Gestational Diabetes

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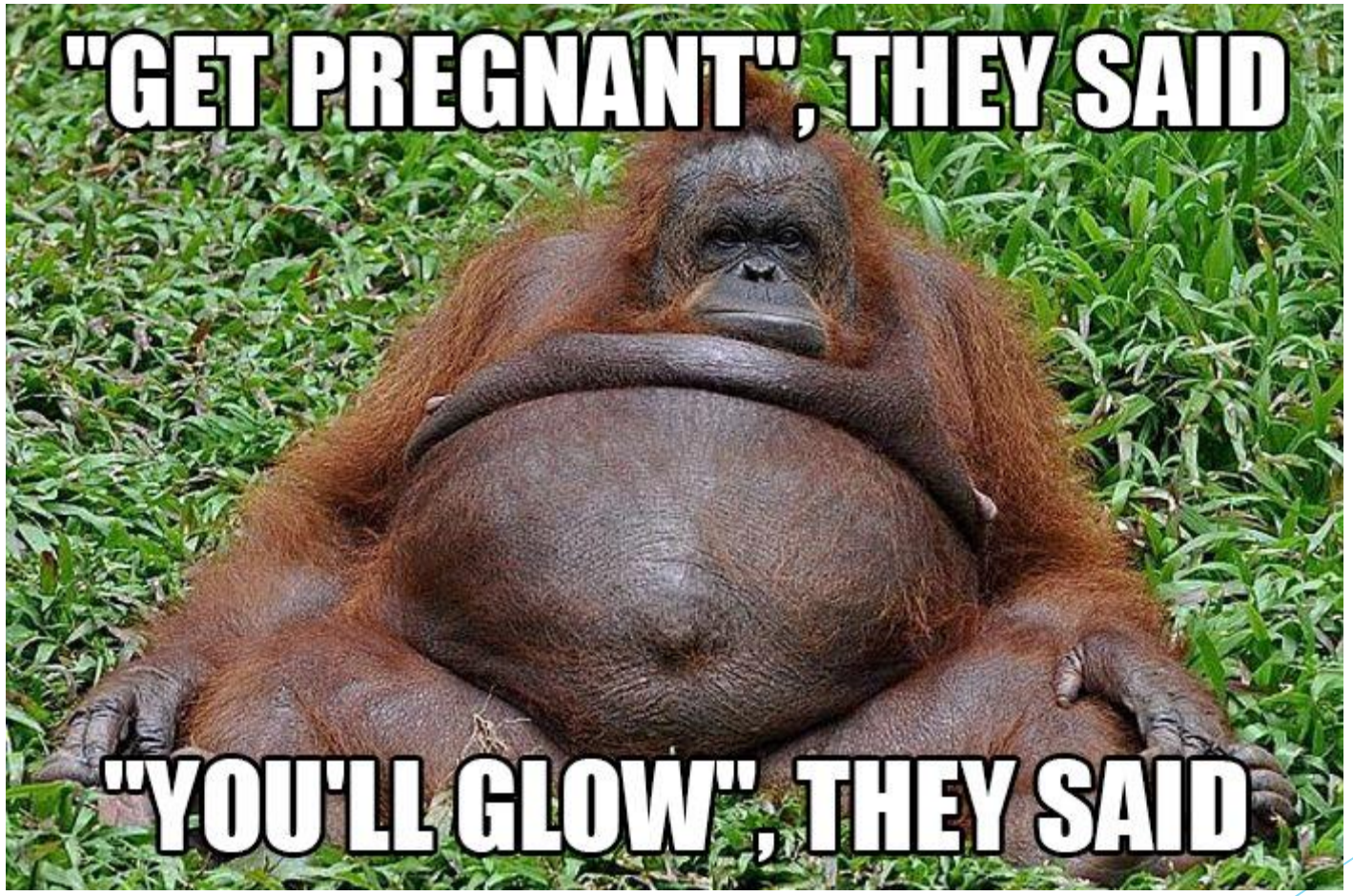

"GET PREGNANT", THEY SAID
"YOU'LL GLOW", THEY SAID

Gestational Diabetes

- Definitions/Classifications
- Incidence
- Screening
- Fetal and Maternal Effects
- Management
- Obstetric Management
- Long term consequences and follow up

Classifications

- Pre-gestational DM
  - Type 1
  - Type 2
  - Monogenic, CF, steroid/med induced
- Hyperglycemia in Pregnancy
  - Diabetes in Pregnancy (DIP) or Over diabetes in pregnancy
  - GDM: early vs standard
    - IADPSG and WHO

Pathophysiology

Increased insulin resistance

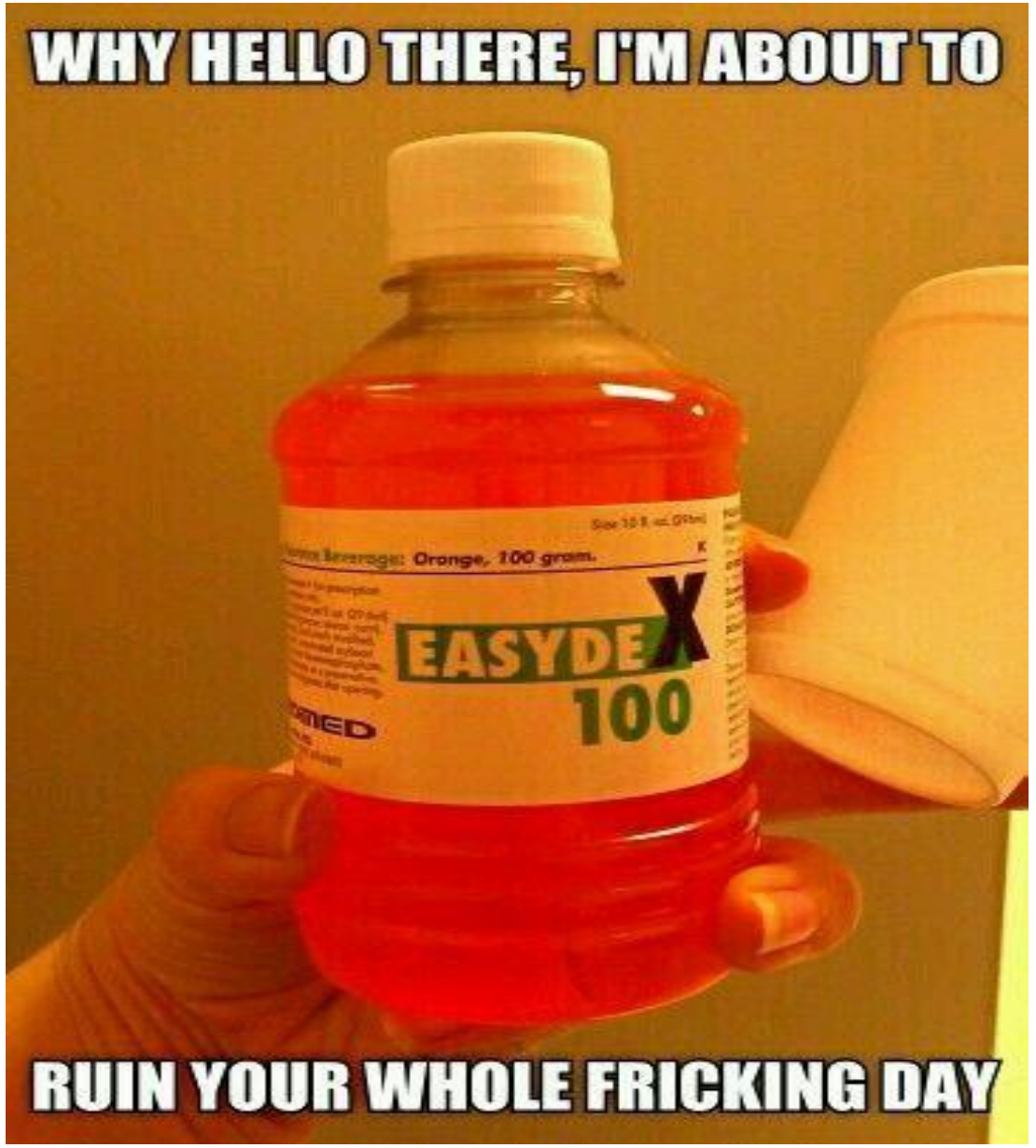
- Increased circulating placental hormones including growth hormone, corticotrophin-releasing hormone, human placental lactogen, prolactin, estrogen, progesterone.
- Facilitated lipolysis late in pg leads FFA exacerbate maternal insulin resistance by inhibiting maternal glucose uptake and increasing hepatic gluconeogenesis.

Relative insulin secretory deficit

- Maternal insulin secretion is unable to compensate for progressive rise in insulin resistance.
- ? Failure of beta cell mass expansion.
- Hyperlipidemia may cause lipotoxic beta cell injury.

Incidence/Prevalence

- 2019 International Diabetes Foundations: 1/6 live births worldwide.
- Varies depending on risk factors.
- Rising internationally secondary to increased incidence obesity in women of childbearing and age rising maternal age.
- Strongest risk factor: history of GDM (recurrence rate up to 84%)
- Ethnicity; S and E Asians, Hispanic, Black, Native Americans, Middle Easterners
  - Study 123,000 Women using ADA dx criteria: Filipinas (10.9%), Asians (10.2%), Hispanics (6.8%), non-Hispanic Whites (4.5%) Black Americans (4.4%) Ref 1.


WHY HELLO THERE, I'M ABOUT TO
Orange, 100 gram.
EASYDEX
100
RUIN YOUR WHOLE FRICKING DAY

Diagnosis

- 95% of Obgyn's use 50 g one-hour GTT as screening tool.
- Historic factors (family or personal history, previous adverse pg outcome, glycosuria, obesity) will miss one half.
- Additionally, low risk women are only 10% of pg women.
- No clear-cut evidence to support cutoff over another (130, 135, or 140) level C – ACOG.
- 2014 US Preventative Services Task Force recommended screen all at 24 wk and beyond.
- ACOG recommends early screening for
  - BMI over 25 (or 23 for Asian Americans) and either physical inactivity, first degree relative with DM, High-risk race/ethnicity, previous infant over 4000 g, previous gdm, htn (140/90 or on therapy), HDL < 35 mg/dl, T greater than 250 mg/dl, pcos, Hba2c > or = 5.7%, CVD history, or other (prepg bmi over 40 kg/m2, acanthosis nigricans.

Diagnosis

- ACOG recommends early screening for
  - BMI over 25 (or 23 for Asian Americans) and either physical inactivity, first degree relative with DM, High-risk race/ethnicity, previous infant over 4000 g, previous GDM, hypertension (140/90 or on therapy), HDL < 35 mg/dl, TG greater than 250 mg/dl, PCOS, Hba1c > or = 5.7%, CVD history, or other (prepregnancy BMI over 40 kg/m2, acanthosis nigricans).
  - No clear recommendations on when and if to repeat.

Diagnosis

- Carpenter Coustan criteria adopted as this increases diagnosis by 50% but these incremental dx had higher rates of perinatal complications.
- One abnormal on 3-hour GTT increased risk adverse perinatal outcomes.
- FBS 95 mg/dl
- 1 hour 180 mg/dl
- Two-hour 155 mg/dl
- Three-hour 140 mg/dl
- Alternatives one step approach 75 g , two-hr GTT endorsed by IADPSG and ADA (levels fbs 92, one hr 180, two hour 153)- would identify 18% of pregnant women in US. There is absence of clear evidence this improves outcomes.

Other Risk Factors

- Family history of type 2 diabetes in a first-degree relative or sibling with GDM.
- Increasing maternal age.
  - Maternal age 35-39 OR 1.8 (1.5-2.1, over 40 yoa 2.4 (1.9-3.1) Ref 2,
- Prepregnancy overweight- increased risk 3x (2.1-3.4 CI 95%) class 1 obesity and 4x (3.1-5.2) Class 2 compared to BMI < 30 kg/m2. Ref 3.
- Multiparity.
- Previous macrosomia.
- h/o perinatal complications.
- Maternal SGA or LGA.
- Low fiber high-glycemic load diets.
- Greater dietary fat and lower carb intake.
- Maternal pre- and early pregnancy hypertension.
- Ref 4.

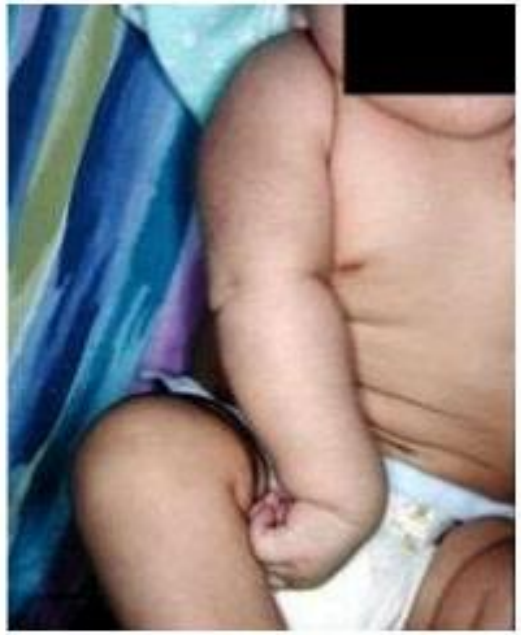
Neonatal Complications: Short Term

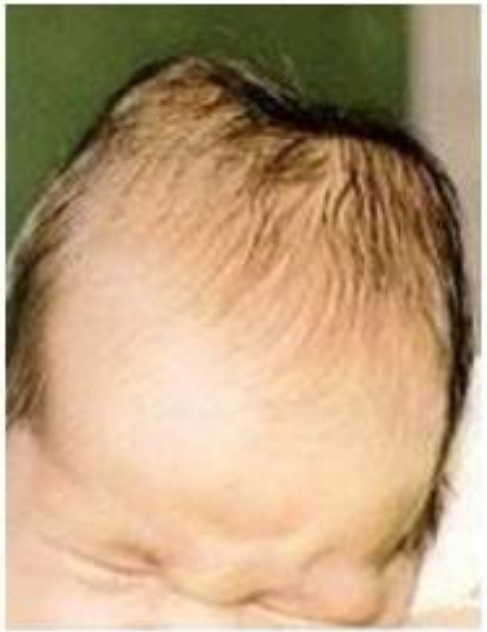
- HAPO study – maternal glucose levels associated linear with each of the levels in the two hr 75 g GTT. Ref 5.
  - LGA, birth weight >90%
  - Shoulder dystocia or birth injury
  - Cesarean delivery
  - Neonatal hypoglycemia, fetal hyperinsulinemia
- Systematic review 207,172- similar positive linear associations for maternal glycemia (GCT, 76 g GTT, or 100 g) **Ref. 6.**
  - Induction of labor.
  - Large for gestational age/macrosomia.
  - Shoulder dystocia

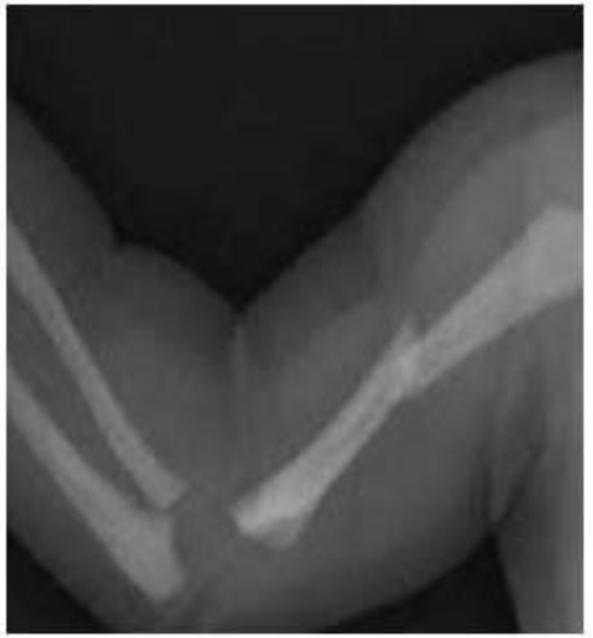
Neonatal Complications : Short Term

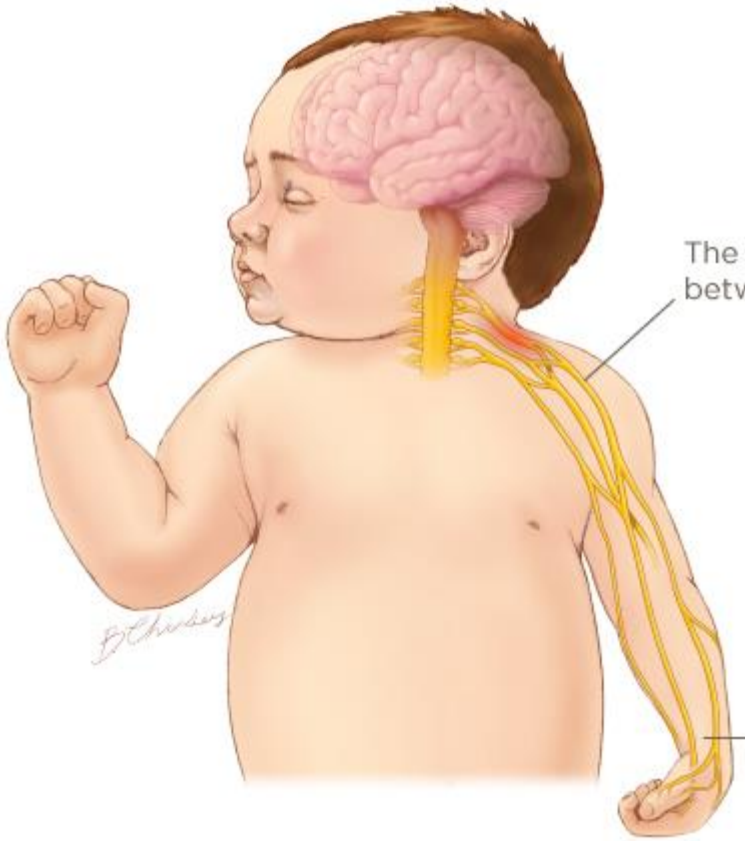
- Neonatal hyperglycemia, hyperbilirubinemia, shoulder dystocia, birth trauma.
- Increased risk still birth but may be confounded by glycemic control.
- Other studies- fetal exposure to maternal diabetes contributes to childhood and adult-onset obesity and diabetes independent of obesity and genetic predisposition.
- A note about shoulder dystocia.

Birth Defects due to Gestational Diabetes









The nerves are the connection between the brain and the muscles.

Symptoms

Babies and children with brachial plexus palsy may have:

- Weakness in the arm or hand
- Arm held against body and elbow straight
- Tightness, and decrease in feeling in the shoulder, arm, or hand.

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Neonatal Risks: Long Term

- Increased early onset CV disease.
- HAPO study Follow up Study (not confounded by treatment: 4832 children age 10-14: maternal hyperglycemia associated with impaired glucose and glucose tolerance, hba1c, and disposition index by age 14, independent of childhood BMI and fam history; also, higher frequencies childhood obesity and measures of adiposity. Ref 5.
- BUT--ACHOIS follow up studies did not demonstrate beneficial impact on childhood obesity and glucose tolerance at five to ten years of age in offspring who received treatment for maternal hyperglycemia. Ref 6.

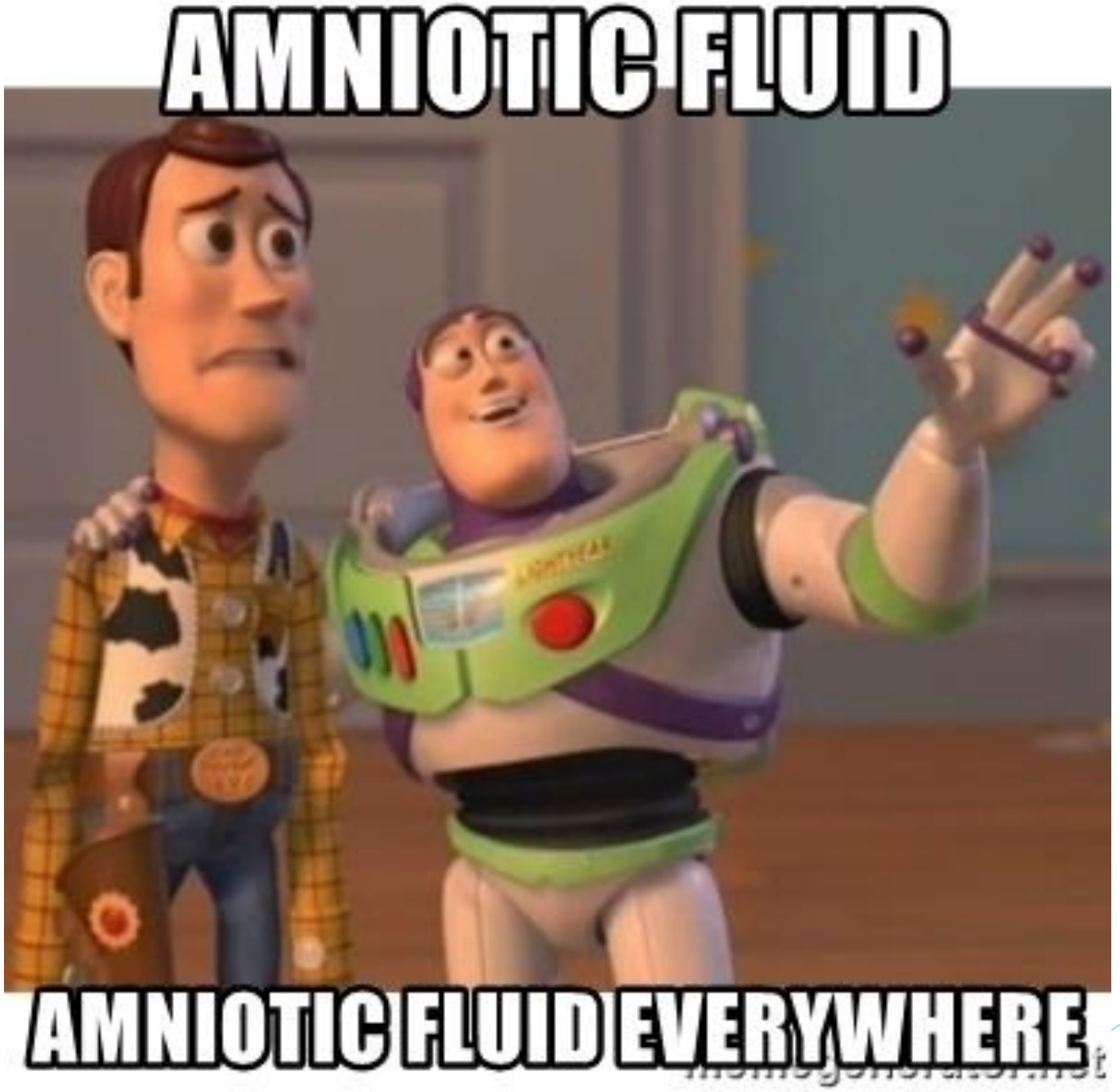
Maternal Complications: Short Term

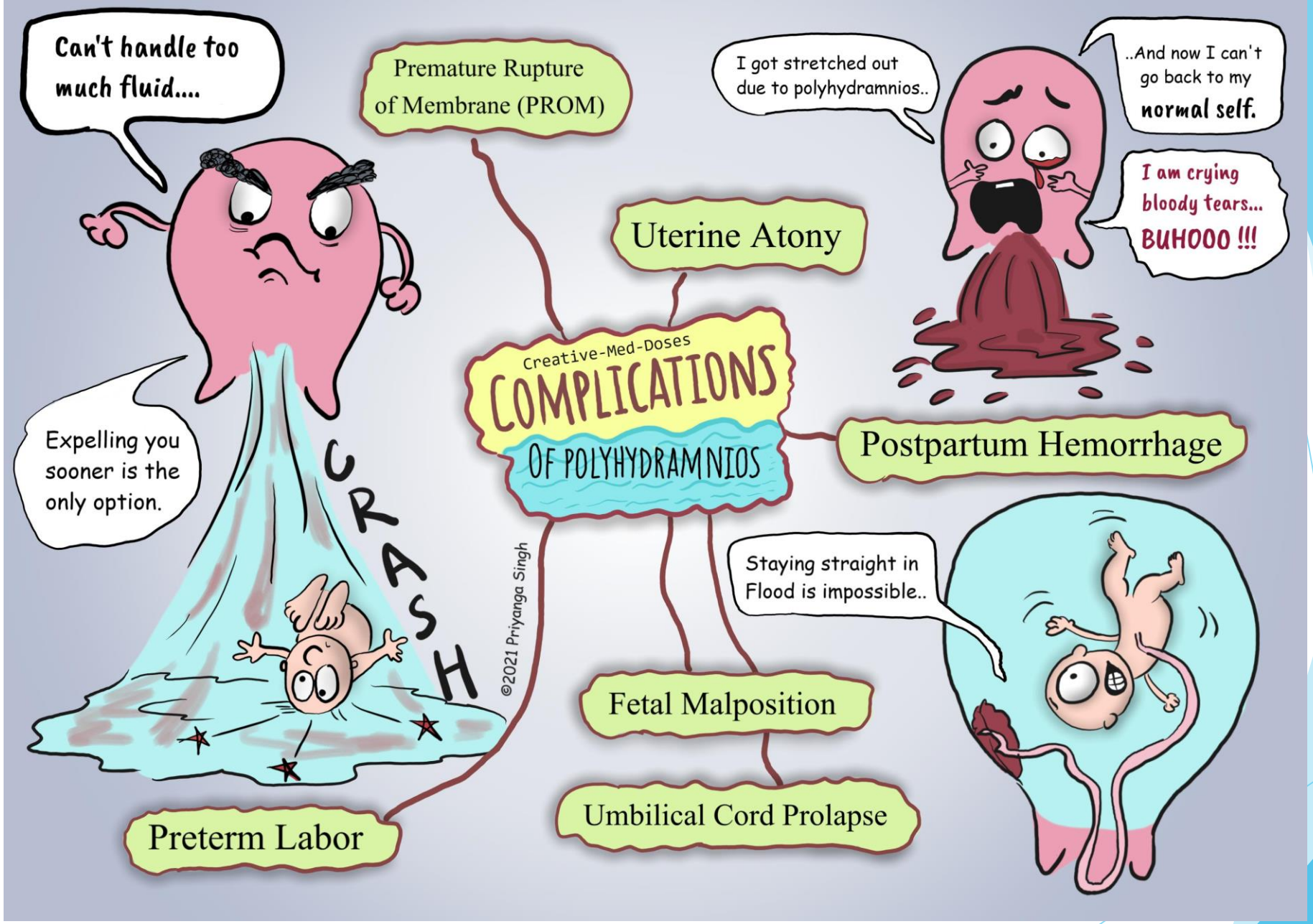
- OB interventions: Induction of labor, cesarean section, instrumental deliveries.
- Increased complications of delivery including perineal lacerations, uterine rupture. Ref 8.
- Increased risk in the HAPO and other trials of gestational hypertension and preeclampsia. Most likely that abnormalities in glucose metabolism affect trophoblast invasion leading to impaired placentation and greater risk for preeclampsia. Also likely through an inflammatory pathway.
- ACOG Bulletin:
  - Risk preeclampsia (9.8% vs 18% if FBS less than 115)
  - C-section (25% vs 17% if require meds vs 9.5% controls)
  - Increased risk lifelong DM- up too 70% within 22-28 years- influenced by race (60% Latin American within 5 years of pg)

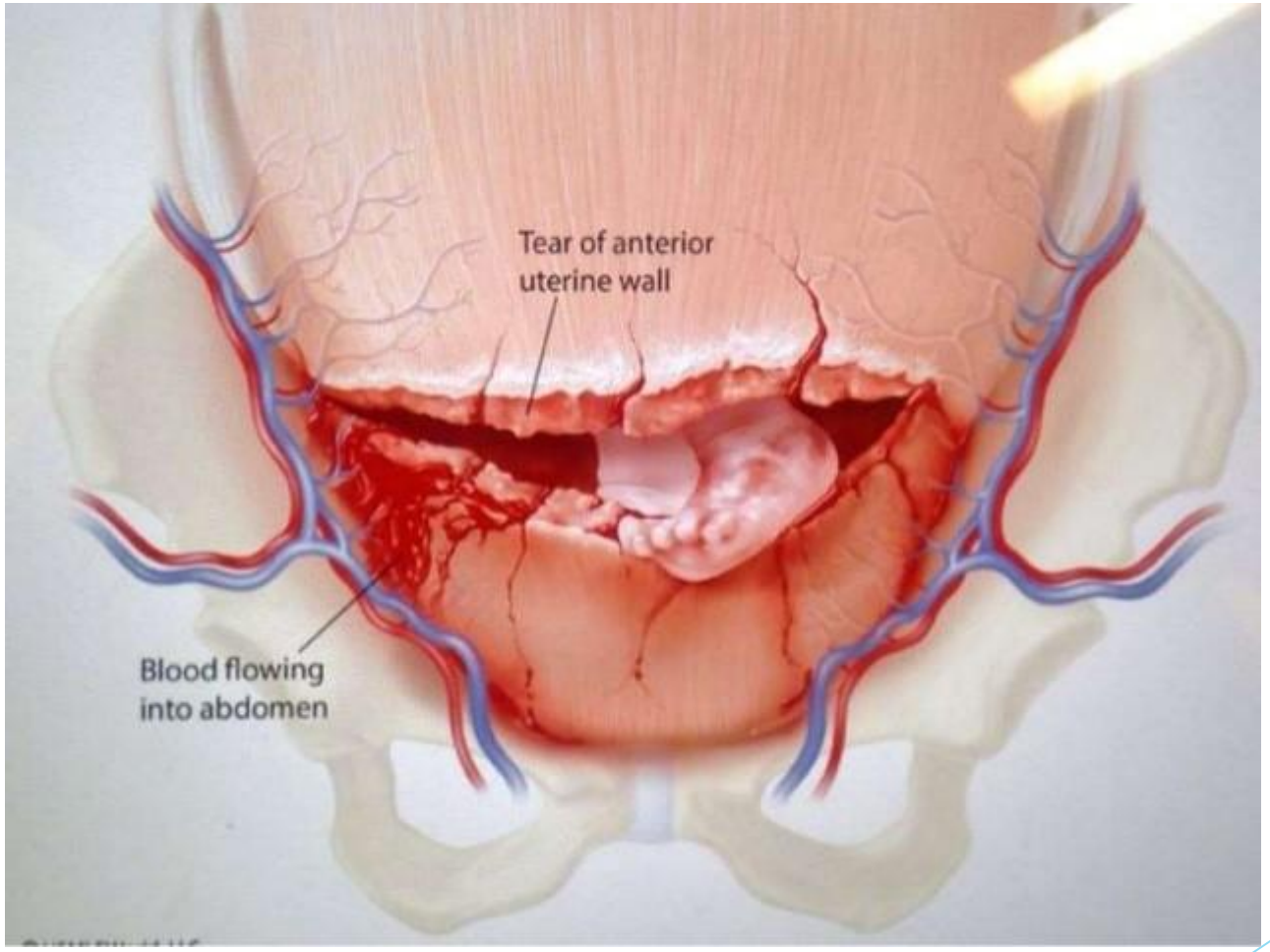
So, you say having a c-section is taking the easy way out? Is using the jaws of life the easy way to get out of a car?

Cesarean Delivery Risks

- Maternal death : 2.2 per 100,000 cesarean deliveries compared to 0.2 vaginal delivery.
- Risks hemorrhage, infection, injury adjacent organs, thromboembolism.
- Fetal injury- generally less than vaginal but include laceration, cephalohematoma, skull fracture, clavicular fracture, brachial plexopathy, facial nerve palsy
- Future pregnancy risk- previa, accreta, rupture.


AMNIOTIC FLUID
AMNIOTIC FLUID EVERYWHERE


Creative-Med-Doses
COMPLICATIONS
OF POLYHYDRAMNIOS
Premature Rupture of Membrane (PROM)
Uterine Atony
Postpartum Hemorrhage
Fetal Malposition
Umbilical Cord Prolapse
Preterm Labor
Can't handle too much fluid....
Expelling you sooner is the only option.
CRASH
I got stretched out due to polyhydramnios..
..And now I can't go back to my normal self.
I am crying bloody tears... BUHOOO !!!
Staying straight in Flood is impossible..
©2021 Priyanga Singh

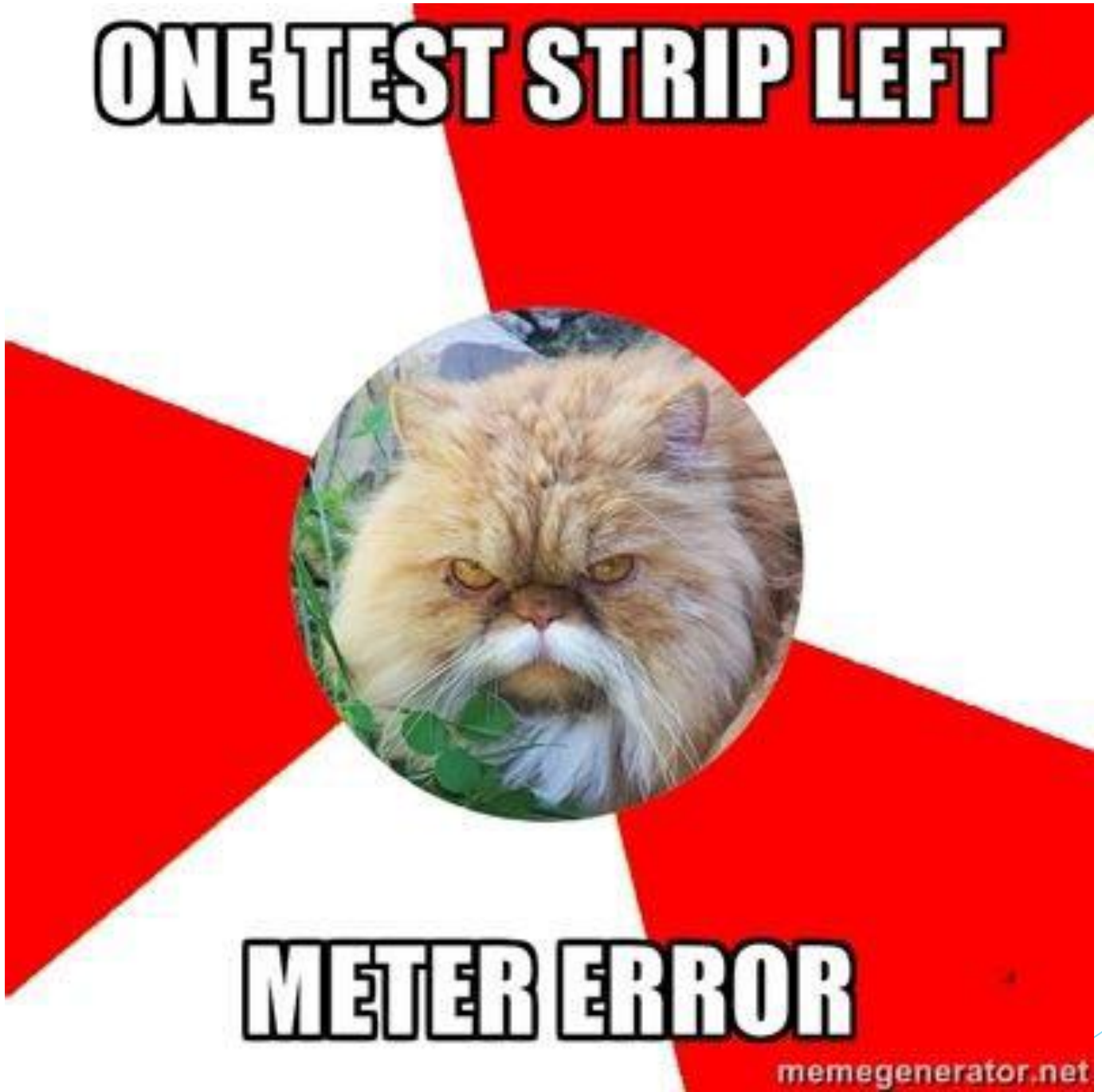

Tear of anterior
uterine wall
Blood flowing
into abdomen

Maternal Risks: Long Term

- Recurrence rates 30-84%.
- 20-fold greater lifetime risk type 2 DM.
- Large meta-analysis and review n 1,332,373 including 67,956 women with history of GDM- 10-fold increased risk type 2 DM, mostly within five years. Ref 9.
- Previous GDM associated with obesity, hypertension, dyslipidemia.
- Lifetime risk CVD 3x higher in women who develop type 2 dm and 1.5-fold higher with women without type 2 DM. Ref 10.
- 26% greater risk hypertension, 43 % greater risk MI/stroke. Ref 11,12.

Management

- Benefits of treatment
  - Randomized multicenter trial 958 women mild GDM in US
    - No differences primary composite outcomes (perinatal death, neonatal hypoglycemia, elevated umbilical cord C-peptide level, birth trauma).
    - Significant differences in secondary outcomes: fewer LGA infants, fewer birth wt over 4000 g, reduced neonatal fat mass, reduced rates cs, shoulder dystocia, hypertensive disorders.
    - Ref 13.
  - U.S. Preventive Services Task Force review
    - Benefits of reduced risks preeclampsia, shoulder dystocia, macrosomia.
    - Ref 14.


ONE TEST STRIP LEFT
METER ERROR
memegenerator.net

Management

- Monitoring- No ideal frequency!
- ACOG- 1- hour postprandial compared to preprandial- better glycemic control, lower incidence of LGA infants, lower rates of cesarean delivery for cephalopelvic dystocia.
- No clear evidence on 1 or 2 hour postprandial (peak is 90 minutes postprandial).
- OK to modify frequency of checks once controlled by diet/exercise.
- No clear evidence for optimum target.
  - ADA and ACOG recommend FBS below 95 mg/dl, postprandial one-hour less than 140, two-hour 120 mg.
- Initially reviewed weekly, then ok to decrease frequency.


STARTED MY NEW HEALTHY DIET TODAY
Breakfast is 2 almonds, I lick an apple for lunch and dinner is yelling at a picture of myself naked.

Management: Diet and Exercise

- Goals achieve normal blood glucose levels, prevent ketosis, provide adequate weight gain and contribute to appropriate fetal growth.
- ADA recommends consult with registered dietician.
- Caloric allotment:
  - 50-60% carbs will result in excessive weight gain and postprandial hyperglycemia.
  - 33-40% carbs but this may be associated with IUGR.
  - Generally complex carbohydrates recommended.
  - In practice three meals and 2-3 snacks per day.
- Exercise- less data- Recommended 30 minutes mod intensity aerobic five days per week.

Management: Medication

- Insulin:
  - First line according to ADA; ACOG ; SMFM either insulin or metformin.
  - Does not cross placenta!
  - Typically, 0.7-1.0 U/kg daily divided into long or intermediate acting and short acting.
  - Prefer lispro or aspart to regular (more rapid onset so can be right before meals.)
  - NPH usually but can use glargine and detemir.

Insulin Pumps

- No data to suggest they are more effective than conventional therapy.
- Higher costs not justified over the short duration of pregnancy.
- Has been described in case reports to be successful in some pregnant women.

Management: Oral Medications

Not approved by FDA for GDM

- **Metformin:** biguanide. Inhibits hepatic gluconeogenesis and glucose absorption and stimulates glucose uptake in peripheral tissues. Lack of long-term data on neonatal safety.
- Meta-analyses show conflicting data:
  - Women randomized to metformin versus insulin- minimal neonatal differences but higher rate preterm birth (RR 1.5) but lower rate gestational hypertension (0.53).; ref 15.
  - Ref 16: Metformin compared to insulin- no superiority for lga, macrosomia, neonatal hypoglycemia, cs. No difference preterm delivery.
- ACOG: 26-46% go on to require insulin.
- Glyburide: crosses placenta. Higher rates macrosomia and hypoglycemia compared to insulin with worse outcomes.

Society for Maternal Fetal Medicine- MFM and Medications

- Statement SMFM Statement: Pharmacological treatment of gestational diabetes May 2018 Ref 17.
- After ACOG recommendation endorsed insulin as preferred first line despite no new evidence.
- Neither insulin, glyburide or metformin is associated with birth defects- long term effects less known.
- ADA endorses insulin as first line therapy
- SMFM points out, multiple doses, less patient preferred.

SMFM

- Metformin compared to insulin less maternal weight gain, lower ga at delivery, less GH, less neonatal hypoglycemia, only 2% discontinue for GI side effects.
- Crosses placenta but some studies:
  - Children age 2 , similar body fat but more sq fat than intraabdominal fat; comparable neurodevelopmental scores.
  - Ref 18.

Management: Antepartum Testing

- Usually recommended for poor control or in the setting of medication requirements (implies poor control at one time).
- Extrapolated from stillbirth data on pregestational diabetes.
- Usually initiated at 32 weeks.
- No consensus if well controlled A1GDM.
- Commonly incorporate periodic AF assessment given the risks of polyhydramnios (PTL, abruption, maternal respiratory compromise, PPROM, malpresentation, etc.)

Management: Assessment of Fetal Weight

- Biometry near term reasonable.
- Caveat- only 22% of LGA infants by US were LGA at birth.
- Estimate up to 588 CS needed to prevent a single case of permanent brachial plexus palsy for EfW 4500 g, and up to 962 needed for 4000 g. Ref 20.
- ACOG: reasonable to offer elective cs for EFW over 4,500 g.


DUE DATE?
I'M COMING WHEN I SAY SO
FunnyBeing.com

Management Obstetric Delivery Timing

- Timing of delivery: delivery by 40.6 low risk GDM with diet; 39 to 39.6 GDM well controlled with treatment.
- **Controversies:**
  - GINEXMAL trial GDM only patient randomized to IOL at 38 wk vs expectant up to 41 wk: no difference cs rates (did not reach full samples size) but higher rate hyperbilirubinemia in induced group. Ref 19.
  - Several smaller trials reduction from 10% to 1.4% with IOL at 38-39 wk; One showed reductions CS IOD before 40 wk,
- **Poorly controlled:** no clear guidance about degree of control lacking tradeoffs between risks prematurity and ongoing risk stillbirth.
- Delivery between 37.0 and 386 usually, but 34.0 to 35.5 for those who fail in hospital attempts or abnormal antepartum testing.


DOES IT HURT? CAN I GET YOU A BEER OR SOMETHING?
WHY NO ONE USES MIDHUSBANDS.

Management in Labor and Delivery

- Intrapartum hyperglycemia increases risk of fetal acidemia and neonatal hypoglycemia.
- Exception- very poor antepartum maternal control since neonatal pancreatic hyperplasia and excessive in utero insulin secretion have occurred. They are much more likely to have severe and prolonged hypoglycemia.
- Active phase of labor has large energy requirements- many give IV glucose (separate IV line).
- No consensus: generally latent phase check every 4-6 hours, active stage every 1-2 hours.
- Insulin drip- goal glucose > 80 and < 125 mg/dl; acog 70-110. levels above 140 associated with increased risk neonatal hypoglycemia.
- More dangerous is neonatal hyperglycemia (increases fetal oxygen requirements) This is worsened by chronic poor maternal control as maternal hemoglobin will carry less oxygen, bind it more tightly and release it less well to placenta.

Guidelines Insulin Infusion

Standard insulin infusion chart

Plasma/Capillary Glucose (mg/dL)	Infusion Rate (U/hr)
<80	Insulin off
80-100	0.5*
101-140	1.0
141-180	1.5
181-220	2.0*
>220	2.5*

*Intravenous bolus of 2-5 units when the rate increases

Reprinted from *Creasy & Resnick's maternal fetal medicine: Principles and practice, 7th Edition* (p 1020), by TR Moore, P Catalano, S Hauguel-DeMouzon, Philadelphia, PA: Saunders/Elselvier. 2014, with permission

Long Term Maternal Follow Up

- Up to 1/3 of women with GDM will have DM or impaired glucose metabolism at postpartum screening.
- Up to 15-70% develop DM later in life.
- Recommendation is to screen 4-12 wk pp for all women with GDM.
- FBS lacks sensitivity.
- 75 g GTT can dx impaired fasting glucose and impaired glucose tolerance.
- Fifth International Workshop on Gestational Diabetes Mellitus recommends women with GDM undergo 76 g two-hour glucose tolerance test in pp period.
- All should follow up with primary care.
- ADA and ACOG recommend repeat testing every 1-3 years .
- Consider more frequent testing between pregnancies.

Long Term Maternal Risks and Follow Up

- Eggleston reviewed insurance claim data 2000 to 2013- only 24 % of women with GDM underwent screening within one year.
- Less than half of those with 2 hr gtt. Ref 20.
- ACOG 2017a- recommends either fasting glucose or 75-g, 2-hour GTT 4-12 wk pp.
- Increased risk CV metabolic syndrome- dyslipidemia, HTN, and abdominal obesity- 47,909 women- 5000 women with gdm were 2.6 times more likely to be hospitalized for CV morbidity. Ref 21.

Postpartum Testing

- There is increasing evidence that ordering the test when patients are still hospitalized after birth increases compliance to nearly 100%.
- 200 patients with GDM did PPD2 and four to twelve pp week 75 g GTT as well as Hba1c one year after delivery Ref 22.
  - No difference between day 2 and four-to-12-week pp gtt in predicting impaired glucose metabolism (a1c >= 5.7 and less than 6.5%) or DM (a1c >=6.5%) at one year,
  - One-year postpartum A1c was consistent with impaired glucose metabolism in 35% and DM in 4% of individuals tested.

Long term maternal follow up

The Diabetes Prevention Program demonstrated that lifestyle intervention and metformin therapy improved insulin sensitivity and preserved beta cell function in women with h/o GDM. Ref 23.


WHEN IS IT OKAY
TO ASK A WOMAN IF SHE IS PREGNANT?
NO NO NO NO NO NO NO NO NO

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