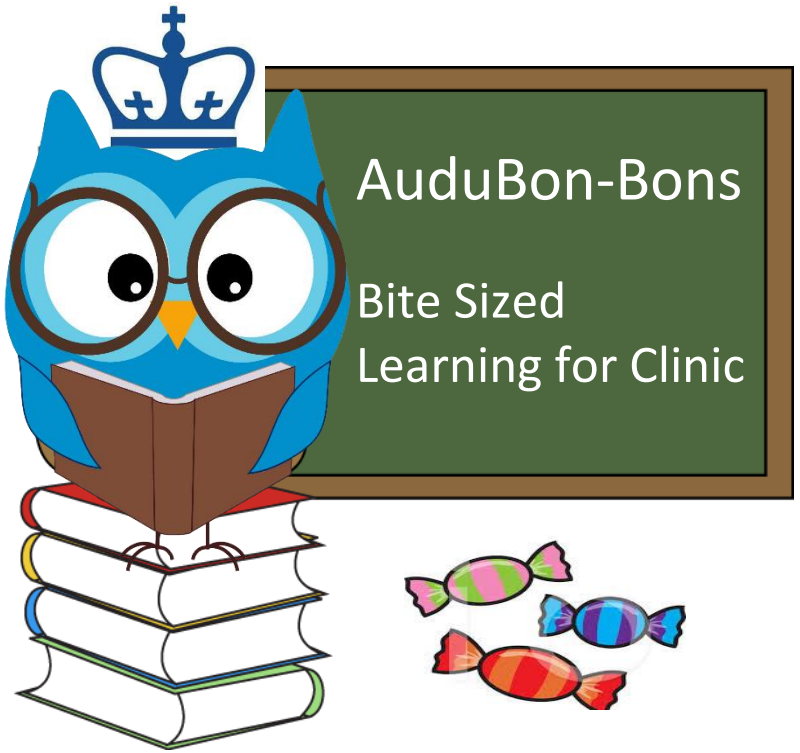
PRENATAL CARE-ALLOIMUNIZATION



Week 86

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Reading Assignment:
ACOG, Practice Bulletin No. 181, August 2017, "Prevention of Rh D Alloimunization"

LEARNING OBJECTIVES

- Understand the background and pathophysiology of Rh D alloimmunization
- Understand the importance and how to prevent Rh D alloimmunization
- Learn how to counsel your patients on the risks and benefits of an Rh D prophylaxis program

CASE VIGNETTE

Patient is a 25 y.o. G3P1011 @ 13w2d who presents for her first prenatal visit. This is a desired pregnancy. She denies any complications in her first pregnancy but recalls needing a shot after delivery.

ROS: denies vaginal bleeding, abdominal pain, abnormal discharge, nausea/vomiting.

FOCUSED HISTORY

What will be pertinent in her history?

- **POB:** G1-FT NSVD, G2-EPF at 6 weeks
- **PGYN:** Menarche @ 12 y.o., regular cycles q28d x 5d; denies STIs, abnormal paps, fibroids, cysts
- **PMH:** Denies
- **PSH:** Denies
- **FH:** Denies
- **SH:** No toxic habits; works as an accountant; married and lives with her husband and daughter; denies IPV
- **Meds:** PNV
- **All:** NKDA

PERTINENT PHYSICAL EXAM FINDINGS

What will be pertinent in her physical exam?

VS: P 99 **BP** 107/80 **Wgt:** 80 kg **Hgt:** 166cm **BMI:** 29.0 kg/m^2

- **General:** NAD, well-appearing
- **Breast:** Symmetrical; no masses, tenderness, discharge, erythema
- **Chest:** CTAB
- **CVS:** RRR
- **Abd:** Soft, NT/ND, no rebound/guarding, no masses
- **GU:** NEFG; normal vaginal mucosa, cervix; no CMT; uterus 13 week size, nontender; no adnexal tenderness or masses
- **Ext:** WWP
- **Bedside US**: SIUP @ 13+2 weeks, FHR 150s

ALLOIMMUNIZATION: BACKGROUND

- Alloimmunization occurs when maternal antibodies are formed against red blood cell antigens not found on maternal red blood cells.
- Nomenclature for the Rh blood group system:
  - 5 major antigens: C, c, D, d, e
  - Majority of Rh alloimmunization cases are due to incompatibility with the D antigen; anti-Rh c and anti Rh E are also common causes of HDFN
- Incidence of Rh negative varies by population:
  - 15% of whites, 5-8% of African Americans, 1-2% of Asians/Native Americans
- Other commonly seen antibodies seen in alloimmunization cases
  - Kell (K1, K2), Duffy (Fy^a, Fy^b), MNS, Kidd (Jk^a, Jk^b), anti-U
  - Lewis (Lea, Leb) and I are IgM antibodies, not associated with fetal complications

PATHOPHYSIOLOGY

- What is the pathophysiology of Rh D alloimmunization?
  - **Fetomaternal hemorrhage (FMH**) stimulates a maternal immune response, with the D antigen eliciting an especially strong immune response
  - Anti-D IgG proliferates rapidly when exposed to the D antigen on fetal cells in subsequent pregnancies.
- What is the volume of fetal blood required to cause alloimmunization?
  - Varies depending on maternal immune responsiveness, immunogenicity of fetal erythrocytes, frequency of bleeding, ABO compatibility
  - FMH volume as **low as 0.1 mL** has led to alloimmunization

PATHOPHYSIOLOGY

- What can cause FMH/alloimmunization?

Box 1. Potential Sensitizing Events in Rh D-Negative Women in Pregnancy ⇦

- Chorionic villus sampling, amniocentesis, cordocentesis
- Threatened miscarriage or miscarriage
- Ectopic pregnancy
- Evacuation of molar pregnancy
- Therapeutic termination of pregnancy
- Antepartum hemorrhage
- Abdominal trauma
- Intrauterine fetal death
- External cephalic version
- Delivery

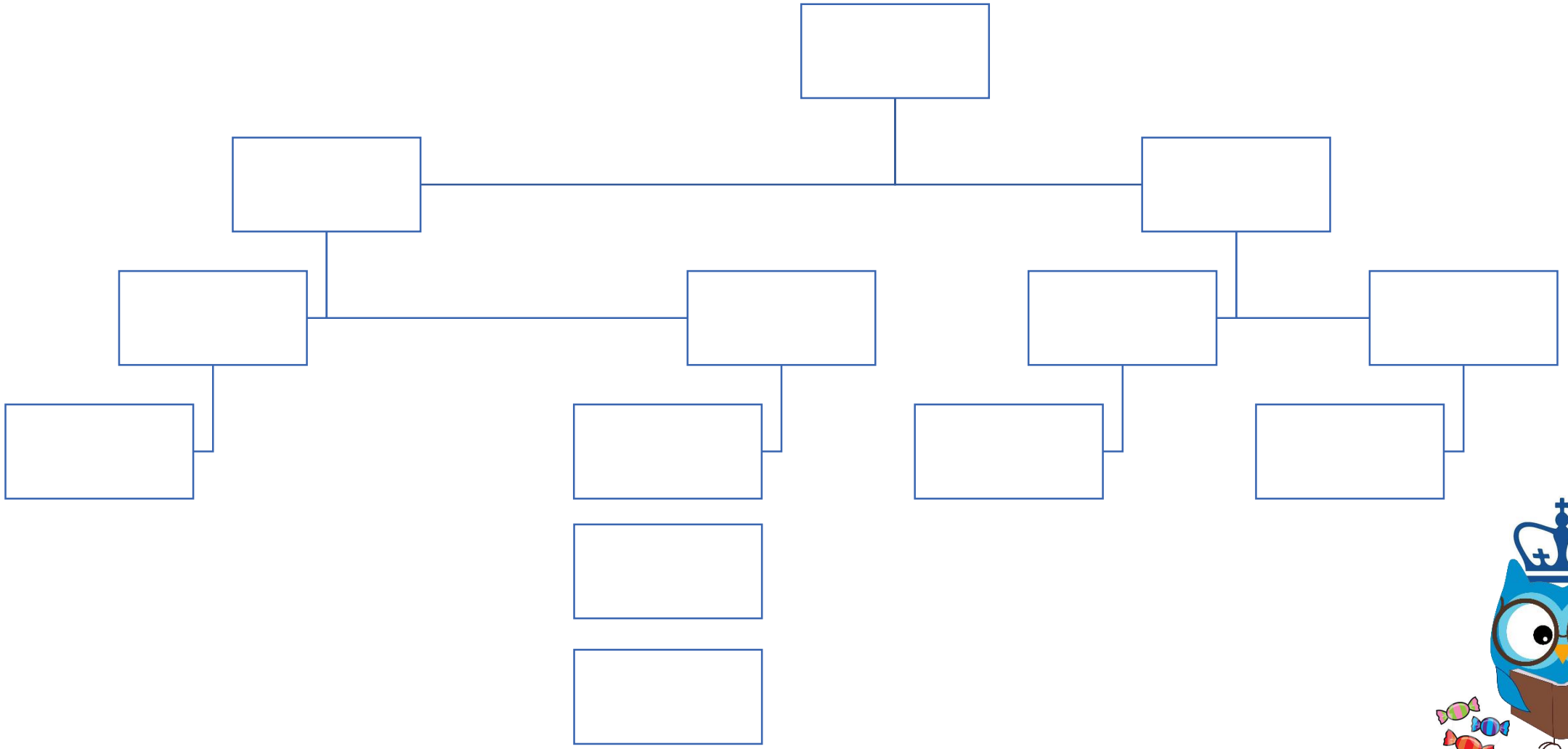
- Rh D antigen appears on fetal RBCs are early **at 38 days from fertilization** (7w3d EGA)
- FMH seen in :
  - 1TM threatened AB: 3-11%, SAB: 1.5-2%
  - 3TM birth: 45%
  - D&C: 4-5%
  - CVS: 14%
  - Amniocentesis: 2-6%
  - ECV: 2-6%

- What is the clinical significance of Rh D alloimmunization in pregnancy?
  - **Hemolytic disease of the fetus and newborn**
  - Anti-D IgG crosses the placenta and binds to fetal erythrocytes, which are then sequestered in the fetal spleen, undergoing extravascular hemolysis; this leads to fetal anemia.
  - Sequelae of fetal anemia include high output cardiac failure, tissue hypoxia
  - Hydrops fetalis (2 or more: ascites, skin edema, pleural effusion, pericardial effusion) seen with fetal hemoglobin deficits of 7g/dL+ (fetal hemoglobin < 5 g/dL)

PREVENTION OF RhD ALLOIMMUNIZATION

- Why is prevention important?
  - **Routine prophylaxis**, including antepartum prophylaxis, with anti-D immune globulin reduces the rate of alloimmunization in at-risk pregnancies **from 13-16% to 0.14-0.2%**
- What tests should you obtain prior to administration of anti-D RhIG?
  - ABO type and antibody screen
  - After deliveries, obtain newborn blood typing: if Rh D negative, no need for RhIG
  - After deliveries and significant FMH events, need to perform a quantitative test (Kleihauer Betke) to determine amount of RhIG needed.
- Administration of anti-D RhIG depends on the following (next slide)

PREVENTION OF Rh D ALLOIMMUNIZATION



PREVENTION OF RhD ALLOIMMUNIZATION

- What is the appropriate dose for prophylaxis?
  - Anti-D RhIG **300 mcg** covers exposure of up to **30 mL** of fetal whole blood or **15 mL** fetal red blood cells
  - 1st 12 weeks EGA: a dose of at least **50 mcg**
    - Lower dose due to lower overall total fetal blood volume is 3 mL
  - After 12 weeks EGA: **300 mcg**
- When do you administer anti-D RhIG?
  - **Within 72 hours** of delivery or possible sensitizing event
  - But, can give up to **13 days** if missed; up to 28 days is recommended by some
- When can you omit anti-D RhIG?
  - If prophylactic dose was given **within 3 weeks** of delivery
- How long is the dose of anti-D RhIG effective?
  - **12 weeks**
  - However, no recommendations for or against repeating dose of RhoGAM if undelivered by 40 weeks if patient received a dose at 28 weeks

PREVENTION OF RhD ALLOIMMUNIZATION

- In cases of chronic antepartum hemorrhage, how should patients be managed?
  - Per ACOG, q3 week indirect Coombs titer: if negative, need to perform K-B to quantify volume of excess FMH and anti-D RhIG dose needed
- What are some concerns regarding Rh D prophylaxis?
  - Theoretical risks of infection as it is obtained from human plasma
    - Historical risks of Hep C, negligible currently
  - Cost effectiveness
    - 40% of Rh D-negative women will have an Rh D-negative fetus
    - Antepartum testing (invasive testing, cffDNA) still less cost effective than routine prophylaxis regimens

MANAGEMENT OF ALLOIMMUNIZED PREGNANCIES

- Refer to your friendly neighborhood Maternal-Fetal Medicine colleagues
- Initially, obtain paternal antigen status and, if risk of Rh D-positive fetus, obtain fetal antigen type via amniocentesis
- Serial maternal serum antibody titers
  - Consider monthly if stable, q 2 weeks if rising
  - Not useful in patients with previously affected pregnancy/neonate
- What is a critical titer?
  - Titer associated with significant risk for severe hydrops
  - Usually between 1:8 and 1:32
  - Is this applicable for patients with Kell-sensitized pregnancies?
    - No, titers do not correspond to severity of fetal hydrops
- Middle cerebral artery doppler testing
  - Peak systolic velocity above 1.5 times the median for the gestational age (>1.5 MoM) is consistent with increased risk of moderate or severe fetal anemia
  - At CUIMC: initiate at diagnosis, perform weekly
- What interventions are available for severe fetal anemia?
  - Cordocentesis for fetal hemoglobin assessment with intrauterine transfusion as indicated
- Timing of delivery
  - If mild anemia only, consider IOL/delivery between 37-38 weeks
  - If severe fetal anemia, consider steroid course for FLM and delivery between 32-34 weeks

CASE, CONTINUED

- What further information would you like to find out regarding the patient?

- If she is Rh negative, how do you counsel her regarding interventions required in pregnancy?

SOCIAL DETERMINANTS OF HEALTH

- Studies have shown that RhD-negative women have felt that information regarding the significance of their Rh D status was not provided adequately by their clinicians, thus reducing their ability to be partners in the decision-making process
- Patients experience anxiety regarding their Rh D status, especially as alloimmunized pregnancies require intense intervention that may not be feasible for patients who have difficulty with accessing medical services due to their social-economic status

The shared decision-making process is vital in the provision of good, patient-centered care, especially in situations with complex medical issues; remember that your role as a clinician is to educate and empower your patients

EPIC .PHRASE

.BBonRhDAllo

Description: Rh D negative pregnancy counseling

We reviewed the significance of an Rh negative antibody status and its implications for the patient's pregnancies. We discussed the risks, benefits, and alternatives to routine prophylaxis with anti-D immune globulin in order to prevent Rh D alloimmunization. We reviewed the risks of not receiving anti-D immune globulin at the recommended times, including becoming Rh D alloimmunized. We discussed the significant morbidity and mortality associated with hemolytic disease of the fetus and neonate, with worsening severity in each subsequent pregnancy.

CODING AND BILLING

- **ICD-10**
  - **Z67.91**, Unspecified blood type, Rh negative
  - **O36.0191**, Maternal care for anti-D Rh antibodies
  - **O36.0990,** Maternal care for other rhesus isoimmunization
  - **Z29.13**, Encounter for prophylactic Rho(D) immune globulin
  - **P56.0**, Hydrops fetalis due to isoimmunization
  - **O36.2,** Maternal care for hydrops fetalis

EVIDENCE

- Prevention of Rh D alloimmunization. Practice Bulletin No. 181. American College of Obstetricians and Gynecologists. Obstet Gynecol 2017;130:e57–70.
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