What are the most common causes of intrauterine growth restriction (IUGR)?

Intrinsic (fetal causes)
- Constitutional
- Genetic
- Toxic
- Infectious
- Teratogenetic
- Behavioral
- In-uterine constraint

Extrinsic (maternal/placental) causes
- Maternal age < 16 years or > 35 years
- Maternal illness
- Placental dysfunction
- Multiple gestation
- Demographic
What causes neonates to be large for gestational age?

- Infants with birth weight above the 90th percentile of the intrauterine growth chart are classified as *large for gestational age*.
- Maternal diabetes is the most common cause of fetal growth acceleration due to the induction of fetal hyperinsulinism during gestation.
- Other causes include fetal hydrops (edema), Beckwith-Wiedemann syndrome, transposition of the great vessels, and maternal obesity.
Is it clinically useful to classify small-for-gestational-age infants as symmetric or asymmetric?

- Infants who are symmetrically growth retarded have proportionally reduced size in weight, length, and head circumference. This type of growth retardation starts early in pregnancy, and it is often secondary to congenital infection, chromosomal abnormalities, and dysmorphic syndromes.

- Most IUGR babies, however, are asymmetrically growth retarded with the most severe growth reduction in weight, less severe length reduction, and relative head sparing.

- Asymmetric IUGR is caused by extrinsic factors that occur late in gestation such as pregnancy-induced hypertension. Infants with asymmetric IUGR have a better long-term growth and developmental outcome than symmetric IUGR infants.
What are the long-term risks of IUGR?

- **Development:** Because this group is heterogeneous, the outcome is dependent on perinatal events, the etiology of growth retardation, and the postnatal socioeconomic environment.

- In general, the asymmetric growth-retarded baby does not show significant differences in intelligence or neurologic sequelae but does demonstrate differences in school performance related to abnormalities in behavior and learning.
What are the long-term risks of IUGR?

- **Health effects:** An increased risk of hypertension is found in adolescents and young adults. Growth-retarded infants with a low ponderal index are at increased risk from syndrome X (non-insulin-dependent diabetes mellitus, hypertension, and hyperlipidemia) and death from cardiovascular disease by the age of 65 years (Barker hypothesis).

- **Growth:** Fetuses that experienced growth failure after 26 weeks' gestation (asymmetric growth retardation) exhibit a period of catch-up growth during the first 6 months of life. However, their ultimate stature is frequently less than an appropriate-for-gestational-age (AGA) baby.
What screening is available for fetal growth assessment?

- The best screening tool to assess fetal growth is fundal height, which is measured from the upper edge of the symphysis pubis to the top of the uterine fundus. Between 20 and 34 weeks' GA, fundal height measurements (in cm) approximate GA (in weeks).

- A discrepancy between measured and expected fundal height measurements of 3 cm or more is suggestive of fetal growth restriction.
what is the next step in determining the degree of impaired fetal growth?

- Fetal biometry should be performed to evaluate possible inappropriate fetal growth. Ultrasonographic measurements of fetal growth are as follows:
  - Biparietal diameter
  - HC
  - Abdominal circumference
  - Femur length
Abdominal circumference is the most sensitive single measurement. These individual growth parameters are commonly input into standard formulas to calculate the estimated fetal weight. When estimated fetal weight is <10th percentile, serial ultrasounds at regular intervals are necessary to monitor growth over time.
Is there a difference between growth retardation and growth restriction? Define fetal growth restriction.

- Because of the pejorative nature of the term *retardation*, the term *restriction* has been substituted. There is no difference between the terms. Intrauterine growth restriction (IUGR) is a deviation in the rate of growth of a fetus that is less than its genetically predetermined growth potential.

- *Symmetric IUGR* is characterized by equal reduction in head, abdominal, and skeletal dimensions. It is indicative of an insult during the period of most active cell division, as seen in chromosomal or congenital abnormalities.

- *Asymmetric IUGR* is distinguished by a reduction in abdominal circumference but sparing of head and skeletal growth. It most likely represents an insult during cell growth from extrinsic factors such as uteroplacental insufficiency or maternal vascular disease.
How do you differentiate a growth-restricted infant from a small-for-gestational-age (SGA) infant and a low-birth-weight (LBW) infant?

- The critical distinction is the fetal growth potential.
- An IUGR infant has failed to meet his or her own growth potential. The term intrauterine growth restriction is frequently used interchangeably, but incorrectly, with SGA.
- SGA refers to an infant whose birth weight is below a preset weight cutoff, typically the 10th percentile for GA, when compared with reference population norms.
- The LBW classification refers to any infant who weighs less than 2500 gm at birth, independent of GA. This category includes term (≥37 weeks' gestation) SGA infants as well as premature infants who may be SGA or of appropriate size relative to their GA.
KEY POINTS: EXTREMES OF FETAL GROWTH

- IUGR: failure to meet growth potential
- SGA: <10th percentile for GA based on population norms
- LBW: birth weight <2500 gm
- Prematurity: normal or altered growth at <37 weeks' GA
Name the major risk factors for fetal growth restriction

- Factors that affect fetal growth are typically categorized as fetal, placental, or maternal in origin. Common examples include the following:
  - Prior maternal history of fetal growth restriction
  - Maternal history of immunologic or collagen vascular disease
  - Maternal TORCH infection: Toxoplasmosis, other (syphilis and other viruses), rubella, cytomegalovirus, and herpes simplex virus
  - Maternal hypertension or preeclampsia
  - Genetic syndromes in the fetus: Trisomy 21, 18, or 13, Turner syndrome
  - Teratogens: Cigarette smoke, retin-A, warfarin, alcohol
  - Advanced maternal diabetes
  - Placental insufficiency
  - Placental infarction
  - Idiopathic factors
RISK FACTORS FOR INTRAUTERINE GROWTH RESTRICTION

Maternal

Placental

Fetal
### Maternal

<table>
<thead>
<tr>
<th>Poor or inadequate nutritional intake</th>
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<tbody>
<tr>
<td>Medical disease</td>
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<tr>
<td>Preeclampsia</td>
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<td>Chronic hypertension</td>
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<td>Collagen vascular disease</td>
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<tr>
<td>Diabetes mellitus with vascular disease</td>
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<tr>
<td>Thrombophilia (congenital or acquired)</td>
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<td>Asthma</td>
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<td>Cyanotic heart disease</td>
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<td>Genetic disorder</td>
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**Environment**

| High altitude                                 |
| Emotional or physical stress                  |

**Medications and drugs**

| Warfarin                                      |
| Anticonvulsants                               |
| Retin-A                                       |
| Cigarette smoking, Alcohol, Cocaine, Heroin   |
Placental

**Abnormal implantation**
- Previa Accreta

**Abnormal morphology**
- Small size
- Bilobed, battledore, or circumvallate
- Velamentous cord insertion

**Lesions**
- Chorioangioma
ta

**Abruptio placentae**

**Infarction**
- Secondary to maternal chronic disease
- Chronic abruption

**Infection**
- Chorionitis
- Chorioamnionitis
- Funisitis
Fetal

**Chromosomal abnormalities**
- Trisomy 13, 18, and 21
- Turner syndrome

**Genetic syndromes**
- Russell-Silver
- Cornelia de Lange

**Congenital malformations**
- Anencephaly
- Congenital heart defect
- Congenital diaphragmatic hernia
- Gastrochisis
- Omphalocele
- Renal abnormalities
- Multiple malformations

**Multiple gestation**
- Twin-twin transfusion syndrome

**Infection**
- TORCH infections: Toxoplasmosis, other (syphilis and other viruses), rubella, cytomegalovirus, and herpes simplex virus
Describe the "brain-sparing effect."

The brain-sparing effect observed in asymmetric IUGR refers to the fetal adaptive response to chronic hypoxia, in which the fetus preferentially redistributes its blood flow to the brain, myocardium, and adrenal glands.

Although still investigational, low middle cerebral artery pulsatility on Doppler ultrasound may provide direct evidence of brain sparing.
What is the ponderal index (PI)?

- The PI is a widely used measurement of the infant's relative thinness or fatness independent of race, gender, and GA:

\[
PI = \frac{\text{weight (gm)} \times 100}{(\text{length [cm]})^3}
\]

- Normal PI values range between 2.32 and 2.85. The PI is normal in symmetric IUGR, low in asymmetric IUGR, and high in the macrosomic fetus.
What is the initial work-up when fetal growth restriction is suspected?

- Perform fetal karyotyping.
- Obtain maternal serology (i.e., TORCH studies) for evidence of recent seroconversion and thrombophilia studies.
- Evaluate the mother for preeclampsia.
- Consider amniotic fluid viral DNA testing.
How should one follow up a fetus at risk for growth retardation?

- Once IUGR is suspected, fetal well-being should be closely monitored with serial antenatal monitoring tests such as the nonstress test and BPP.

- Qualitative assessment of the amniotic fluid level gives an estimate of the chronicity of the insult.

- The timing of delivery is based on fetal maturity, signs of fetal distress, and worsening maternal disease. Evaluation of placental Doppler blood flow may be helpful in this decision.

- Electronic fetal monitoring during labor is essential in the care of an IUGR fetus. Intrapartum fetal acid-base status is another indicator that can be used to confirm electronic fetal monitoring findings.
What role does Doppler ultrasonography have in the management of a growth-restricted fetus?

- In pregnancies at risk for IUGR, Doppler analysis is used to evaluate placental disease and fetal compromise and may improve fetal and neonatal outcomes.

- Normal umbilical arterial Doppler flow is reassuring and rarely associated with significant morbidity.

- Absence of end-diastolic flow in the umbilical artery is indicative of fetal hypoxia.

- Reversal of flow is suggestive of worsening fetal status and impending demise.

- Abnormalities in venous circulation (e.g., ductus venosus pulsatility) represent worsening circulatory compromise and may reflect a greater risk of imminent fetal demise than abnormalities in the arterial circulation.
What are the delivery implications for a growth-restricted fetus?

- The timing of delivery is determined by the GA and clinical status of the fetus.

- For an IUGR fetus at term or near term with documented pulmonary maturity, delivery is indicated if fetal distress is present, minimal fetal growth is observed over serial ultrasounds, or maternal status is worsening (e.g., hypertension).

- For an IUGR fetus <32 weeks' GA, optimal timing of delivery is still unresolved. If the indication for delivery is uncertain, the fetus should undergo continuous monitoring.

- The IUGR fetus is at increased risk of metabolic acidosis, hypoxia, and mortality during labor because of a reduced capability to withstand insults.