

Medical Complications of Pregnancy

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 - ▣ Research focus: Long term sequelae of GDM and preeclampsia
 - ▣ Clinical focus: Endocrine and hypertensive complications of pregnancy

Disclosures:



None

Objectives



- To understand the implications of common medical conditions on pregnancy
- To be able to appropriately change medical management of patients prior to pregnancy
- To understand differences in disease management goals in pregnancy

Common Complicating Medical Conditions that Precede Pregnancy

- Hypertension ~5-10%
- Diabetes Mellitus ~1-2%
- Hypothyroidism ~2-3%
 - Leading causes of hospitalization in pregnancy:
 - Preterm labor
 - Hypertension
 - Diabetes Mellitus
 - Bleeding

Why Is it Important for Medical Caregivers to Know about these?



- Prepregnancy Planning and Counseling Key to Successful Pregnancy Outcome
- At least 50% pregnancies are unplanned in US.



The American College of
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WOMEN'S HEALTH CARE PHYSICIANS

ACOG PRACTICE BULLETIN

Clinical Management Guidelines for Obstetrician–Gynecologists

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Chronic Hypertension in Pregnancy

Hypertension

Volume 79, Issue 2, February 2022; Pages e21-e41
<https://doi.org/10.1161/HYP.0000000000000208>



AHA SCIENTIFIC STATEMENTS

Hypertension in Pregnancy: Diagnosis, Blood Pressure Goals, and Pharmacotherapy: A Scientific Statement From the American Heart Association

Hypertensive Disorders in Pregnancy

Chronic Hypertension:

Hypertension prepregnancy or < 20 weeks gestation; or hypertension diagnosed for the 1st time in pregnancy & does not resolve postpartum

Preeclampsia:

SBP ≥ 140 , or DBP ≥ 90 mm Hg, or both on 2 occasions ≥ 4 hrs apart, >20 weeks gestation and prior normal BP or severe range hypertension, with proteinuria or other end organ manifestations

Gestational Hypertension:

SBP ≥ 140 , or DBP ≥ 90 mm Hg, or both on 2 occasions ≥ 4 hours apart, *after* 20 weeks gestation with previously normal BP

Superimposed Preeclampsia:

Preeclampsia (with proteinuria or other end organ manifestations) in a woman with hypertension before pregnancy or < 20 weeks gestation

Risks of Hypertension in Pregnancy

- Fetus/Neonate
 - Low birth weight
 - Prematurity (induced)
- Mother
 - Exacerbation of hypertension and risk of stroke, MI, renal failure
 - Superimposed preeclampsia

Chronic Hypertension and Preeclampsia Rates

□ General population	4-5%
□ Preexisting hypertension	25 %
< 4 y duration	22%
≥ 4 y duration	31%
DBP <100 mm Hg	24%
DBP 100-110 mm Hg	42%

Based on BP at visit regardless of antihypertensive Rx

Adapted from Sibai Am Obstet Gyn 2002;100:369

ASA for preeclampsia prevention

- USPSTF recommends low dose ASA for women with chronic hypertension starting at 12 wks
- Risk reduction ~15%

Preexisting Hypertension in Pregnancy

- Pregnancies do well unless superimposed preeclampsia develops
- Goal SBP ≥ 120 to < 160 ; DBP ≥ 80 to < 110 mm Hg *
- Antihypertensives generally can be tapered during pregnancy to lower fetal exposure

* *ACOG Practice Bulletin No 203: Chronic Hypertension in Pregnancy, 2019*

Antihypertensive Rx for Preexisting Hypertension in Pregnancy

1st line


- Alpha-Beta blocker
 - ▣ labetalol
- Calcium channel blocker
 - ▣ nifedipine long acting alternative first line

2nd line

- Methyldopa
 - ▣ used since 1960s
 - ▣ infant F/U to 7½ yrs (*Cockburn J et al. Lancet 1982;1(8273):647*)
 - ▣ Less favored now due to side effects/efficacy
- Diuretics
 - ▣ concern of dehydration

ACOG Practice Bulletin No 203: Chronic Hypertension in Pregnancy, 2019

Antihypertensive Rx for Preexisting Hypertension in Pregnancy

-  CEs and ARBs prior to conception
 - ▣ fetal anuria and oligohydramnios (2nd & 3rd trimester)
 - ▣ neonatal renal failure (2nd & 3rd trimester)
 - ▣ birth defects controversial (1st trimester Cooper et al. N Engl J Med, 354: 2443-51 2006 versus Li DK et al. BMJ. 2011 Oct 18;343:d5931; Bateman et al, Am J Ob Gyn 2015)
 - ▣ MR blockers spironolactone, eplerenone
- Not recommended: atenolol-Concern for growth restriction

Goals for BP in Pregnancy

- Magee et al 2015:
 - ▣ Tight control: target diastolic blood pressure, 85 mmHg
 - ▣ Less-tight control: target diastolic bp, 100 mmHg
- In 987 pregnant women with preexisting or gestational hypertension and diastolic bp of 90-105 mmHg
 - ▣ Women assigned to tight control vs prior goals (less-tight control) developed lower rates of severe hypertension ($\geq 160/110$ mmHg) – (27.5% vs 40.6%, $p < 0.001$).
 - ▣ No significant differences between groups in risk of pregnancy loss or overall maternal complications

ACOG Clinical Guidance for the Integration of the Findings of the Chronic Hypertension and Pregnancy (CHAP) Study. April 2022.

Magee LA, Singer J, von Dadelszen P; CHIPS Study Group. Less-tight versus tight control of hypertension in pregnancy. *N Engl J Med*. 2015;372(24):2367-2368. doi:10.1056/NEJMc1503870

Summary: Chronic Hypertension and Pregnancy

- Importance of family planning with all women with hypertension
- Awareness re need to switch from certain antihypertensives (ACEIs, ARBs)
- Knowledge that BP goals differ during pregnancy
- Awareness of hypertensive complications of pregnancy
- 140/90 threshold for initiation or titration of therapy

Review

> [Diabetes Care](#). 2025 Jan 1;48(1 Suppl 1):S306-S320. doi: 10.2337/dc25-S015.

15. Management of Diabetes in Pregnancy: Standards of Care in Diabetes-2025

American Diabetes Association Professional Practice Committee

Collaborators — collapse

Collaborators

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PMID: 39651985 PMCID: PMC11635054 (available on 2026-01-01) DOI: [10.2337/dc25-S015](#)

Diabetes Mellitus

- Birth defect risk rises related to level of HbA_{1c} at conception- as high as 20%
- Preconception glucose control can reduce birth defects to ~1% over general population

Risks of Diabetes Mellitus in Pregnancy

□ Fetus/Neonate

- ▣ Birth defects
- ▣ Macrosomia
- ▣ Prematurity (induced)
- ▣ Birth Trauma
- ▣ Neonatal Hypoglycemia

□ Mother

- ▣ Progression of diabetic complications: retinopathy, nephropathy
- ▣ Preeclampsia (start ASA after 12 wks if high risk per ACOG)
- ▣ Increased chance for C-section

Prepregnancy Planning for Women with Diabetes

- Discuss family planning at least yearly and stress the importance of prepregnancy glucose control
- If HbA_{1c} not in normal range, plan with patient 6 months to achieve glucose control prior to conception
- Counseling re risks
- Prepregnancy determination of retinopathy, nephropathy and other complications (i.e. gastroparesis)
- Adjustment of diabetes medications (*including* BP meds)

Optimal Diabetes Control for Conception

American Diabetes Association control goal:

- As close to $\text{HbA}_{1\text{C}} < 6.5\%$ as safely possible to reduce risks of
 - ▣ Congenital anomalies
 - ▣ Preeclampsia
 - ▣ Macrosomia
 - ▣ Other complications

Preeclampsia Prophylaxis

- Women with type 1 or type 2 DM should be prescribed low-dose aspirin 100–150 mg/day starting at 12 -16 weeks gestation to lower risk of preeclampsia.
- Dosage 162 mg/day may be acceptable; in U.S., low-dose aspirin available in 81-mg tabs.

Management of Diabetes Mellitus

Preconception and During Pregnancy

- Diet and home glucose monitoring are the mainstay of management
- Insulin is the preferred agent for preexisting diabetes in pregnancy.
- For Type 2 DM on oral/other agents, change to insulin
- Benefits/risks of oral agents or GLP1 RAs for Type 2 DM during pregnancy- the jury is out.
- Preconception counseling should begin at puberty

Insulin in Management of Diabetes Mellitus

Preconception and During Pregnancy

- ❑ Long experience with NPH and regular
- ❑ Shorter acting- lispro and aspart commonly used
- ❑ Longer acting:
 - ▣ Levemir- was preferred by many, esp in Europe, now off market
 - ▣ Glargine- was controversial due to increased IGF-1-receptor affinity/mitogenic potency in human osteosarcoma cell-culture model; not reported in humans and is widely used
- ❑ MDI or pumps or can be used (= by Cochrane systematic review)
- ❑ No data to recommend any specific insulin regimen over another (Cochrane systematic review)

O'Neill SM, et al. Different insulin types and regimens for pregnant women with preexisting diabetes. Cochrane Database Syst Rev 2017;2:CD011880

Farrar D et al Continuous subcutaneous insulin infusion versus multiple daily injections of insulin for pregnant women with diabetes. Cochrane Database Syst Rev 2016;6:CD005542

Insulin resistance during pregnancy

- Insulin resistance increases as pregnancy progresses
- Insulin requirements typically increases in pregnancy but may decrease just before delivery; therefore doses needed to be adjusted throughout pregnancy

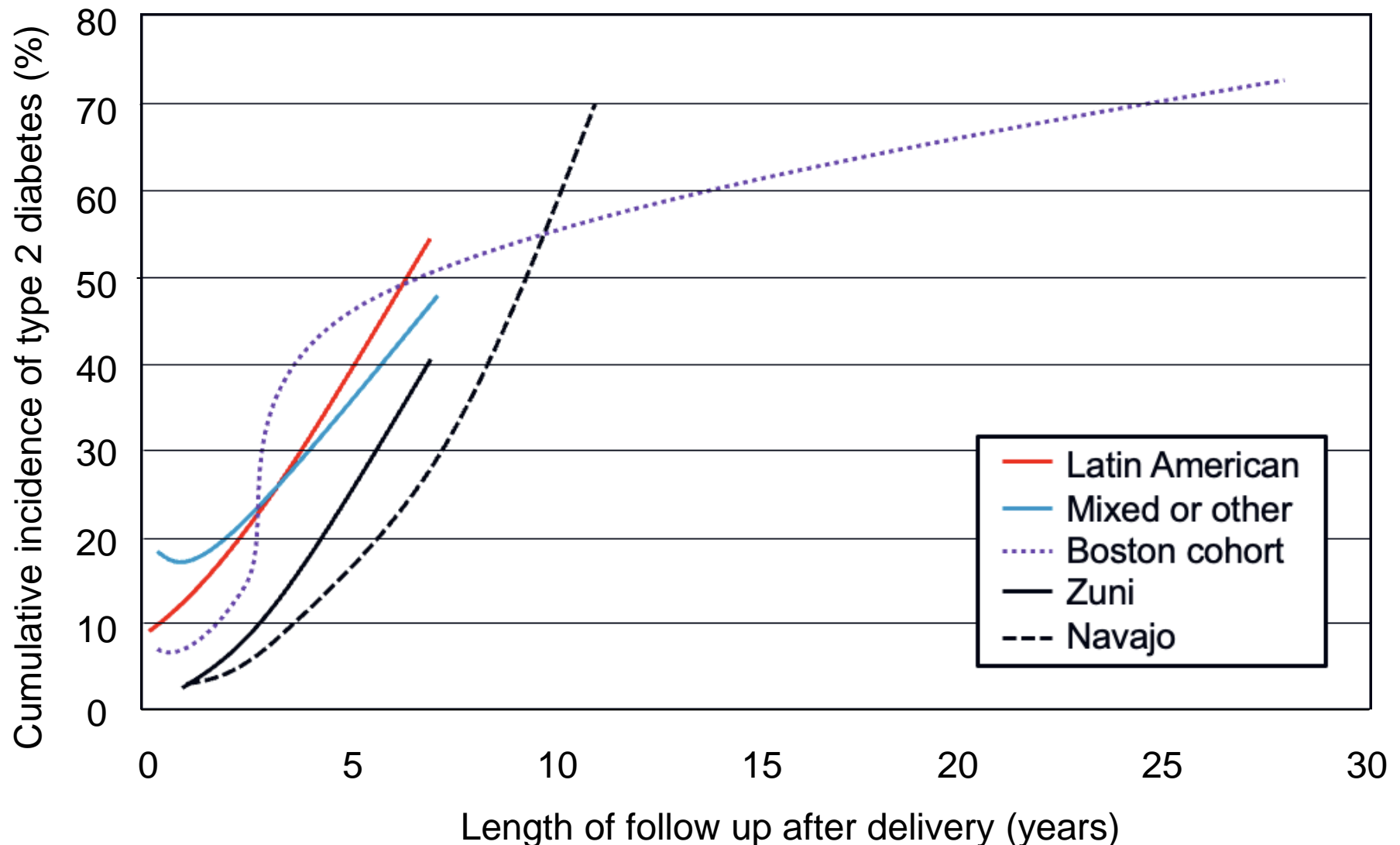
Glucose goals during pregnancy

- FBS <95 mg/dl
- Post meals
 - 1 hr <140 mg/dl
 - 2 hr <120 mg/dl
- HbA₁C <6% (if achievable without too much hypoglycemia)

Gestational Diabetes Mellitus and the Primary Care Physician

- GDM: Diabetes first diagnosed in pregnancy after the 1st trimester, resolves with delivery
- Risk of future Type 2 DM as high as 60-70%

Gestational diabetes and the incidence of type 2 diabetes



Adapted from Kim C et al. *Diabetes Care*. 2002 Oct;25(10):1862-8.

Recommendations for PP screening of women with a hx GDM for diabetes detection

	Early PP	Subsequent
ADA 2025	Fasting glucose or 75 gm 2h-OGTT	Reassess at a minimum of <u>every 3 years</u> if normal glucose tolerance with HbA ₁ C/FBG/OGTT. Reassess <u>annually</u> if IFG or IGT is detected.

- Only 50% or less women receive early PP testing
- Only 50% receive long-term testing

Zera CA, Obstet Gynecol. 2015

Summary: DM and Pregnancy

- ❑ Need for pregnancy planning to normalize HbA_{1c}
- ❑ May need to switch medications (both glycemic and antihypertensive meds) before conception
- ❑ Insulin doses require adjustment throughout pregnancy
- ❑ Women with a history of GDM should receive regular screening for Type 2 DM

Hypothyroidism

2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and the Postpartum

Thyroid Volume 27, Number 3, 2017

Erik K. Alexander,^{1,*} Elizabeth N. Pearce,^{2,*} Gregory A. Brent,³ Rosalind S. Brown,⁴ Herbert Chen,⁵
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New ATA Pregnancy Guidelines in preparation 2025

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Thyroid Disease in Pregnancy

Hypothyroidism: Diagnosis In Pregnancy

- ❑ 2-10% of pregnancies
- ❑ Universal screening not recommended by ACOG, the Endocrine Society, or American Association of Clinical Endocrinologists
- ❑ Diagnosis made by elevated TSH
- ❑ Symptoms:
 - ▣ weight gain (typical of normal pregnancy)
 - ▣ constipation (typical of normal pregnancy)
 - ▣ cold intolerance (not typical of pregnancy)

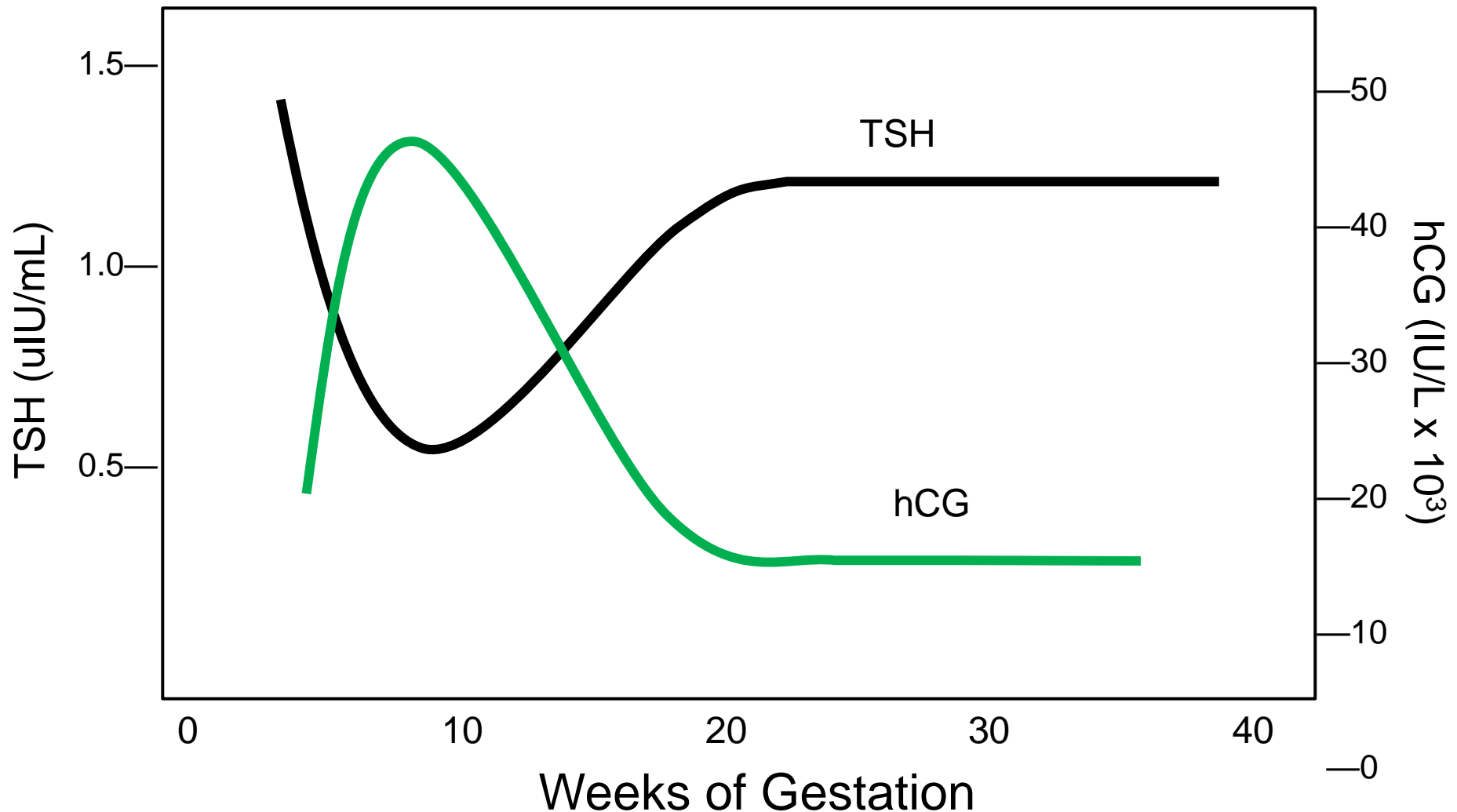
Screen women with

- personal or family history of thyroid disease
- type 1 diabetes mellitus
- clinical suspicion of thyroid disease- sx or signs on physical exam
- No recommendation for universal screening

Thyroid Hormone Changes in Pregnancy

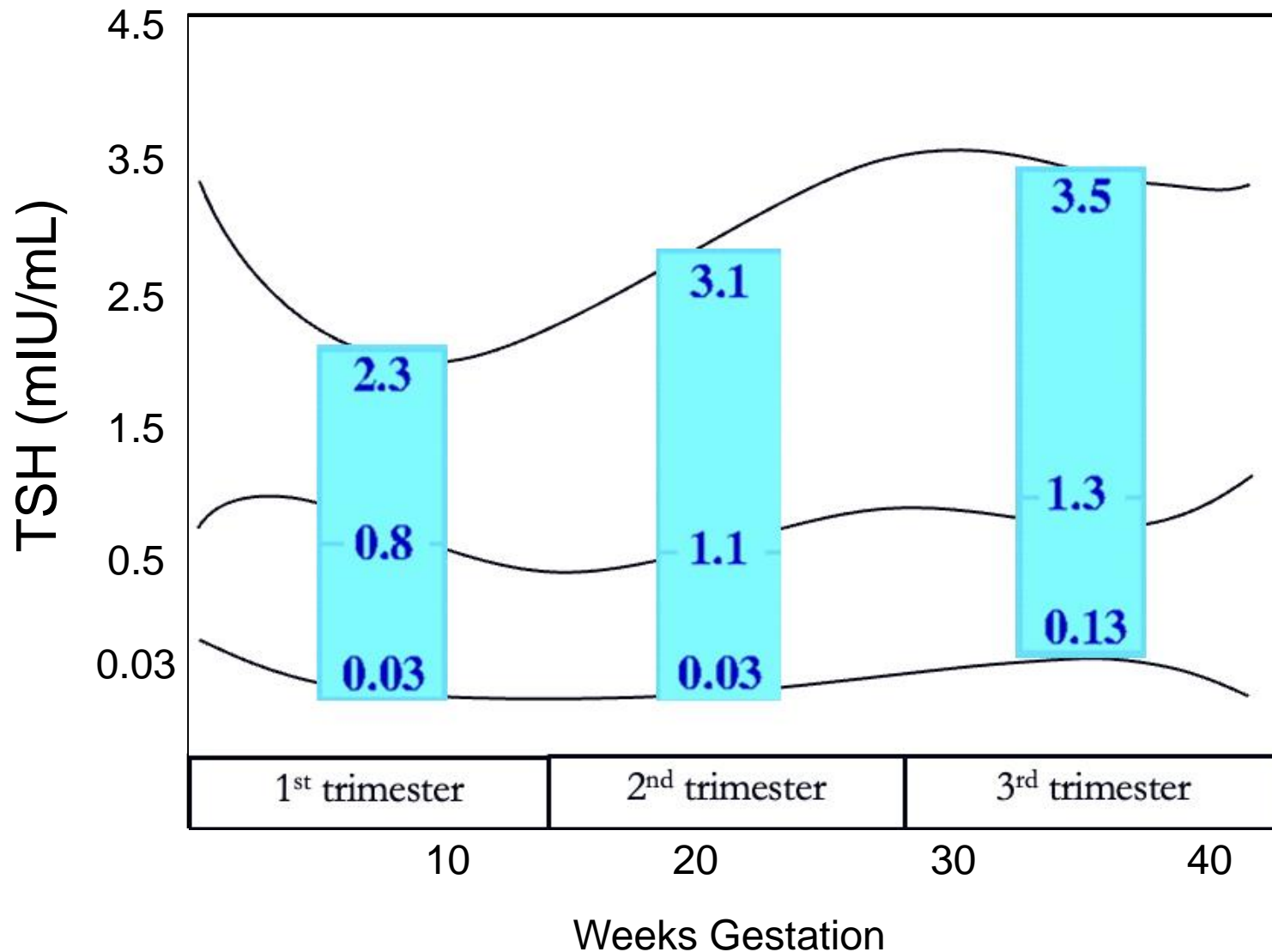
- ❑ Diagnosis often complicated by the changes in thyroid function that take place in normal pregnancy.
- ❑ Early pregnancy, rise in HCG (has thyroid stimulatory activity), leads to compensatory fall in TSH.
- ❑ TSH concentration is usually within the normal range; in some women falls

Relationship between TSH and hCG



Adapted from Glinoer et al. JCEM 1990; 71(2):282

Serum TSH in Pregnancy: Mean and 95% CI



TSH normal range in pregnancy

- Use pregnancy specific normal range of your lab
- If trimester-specific reference ranges for TSH are not available reduce lower reference range for TSH by 0.4 and upper by 0.5 milliunits/L in late 1st trimester

Clinical Hypothyroidism: Risks to Pregnancy

Defined as Elevated TSH and low T₄

- Fetal/Infant

- ▣ Preterm Birth
- ▣ Pregnancy loss
- ▣ Stillbirth
- ▣ Impaired neuropsychologic development

- Maternal

- ▣ Increases risk for preeclampsia, placental abruption (preterm delivery)

Subclinical Hypothyroidism: Risks to Offspring

Defined as Elevated TSH and normal T₄

- Observational studies suggested impaired neurodevelopment and decreased IQ
- Two prospective randomized controlled studies showed no benefit of thyroid hormone administration with f/u to age 5 yrs.

Haddow JE et al. N Engl J Med 1999;341:549–55; Pop VJ et al. Clin Endocrinol (Oxf) 1999;50:149–55. ;Lazarus JH et al. N Engl J Med 2012;366:2012;366:493–501.

Casey BM et al. N Engl J Med 2017;376:815–25.

Subclinical Hypothyroidism: Risks to Pregnancy Controversial

- ❑ Preterm birth
- ❑ Preeclampsia
- ❑ Gestational diabetes
- ❑ Placental abruption
- ❑ NICU admission

Given clear risk a/w clinical hypothyroidism and potential a/w subclinical, pregnant women are treated with levothyroxine to achieve a nl TSH for pregnancy

Hypothyroidism: Treatment Prior to and During Pregnancy

- Aim for TSH <2.5 at conception
- Check TSH as soon as pregnancy test positive
- Requirement for thyroid hormone characteristically increases in pregnancy and returns to prepregnancy requirement postpartum
- Titrate thyroid hormone dose to maintain TSH <2.5
- Reduce thyroid hormone dose to prepregnancy dose at delivery and check TSH at 6 wk pp visit

Summary Hypothyroidism and Pregnancy



- TSH values vary through pregnancy and may be suppressed in first trimester due to rise in HCG
- TSH levels run lower in pregnancy so aim for T₄ replacement is a lower TSH.

Overall Summary



- Women with medical problems should receive regular family planning counseling
- Adjustment of medications is often necessary prior to and during pregnancy
- Goals for treatment of medical problems may differ during pregnancy

Potential Conflicts:

None

Question 1

You see a 34 yo woman with Type 2 diabetes and hypertension who has recently stopped using contraception. She is taking glyburide and lisinopril. Her last HbA_{1c} was 9%.

Your recommendations include all of the following except:

- a) Change to insulin and aim for HbA_{1c} <6.5%.
- b) D/C lisinopril and substitute labetalol before she tries to become pregnant
- c) D/C lisinopril and substitute an angiotensin 2 receptor blocker (ARB) to help protect her kidneys during pregnancy
- d) Eye exam for retinopathy assessment

Question 1-Answer

Your recommendations include all of the following except: Answer C

- a) Change to insulin and aim for HbA_{1c}<6.5%. *This is a correct goal for conception per ADA.*
- b) D/C lisinopril and substitute labetalol before she tries to become pregnant. *Lisinopril is contraindicated in pregnancy and labetalol is a 1st line medication.*
- c) D/C lisinopril and substitute an angiotensin 2 receptor blocker (ARB) to help protect her kidneys during pregnancy. *Both ACEIs and ARBs cause fetal renal damage.*
- d) Eye exam for retinopathy assessment. *An eye exam should be performed prior to pregnancy in women with diabetes.*

Question 2

A 24 yo woman reports a home positive pregnancy test and having missed her period. Because of fatigue, another clinician ordered a TSH to rule out hypothyroidism and which returned at 5.0 mIU/L. She has no other symptoms.

You:

- a) Recommend recheck of TSH in 4 wks.
- b) Explain that TSH values may increase over the course of normal pregnancy due to the rise in HCG.
- c) Start T4 with a goal TSH < 4.5.
- d) Start T4 with a goal TSH < 2.5

Question 2 Answer

You: Answer **D**

- a) Recommend recheck of TSH in 4 wks. *Incorrect: T₄ requirement rises over the course of pregnancy.*
- b) Explain that TSH values usually increase in 1st trimester of normal pregnancy due to rise in HCG. *Incorrect: TSH levels typically fall in the 1st trimester due to rise in HCG.*
- c) Start T₄ with a goal TSH < 4.5. *Incorrect: TSH goals are lower in pregnancy. Do not use non pregnant nl range.*
- d) Start T₄ with a goal TSH < 2.5. *Correct: TSH goals are lower in pregnancy.*

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