2025 Hot Topics in Obstetrics
A Montana Update

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BENJAMIN BRYDEN MD, MPH
ASSOCIATE PROFESSOR OF MEDICINE
FAMILY MEDICINE RESIDENCY OF WESTERN MONTANA

Disclosures

NONE

Learning Objectives

- Understand the role of the family physician for maternity care in Montana
- Discuss the implementation of tailored pregnancy care to address access issues
- How to respond to patients about controversial topics in obstetric care
- Review evidence behind risks of acetaminophen and SSRIs in pregnancy
- Review BP targets from the CHAP trial
- Review new prevention strategies for infections that may impact pregnancy
- Understand the impact of syphilis in Montana
- Understand the use of NIPT for RhD status in the era of Rhogam shortage

Which Best Reflects Your Current Role in Pregnancy Care?

- Full spectrum antepartum care including deliveries and surgical obstetrics?
- Full spectrum antepartum care including vaginal deliveries?
- Outpatient Limited OB Care, some antepartum care in 1st / 2nd trimester, then transfer?
- Pregnancy confirmation only?
- No involvement in pregnancy care?

The Montana Context: Why We Are Essential

The Problem: The Maternal Care Access Crisis in Montana

50% of Montana's counties are Pregnancy Care Deserts (no birthing facility OR obstetric clinician).

Pregnant mothers in Montana face some of the **longest drive times** to care in the country (average of ~23 minutes, but often > 1 hour).

This crisis is often borne by our Indigenous patients (Preterm birth rate for American Indian/Alaska Native birthing people is **1.3x higher**).

The Solution

We, as Family Physicians, are often the **sole pregnancy care providers** in these deserts. Our role is non-negotiable and requires up-to-date, efficient, and equitable practices.

Recently closed obstetric units

- Providence St. Patrick, Missoula
- Clark Fork Valley Hospital, Plains
- Logan Health, Cut Bank

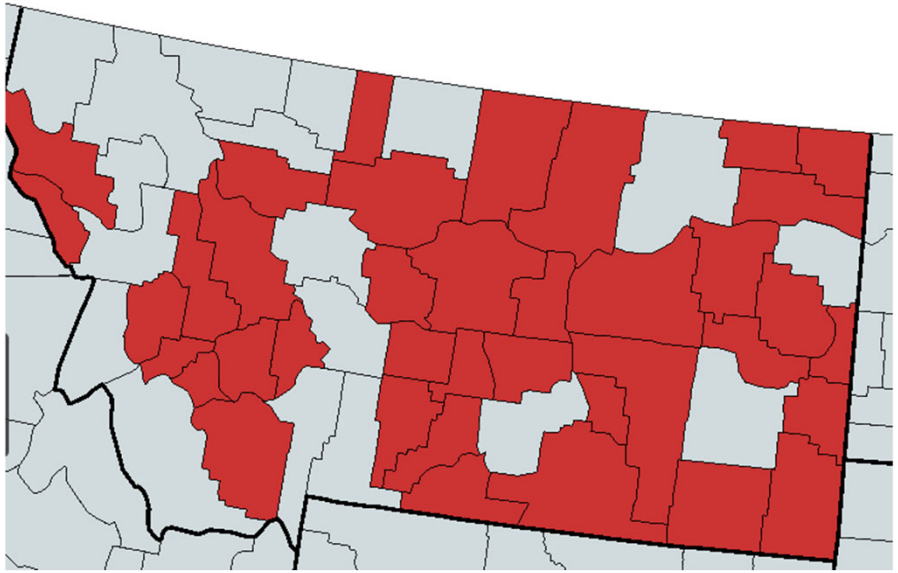
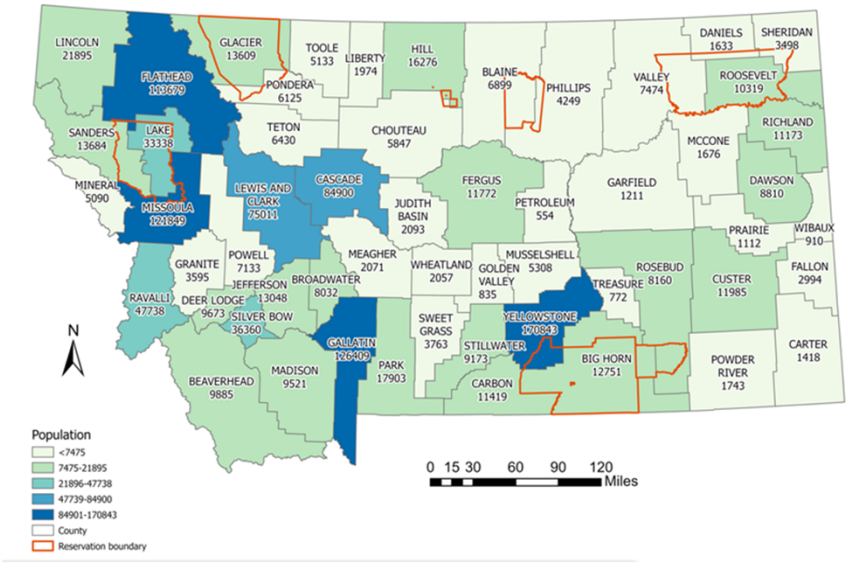


Figure 3. Montana population by county, 2022

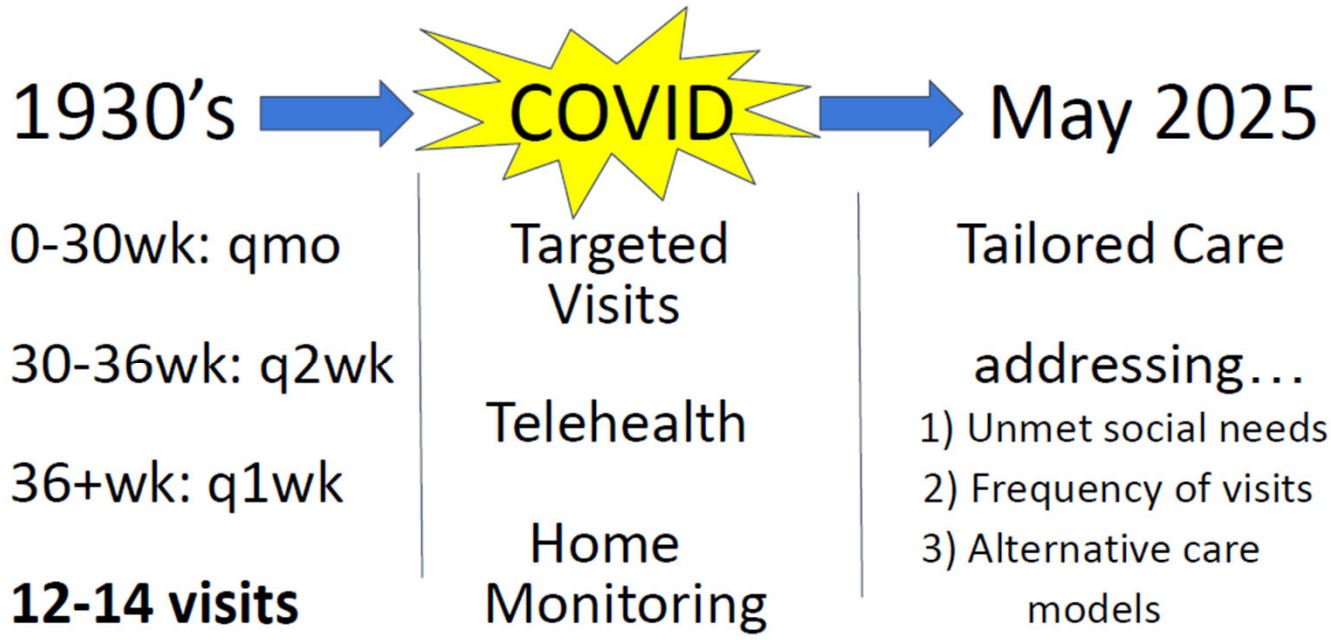


Counties in Montana with no Labor and Delivery

Possible Solution: Tailored Prenatal Care

- ACOG Clinical Consensus May 2025

- Tailored Prenatal Care Delivery for Pregnant Individuals: ACOG Clinical Consensus No. 8. Obstet Gynecol. 2025 May 17; 145(5):565-577.


1930's
COVID
May 2025
0-30wk: qmo
30-36wk: q2wk
36+wk: q1wk
12-14 visits
Targeted Visits
Telehealth
Home Monitoring
Tailored Care
addressing…
1) Unmet social needs
2) Frequency of visits
3) Alternative care models

Plan for Appropriate Tailored Healthcare in Pregnancy (PATH)

- The problem:
  - 23% of patients don't present until second trimester
  - 50% don't receive the all recommended services in a timely manner
  - Social and structural drivers of health contribute to poor maternal and neonatal outcomes
  - Gaps in prenatal care are associated with adverse pregnancy outcomes
  - Montana: geographic isolation
- Need to reassess standards and improve processes of prenatal care
- Consensus developed with goal of equity (over equality) for reproductive health justice and quality improvement

PATH Conclusions

- Provide an alternate approach to prenatal care
- Expand the COVID care model
- Look at individualized care and equity

- "The goal is to improve access to care while also improving operational efficiency and cost-effectiveness. By streamlining the number of visits for average-risk patients, we can improve availability for higher-risk patients with more complex needs."

Mark Turrentine, MD, FACOG - co-author ACOG Clinical Consensus on Tailored Care

Key PATH Recommendations

Comprehensive prenatal needs assessment

Table 1. Sample Components of Maternal Risk Assessment

Obstetric or Gynecologic	Medical	Family History	Social Drivers of Health*
Prior pregnancies and outcomes Menstrual history Infertility, ART Current pregnancy symptoms EDD confirmation Gynecologic history, including PAP testing and results Sexual history, including past STIs and current risk Teratogen exposures since pregnancy and ongoing risk	Chronic conditions History of mental health diagnoses and treatment, including substance use and substance use disorder and eating disorders Surgeries Allergies Immunizations Medications and supplements Oral health Infectious diseases—past and ongoing risk	Genetic or congenital defects or conditions in the genetic family of the fetus Recurrent pregnancy loss Pregnancy complications Chronic conditions Cancer	Demographic characteristics and identities associated with health outcomes and experience of marginalization (eg, race, ethnicity, gender identity, sexual orientation, religion, nationality, geographic location, primary language) Social network and support (eg, family structure, partner, father of baby if applicable, individuals in the home, history of trauma or intimate partner violence) Material needs (eg, housing, access to nutritious foods, transportation, financial resources strain, health care affordability) Education and employment (eg, highest school completed, health literacy, current work)

ART, assisted reproductive technology; EDD, estimated due date; STI, sexually transmitted infection.

AAP/ACOG Guidelines for perinatal care. 8th ed. 2017.

- Engage pregnant people in their care plan
- Refer / coordinate assistance with unmet social needs

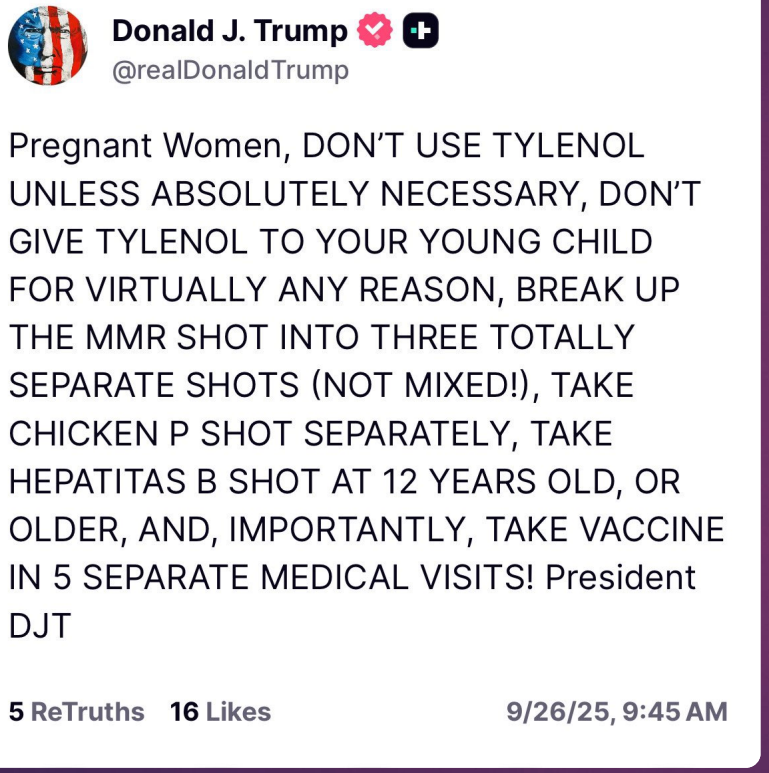
Table 2. Potential Examples of Unmet Social Needs Matched With Possible Assistance and Adjustment*

Unmet Social Need	Potential Assistance (Health System, Community, and Local Resources Provided to Alleviate the Unmet Social Need)	Potential Care Adjustment (Modifications to Care Delivery by Maternity Care Professionals to Improve Accessibility)
Transportation insecurity	Ride share vouchers Coordinated transportation	Targeted visit schedule Telemedicine Local completion of laboratory tests and vaccinations
Social isolation	Peer-support programs Doula services Prenatal support groups	Group prenatal care Doula or peer support at prenatal visits

Data from: National Academies of Sciences, Engineering, and Medicine. Integrating social care into the delivery of health care: moving upstream to improve the nation's health. National Academy of Sciences; 2019.

- Adjust prenatal care to be accessible to the individual
  - Tailored visit schedule
  - Telehealth
  - Group prenatal care
- Tailor visit frequency and monitoring
  - Visits: 6-10 vs 12-12 (equivalent outcomes with 3 sys reviews)
  - Monitoring: BP, weight, FH / +/- FHT / no U/A
- Alternative models may help to meet care guidelines
  - Telemedicine: addresses cost / access
  - Group care: benefits marginalized populations
- Individualize monitoring options
  - Pharmacies, home visits, home monitoring

My friend told me not to take …



What about Tylenol?

Tylenol in pregnancy…

- Controversy from observational evidence that suggest prenatal acetaminophen exposure may be associated with increased risks of asthma, ADHD, autism spectrum disorders, and other neurodevelopmental disorders
  - Studies are limited by confounding factors and have not demonstrated a clear causal relationship
  - Short term medically indicated use likely low / no risk
  - Prolonged frequent use may be associated with higher risk though unproven risks should not be overstated and may lead to the use of more harmful medications

Lowest effective dose for the shortest time necessary…

- **AAFP**: "Acetaminophen is considered the safest over the counter pain reliever for use during pregnancy when taken as directed."
  - Recommended first line for pain and fever and no conclusive evidence of a causal link between its use and neurodevelopment disorders
- **SMFM**: "physicians should communicate the risks vs benefits of acetaminophen use during pregnancy and consider it a reasonable and appropriate medication for pain or fever in pregnancy"
- **ACOG**: "One of the only safe pain relievers for pregnant patients with no clear evidence that provide a direct relationship between the use of acetaminophen during any trimester and fetal development issues, and that any medication should be used only as needed, in moderation, and after the pregnant patient has consulted with their health care professional"

Recent evidence summary

2019

Australian systemic review and meta-analysis of eight prospective cohort studies (n = 244,940) found association with increased risk of ADHD in prolonged antepartum use of acetaminophen (>28 days) during third trimester

- Fever and infections confounding variables also associated with increased risk of ADHD and may have been the reason for increased acetaminophen use

2024

Swedish study (n = 2,480,797) found no increased incidence of autism or ADHD in children of mothers who used acetaminophen during pregnancy with siblings as control

- Suggested prior associations (2019 study) may have been from familial confounding

2025

BMJ "Umbrella review"

- Conventional cohort studies report modest increased risk of ADHD and ASD
- Associations disappear when controlled for sibling analysis

How to talk to patients about conflicting information?

- "Authority bias" (trusting the president) vs "expert bias" (trusting you, their doctor)
- For any medication in pregnancy lowest dose for least time necessary
- Counseling points:
  - Treat the fever, not just the pain
    - Fever is known to be dangerous in pregnancy and may have teratogenic effects, link between acetaminophen and NDD is inconclusive with weak if any supporting evidence
  - Lack of alternatives
    - "We don't have other options. NSAIDs (like Ibuprofen/Advil) can cause heart/kidney issues in the baby and are strictly unsafe in later pregnancy. Tylenol remains the safest choice when necessary."

What about antidepressants?

July 2025 FDA expert panel on SSRIs in pregnancy noted:

Concerns about "heart defects, autism, and developmental issues"	Discussed risk of pregnancy complications including risk of spontaneous abortion, post partum hemorrhage, and pre eclampsia	Neonatal issues including persistent pulmonary hypertension of the newborn (PPHN)	Did acknowledge the severe dangers of untreated maternal depression (suicide, preterm birth, substance use)

Concerns about misleading information to the public about risks of SSRIs in pregnancy

Widely reported by media as "misinformation"

ACOG / SMFM Response

- "Panel was alarmingly unbalanced and did not adequately acknowledge the harms of untreated perinatal mood disorders in pregnancy"
- "unsubstantiated and inaccurate claims made by FDA panelists"
- "For pregnant people who need SSRIs, they are life changing and lifesaving. Mental health conditions are already the most frequent cause of pregnancy related death."
- "misinformation about depression and its treatment creates confusion and doubt among patients and the public leading to unnecessary barriers to care."
- "ACOG recommends against withholding or discontinuing medications for mental health conditions due to pregnancy or lactation status alone"

What does the evidence say?

- Mental illness is common in pregnancy but often not treated or undertreated
- Risks of undertreatment or no treatment are severe
- Antidepressants do have risks in pregnancy but risks generally outweigh benefits if there is potential for severe untreated mental illness
  - Exposures should be thoughtfully weighed and shared decision making is paramount

- **Suicide is currently the leading preventable contributor to maternal mortality in the United States**, exceeding hemorrhage and hypertensive disorders

Counseling points

- ACOG recommends that obstetricians be prepared to counsel patients on the benefits and risks of psychopharmacotherapy for perinatal mental health conditions when clinically indicated.

Table 1. General Approach to Risk Counseling for Depression Psychopharmacotherapy

Risks of under-treatment or no treatment for depression during pregnancy include…	Risks of antidepressant use during pregnancy include…*
Limited engagement in medical care and self-care	PPHN
Substance use	Transient neonatal adaptation syndrome
Preterm birth	Preeclampsia (SNRIs)
Low birth weight	Spontaneous abortion (SNRIs)
Preeclampsia	
Postpartum depression	
Impaired infant attachment (which carries long-term developmental effects)	
Disrupted relationship with partner	
Suicide†	

PPHN, persistent pulmonary hypertension of the newborn; SNRI, serotonin-norepinephrine reuptake inhibitor.

*Data derived from literature that accounts for the underlying indication for antidepressant use.

†Suicide is a leading preventable contributor to maternal mortality in the United States, exceeding hemorrhage and hypertensive disorders.

Data from Trost SL, Beauregard J, Njie F. Pregnancy-related deaths: data from maternal mortality review committees in 36 US states, 2017–2019. Centers for Disease Control and Prevention; 2022. Accessed December 7, 2022. https://www.cdc.gov/reproductivehealth/maternal-mortality/erase-mm/data-mmrc.html *and* Viswanathan M, Middleton JC, Stuebe A, Berkman N, Goulding AN, McLaurin-Jiang S, et al. Maternal, fetal, and child outcomes of mental health treatments in women: a systematic review of perinatal pharmacologic interventions. Comparative Effectiveness Review, No. 236. Agency for Healthcare Research and Quality; 2021. Accessed February 8, 2023. https://www.ncbi.nlm.nih.gov/books/NBK570101/

Neonatal risks of SSRIs

- Persistent pulmonary hypertension of the newborn
  - Rare but potentially fatal
  - Respiratory distress in first few hours of life with 10-20% mortality risk
  - FDA issued public health advisory in 2006
  - Absolute risk low and SSRIs may contribute to 1-2/1000 additional cases of PPHN
  - FDA updated guidance after 2006 advising physicians to not alter prescribing practice when treating depression in pregnancy due to concerns for PPHN
- Neonatal adaptation syndrome

Neonatal adaptation syndrome

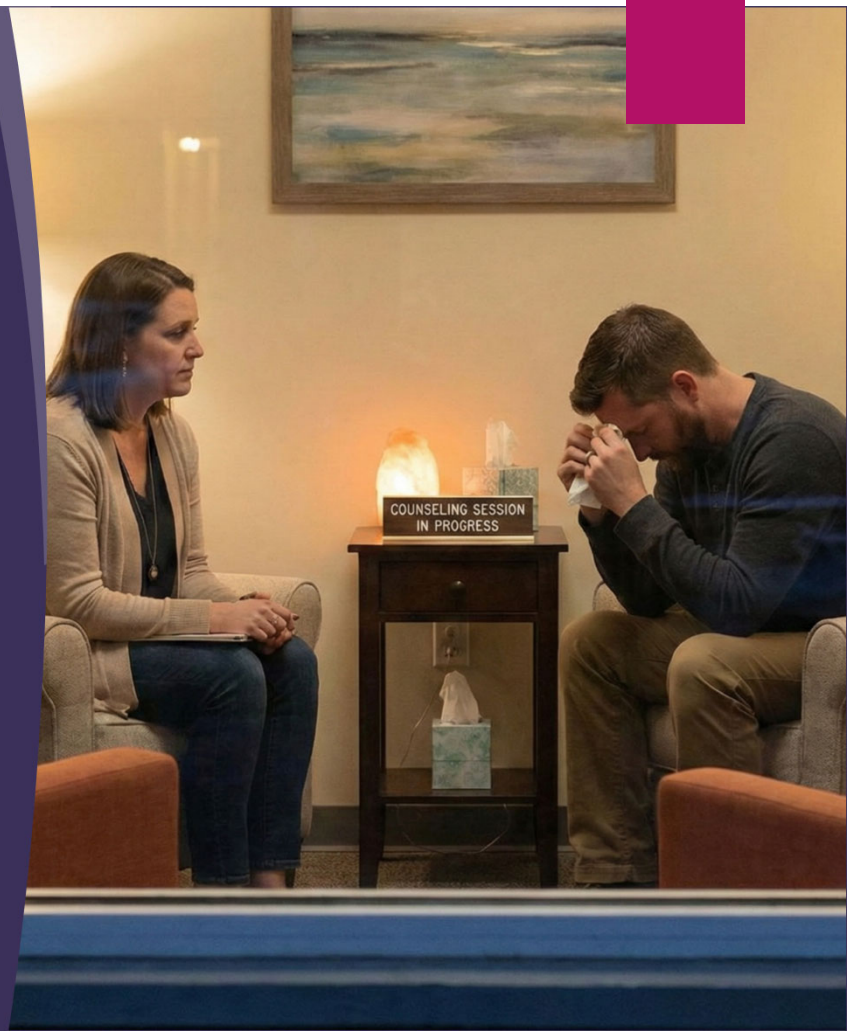
- Irritability, restlessness, tremors, hyperreflexia, hypoglycemia, hypothermia, sleep disruptions, poor feeding, rarely seizures
- Symptoms usually start in first few days of life and resolve by 2 weeks
- Almost always self limited **without evidence of long term harm**
- Incidence between 10-30%
- **Fluoxetine** and **paroxetine** more commonly implicated
- Poorly understood but may be from serotonergic withdrawal
- ACOG recommends "**Pregnant individuals taking an SSRI or SNRI should deliver in a hospital** to facilitate pediatric assessment and monitoring if needed"
- Treatment includes supportive measures such as skin to skin and frequent feeding
- Tapering antidepressants not recommended to avoid NAS and increases risk of symptom relapse

What to avoid?

- Any SSRI may be used in pregnancy but some may have higher risks than others
- **Fluoxetine**
  - Long half life
  - Higher risk of neonatal adaptation syndrome and accumulation in breast milk
  - Does not preclude use of fluoxetine if previously effective outside of pregnancy
- **Paroxetine**
  - Higher risk of neonatal adaption syndrome

Prevention?

- Data supports prevention of perinatal depression for those at risk
  - Counseling (CBT, Mothers and Babies)
  - Interpersonal therapy (the ROSE program [Reach Out, Stay Strong, Essentials for mothers of newborns)



Depression Treatment approach

- Psychotherapy is first line treatment for mild – moderate perinatal depression
  - Not always accessible or acceptable to individuals
- SSRIs are first line pharmacotherapy for perinatal depression
  - SNRIs are reasonable alternatives
- Sertraline or escitalopram are first line medications
- Individualize treatment based on prior response to therapy (if applicable)

General Depression Treatment Approach

- Use the lowest effective dose
- Avoid polypharmacy
  - Use single agent if possible, polypharmacy increases exposures and risk of adverse outcomes
- Minimize switching medications
  - Transitioning can require a cross taper and increase exposure
- Consider untreated or inadequately treated mental health disorders an exposure and pregnancy risk
- Don't forget adjunctive support and social determinants of health
- Up titrate quickly

- Choose antidepressant that has worked before. If antidepressant naïve, choose antidepressant based on table below with patient preference in consideration. Antidepressants are similar in efficacy and side effect profile.
- In late pregnancy, you may need to increase the dose above usual therapeutic range (e.g., sertraline 250mg rather than 50-200mg).
- If a patient presents with pre-existing mood and/or anxiety disorder and is doing well on an antidepressant, do not switch it during pregnancy or lactation. If patient is not doing well, see Figure 2: *Follow-Up Treatment of Perinatal Mental Health Conditions*.
- Evidence does not support tapering antidepressants in the third trimester.
- Minimize exposure to both illness and medication.
  - Untreated/inadequately treated illness is an exposure
  - Use lowest effective doses
  - Minimize switching of medications
  - Monotherapy preferred, when possible

First-line Treatment Options for Mild, Moderate, or Severe Depression, Anxiety Disorder, and PTSD

Medication	sertraline*	fluoxetine	citalopram**	escitalopram**
Starting dose and timing	25 mg qAM (if sedating, change to qHS)	10 mg qAM	10 mg qAM	5 mg qAM
Initial increase after 4 days	↑ to 50 mg	↑ to 20 mg	↑ to 20 mg	↑ to 10 mg
Second increase after 7 more days	↑ to 100 mg			
Reassess Monthly (increase as needed until symptoms remit)	↑ by 50 mg	↑ by 20 mg	↑ by 10 mg	↑ by 10 mg
Therapeutic range***	50-200 mg	20-80 mg	20-40 mg	10-20 mg
Individualized approach to titration	Slower titration (e.g., every 10-14 days) is often needed for patients who are antidepressant naïve			

Adjunctive Support and Social Determinants of Health

Adjunctive Support Options	Social and Structural Determinants of Health
Talk to your patient about adjunctive support options such as: • Self-care • Balanced nutrition • Substance avoidance • Sleep hygiene • Mindfulness • Exercise • Books and workbooks	Ask about/consider social and structural factors that can be a barrier to engagement in care: • Access to stable housing • Access to food/safe drinking water • Utility needs • Safety in home and community • Immigration status • Employment conditions • Transportation • Childcare • Refer to social services as indicated

Post partum depression – new

- IV brexanolone can be used for moderate – severe depression with onset in 3rd trimester or up to 4 weeks post partum
  - Rapid onset of access
  - Does require hospitalization
    - Limited access

Medication Treatment for Moderate/Severe Depression with Onset in Late Pregnancy or Within 4 weeks postpartum – Brexanolone	
Brexanolone is an FDA-approved medication that can be considered for treatment of moderate to severe postpartum depression.	
Brexanolone: – is a formulation of intravenous allopregnanolone (a neurosteroid) that acts on GABA-A receptors – requires an IV infusion over 60 hours – has a faster onset of action (symptom reduction in 1-2 days) compared to available oral antidepressants, which generally take 4-8 weeks to work – has been shown to maintain the reduction in depression symptoms at 30 days post-infusion	When is Brexanolone indicated? If onset of depression occurs in 3rd trimester through 4 weeks postpartum and if patient is <6 months postpartum at screening, consider Brexanolone (IV allopregnanolone infusion over 60 hours in an inpatient setting).
More information can be found at Reprotox and LactMed on all pharmacological treatments	

New BP Targets for chronic hypertension in pregnancy

CHAP TRIAL

What is the goal blood pressure for chronic hypertension in pregnancy? CHaP Trial

- **Treat BP in pregnancy when consistently > 140/90**
  - Major practice change from prior recommendations to treat BP in pregnancy when consistently >160/110 and stop anti-hypertenstive therapy if BP <120/80
- Primary outcomes:
  - Reduced risk of PEC w SF, preterm birth <35w, placental abruption, fetal / neonatal death
- Other serious maternal / neonatal complications similar and incidence of low birth weight similar between groups

Infectious Update – RSV and Syphilis

JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 20, 2023 VOL. 388 NO. 16

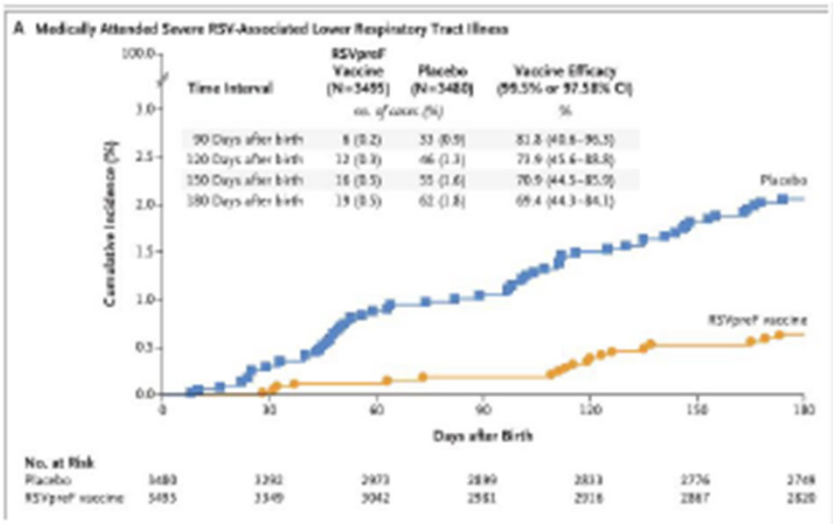
Bivalent Prefusion F Vaccine in Pregnancy to Prevent RSV Illness in Infants

B. Kampmann, S.A. Madhi, I. Munjal, E.A.F. Simões, B.A. Pahud, C. Llapur, J. Baker, G. Pérez Marc, D. Radley, E. Shittu, J. Glanternik, H. Snaggs, J. Baber, P. Zachariah, S.L. Barnabas, M. Fausett, T. Adam, N. Perreras, M.A. Van Houten, A. Kantele, L.-M. Huang, L.J. Bont, T. Otsuki, S.L. Vargas, J. Gullam, B. Tapiero, R.T. Stein, F.P. Polack, H.J. Zar, N.B. Staerke, M. Duron Padilla, P.C. Richmond, K. Koury, K. Schneider, E.V. Kalinina, A.S. Anderson, K.A. Swanson, W.C. Gruber, and A. Gurtman, for the MATISSE

Prevent neonatal RSV?

RSV Vaccine for Pregnant patients

- Single dose of RSV vaccine for pregnancy patients between 32w0d and 36wd6 EDD during RSV season (September – January)
  - **Reduced risk of infant hospitalization for RSV by 68% (birth – 3 month)**
  - **Reduced risk of severe RSV disease by severe RSV disease by 82% (birth – 3 months and by 69% (birth to 6t months)**
- Adverse effects: Low birth weight and neonatal jaundice however not statistically significant vs placebo

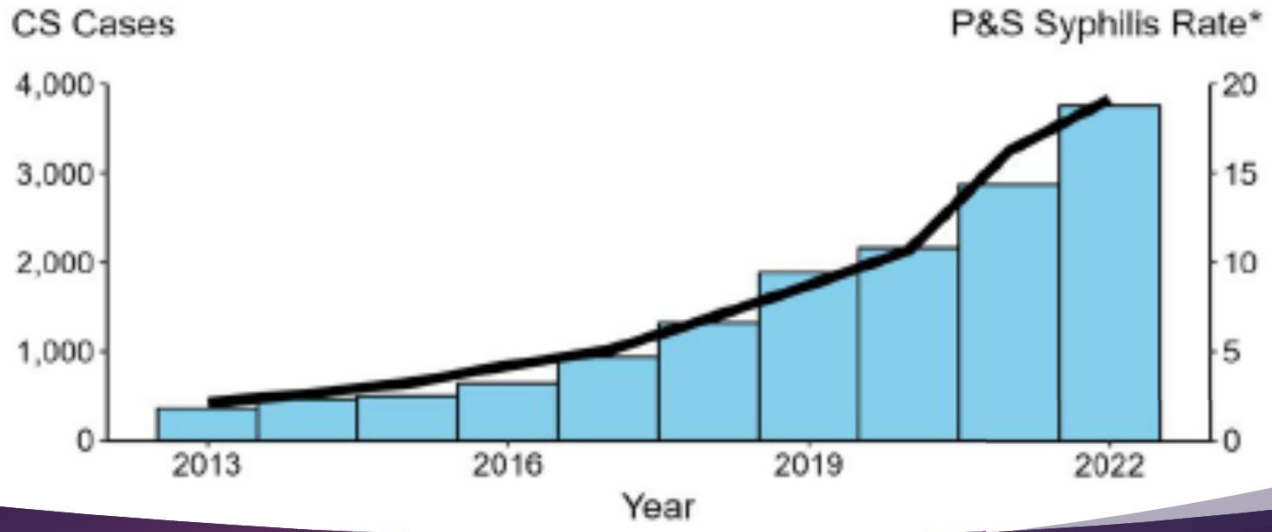


When to vaccinate the newborn?

- Infant younger than 8 months old entering first RSV season (October through March 31)
  - Mother did not receive RSV vaccine
  - Mother's RSV vaccination status is unknown
  - Infant born within 14 days of maternal RSV vaccination
  - Increased risk of severe infection
  - Consider for infants of mothers vaccinated in prior pregnancies
  - Ideally should be given in hospital before discharge

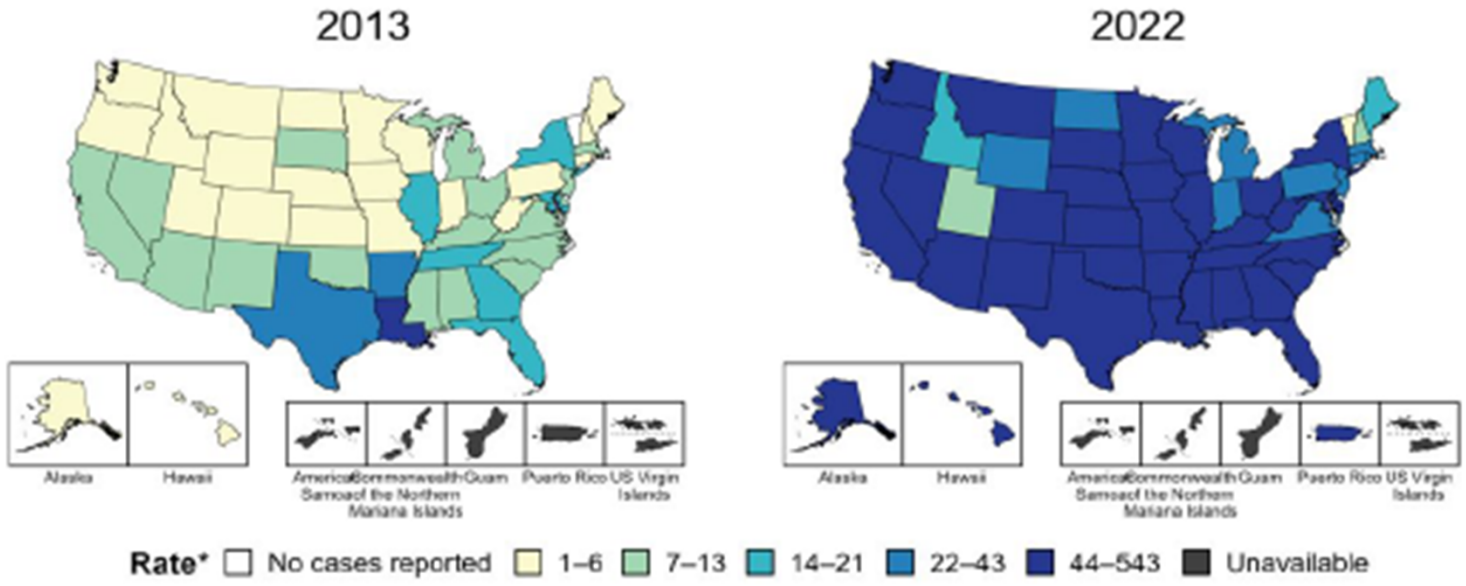
Syphilis on the rise

Cases of Primary and Secondary Syphilis Among Women Aged 15–44 Years, United States, 2013–2022



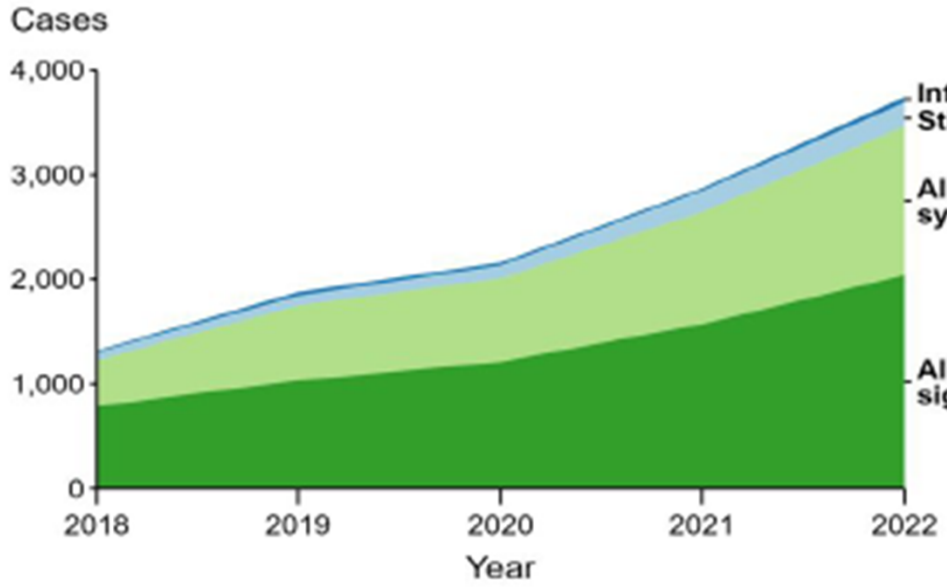
Syphilis on the rise

Syphilis (All Stages) — Rates of Reported Cases Among Women Aged 15–44 Years by Jurisdiction, United States and Territories, 2013 and 2022



* Per 100,000

Congenital Syphilis — Reported Cases by Vital Status and Clinical Signs and Symptoms* of Infection, United States, 2018–2022

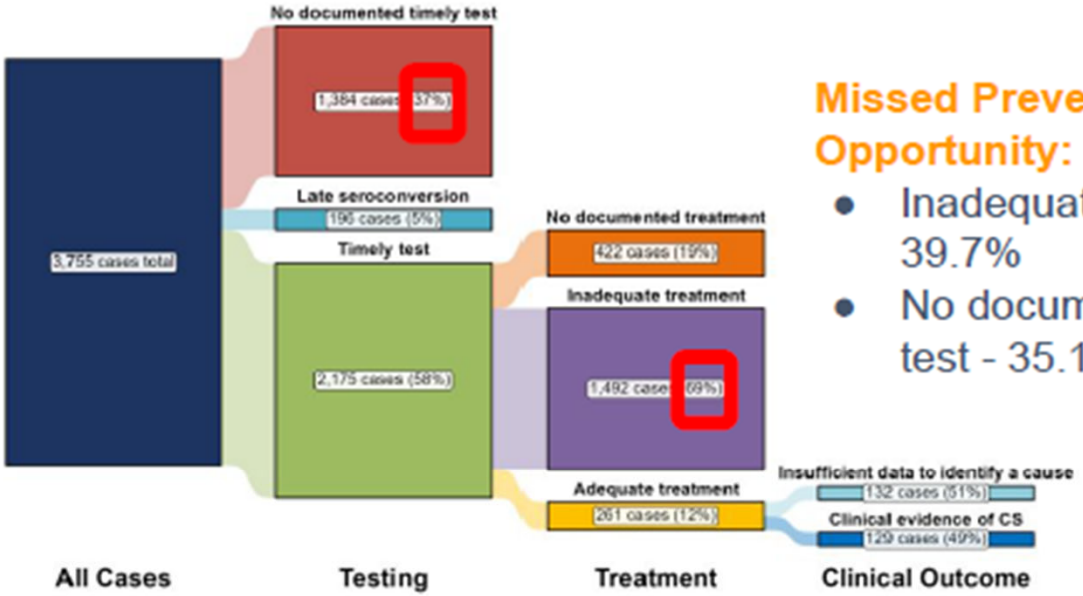


(54.3%)

* Infants with signs and/or symptoms of congenital syphilis have documentation of at least one of the following: long bone changes consistent with congenital syphilis, snuffles, condylomata lata, syphilitic skin rash, pseudoparalysis, hepatosplenomegaly, edema, jaundice due to syphilitic hepatitis, reactive CSF-VDRL, elevated CSF WBC or protein values, or evidence of direct detection of *T. pallidum*.

NOTE: Of the 11,999 congenital syphilis cases reported during 2018 to 2022, 33 (0.3%) did not have sufficient information to be categorized.

Congenital Syphilis — Distribution of Receipt of Testing and Treatment by Pregnant Persons with a Congenital Syphilis Outcome, United States, 2022



Missed Prevention Opportunity:

- Inadequate treatment - 39.7%
- No documented timely test - 35.1%

(Center for Disease Control and Prevention, 2022)

Figure 35. Percentage of syphilis cases by sex, Montana, 2023

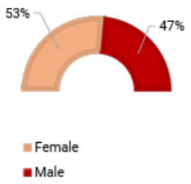


Figure 36. Percentage of syphilis cases by race, Montana, 2023

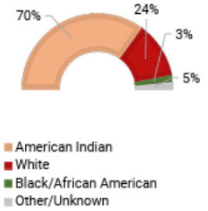
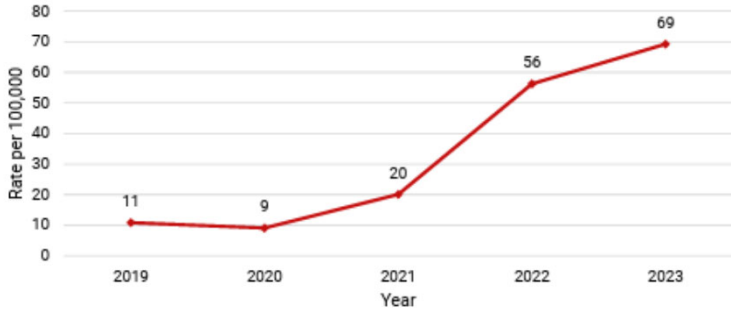
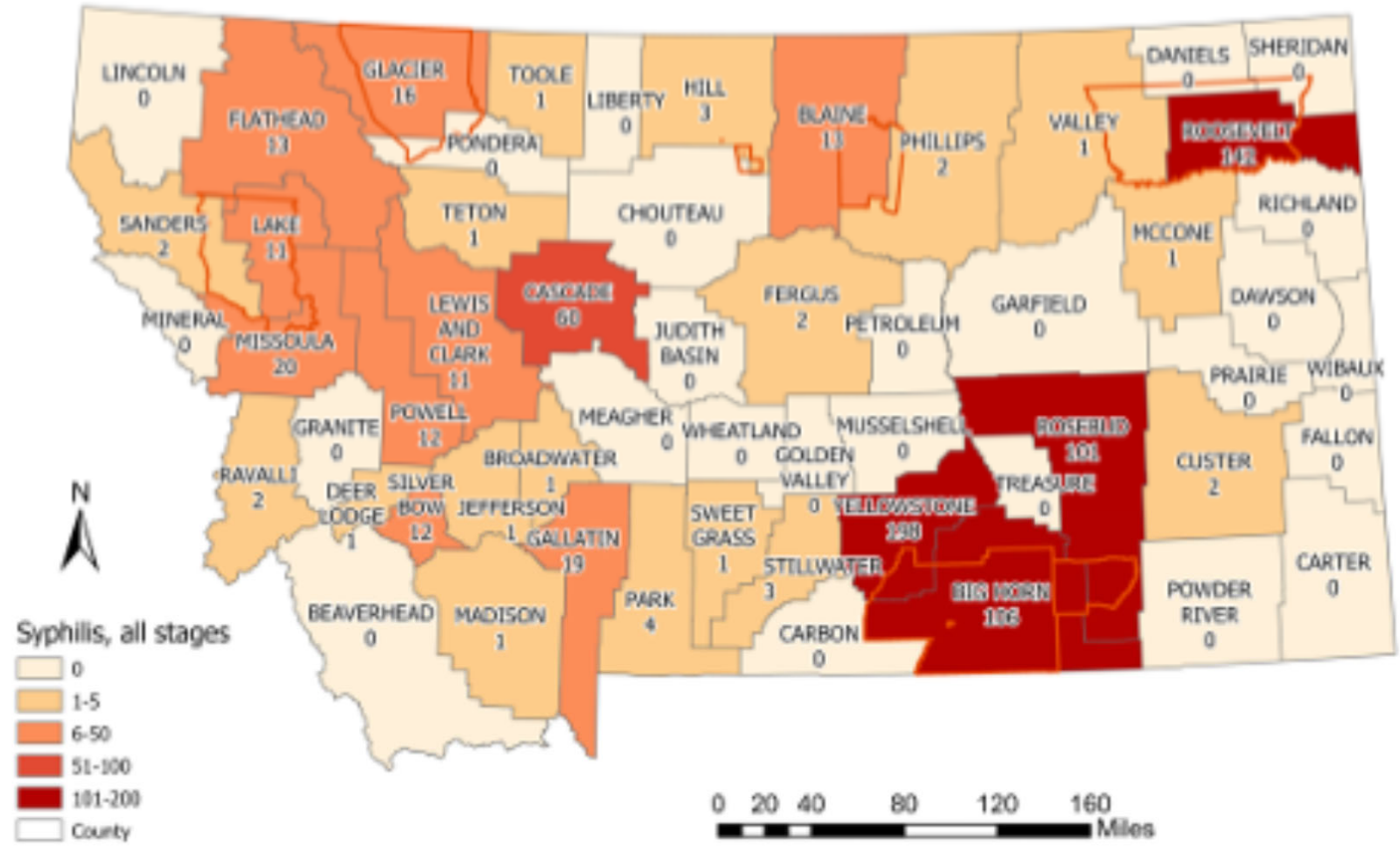


Figure 33. Syphilis cases per 100,000 population, Montana, 2019-2023



Syphilis in Montana

Figure 40. Number of syphilis cases (all stages) by county, Montana, 2023



Syphilis screening

- Maternal
  - First prenatal visit (CDC / ACOG)
  - AND 28-32 w AND at delivery
    - All pregnant patients (ACOG 2024)
    - High risk or living in area with high syphilis prevalence (CDC)
  - Stillborn evaluation
- 37% of congenital syphilis cases had no prenatal care
  - Need to tailor prenatal care!
- Reverse sequence favored over traditional algorithms
- Fetal
  - If positive maternal screen >20w GA need detailed anatomy ultrasound

Is Screening Mandatory?

Legal requirements for syphilis screening among pregnant women by time of test and state

	First Visit	Third Trimester	Delivery
Alabama	X	X	X
Alaska	X		
Arizona	X	X	X
Arkansas	X	X	
California	X	X	O
Colorado	X		
Connecticut	X	X	
Delaware	X	X	
DC	X	X	
Florida	X	X	O
Georgia	X	X	X
Hawaii			
Idaho	X		
Illinois	X	X	
Indiana	X	O	
Iowa			
Kansas	X		
Kentucky	X		
Louisiana	X	X	O
Maine			
Maryland	X	X	O
Massachusetts	X		
Michigan	X	X	O
Minnesota			
Mississippi	X	X	X
Missouri	X	O	O
Montana	X		
Nebraska	X		
Nevada	X	X	O
New Hampshire			
New Jersey	X		X
New Mexico	X		
New York	X	X	
North Carolina	X	X	X
North Dakota			
Ohio	X		
Oklahoma	X	O	O
Oregon	X		
Pennsylvania	X	O	
Rhode Island	X		
South Carolina	X		
South Dakota	X		
Tennessee	X	O	
Texas	X	X	X
Utah	X		
Vermont	X		
Virginia	X		
Washington	X		
West Virginia	X		
Wisconsin			
Wyoming	X		

X	Screening required
O	Screening Required only if at increased risk

Syphilis treatment – rapid overview

- High risk for vertical transmission if
  - Early stage syphilis (<12 mo)
  - High nontreponemal titers (>1:8)
  - Delivery <30 days after treatment
- Reduces vertical transmission from 70-100% to 1-2%
- Reduces stillbirth 82%, preterm birth 65%, neonatal death 80%, and clinical disease in newborn 97%

Recommended Treatment:

- Benzathine penicillin G 2.4m units IM
  - Single dose for early disease, consider x2
- 1 dose q7d x3 for late latent syphilis
- If true PCN allergy, first complete desensitization
- Ensure partner(s) also evaluated
- Screen for HIV
- Jarisch-Herxheimer reaction, consider treatment in hospital

- Follow up
  - Repeat nontreponemal titer 28-32w, delivery, 6mo, and 12 mo
  - If unknown duration or late also repeat at 24mo

NIPT Updates

RhD negative pregnancies during a RhoGAM shortage

- National shortage of Rho(D) Immune Globulin (RhoGAM) since 2023
- RhoGAM is a human blood product and requires alloimmunized donors to create the product and supply may be diminishing
- Limited pool of human donors

RhoGAM preservation strategies

1

Test blood type of father (if certain paternity)

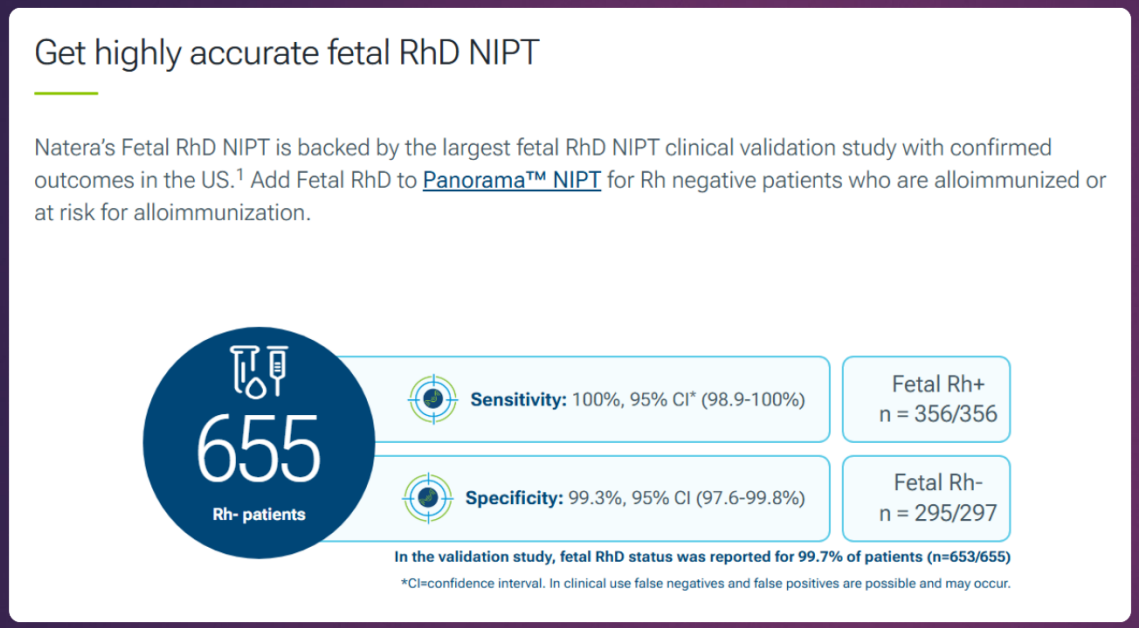
2

Follow ACOG guidance about RhoGAM use in early pregnancy

- Generally not indicated for bleeding / EPL <12 weeks

3

Use NIPT to test the fetus



NIPT / cfDNA that includes RhD status now widely available as an add on to standard NIPT

February 2025 in AJOG

Clinical Opinion ajog.org

The use of free DNA for fetal *RHD* genotyping in the Rh negative pregnant patient—the time has come

Kenneth J. Moise Jr, MD

TABLE 3
Validation of a single-well MassARRAY *RHD* assay in 150 precharacterized clinical samples provided by the University of Göttingen (Professor Tobias Legler)

Variable	Real-time PCR *RHD* positive	Real-time PCR *RHD* negative
MassARRAY *RHD* positive	86	0
MassARRAY *RHD* negative	0	62
	Serologically RhD positive	**Serologically RhD negative**
MassARRAY *RHD* positive	85	1[a]
MassARRAY *RHD* negative	0	62

Two samples were inconclusive with the MassARRAY RHD test and were excluded from the data comparison depicted here.
PCR, polymerase chain reaction; RHD, Rh blood group D antigen gene.
[a] Called *RHD* positive by real-time PCR; individual had been classified as RHD-unexpressed; child has been subsequently retested and is serologically RhD positive. The molecular tests were correct.

Tynan. Multiplexed noninvasive prenatal RHD testing. Am J Obstet Gynecol 2011.

Tynan 2010

TABLE
Correlation studies of 2 U.S. based free DNA assays for fetal *RHD*

No of samples/patients	*RHD pos* NIPT	*RHD neg* NIPT	Rh *pos* result	Rh *neg* result	Sensitivity (95% CI)
Initial U.S. assay[a]					
456[24]	254	191	454	192	100% (98.6–100)
401[25]	261	140	261	140	100% (98.6–100)
Second U.S. assay[b]					
110[26]	70	40	70	40	100% (94.9–100)
655[27]	358[c]	295	356	297	100% (98.9–100)

NIPT, noninvasive prenatal testing.
[a] UNITY assay (BillionToOne, Inc); [b] Panorama (Natera, Inc); [c] Two false positive results (fetal *RHD* result: *RHD* pos; neonate RhD negative by serology).

the product from the four manufacturers, the American College of Obstetricians and Gynecologists (ACOG) offers the following prioritization and conservation strategies for consideration:

- Although current ACOG guidance does not recommend routine use of noninvasive prenatal testing (NIPT) to determine fetal Rh(D) status based on cost-effectiveness analyses, ***the use of NIPT to prioritize use of RhIg and conserve RhIg supply is a reasonable consideration in the practice setting that is experiencing RhIg shortages***. Noninvasive fetal red blood cell antigen genotyping utilizing cell-free DNA (cfDNA) isolated from maternal plasma has demonstrated high sensitivity and specificity for detection of fetal Rh(D) antigen status. **If cfDNA testing results confirm an Rh(D)-negative fetus, RhIg would not need to be routinely administered in the antepartum period (for bleeding, abortion, pregnancy loss, or at 28 weeks of gestation)**. Available cfDNA testing options for Rh(D) may vary depending on location and practice setting (eg, companies offering the test; whether the test is offered as a stand-alone or combined with aneuploidy testing; timing of results; insurance coverage) and should be confirmed before implementation.

Questions

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