

# Pregnancy: What the non-Ob needs to know



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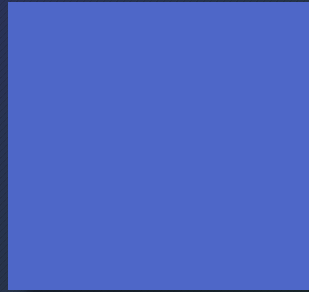
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Disclosures



Non relevant

# Overview

- Hot topics in Obstetrics
  - The maternal mortality crisis
  - Rising CS rates
  - Doulas
- Common complications in Pregnancy
  - Cardiovascular changes and hypertensive disorders of pregnancy
  - Gestational diabetes
- Breastfeeding: impacts on CV disease and DM

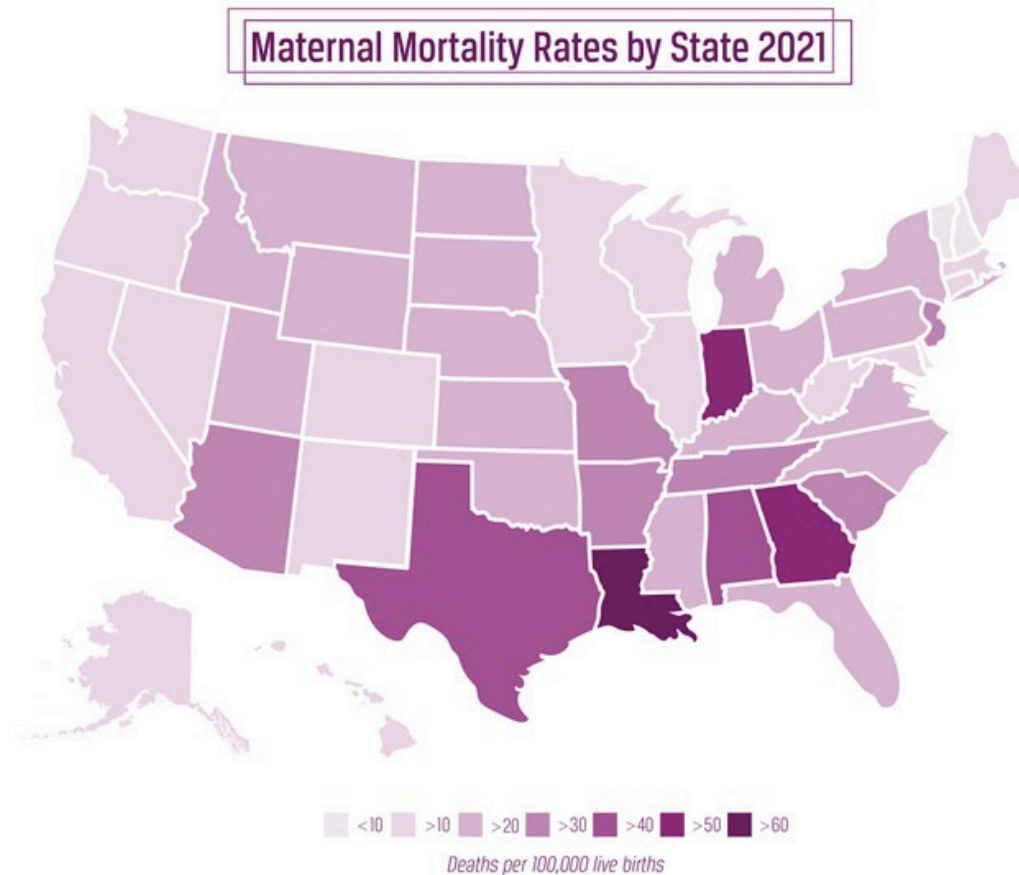
Pregnancy:  
A time of joy and  
apprehension



Martha  
Jefferson



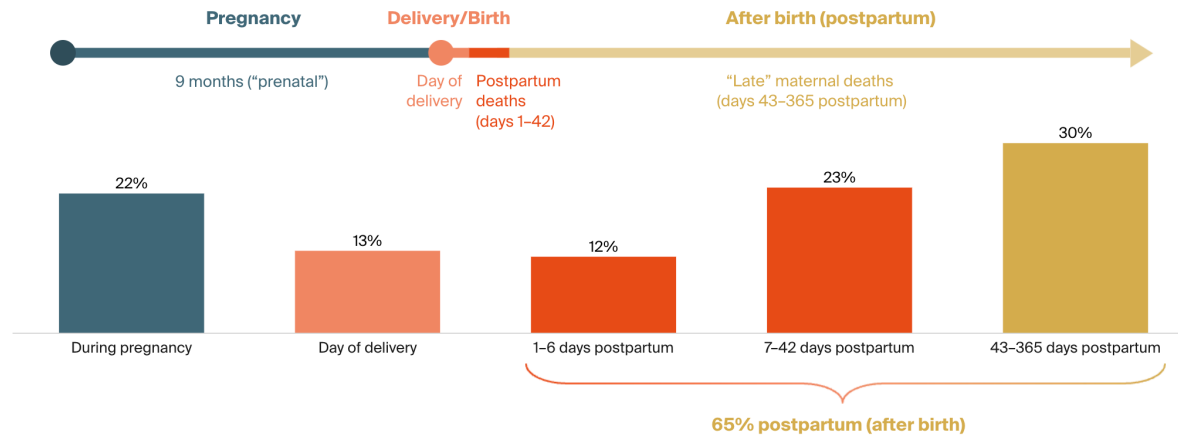
# Maternal Mortality by State, 2021



SOURCE: "Maternal Mortality by State 2021," *World Population Review*, accessed April 8, 2021, <https://worldpopulationreview.com/state-rankings/maternal-mortality-rate-by-state>.

## Two-thirds of U.S. pregnancy-related deaths occur during the postpartum period.

Distribution of pregnancy-related deaths by timing of death in relation to pregnancy, 2017–2019



Notes: Data from Maternal Mortality Review Committees in 36 US states; specific timing information is missing (n=2) or unknown (n=14) for 16 (1.6%) pregnancy-related deaths.

Data: Susanna Trost et al., *Pregnancy-Related Deaths: Data from Maternal Mortality Review Committees in 36 US States, 2017-2019* (Centers for Disease Control and Prevention, 2022).

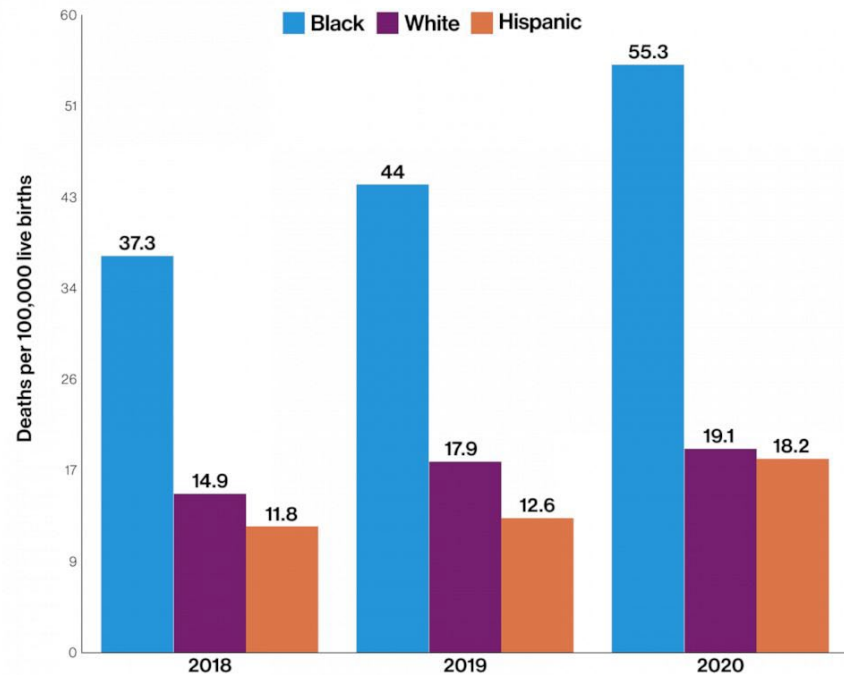
Source: Munira Z. Gunja et al., *Insights into the U.S. Maternal Mortality Crisis: An International Comparison* (Commonwealth Fund, June 2024). <https://doi.org/10.26099/cthn-st75>

# Timing of pregnancy-related deaths

The crisis:  
Racial  
disparities in  
maternal  
mortality

## Maternal Mortality Rates in the U.S. by Race and Ethnicity

2018-2020

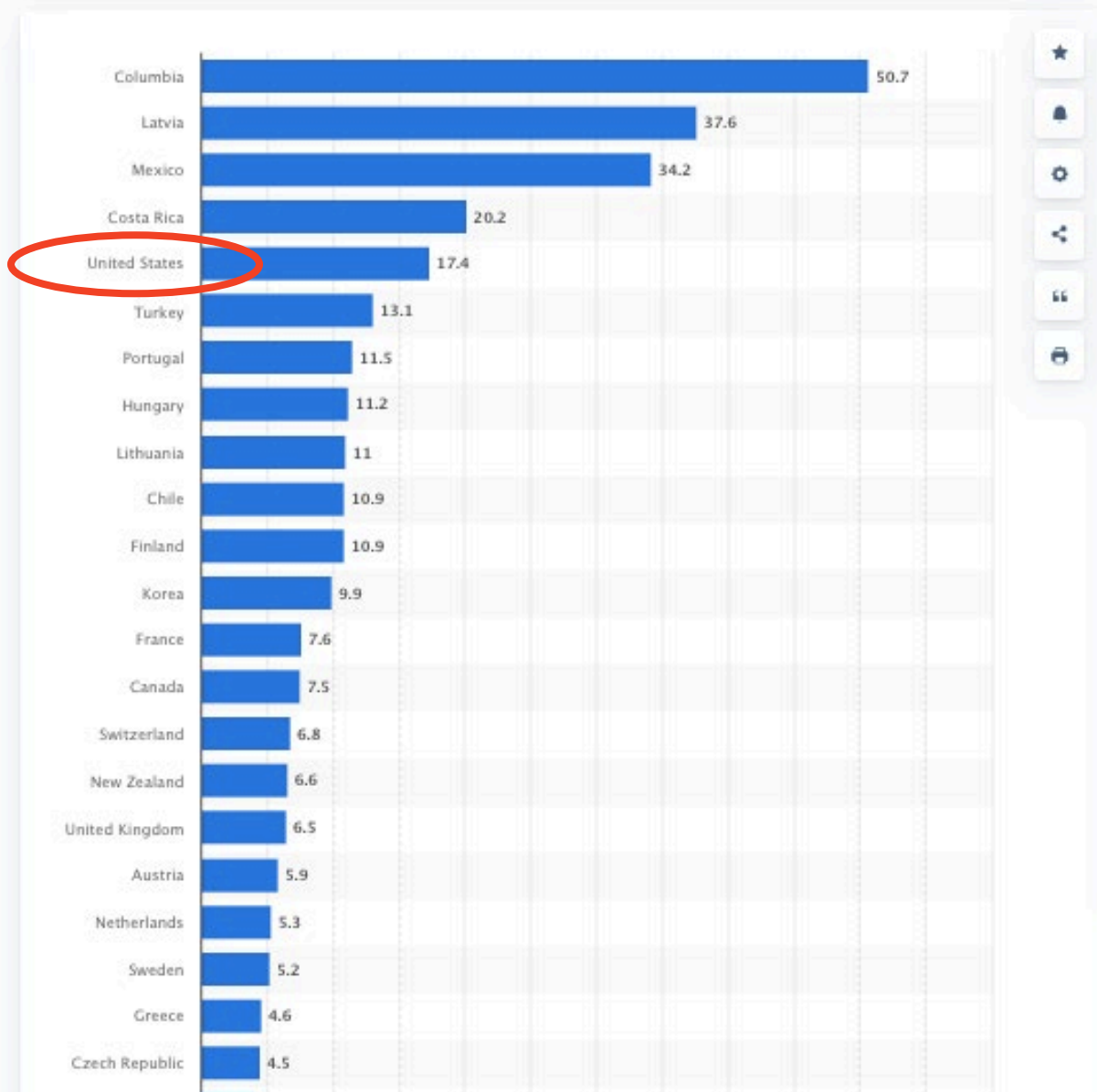


SOURCE: National Center for Health Statistics, National Vital Statistics System

abc NEWS

# Maternal mortality rates worldwide in 2019, by country

(per 100,000 live births)



## Pregnancy-Related Deaths: Data from 14 U.S. Maternal Mortality Review Committees, 2008-2017



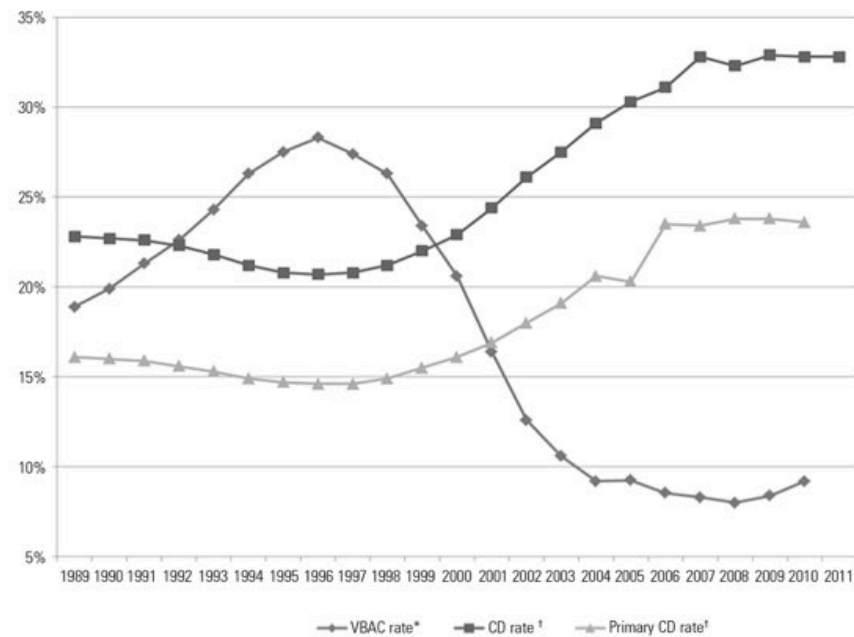
- 8-9 % of all maternal deaths related to suicide, overdose, homicide, substance use disorder, mental health conditions.
- 67% occur after 6-wks PP.

**Table 3.** Leading underlying causes of pregnancy-related deaths, overall and by race-ethnicity, data from 14 maternal mortality review committees, 2008-2017.\*

	Total		non-Hispanic Black		non-Hispanic White	
	N	%	n	%	n	%
Cardiovascular Conditions <sup>†</sup>	58	13.8	22	13.9	27	13.4
Hemorrhage	55	13.1	17	10.8	27	13.4
Infection	48	11.4	16	10.1	25	12.4
Embolism <sup>‡</sup>	40	9.5	16	10.1	16	8.0
Cardiomyopathy	39	9.3	22	13.9	16	8.0
Mental Health Conditions <sup>§</sup>	37	8.8	--	--	30	14.9
Preeclampsia and Eclampsia	35	8.3	18	11.4	13	6.5

\*Specific cause of death was missing or listed as "Unknown" for a total of 34 (7.5%) pregnancy-related deaths. Numbers are not presented when cell size is <5. Deaths among women not classified as non-Hispanic Black or non-Hispanic White are included in the total number of deaths.

# The Problem: Rising Cesarean rates



Cesarean rate

Primary Cesarean rate

Vaginal birth after CS rate

**Fig. 1.** U.S. delivery rates, 1989–2011. Data from National Vital Statistics. Abbreviations: CD, cesarean delivery; VBAC, vaginal birth after cesarean delivery. \*Percent of women who have a vaginal birth after prior cesarean delivery. †Rate based on total number of deliveries. ‡Rate based on total number of deliveries. (Data from Martin JA, Hamilton BE, Ventura SJ, Osterman MJ, Mathews TJ. Births: final data for 2011. Natl Vital Stat Rep 2013;62(2):1–90.)

# C-section rates differ by race/ethnicity

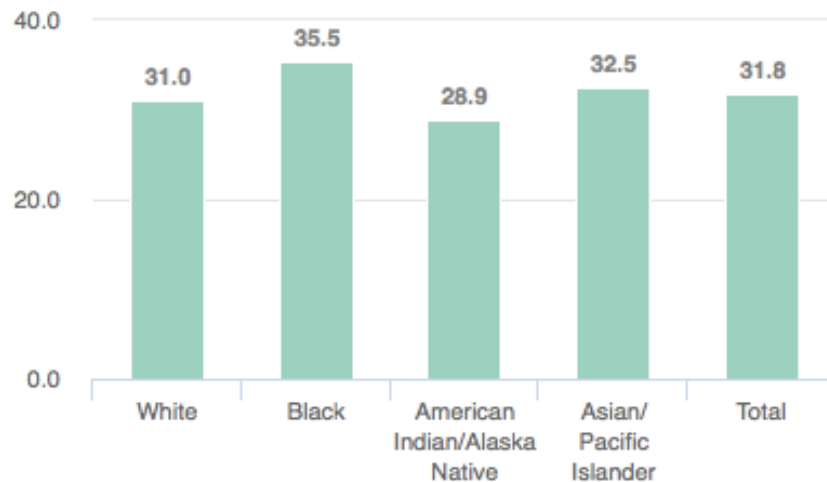
HEALTHY  
MOMS.  
STRONG  
BABIES.



PERISTATS

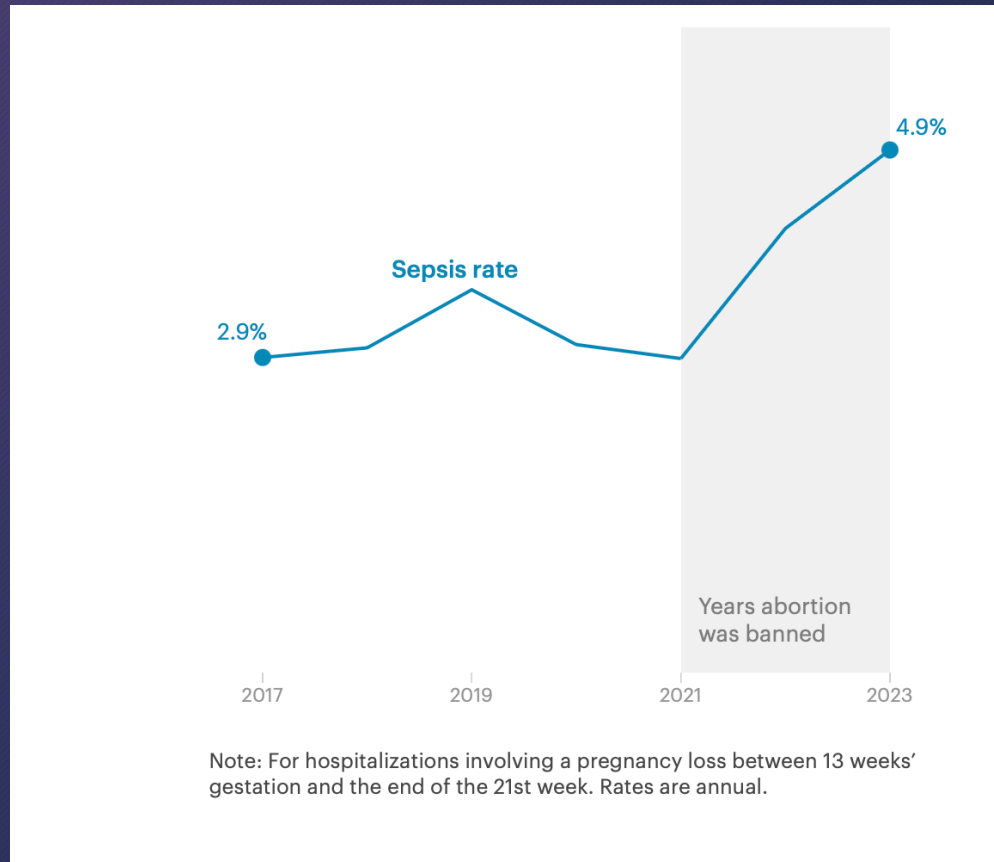
## Total cesarean deliveries by race: United States, 2017-2019 Average

Percent of live births





# Pregnancy related sepsis: Texas



# Oral contraception is low risk/high benefit

- **Oral contraceptive pills are available over the counter in > 100 countries**
- Efforts underway to increase OTC access in the US
- **Combined OCP**
  - Estrogen and progesterone
  - Estrogen dose varies, progestin type and dose varies
  - Low dose estrogen is preferable (20 mcg)
  - Somewhat resilient to occasional missed doses
  - Example: norethindrone acetate 1 mg/ethinyl estradiol 20 mcg
- **“Minipill” = POP = progesterone only pill (norethindrone 35 mcg)**
  - No increased risk of clotting
  - No withdrawal bleed
  - \*High failure rate with missed doses



# Hot topic: Doulas

## Perceptions and experiences of labour companionship: a qualitative evidence synthesis

Meghan A Bohren<sup>1</sup>, Blair O Berger, Heather Munthe-Kaas, Özge Tunçalp

A doula is a trained companion who is not a healthcare professional and who supports another individual through a significant health-related experience

- Emotional support: using praise and reassurance to help women feel in control and confident, and providing a continuous physical presence.
- Practical support: including encouraging women to move around, providing massage, and holding her hand.
- Informational support: providing information about childbirth, bridging communication gaps between health workers and women, and facilitating non-pharmacological pain relief.
- Advocates: spoke up in support of the woman

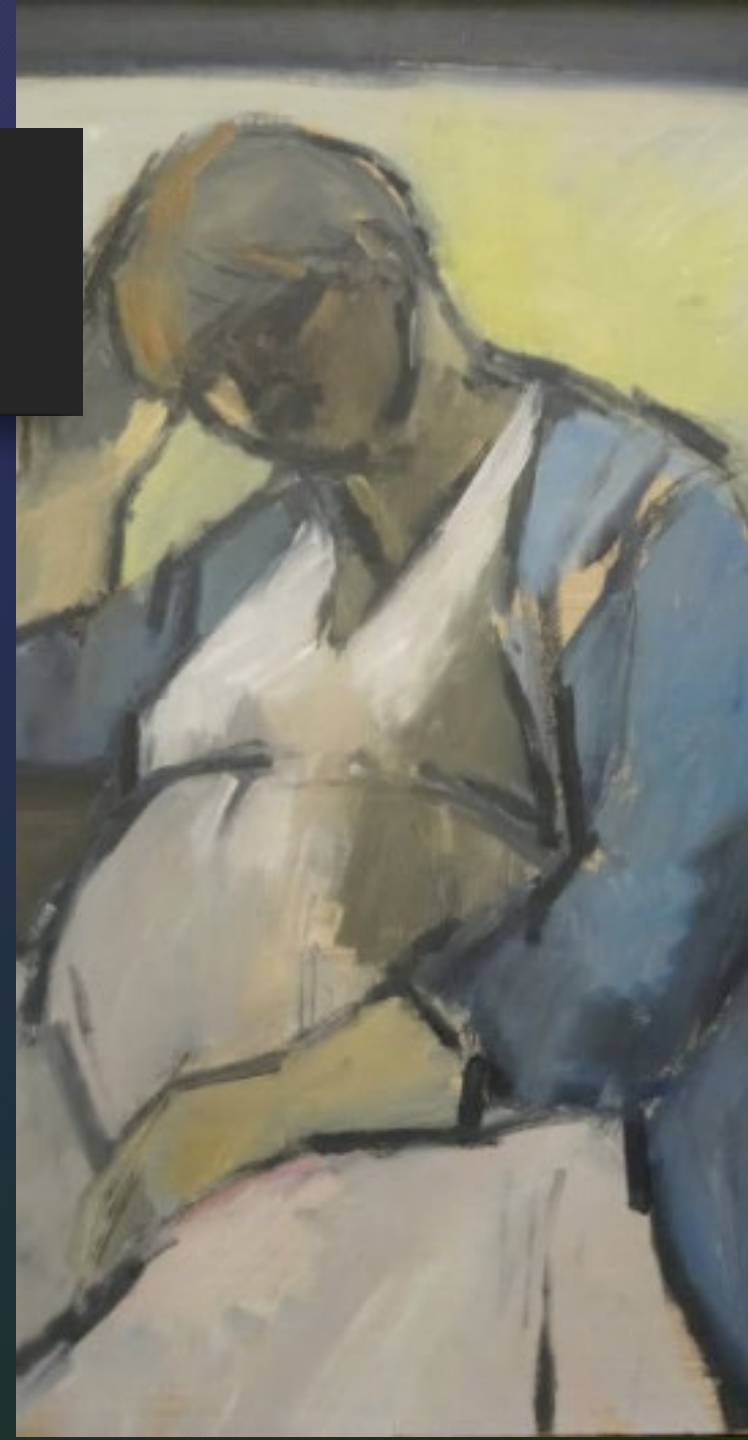
# Continuous labor support: Cochrane review

- 15,858 women across 26 studies
  - 13 high income countries, 13 middle income countries
  - Labor support by doula, medical team, or friend/family
- “Continuous labor support appears to offer impressive benefits and no harms to women and newborns, especially when provided by someone in a doula role.”
- Statistically significant INCREASE
  - Vaginal birth
  - Shorter labor
- Statistically significant DECREASE
  - Cesarean birth
  - Operative vaginal deliver
  - Use of regional anesthesia
  - Negative birth experience
  - Low 5 minute Apgar score



# Hot topic: Psych meds - yes or no?

- Balance risk of untreated disease with risk of medication
- Untreated depression and anxiety may have long term consequences for both mother and baby
- Most psych meds are compatible with pregnancy!
- Lowest EFFECTIVE dose of lowest number of meds, but polypharmacy is OK when indicated!



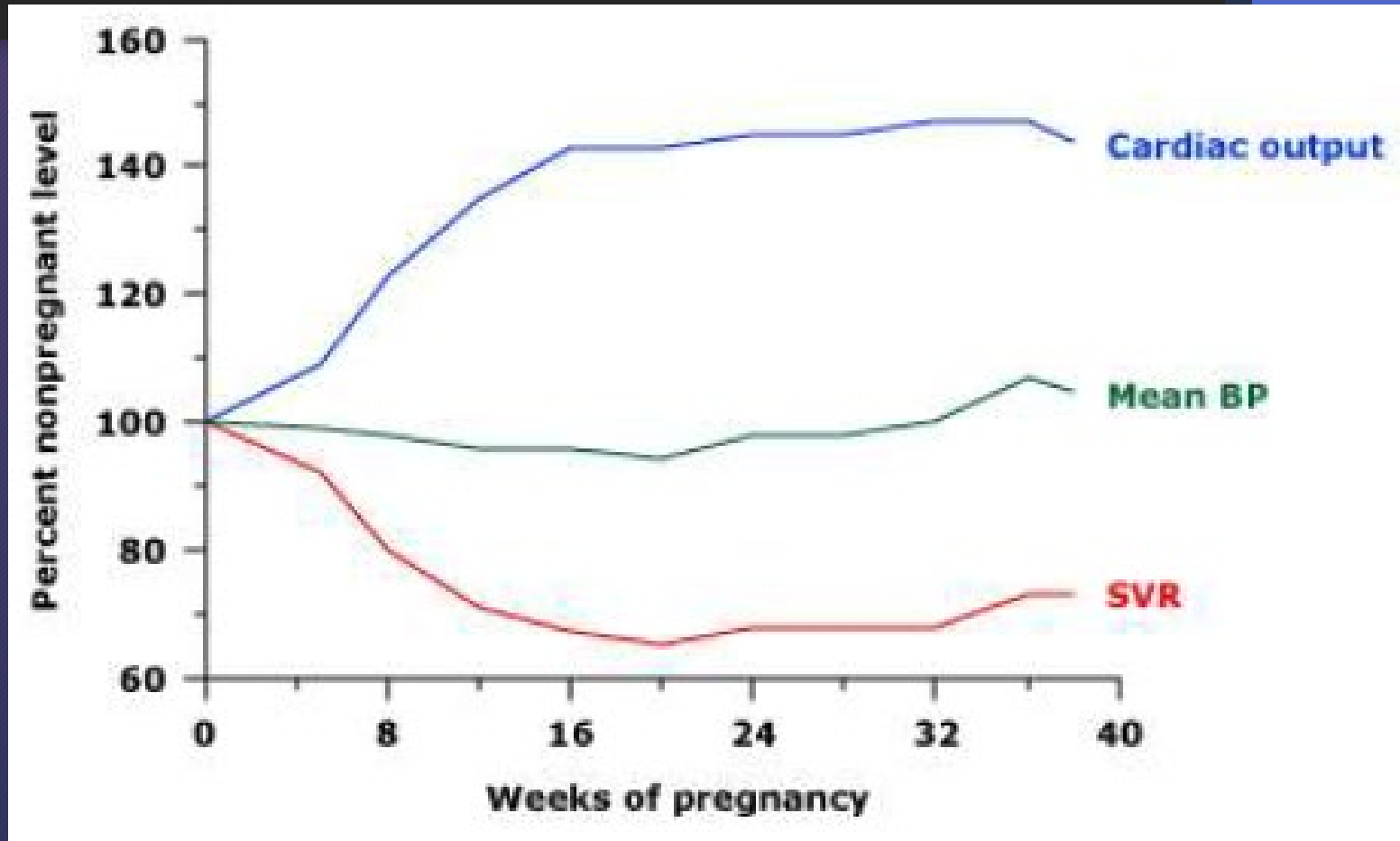
# Obstetric Physiology and Pathology

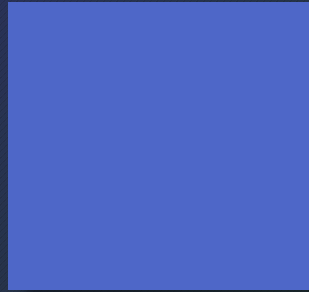
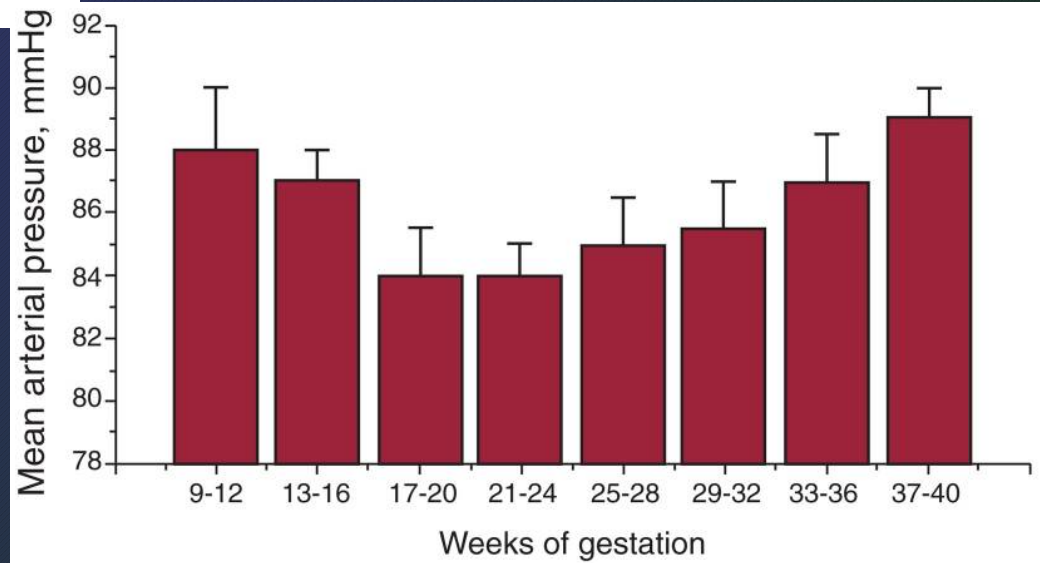
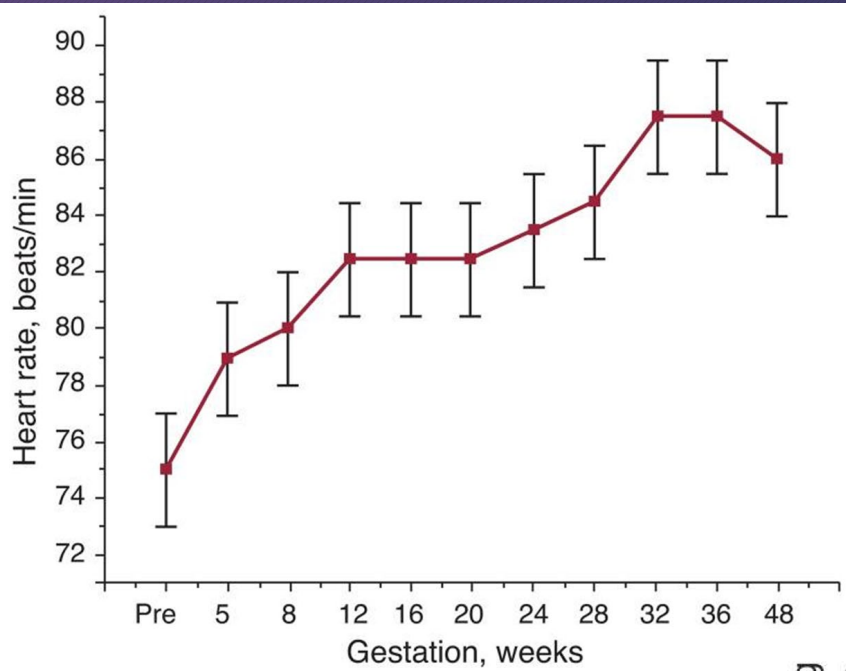


Cardiovascular  
changes &  
hypertensive  
disorders of  
pregnancy

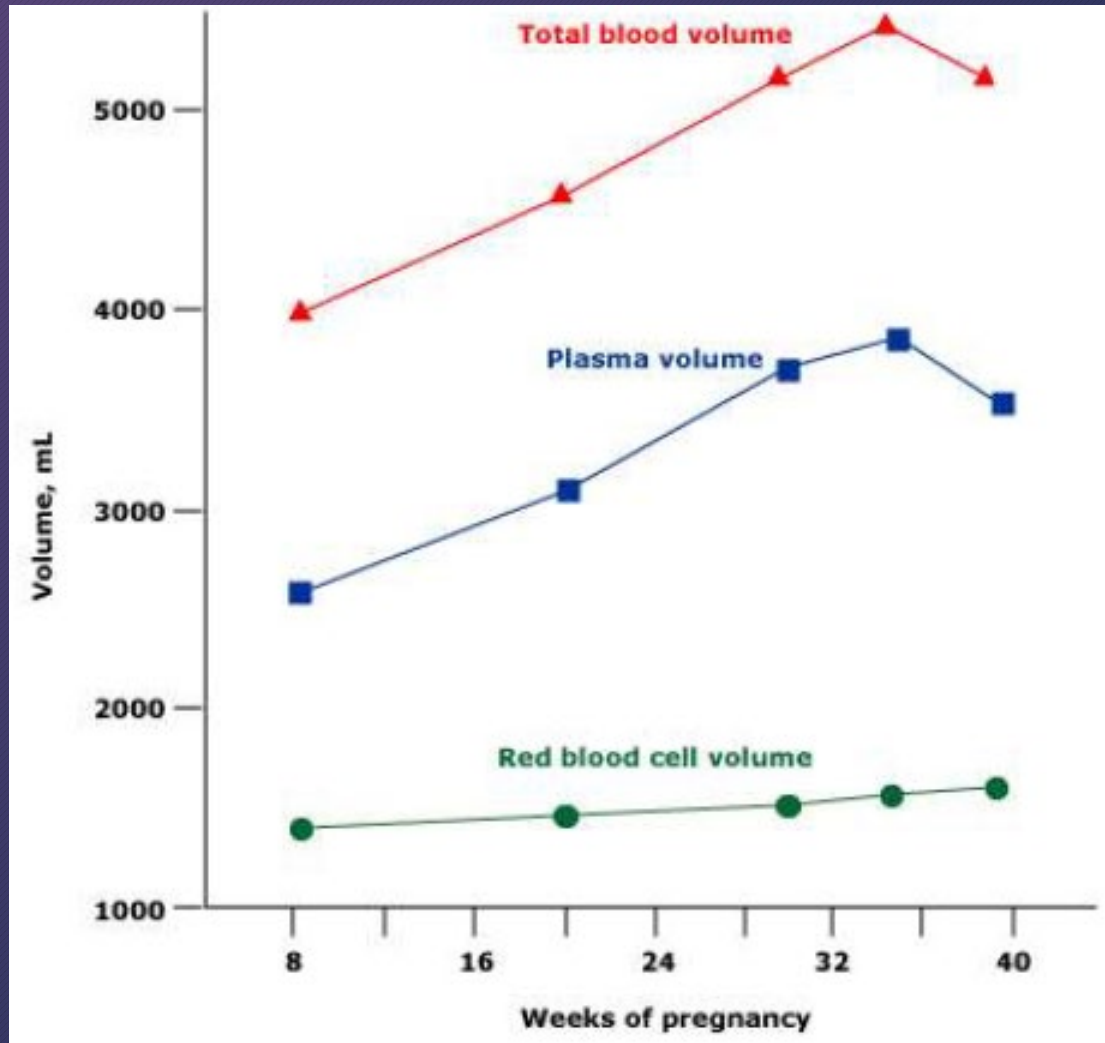


# Physiology: CV changes



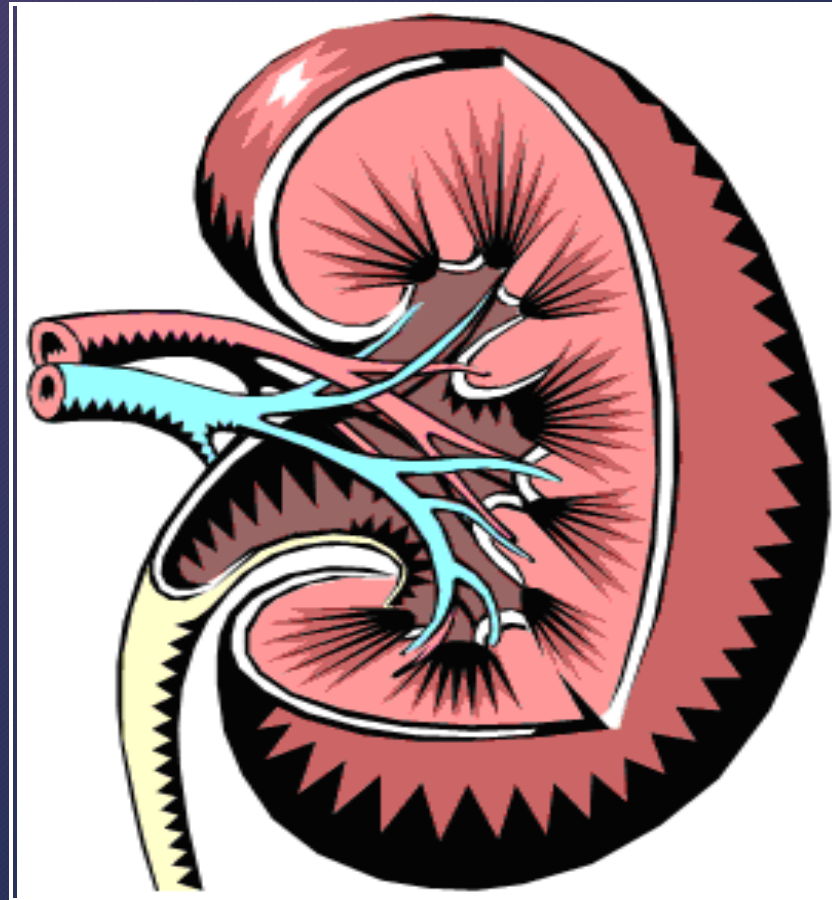


# Circulating Volume

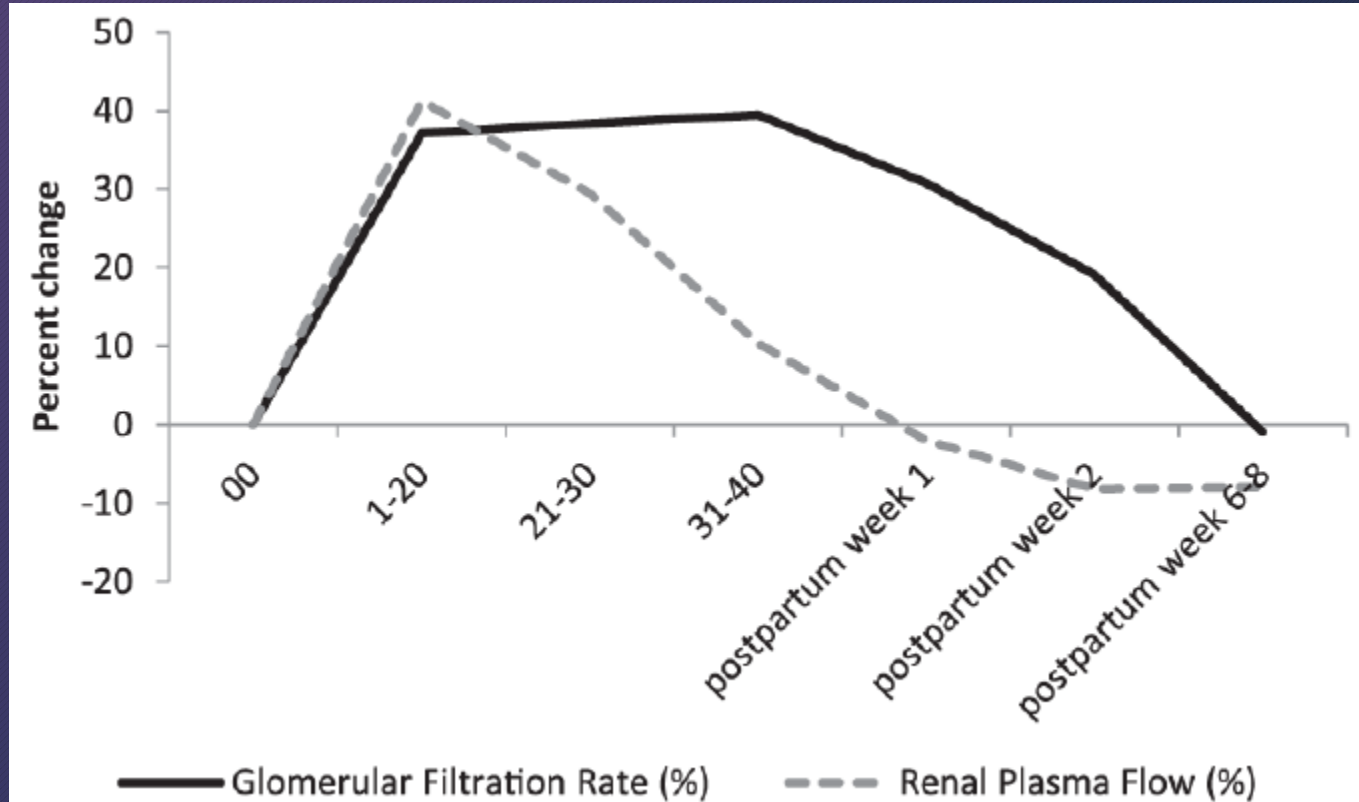


Plasma volume increases  
1200 - 1600 mL  
~40% above baseline

# Renal

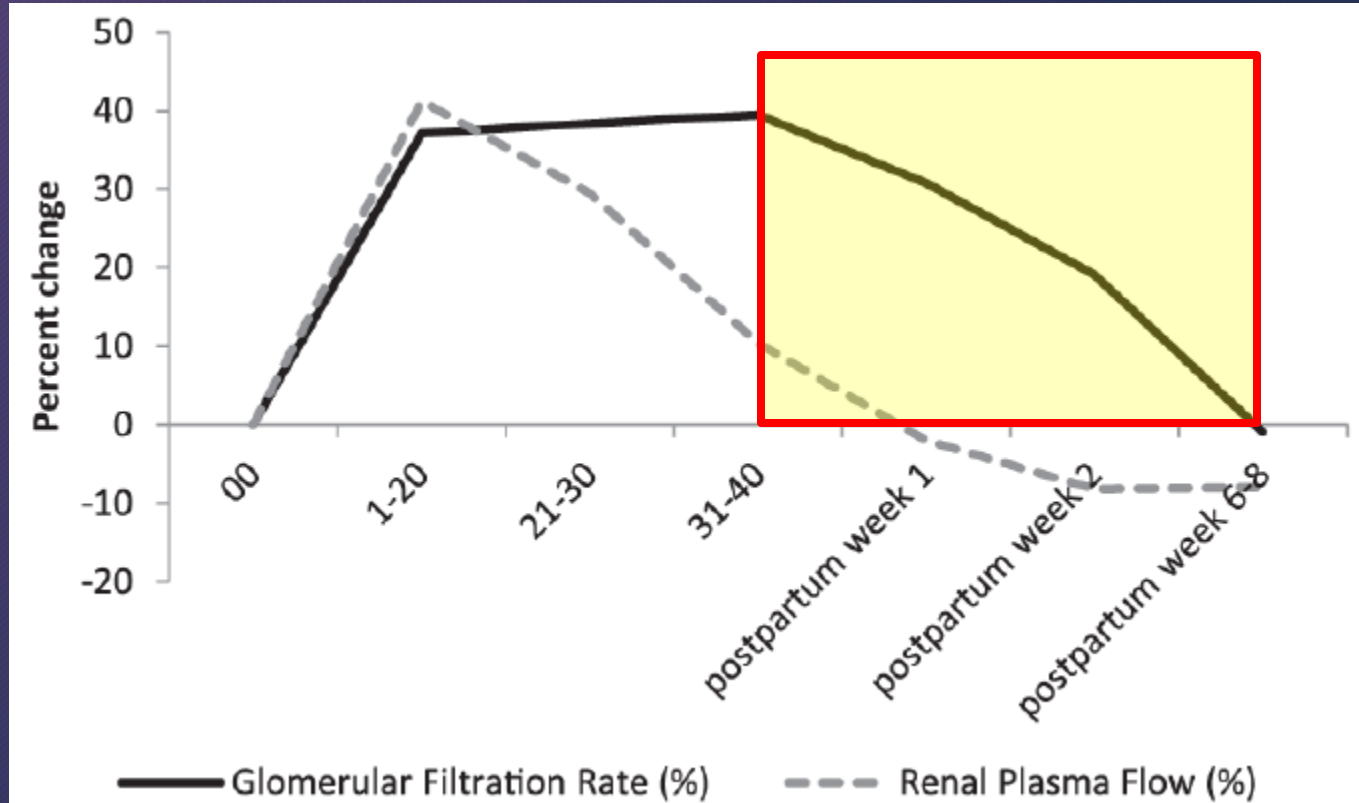


# Renal



30-50% increase in renal clearance due to increases in renal blood flow and glomerular filtration rate.

# Renal

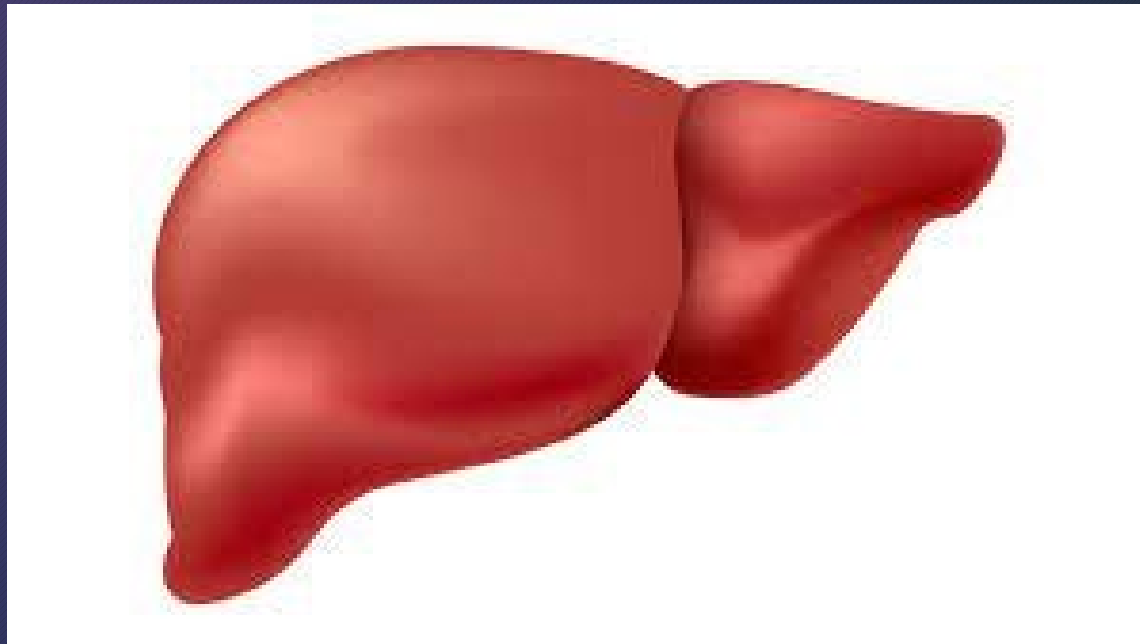


30-50% increase in renal clearance due to increases in renal blood flow and glomerular filtration rate.

# Volume Changes Post-Partum

- Postpartum diuresis
  - Hct difference PP w SVD: +5.2% on day 3
  - Hct difference PP w C-sec: -5.8 % on day 5
- Most of the volume loss in following SVD is due to diuresis
  - Diuresis normally occurs b/w days 2-5 PP
  - Allows for loss of excess ECF accumulated in pregnancy
  - Average ~6lb weight loss

# Hepatic



# Hepatic

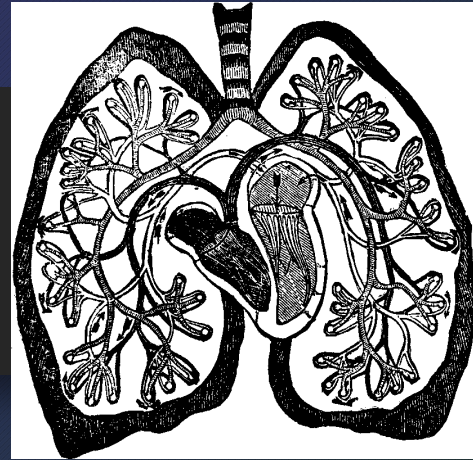
## Pregnancy-induced changes in hepatic enzymes

Enzyme (references)	Pregnancy-induced change	Potential substrates in obstetrics
CYP3A4 <sup>19,20,77,78</sup>	Increased	Glyburide, nifedipine, and indinavir
CYP2D6 <sup>77,79</sup>	Increased	Metoprolol, dextromethorphan, paroxetine, duloxetine, fluoxetine, and citalopram
CYP2C9 <sup>18,80</sup>	Increased	Glyburide, NSAIDs, phenytoin, and fluoxetine
CYP2C19 <sup>18,80</sup>	Decreased	Glyburide, citalopram, diazepam, omeprazole, pantoprazole, and propranolol
CYP1A2 <sup>17,23,77,81</sup>	Decreased	Theophylline, clozapine, olanzapine, ondansetron, and cyclobenzaprine
UGT1A4 <sup>82-84</sup>	Increased	Lamotrigine
UGT1A1/9 <sup>25</sup>	Increased	Acetaminophen
NAT2 <sup>17,24,85</sup>	Decreased	Caffeine

# Take home point for small molecule meds



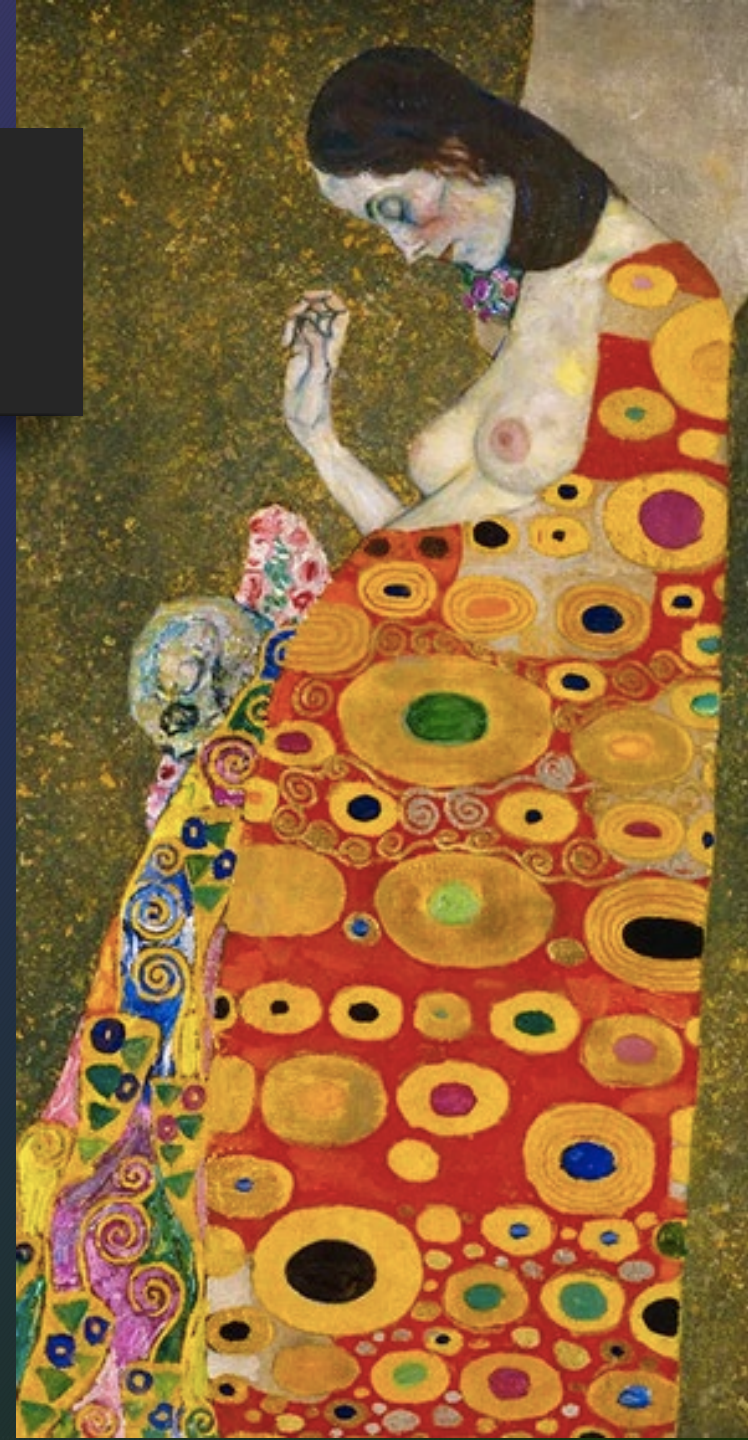
# Physiology: Dyspnea



- Common symptom in pregnancy
  - Up to 70% of women experience this sensation in a normal pregnancy
- The obstetric patient presenting with an acute onset of shortness of breath deserves a careful evaluation
- Cardiovascular diseases as a cause of dyspnea complicate 1-4% of pregnancies.
  - Peripartum cardiomyopathy is an uncommon but life threatening complication of pregnancy
  - Women with underlying valvular disease may poorly tolerate plasma volume expansion

# Preeclampsia

1. Preeclampsia diagnosis (updated by ACOG, 2013)
2. Preeclampsia management
3. Preeclampsia prevention (low-dose aspirin)
4. Postnatal counseling



# Classic presentation

- C.M., a 32 year old prima gravida
- Initiated prenatal care: 16 weeks GA
  - BP 106/70 mmHg, no proteinuria
  - Weight 102 pounds
- Pregnancy proceed unremarkably
- At 36 weeks:
  - Edema of the hands and face
  - BP 160/115 mmHg
  - Urine contained 6g of albumin in a 24 hour sample
  - 30 pound weight gain, 11 in last 4 weeks



Admitted to Boston Lying In Hospital in 1862

**TABLE E-1. Diagnostic Criteria for Preeclampsia** ↵

Blood pressure	<ul style="list-style-type: none"><li>• Greater than or equal to 140 mm Hg systolic or greater than or equal to 90 mm Hg diastolic on two occasions at least 4 hours apart after 20 weeks of gestation in a woman with a previously normal blood pressure</li><li>• Greater than or equal to 160 mm Hg systolic or greater than or equal to 110 mm Hg diastolic, hypertension can be confirmed within a short interval (minutes) to facilitate timely antihypertensive therapy</li></ul>
and	
Proteinuria	<ul style="list-style-type: none"><li>• Greater than or equal to 300 mg per 24-hour urine collection (or this amount extrapolated from a timed collection)</li><li>or</li><li>• Protein/creatinine ratio greater than or equal to 0.3*</li><li>• Dipstick reading of 1+ (used only if other quantitative methods not available)</li></ul>
Or in the absence of proteinuria, new-onset hypertension with the new onset of any of the following:	
Thrombocytopenia	<ul style="list-style-type: none"><li>• Platelet count less than 100,000/microliter</li></ul>
Renal insufficiency	<ul style="list-style-type: none"><li>• Serum creatinine concentrations greater than 1.1 mg/dL or a doubling of the serum creatinine concentration in the absence of other renal disease</li></ul>
Impaired liver function	<ul style="list-style-type: none"><li>• Elevated blood concentrations of liver transaminases to twice normal concentration</li></ul>
Pulmonary edema	
Cerebral or visual symptoms	

\* Each measured as mg/dL.

# Preeclampsia Diagnosis

# Hypertensive disorders of pregnancy

---

Chronic Hypertension

---

Preeclampsia

---

Superimposed Preeclampsia

---

Gestational Hypertension

---

Eclampsia

---

HELLP Syndrome

# Differential diagnosis: It's complicated...

## Chronic Hypertension

- Hypertension prior to pregnancy
- Hypertension prior to 20 wks GA
- Hypertension first seen after 20 weeks but persisting >12 weeks PP
- Medication optimization

## Gestational Hypertension

- Not preeclampsia
- $BP \geq 140/90$
- May be associated with adverse outcomes
- 10% of eclamptics seize without proteinuria

## Superimposed preeclampsia

- New proteinuria in chronic hypertensive after 20 weeks
- Sudden increase in protein, pressures, other findings in patients with nephrotic syndrome and hypertension prior to 20 weeks

## HELLP syndrome

- RUQ pain (80%)
- Hemolysis, elevated LFTs, low platelets

# Epidemiology

## Overall:

4.6% of pregnancies worldwide

3.4% in US (1.5-2x increase in first pregnancy)

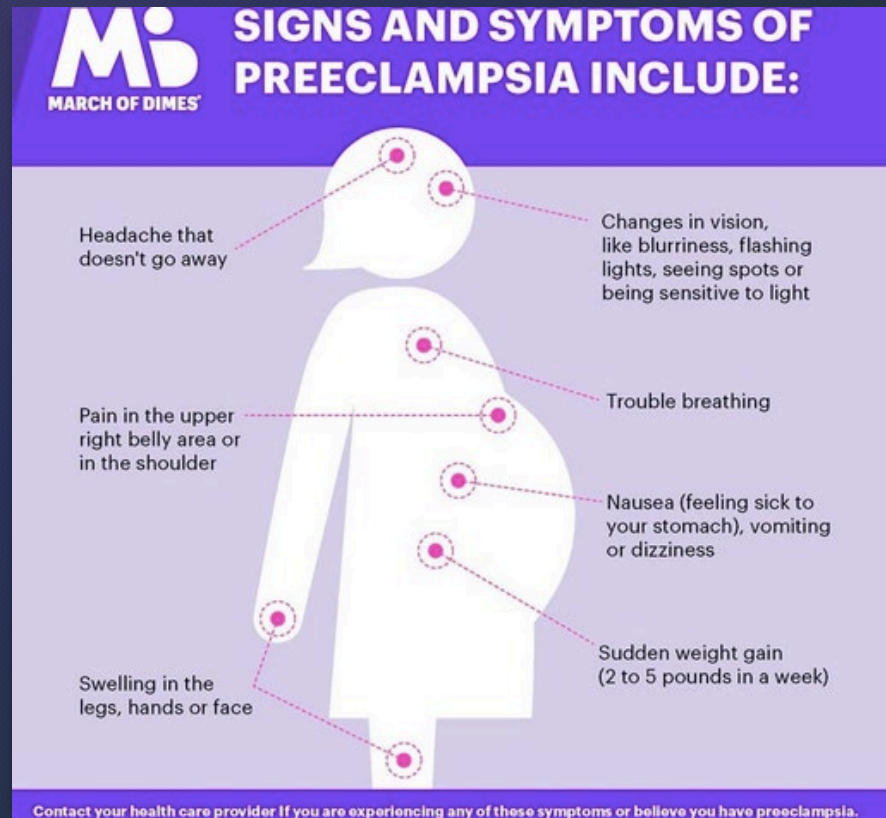
## By gestational age:

< 34 weeks: 0.3%

≥ 34 weeks: 2.7%

Up to 23 days postpartum

\*Comprehensive evaluation for other sources should be undertaken for late occurrence



# Differential diagnosis

- Preexisting hypertension vs. preeclampsia
- Chronic hypertension vs. superimposed preeclampsia
- Exacerbation of preexisting renal disease
- Antiphospholipid syndrome
- Acute fatty liver of pregnancy (AFLP)
- TTP (thrombotic thrombocytopenic purpura) or HUS (hemolytic uremic syndrome)
- SLE exacerbation
- Pheochromocytoma
- Mirror syndrome (assoc w/ fetal hydrops)

# Preeclampsia Risk Factors

Prior preeclampsia (RR 8.4)

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Chronic hypertension (RR 5.1)

---

Pregestational diabetes (RR 3.7)

---

Multifetal gestation (RR 2.9)

---

Family history preeclampsia (RR 2.9)

---

Autoimmune disease (SLE, RR 1.8; APS, RR 2.8)

---

BMI >30 (RR 2.8)

---

First pregnancy (RR 2.1)

---

Chronic kidney disease (RR 1.8)

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# Short Term Maternal Complications

- Liver rupture/ hemorrhage
- Acute pancreatitis
- Posterior reversible leukoencephalopathy syndrome (PRES)
- Cortical blindness (usually transient) or retinal pathology (can be permanent)
- Stroke (most are hemorrhagic):
- 36% of strokes during pregnancy are due to preeclampsia/ eclampsia



# Fetal/Neonatal Complications

- Growth restriction
- Preterm delivery
- Fetal demise
- Long-term health consequences



# Management: Gestational Age Dependent

If preeclampsia with severe features, deliver if  $\geq 34$  weeks gestation

- Delivery minimizes maternal and fetal complications
- Also deliver if previsible gestational age or if maternal or fetal status not stable

If  $< 34$  weeks and stable, expectant management

- Administer antenatal corticosteroids
- Blood pressure control and maternal/fetal surveillance
- Delivery at 34 weeks if severe features
- Delivery at 37 weeks without severe features
  - HYPITAT trial: women induced had 30% decrease in maternal morbidity/mortality, decreased c-section rate (14 vs 19%), no difference in neonatal outcome

# Why do pregnant women develop preeclampsia?



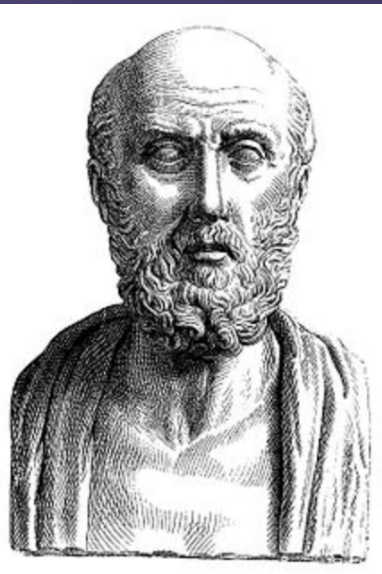
- We still lack the ability to predict which women will develop preeclampsia
- Preventative and therapeutic options are limited
- Delivery remains the primary intervention



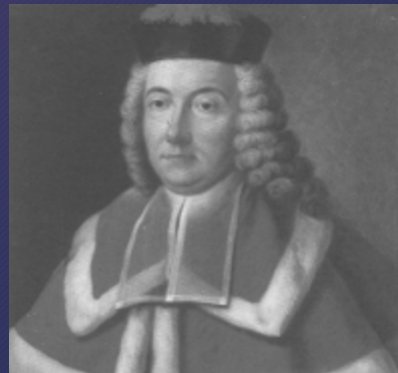
# 3000 Years of eclampsia

Eclampsia: the development of generalized tonic clonic seizures in a pregnant patient without history of a seizure disorder

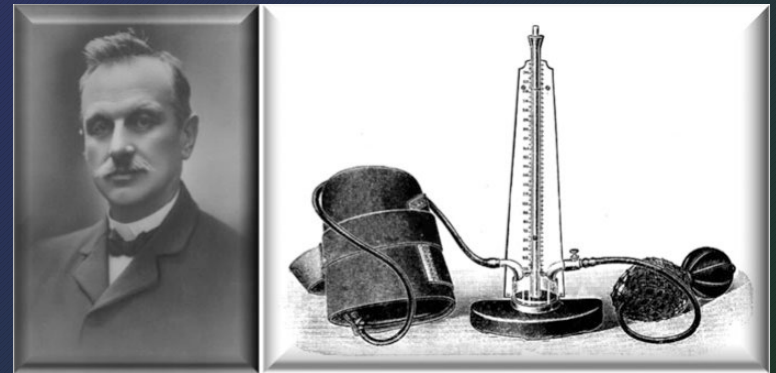
# Eclampsia



Hippocrates (400 BCE)



Bossier du Sauvages  
(1710-1795)  
*First to use the Greek  
term “eclampsia”*



Scipione Riva-Rocci's sphygmomanometer: 1896

# Eclampsia

## Incidence

- Ranges from 1/2000-3448 pregnancies

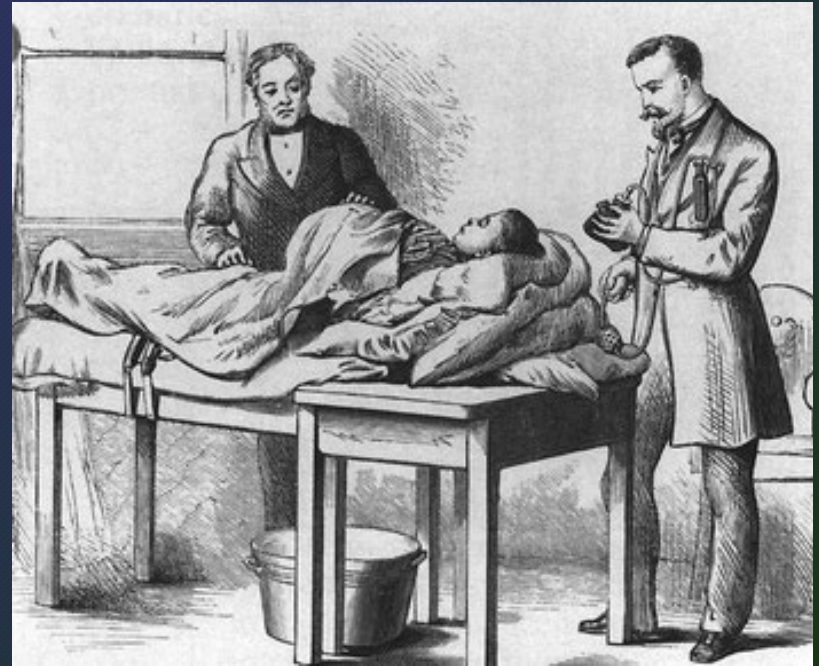
## Symptoms

- May occur before or after convulsions
- Persistent occipital or frontal headache
- Blurred vision
- Photophobia
- Epigastric or RUQ pain
- Altered mental status



# Seizure prophylaxis: Magnesium

- Intramuscular magnesium was introduced in the 1900s
- Intravenous injection in the 1920s
- 1990s brought RCTs demonstrating superiority over other methods.
- Magnesium sulfate IV:
  - 6 g load, 2 g IV (or 4/1)
  - or 5 g / buttock IM
- NNT = 60 (prevention of eclampsia in preeclampsia with severe features)



# Preeclampsia: Postpartum course

- Acute features generally resolve postpartum
- Some symptoms resolve within hours (headache), others take weeks or months (proteinuria, hypertension)
- Mobilization of 3<sup>rd</sup> spaced fluid: within 48 hrs of delivery
- Hypertension can worsen 1-2 weeks postpartum, usually normalizes by 4 weeks

# Preeclampsia: prevention

- Low-dose aspirin (60-150 mg/day; by 16 weeks) decreases preeclampsia by 10-20% in women at moderate to high risk
- Excellent safety profile
- 2019 Cochrane meta-analysis
  - 74 trials, >40,000 women; RR 0.82



# Preeclampsia: Postnatal counseling

History of preeclampsia is associated with increased lifelong risks

Condition	Lifetime RR
Hypertension	3.7
Ischemic heart disease	2.2
Stroke	1.8
VTE	1.8

Absolute risk by age 50-59:  
18% with preeclampsia hx vs  
8% without.

- Gradation in risk by severity and GA at delivery
  - Mild disease: RR 2.0
  - Moderate preeclampsia: RR 3.0
  - Severe preeclampsia: RR 5.3
- Lifestyle interventions may decrease risk by 4-13 %



## HEAR HER Campaign

EXPLORE TOPICS ▾

Resources for non-Ob health care providers

- Pregnancy complications: 1/3 maternal deaths occur within the year postpartum
- Always ask if your patient is pregnant or was pregnant in the last year
- Recognize urgent maternal warning signs



# Which one of these people was recently pregnant?

It may not be obvious, but knowing could help save a life.

Life-threatening complications can happen up to a year after pregnancy.

**Ask your patient if they are pregnant or have been pregnant in the last year.**

**HEAR**<sup>™</sup>  
HEAR HER CONCERNS

Learn more at [cdc.gov/HearHer](https://cdc.gov/HearHer)



## Pregnant now or within the last year?

Get medical care right away if you experience any of the following symptoms:



Headache that won't go away or gets worse over time



Dizziness or fainting



Changes in your vision



Fever of 100.4° F or higher



Extreme swelling of your hands or face



Thoughts of harming yourself or your baby



Trouble breathing



Chest pain or fast beating heart



Severe nausea and throwing up



Severe belly pain that doesn't go away



Baby's movement stopping or slowing during pregnancy



Severe swelling, redness or pain of your leg or arm



Vaginal bleeding or fluid leaking during pregnancy



Heavy vaginal bleeding or discharge after pregnancy



Overwhelming tiredness

These could be signs of very serious complications. If you can't reach a healthcare provider, go to the emergency room. Be sure to tell them you are pregnant or were pregnant within the last year.

Learn more at [www.cdc.gov/HearHer/AIAN](http://www.cdc.gov/HearHer/AIAN)

**HEAR**  
HEAR HER CONCERNS



This list of urgent maternal warning signs was developed by the Council on Patient Safety in Women's Health Care.

# Diabetes in Pregnancy



# Gestational Diabetes

- First documentation in 1824, of hyperglycemia and stillbirth of a macrosomic infant at 22 weeks
- *“Of pregnancy and progeny:” 1980*
- Carbohydrate intolerance of variable severity with onset or first recognition during pregnancy
- May not depend on treatment with insulin
- Complicates 7% of pregnancies



# Two Step Process

- Screen with 50 gm load, test one hour
  - Abnormal  $\geq 140$  mg/dl (130 in some sites)
- 100 gm 3 hr OGTT performed fasting
  - 2 values  $\geq$  fasting 95 mg/dl, 1 hr 180, 2 hr 155, 3 hr 140 (Carpenter-Coustan) Or fasting 105 mg/dl, 1 hr 190, 2 hr 165, 3 145 (NDDG)



# Diagnosis of Gestational DM

- Usually screen 24-28 weeks gestation
- Two step endorsed by ACOG (6-7% of patients)
- One step endorsed by ADA and IADPSG (15-20% of patients)
- NIH consensus recommend two step continue
  - Vandorsten et al, NIH Concens State Sci 2013;29(1):1

ACOG=American College of Obstetrics and Gynecology

ADA= American Diabetes Association

IADPSG= International Association Diabetes and Pregnancy Groups

# Principles of Treatment

- Daily self monitoring
  - Fasting and 1 or 2 hour postprandial
- Individual medical nutrition therapy (70%)
  - Restrict diet to 35-40% CHO
- Insulin is the therapy most tested to reduce fetal morbidity
  - Fasting <90 1 Hr PP <140
- Fetal surveillance due to increased risk of stillbirth when poorly controlled sugars

# Postnatal counseling- Diabetes

- 50% risk of Type 2 diabetes in women with gestational diabetes
- Encourage 75 g testing at 6 weeks postpartum



# Mitigating obstetric risk

Optimize maternal conditions prior to pregnancy

Screen postpartum for T2DM in patients with GDM

Early GDM screen in patients with risk factors (HbA1c <5.7)

LDASA to prevent preeclampsia

MFM consultation for medications rather than abrupt discontinuation

# Breastfeeding



# Breastfeeding: Medicine and Culture



Risk of harm



Risks and benefits to birthing person- infant dyad

# Breastfeeding: Medicine and Culture

- How to move the needle?
  - Better understanding of benefits of breastfeeding to mothers/lactating persons
  - Better understanding of risk of medication exposure in breastmilk to newborns and babies



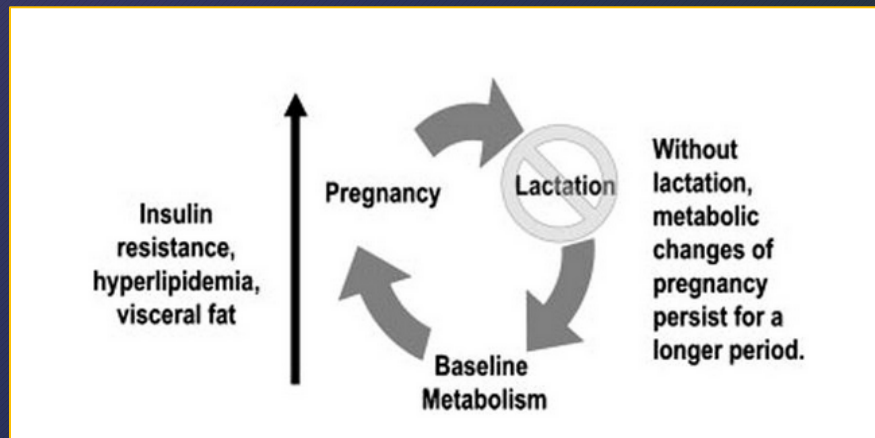


## Breastfeeding: Medicine and Culture

- Breastfeeding is not the right choice for every individual
- Complex relationships between mood and breastfeeding
- Breast surgeries may reduce/eliminate supply
- Despite best efforts, sometimes breastfeeding is not successful

# Importance of Lactation

- For maternal metabolism, pregnancy ends with weaning, not birth.
- Pregnancy is a time of increases in visceral fat, insulin production, insulin resistance, and circulating lipid levels
- In the absence of lactation, these changes persist for longer duration



Stuebe A, Am J Perinatol. 2009 Jan; 26(1): 81-88

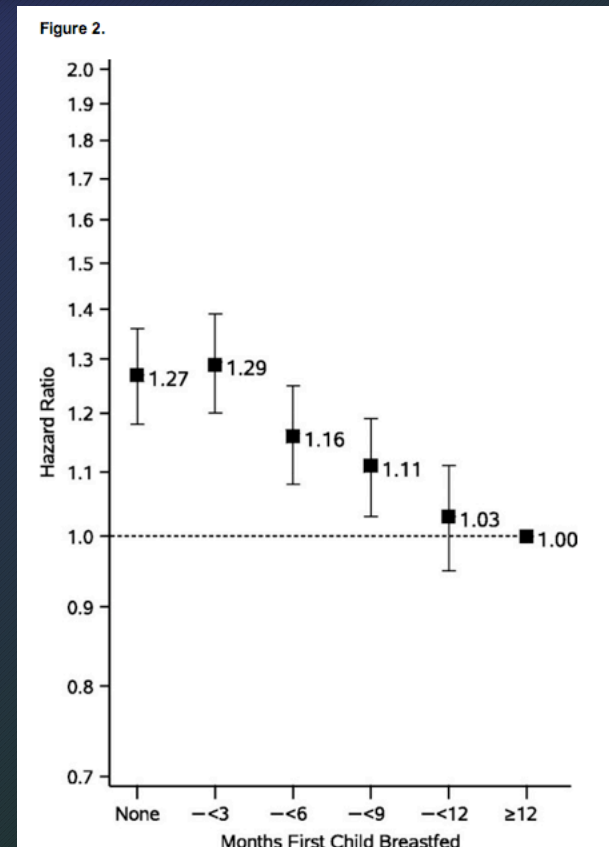
# How to understand long term health benefits

- Comparison of 3 groups:
  - Never pregnant
  - Pregnant, no lactation
  - Pregnant, + lactation



# Breastfeeding: Reduced risk heart disease

- 89,326 women from the Nurses Health Study
- BF for lifetime total 2 years +
  - 23% lower risk of CVD (95%CI 6-38),  $p=0.02$ ) controlled for age, parity, stillbirth history, early-adult adiposity, parental history, and lifestyle factors.
- Observational cohort of 55,636 parous women in US Nurses' Health Study II
- Never or curtailed lactation was associated with an increased risk of incident HTN compared with >6 months of exclusive (HR 1.29) or >12 months of total lactation per child (1.22)



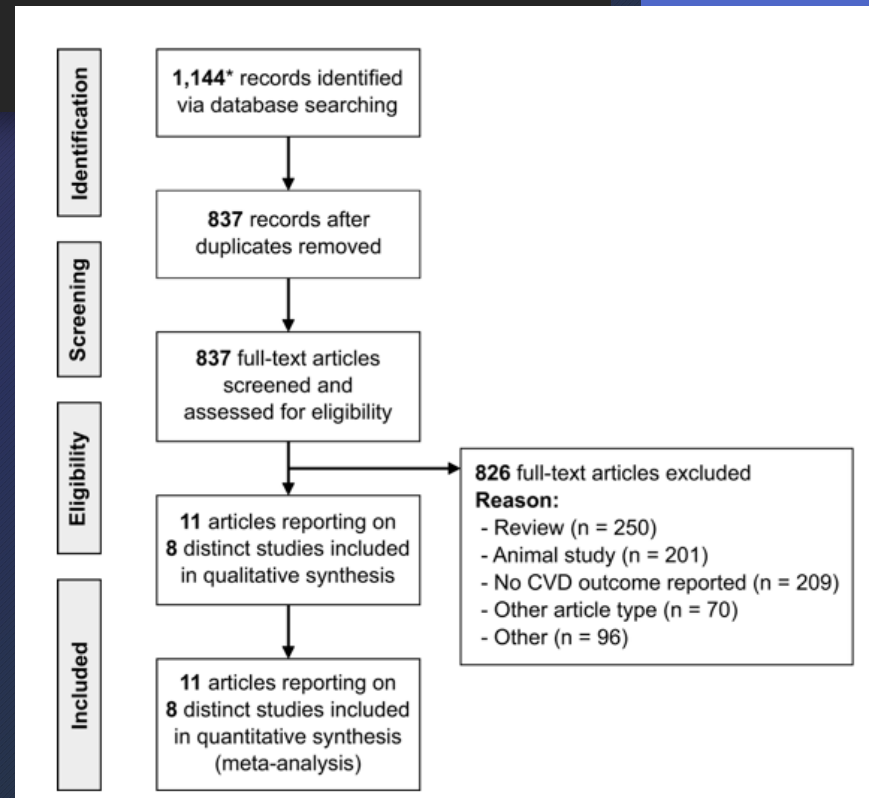
# Breastfeeding Is Associated With a Reduced Maternal Cardiovascular Risk: Systematic Review and Meta-Analysis Involving Data From 8 Studies and 1 192 700 Parous Women

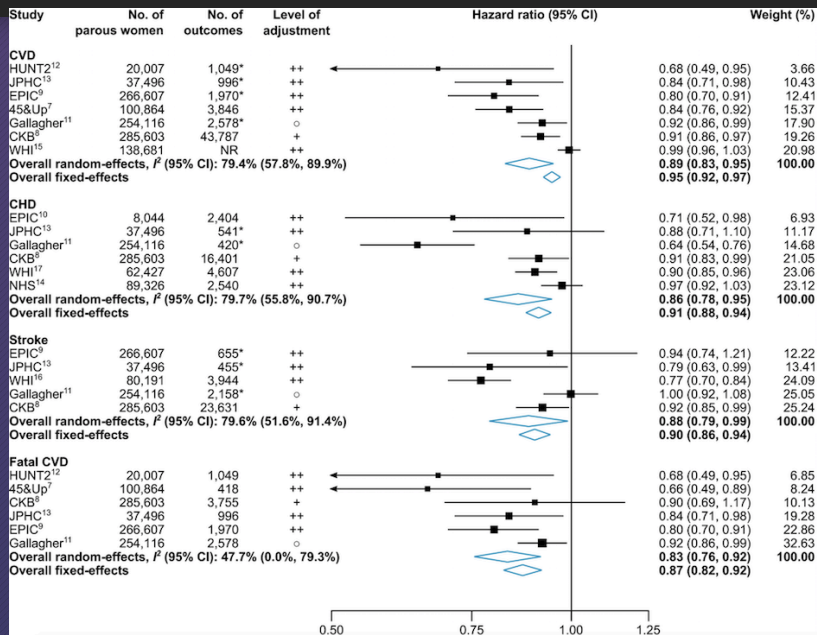
Lena Tschiderer, Lisa Seekircher, Setor K. Kunutsor, Sanne A. E. Peters, Linda M. O’Keeffe and Peter Willeit

Originally published 11 Jan 2022 | <https://doi.org/10.1161/JAHA.121.022746> | Journal of the American Heart Association. 2022;11:e022746

## Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram.

CVD indicates cardiovascular disease. \*A total of 514 from PubMed and 630 from Web of Science.





**Figure 2. Forest plot for CVD, CHD, stroke, and fatal CVD comparing parous women who ever breastfed vs never breastfed.**

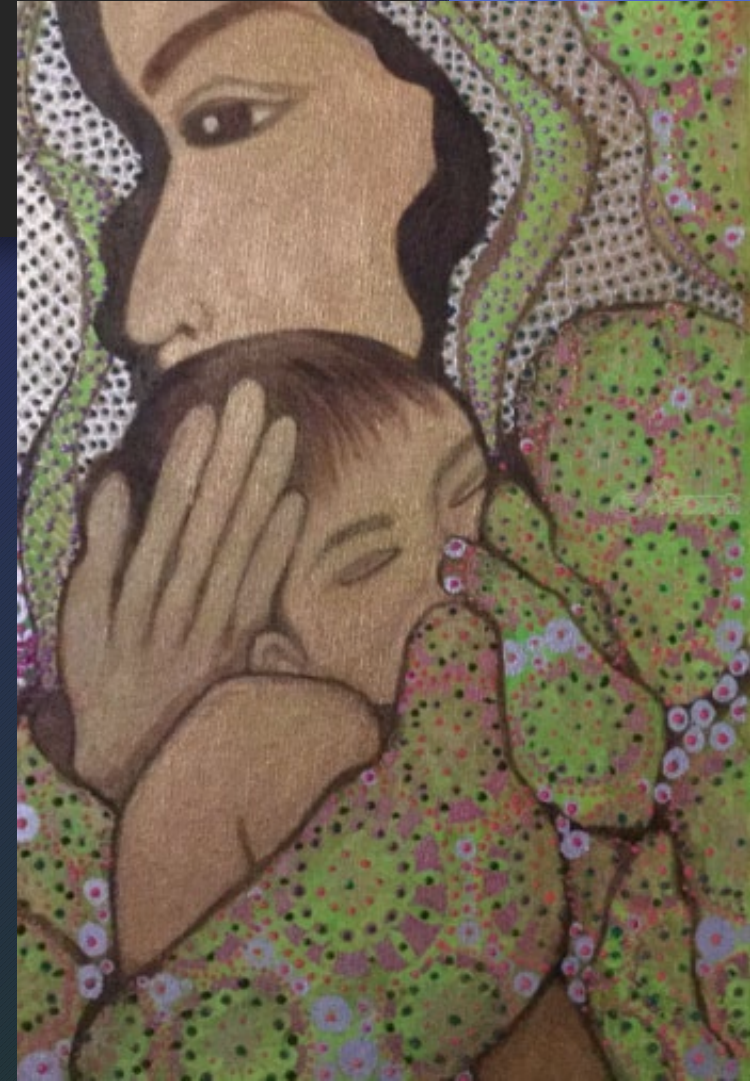
\*Only fatal events included. ○, adjusted for demographics and reproductive factors; +, adjusted for demographics and cardiovascular risk factors; ++, adjusted for demographics, reproductive factors, and cardiovascular risk factors. Full study names are provided in the footnotes of the Table. CHD indicates coronary heart disease; and CVD, cardiovascular disease.

# Breastfeeding: Protection from T2DM

- 2233 women in California (Kaiser)
- 56% BF for >1 month
- BF>1 mo had similar rates of T2DM as nulliparas
  - (OR 1.01 95%CI 0.56-1.81)
- No BF more likely to develop T2DM than nulliparas
  - (OR 1.93 95%CI 1.14-3.27)
- No BF more likely to develop T2DM than BF 1-3 months
  - (OR 1.52 95% CI 1.11-2.1)

**Risk of type 2 diabetes increases when term pregnancy is followed by <1 month of BF, independent of physical activity and BMI later in life**

Schwartz Am J Med 2010



# Type 2 Diabetes

- Longer lifetime lactation is associated with lower incidence of type 2 diabetes
- Nurses Health Study cohorts: lifetime duration of lactation was associated with reduced likelihood of incident type 2 diabetes in the 15 years since a woman's last birth
  - HR per year lifetime lactation NHS 0.85 (95% CI 0.73-0.99)
  - In NHS II 0.86 (95% CI 0.79-0.93)
- Longer lactation also associated with reduced DM risk in Women's Health Initiative, Reproductive Risk factors for Incontinence Study at Kaiser, the Shanghai Women's Health Study, and EPICPotsdam Study

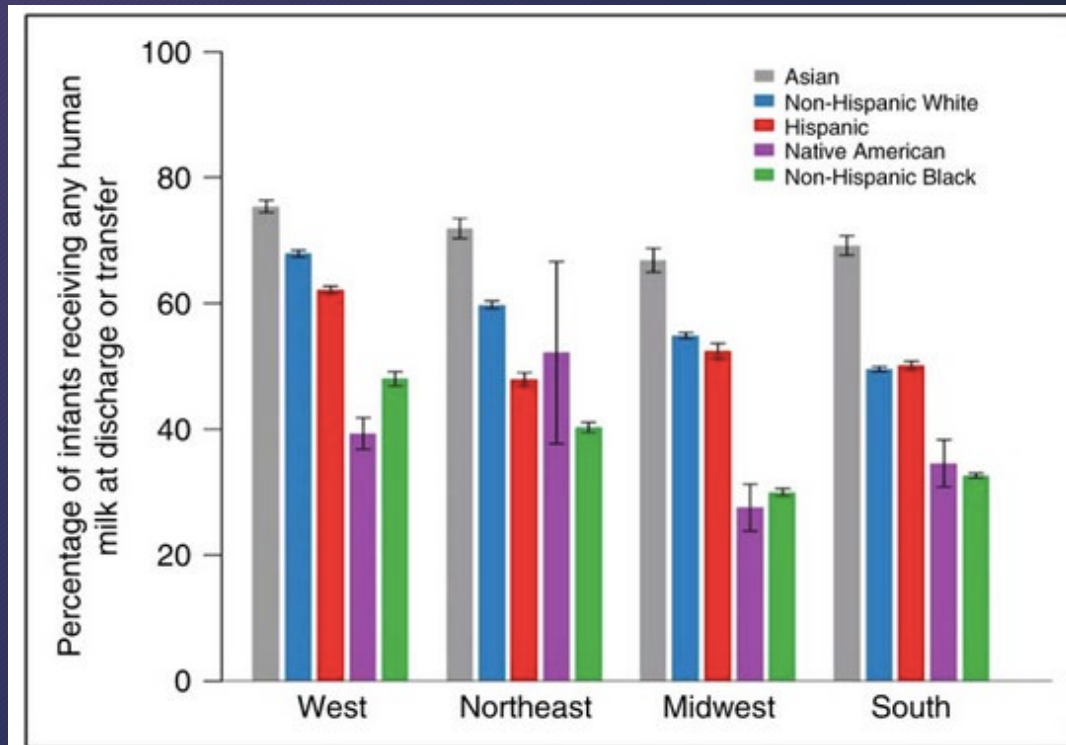
Jager 2014, Schwarz 2010, Stuebe 2005, Villegas 2008, Schwarz 2009



## Additional benefits to mother and baby

- Reduced risks of breast and ovarian cancer
- Reduced newborn infections
- Reduced asthma, type 1 diabetes, obesity, SIDS in children

# US variation in any human milk at NICU discharge by maternal R/E



# Caveats and confounders

- Pre-pregnancy obesity is associated with reduced BF initiation and duration
- Obesity associated with delayed lactogenesis
- Perinatal depression and anxiety disorders may mediate associations between lactation and metabolic disease
- Maternal metabolic health may affect lactation performance

Stuebe 2015



# How to calculate risk when medication is needed?

1. What is the benefit of the medication to disease control?
2. What is the risk of harm if medication is not administered?
3. Is there a risk of harm to newborn?
4. How to mitigate that risk?



For drugs that are not systemically absorbed, there is a standard statement indicating that maternal use is not expected to result in infant exposure

For drugs that are systemically absorbed, the risk summary must be a description of the following information or it will state that it is not available:

- Effects of drug on milk production
- Presence of drug in human milk
  - If drug not detected, it will state limits of assay
  - If drug is detected, provide drug concentration in milk and estimated infant daily dose (actual and compared to pediatric or maternal doses)
  - Effects of the drug on the breastfed child
- If data show that the drug does not affect the quantity and quality of breast milk and there is reasonable certainty that either the drug is not detectable in breast milk or will not adversely affect the breastfed child, then it will state:
  - “The use of [name of drug] is compatible with breastfeeding.”

#### **Clinical Considerations**

This section must provide, when available, information on:

- Ways to minimize exposure of the breastfed infant to the drug
- Dosing adjustments during lactation

Evaluating safety of specific medications:  
FDA guidelines

# Evaluating safety of specific medications: Lactmed

Drugs and Lactation Database (LactMed®) [Internet]. ◀ Prev Next ▶

 [Show details](#)  
[Contents](#) 

## Rituximab

Last Revision: February 15, 2023.  
Estimated reading time: 6 minutes  
CASRN: 174722-31-7

[Drug Levels and Effects](#) Go to: 

### Summary of Use during Lactation

Rituximab is a genetically engineered chimeric murine/human monoclonal antibody that targets CD20, a B-cell-specific surface antigen. The amount in milk is very low and absorption is unlikely because it is a protein with a molecular weight of 143,860 Da. It is likely to be partially destroyed in the infant's gastrointestinal tract and absorption by the infant is probably minimal.<sup>[1,2]</sup> Several breastfed infants appeared during maternal use of rituximab, including no adverse effect on the CD19 +B cell count of 6 breastfed infants. The manufacturer recommends that breastfeeding be discontinued during rituximab therapy and for 6 months after the last dose. However, the American College of Rheumatology and others consider rituximab to be acceptable for use during breastfeeding.<sup>[3-5]</sup> Until more data become available, rituximab should be used with caution during breastfeeding, especially while nursing a newborn or preterm infant.<sup>[6-8]</sup>

### Drug Levels

**Maternal Levels.** A patient who had granulomatosis with polyangiitis received rituximab 500 mg intravenously while exclusively breastfeeding her infant. Milk samples were collected daily for 4 weeks post-infusion. Milk rituximab concentrations averaged 0.5 mcg/L (range 0.4 to 0.6 mcg/L). The relative infant dose to the infant was estimated to be 0.007%.<sup>[9]</sup>

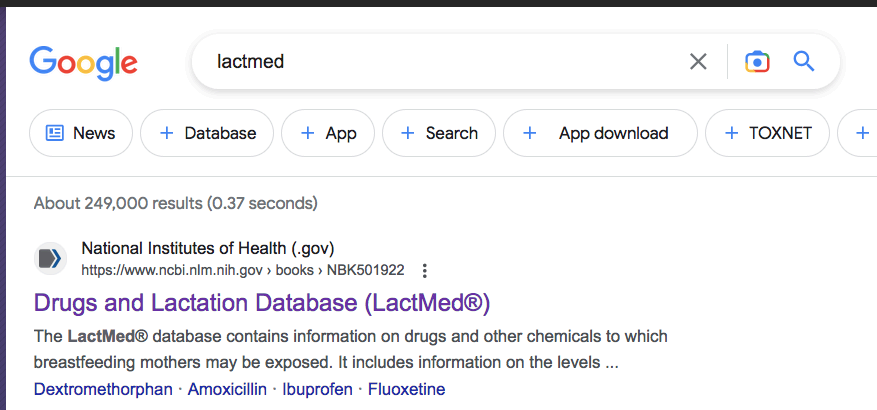
A woman with ANCA-associated vasculitis was treated with rituximab 500 mg intravenously. The median concentration of rituximab in milk samples collected on 4 consecutive days was 290 mcg/L, which occurred in a woman with a single breast milk sample.<sup>[10]</sup> Breastmilk samples were collected from 9 women with multiple sclerosis who received rituximab once or twice while breastfeeding. Four patients provided samples before 7 days, and 18 to 21 days after a dose. Five additional patients provided 1 or 2 samples during breastfeeding. The median average rituximab concentration in mature breast milk was 41 mcg/L in the 4 patients with serial breast milk collection, with an estimated median concentration of 290 mcg/L in the 5 patients with single breast milk collection. Most patients had a peak milk concentration at 1 to 7 days after infusion. The highest concentration reported was in one woman who had a milk concentration of 250 mcg/L. The median average concentration in the breastmilk of the 6 women was 41 mcg/L.<sup>[12]</sup>

**Infant Levels.** A woman received rituximab 375 mg/square meter once weekly for 4 weeks beginning at week 30 of gestation. Her infant was born at 40 weeks of gestation and was exclusively breastfed with no major health issues. At 4 months of age, trace amounts of rituximab heavy and light chains were detected, but not quantified, in the infant's serum. Whether the drug was acquired transplacentally or during breastfeeding was not determined.<sup>[13]</sup>

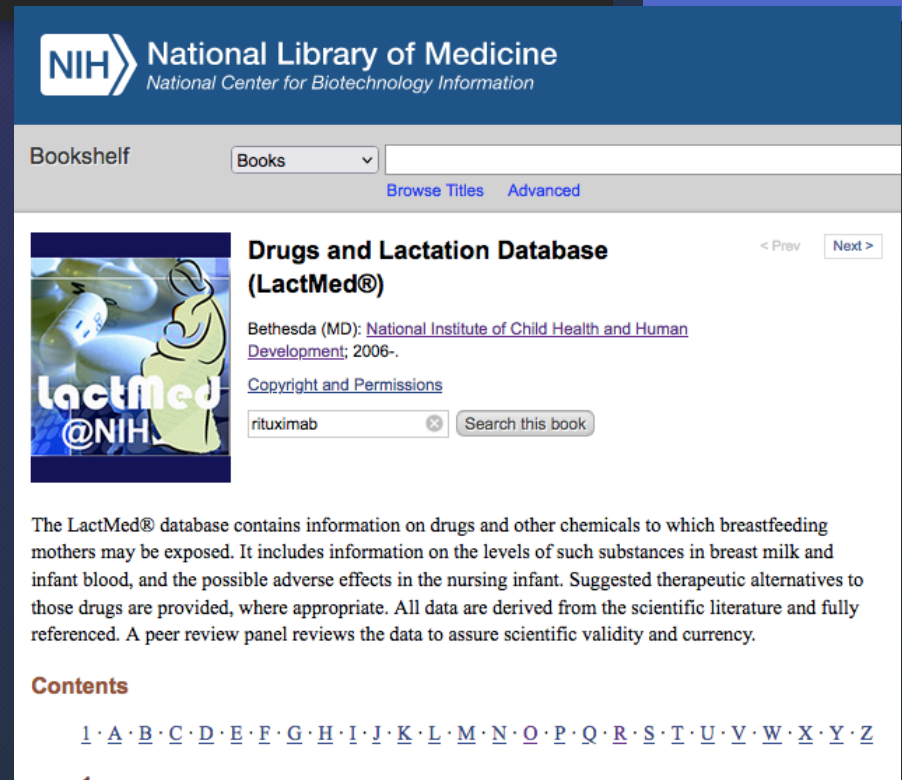
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# How to find Lactmed



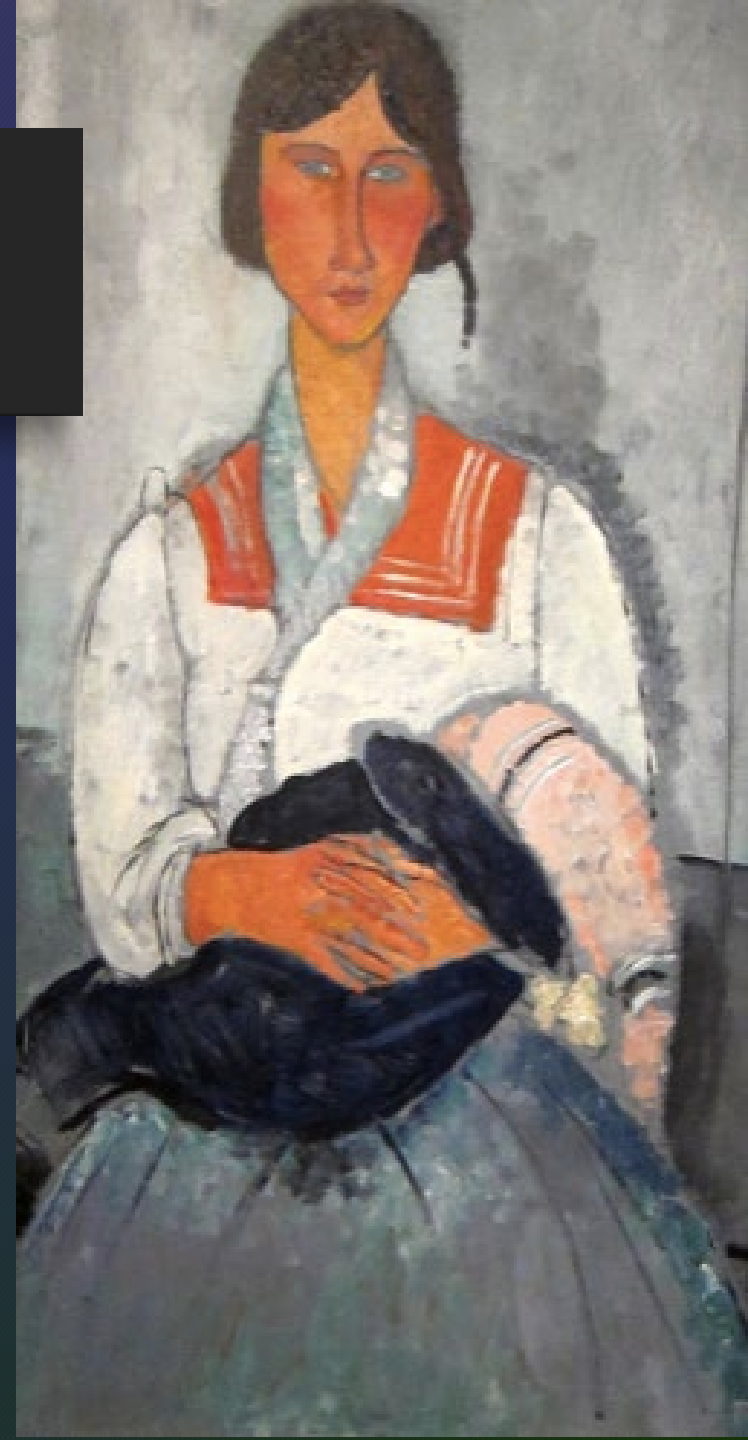
A screenshot of a Google search for "lactmed". The search bar shows "lactmed" with a magnifying glass icon. Below the search bar are filters for News, Database, App, Search, App download, and TOXNET. The results show "About 249,000 results (0.37 seconds)". The top result is from the National Institutes of Health (.gov) with the URL "https://www.ncbi.nlm.nih.gov/books/NBK501922". The title is "Drugs and Lactation Database (LactMed®)". The description states: "The LactMed® database contains information on drugs and other chemicals to which breastfeeding mothers may be exposed. It includes information on the levels ...". Below the description are links for "Dextromethorphan", "Amoxicillin", "Ibuprofen", and "Fluoxetine".



A screenshot of the National Library of Medicine (LactMed) website. The header features the NIH logo and the text "National Library of Medicine National Center for Biotechnology Information". Below the header is a "Bookshelf" section with a dropdown menu set to "Books" and a search bar. The main content area displays the title "Drugs and Lactation Database (LactMed®)" with a "Prev" and "Next" navigation bar. Below the title is a description: "Bethesda (MD): National Institute of Child Health and Human Development; 2006-." and a link for "Copyright and Permissions". A search bar contains the text "rituximab" and a "Search this book" button. Below the search bar is a paragraph of text: "The LactMed® database contains information on drugs and other chemicals to which breastfeeding mothers may be exposed. It includes information on the levels of such substances in breast milk and infant blood, and the possible adverse effects in the nursing infant. Suggested therapeutic alternatives to those drugs are provided, where appropriate. All data are derived from the scientific literature and fully referenced. A peer review panel reviews the data to assure scientific validity and currency." Below this text is a "Contents" section with a list of letters: "I · A · B · C · D · E · F · G · H · I · J · K · L · M · N · O · P · Q · R · S · T · U · V · W · X · Y · Z".

# Breastfeeding Summary

- Breastfeeding has significant health benefits
- Most medications are compatible with breastfeeding
- Recommendations against breastfeeding have significant health consequences and should be thoughtfully given
- In most cases, disease treatment for mothers/birthing persons can be optimized while breastfeeding continues.



# Take Aways

- Maternal mortality and racial disparities in morbidity and mortality are a current crisis in the US
- Mitigating obstetric risk is feasible with optimization of maternal medical conditions and close surveillance of pregnancy complications
- Breastfeeding has important lifetime health benefits and should be supported whenever possible.

# Acknowledgements- historical references

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## **HISTORICAL PERSPECTIVE**

**The History of Preeclampsia and Eclampsia  
as Seen by a Nephrologist**

**2012 Benson and Pamela Harer Seminar on History Lecture**

Marshall D. Lindheimer, MD, FACP,

FRCOG (London, ad eundem)

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University of Chicago, Division of Biological Sciences\*



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