Large for gestational age (LGA)
Small for gestational age(SGA)
Hypoglycemia

SGA describes an infant whose birth wt is statistically less than the 10th centile or 2 SD below the mean BWt for gestational age

IUGR represents a deviation from expected growth patterns.

The ↓ fetal growth associated with IUGR is an adaptation to unfavorable I.U conditions that result in permanent alterations in metabolism , growth&development

IUGR most frequently occurs with a variety of maternal conditions that are associated with preterm delivery

Etiologies for IUGR & SGA at Birth

Maternal Factors **Age (young & advanced) Cigarette smoking Genetics (short stature, wt) Illnesses during pregnancy (PET, severe DM, ch.HT ,CTD) Infections (intrauterine(TORCHS) Lack of good ANC ,Oligohydramnios Poor nutrition &Race (Black)**

Fetal Factors **Chromosomal abnormality &nonchromosomal syndrome Congenital infections IEM &Multiple gestations**

Maternal Medications Antimetabolites (MTX) Heavy metals (Hg, Pb) Hydantoin Narcotics (morphine, methadone) Steroids (prednisone) Substance & illicit drug use (alcohol, cocaine) &Warfarin

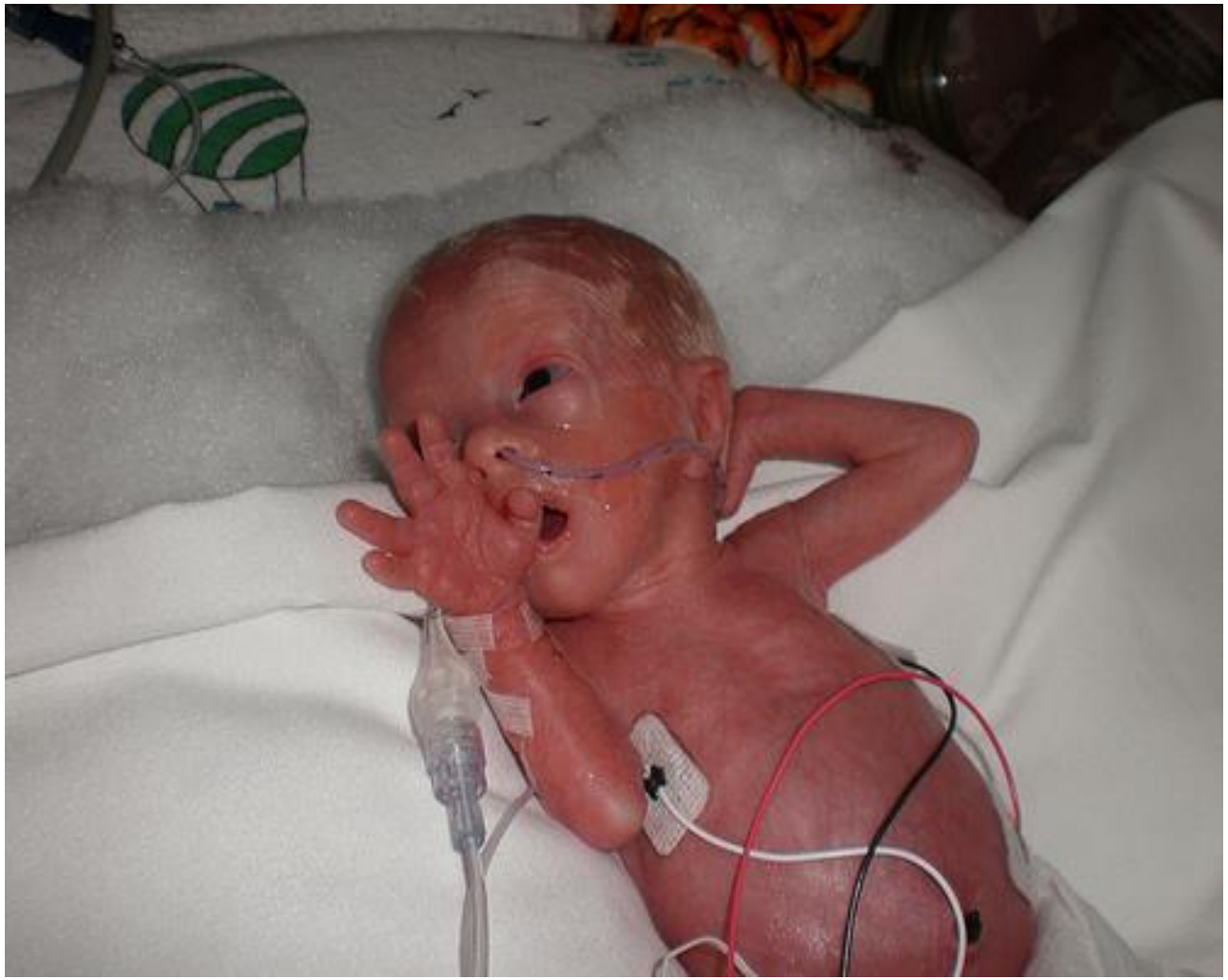
Placental &Uterine Abnormalities Abruptio placentae ,Abnormal implantation ,Abnormal placental vessels : Chorioangioma ,Circumvallate placenta, Fetal vessel thrombosis ,Ischemic villous necrosis

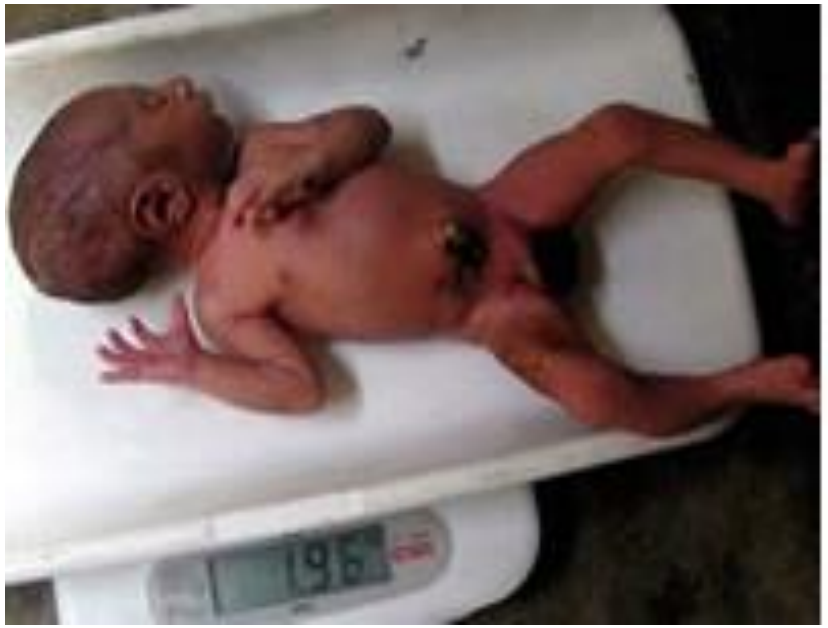
Multiple gestations ,True knots in umbilical cord &Villitis (congenital infection)

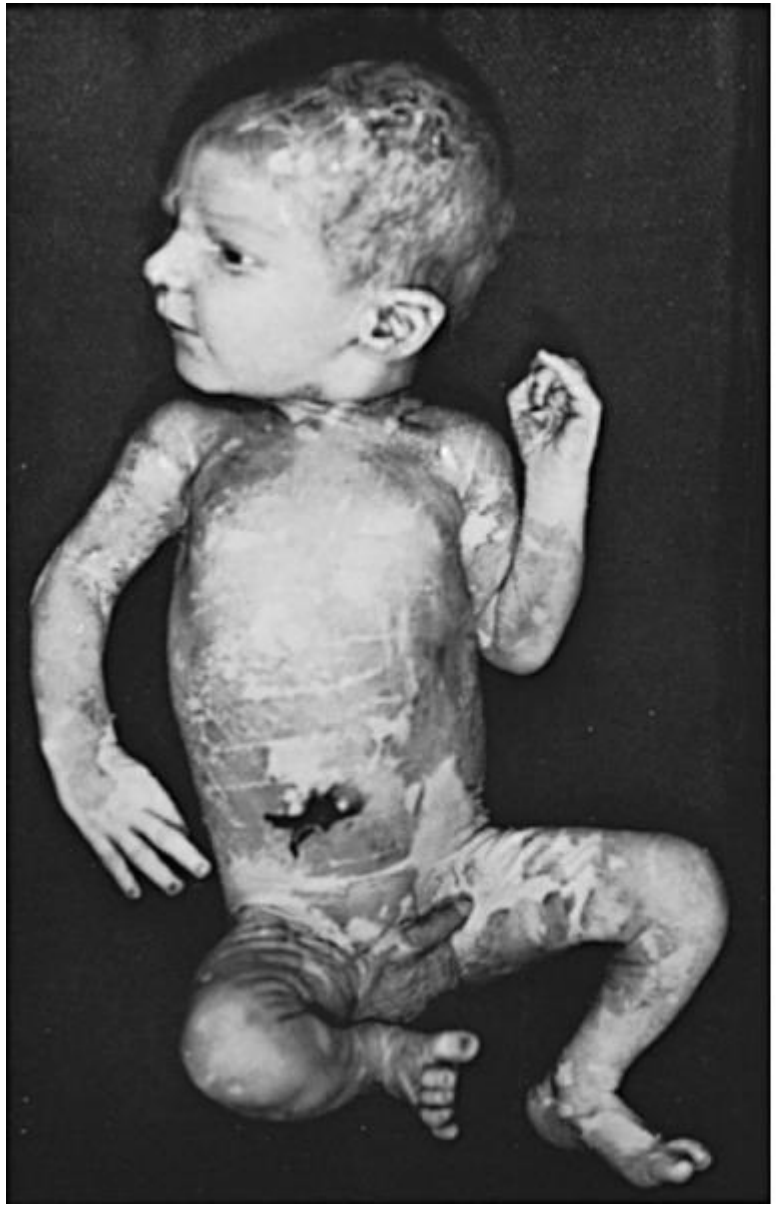
SGA appear smaller than normal with decreased s.c fat. More severely affected infants may present with a "wasted appearance" with asymmetric findings including larger heads for the size of the body (CNS sparing), widened AF , small abdomen, thin arms & legs, dry &redundant skin, ↓ M. mass, & thin (often meconium-stained) umbilical cord.

Gestational age is often difficult to assess when based on physical appearance & perceived advanced neurologic maturity.

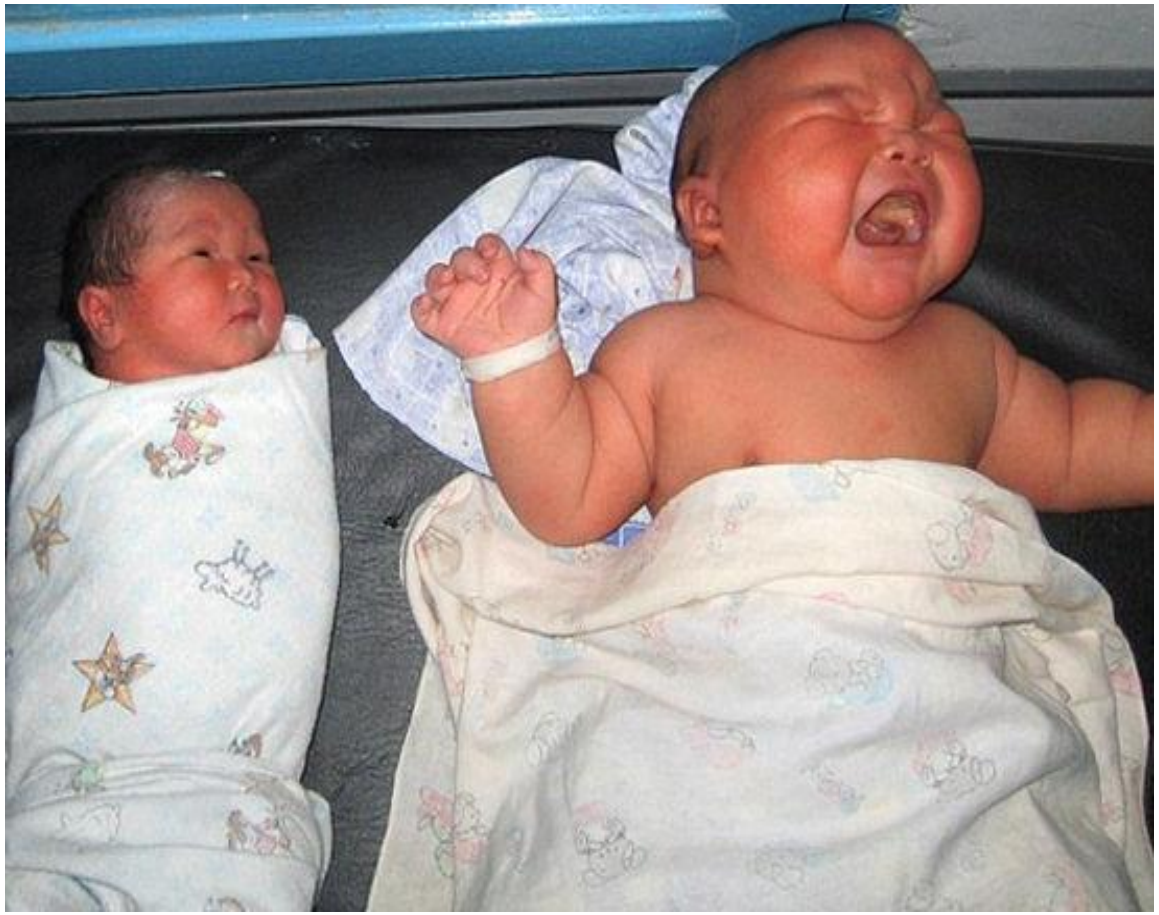
Physical examination should detail the presence of dysmorphic features, abnormal extremities, or gross anomalies that might suggest underlying congenital malformations, chromosomal defects, or exposure to teratogens







Infant with IUGR as a result of placental insufficiency. Note the long, thin appearance with peeling, parchment-like dry skin, alert expression, meconium staining of the skin, & long nails



Problems of IUGR (SGA) Infants

PROBLEM	PATHOGENESIS
Intrauterine fetal demise	Hypoxia, acidosis, infection, lethal anomaly
Perinatal asphyxia	↓ Uteroplacental perfusion during labor ± chronic fetal hypoxia-acidosis; meconium aspiration syndrome
Hypoglycemia	↓ Tissue glycogen stores, ↓ gluconeogenesis, hyperinsulinism, ↑ glucose needs of hypoxia, hypothermia, large brain
Polycythemia-hyperviscosity	Fetal hypoxia with ↑ erythropoietin production
↓O_2 Consumption/hypothermia	Hypoxia, hypoglycemia, starvation effect, poor subcutaneous fat stores
Dysmorphology	Syndrome anomalads, chromosomal-genetic disorders, oligohydramnios-induced deformation, TORCH infection

Infants with **severe IUGR or SGA**, esp. in conjunction with fetal distress, may have problems at birth that include resp. acidosis, metabolic acidosis, asphyxia, hypoxemia, hypotension, hypoglycemia, polycythemia, meconium aspiration syndrome, & PPHN

Management of IUGR & SGA infants is usually symptomatic & supportive

MR of infants severely affected are 5 - 20 times the MR of infants who are appropriate for gestational age

Infants born at a weight > the 90th centile for their age are considered large for gestational age (LGA). Among the risks associated with being LGA are all the risks of the infant of a diabetic mother & risks associated with postmaturity

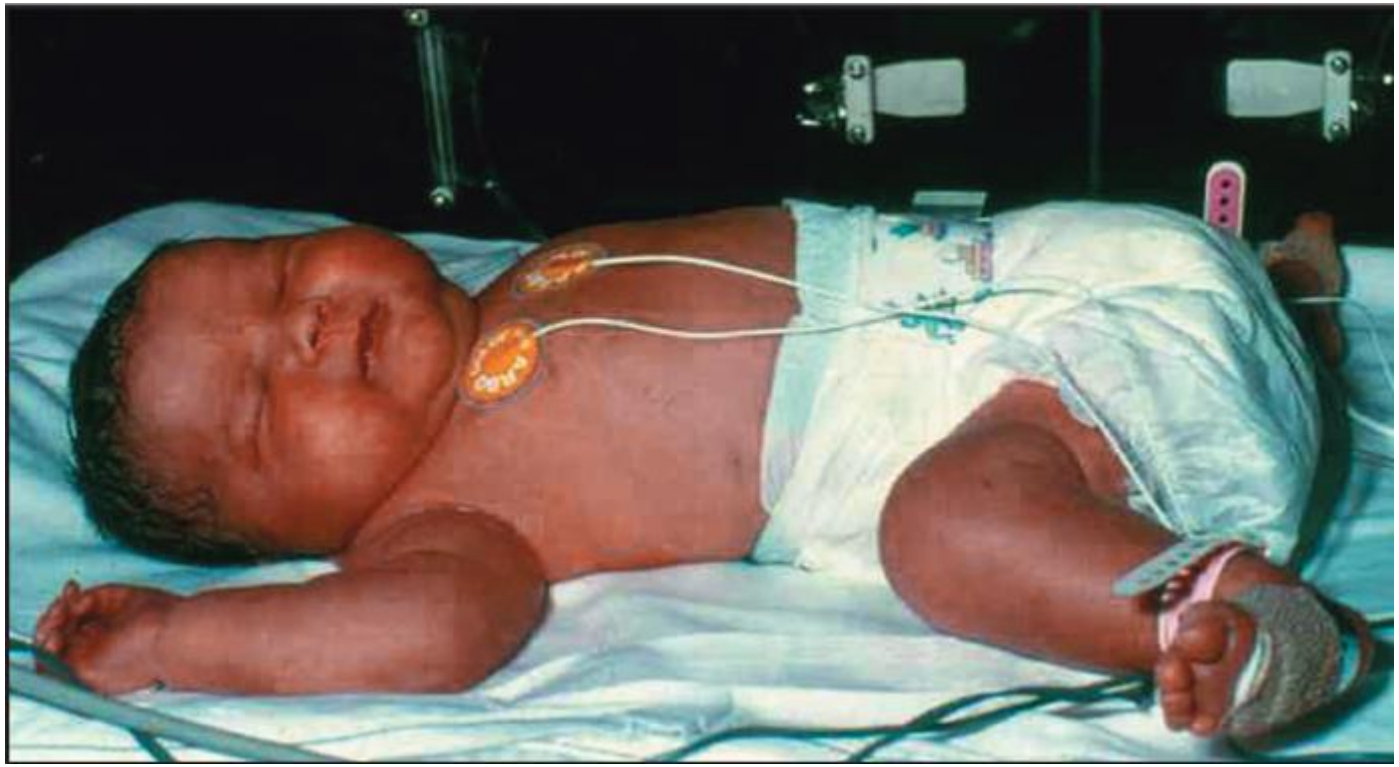
The problems associated with being LGA are:

1- Birth asphyxia from a difficult delivery

2-Birth trauma, especially from shoulder dystocia at delivery (difficulty delivering the shoulders from impaction behind maternal symphysis pubis)

3-Hypoglycemia due to hyperinsulinism

4-Polycythemia.



Infant of a diabetic mother showing macrosomia & plethora. Born vaginally at 36 /52 gestation, she weighed 5.5 kg & suffered a right-sided brachial plexus injury.

Fetal problems associated with maternal diabetes

***Congenital malformations*.** there is a 6% risk , a 3 fold increase. The range of anomalies is similar to that for the general population, apart from an ↑ incidence of cardiac malformations, sacral agenesis (caudal regression syndrome) & hypoplastic left colon.
Studies show that good diabetic control periconceptionally ↓ the risk of congenital malformations.

(IUGR). **There is a 3 fold increase in growth restriction in mothers with long-standing microvascular disease.**

Macrosomia **. Maternal hyperglycemia causes fetal hyperglycemia as glucose crosses the placenta. As insulin does not cross the placenta, the fetus responds with ↑ secretion of insulin which promotes growth by ↑ both cell no.& size.**
~ 25% of such infants have a birth wt >4 kg compared with 8% of non-diabetics.

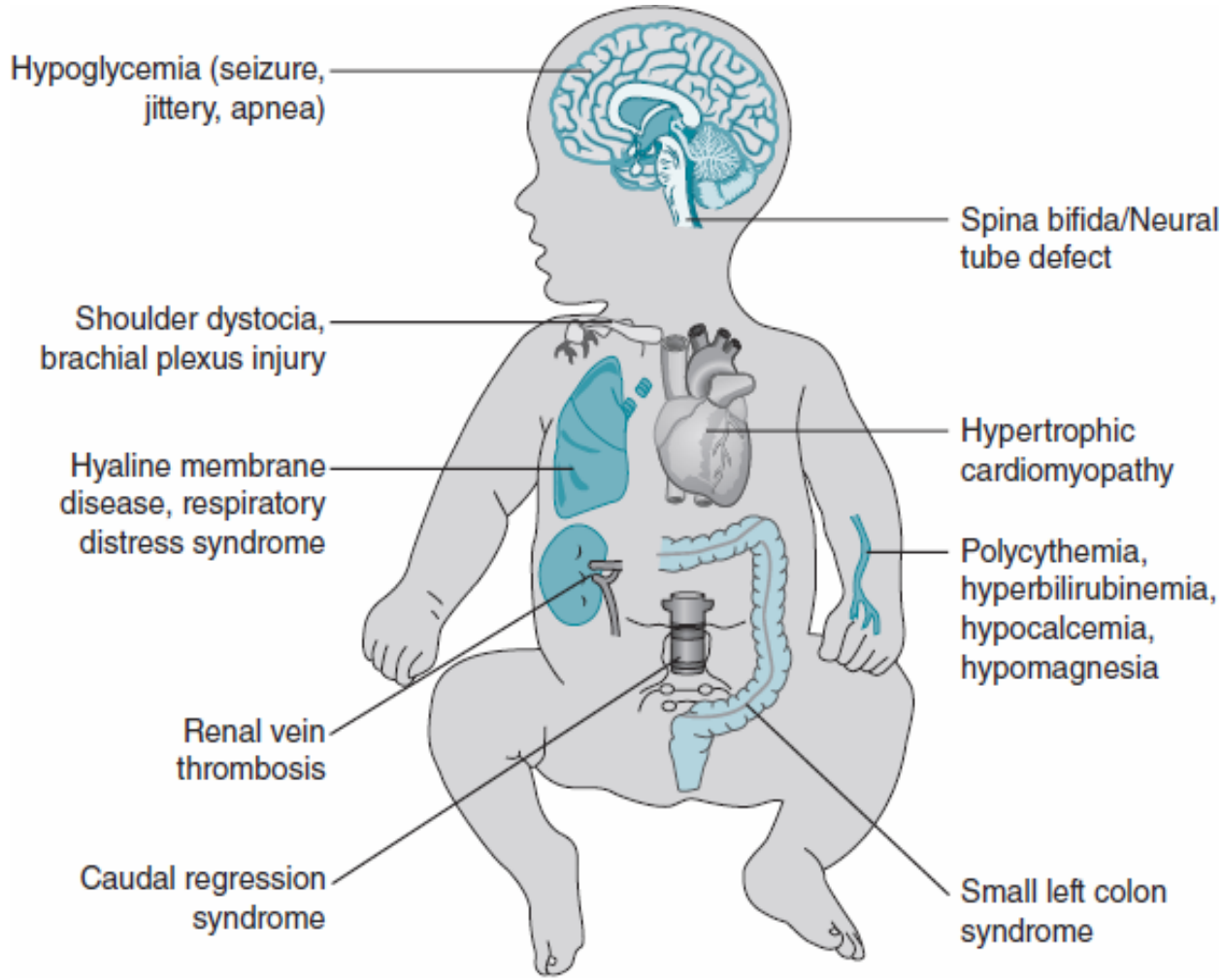
Neonatal problems include:

Hypoglycemia..

(RDS). More common as lung maturation is delayed.

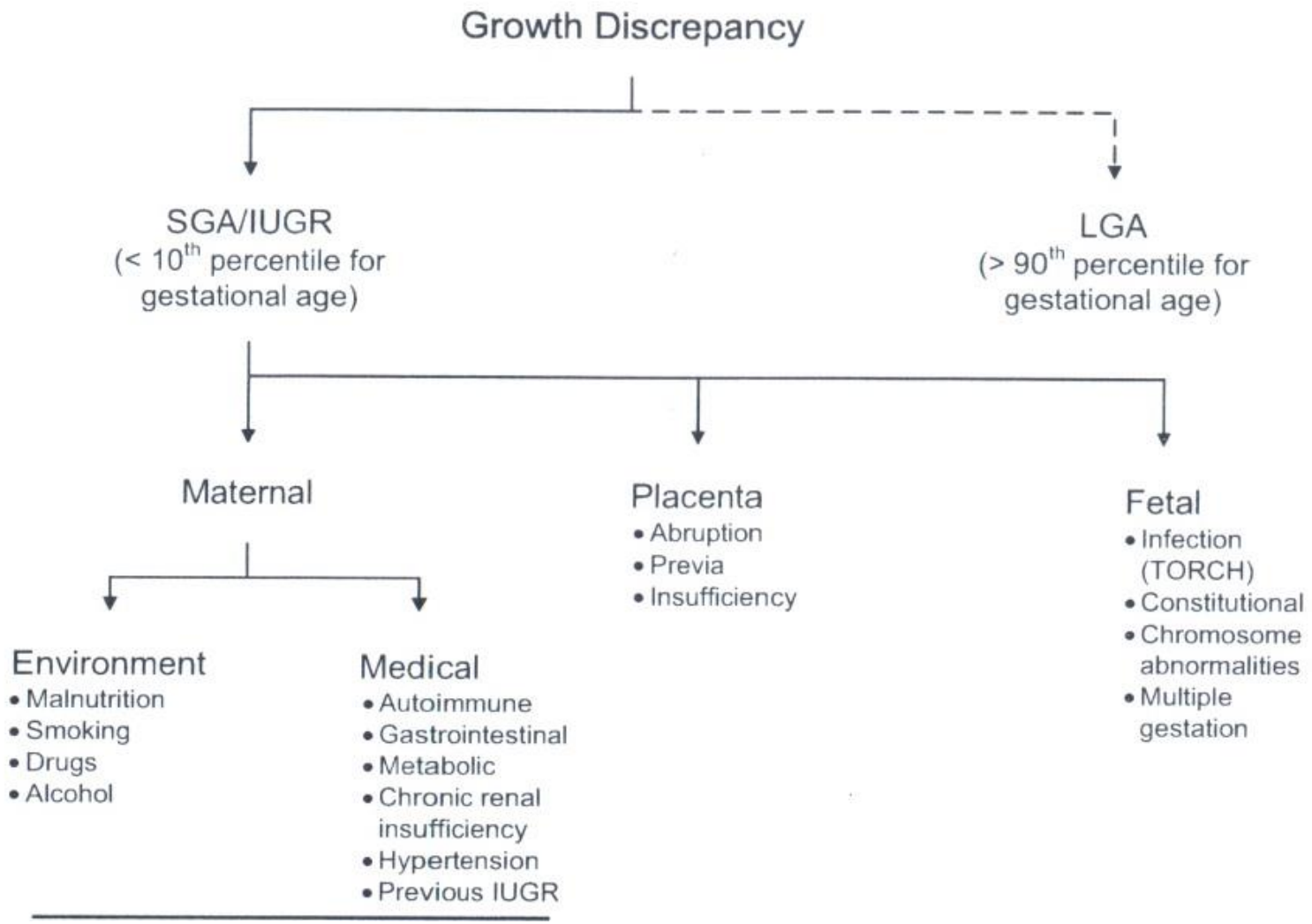
Hypertrophic CMP **. Hypertrophy of the cardiac septum occurs in some infants. It regresses over several wks but may cause HF from ↓ LV function**.

Polycythemia (venous hematocrit >0.65). Makes the infant look plethoric.
Treatment with partial exchange transfusion to reduce the hemocrit & normalise viscosity may be required



Source: E.C. Toy, M.D. Hormann, R.J. Yetman, M.C. McNeese, S.L. Lahoti, M.J. Sanders, A.M. Geltemeyer: Case Files®: Pediatrics, 5th Edition, www.mhmedical.com

GROWTH DISCREPANCY: Small for Gestational Age (Intrauterine Growth Restriction)



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Hypoglycemia:

BG levels decline after birth until 1–3 hr of age, when levels spontaneously ↑in normal infants.

In healthy term infants, RBG values are rarely <35 mg/dL between 1 -3 hr of life, <40 mg/dL from 3 - 24 hr, & <45 mg/dL (2.5 mmol/L) after 24 hr.

Both premature & term infants are at risk for serious neurodevelopmental deficits from equally low glucose levels.

This risk is related to the depth & duration of the hypoglycemia

Physiology

- Glucose provides 60-70% of energy to fetus and newborn.
- Fetal glucose is approximately 2/3 of maternal levels.(Trans placental facilitated diffusion)

<u>Why prone to develop hypoglycemia:-</u>

1. Umblical cord cutting at birth.
2. Inadequate storage of glycogen.
3. Immature adaptive mechanisms.
4. Prone to long term neurological damage.

Hypoglycemia is likely to occur in the first 24 hrs of life in babies who had **IUGR, who are preterm, born to mothers with DM , are LGA , hypothermic, polycythemic or ill for any reason**. Growth-restricted & preterm infants have poor glycogen stores, whereas the infants of a DM mother have sufficient glycogen stores, but hyperplasia of the islet cells in the pancreas causes high insulin levels

The incidence of symptomatic hypoglycemia is highest in SGA infants . The incidence of symptomatic hypoglycemia probably varies between 1 -3 / 1,000 live births & affects ~ 5–15% of growth-restricted infants.

The onset of symptoms varies from a few hrs to a wk after birth.

Symptoms include:

jitteriness or tremors, apathy, episodes of cyanosis, convulsions, intermittent apneic spells or tachypnea, weak or high-pitched cry, limpness or lethargy, difficulty feeding, & eye rolling. Episodes of sweating, sudden pallor, hypothermia, & cardiac arrest & failure also occur.

Frequently, a clustering of episodic symptoms may be noted.

Because these CF may result from various causes, so measurement of blood glucose levels is important ,whether they disappear with the administration of sufficient glucose , ***if they do not, other diagnoses must be considered.***

When symptoms other than seizures are present, an i.v (2 mL/kg) of 10% glucose is effective in elevating the blood glucose conc..

In the presence of convulsions, 4 mL/kg of 10% glucose as a bolus injection is indicated.

Then , a glucose infusion should be given at 8 mg/kg/min. If hypoglycemia recurs, the infusion rate & conc. should be increased until 15–20% glucose is used. If an i.v infusions of 20% glucose are inadequate to eliminate symptoms & maintain BG , glucagon or hydrocortisone can be given. if no response hyperinsulinemia is probably present & diazoxide should be administered. If the diazoxide is unsuccessful, octreotide may be useful;

infants with severe persistent hyperinsulinemic hypoglycemia may eventually need to undergo subtotal pancreatectomy .

The serum glucose level should be measured every 2 hr after initiating therapy until several determinations are >40 mg/dL. Subsequently, every 4–6 hr & the treatment gradually reduced & finally discontinued when BG value has been in the normal range & the baby asymptomatic for 24–48 hr. Treatment is usually necessary for a few days to a wk, rarely for several wks.

Infants at increased risk for hypoglycemia should have their BG measured within 1 hr of birth, every 1–2 hr for the 1st 6–8 hr, & then every 4–6 hr until 24 hr of life.

Normoglycemic high-risk infants feeding started at 1–3 hr of age & continued at 2–3 hr intervals for 24–48 hr.

HYPOCALCEMIA

- DEFINITION:
- **Hypocalcemia** is defined as total serum calcium of less than **7** mg/dL (1.75 mmol/L) or ionized calcium less than **4** mg/dL (1 mmol/L)
- In very low BW infants the ionized calcium levels of 0.8 to 1mmol/L are common & not usually associated with clinical symptoms

TYPES OF NEONATAL HYPOCALCEMIA

The early onset hypocalcemia:

presents within 72 h requires treatment with Ca supplementation for at least 72 hr.

late onset hypocalcemia:

usually presents after 7 days & requires longer term therapy.

CAUSESOF EARLY ONSET HYPOCALCEMIA

- Prematurity
- Preeclampsia
- Infant of Diabetic mother
- Peri-natal stress/ asphyxia
- Maternal intake of anticonvulsants (phenobarbitone, phenytoin sodium)
- Maternal hyperparathyroidism
- Iatrogenic (alkalosis, use of blood products, diuretics, phototherapy, lipid infusions etc

CLINICAL FEATURES

- Asymptomatic
- Symptomatic:

a) Neuromuscular irritability , Myoclonic jerks

Jitteriness, Exaggerated startle Seizures

b)Cardiac involvement :Tachycardia, prolonged QT Interval, decreased contractility,

c)Other symptoms like

apnea, cyanosis,tachypnea,laryngospasm are noted

Diagnosis

- Lab. : measuring total or ionized serum Ca+2
- Ionized calcium is preferred mode for measuring hypocalcemia
- ECG: QoTc>0.22 seconds or QTc>0.45 sec
- QoT is measured from origin of q to origin of t wave
- QT is measured from origin of q wave to end of t wave

Management of EOH

Hypocalcemia
Total serum Cal <7 mg/dl

Asymptomatic
80 mg/kg/day for 48 hrs
(8 mL/kg/day of 10% calcium gluconate)
⇩
Taper to 40 mg/kg/day for one day
Then stop

Symptomatic
Bolus of 2 mL/kg calcium gluconate 1:1 diluted with 5 % dextrose over 10 minutes under cardiac monitoring
⇩
Followed by continuous infusion 80 mg/kg/day for 48 hrs
(8 mL/kg/day of 10% calcium gluconate)
Document normal calcium at 48 hrs
⇩
Then taper to 40 mg/kg/day for one day
Then stop

Prophylactic

Preterm< 32 wk, sick IDM,severe asphyxia

40 mg/kg/day for 3 days

(4ml/kg/day of 10% calcium gluconate)

IV or oral if can tolerate per oral

- *Treatment is for 72 hrs*
- *Continuous infusion is better than bolus*
- *Symptomatic babies treatment is 48 hrs continuous infusion*

In case the hypocalcemia does not correct with the above by 72 hrs then investigate for causes of late hypocalcemia.- Refer Table 2

Side effects of calcium:

- Bradycardia
- Arrythmias
- Skin & subcutaneous tissue necrosis may occur due to extravasation
- Hepatic necrosis may occur if tip of UVC lies in branch of portal vein

LATE ONSET NEONATAL HYPOCALCEMIA

- presents at the end of the 1st wk of life. It is usually symptomatic in the form of neonatal tetany or seizures.
- This is usually caused by high phosphate intake (iatrogenic).

CAUSES OF LATE ONSET HYPOCALCEMIA

- Increased phosphate load
- Cow milk, renal insufficiency
- Hypomagnesemia
- Vitamin D deficiency
- Maternal vitamin D deficiency
- Malabsorption
- Renal insufficiency
- Hepato-biliary disease
- PTH resistance
- Transient neonatal pseudo-hypoparathyroidism

- **Hypoparathyroidism**
- Primary

  Hypoplasia, aplasia of parathyroid glands - (Di George's syndrome), CATCH 22 syndrome ,activating mutations of calcium sensing receptor
- Secondary

  Maternal hyperparathyroidism

  Metabolic Syndromes

  Kenny-caffey syndrome

  Long-chain fatty A . acyl CoA dehydrogenase deficiency

  Kearns-sayre syndrome

- **Iatrogenic**
- Citrated blood products, Lipid infusions, Bicarbonate therapy
- Diuretics, Glucocorticosteriods Phosphate therapy ,
- Alkalosis
- Phototherapy ??

Table 3 Investigations required in infants with persistent / late onset hypocalcemia

Investigations required			
	First line	Second line	Others
	Serum phosphate	Serum magnesium	CT brain for calcification
	Serum alkaline phosphatase (SAP)	Serum parathormone levels (PTH)	Echocardiography
	Liver function tests	Urine calcium creatinine ratio	Vitamin D levels (1,25 D3)
	Renal function tests	Maternal calcium, phosphate, and alkaline phosphatase	Hearing evaluation
	X ray chest/ wrist		Serum cortisol
	Arterial pH		Thyroid function tests
S No	*Disorder causing hypocalcaemia*	*Findings*	
1	Hypoparathyroidism	High : Phosphate	
		Low : SAP, PTH, 1,25 D3	
2	Pseudo Hypoparathyroidim	High : SAP, PTH, Phosphate	
		Low : 1,25 D3	
3	Chronic renal failure	High : phosphate, SAP, PTH, pH (acidotic), deranged RFT	
		Low : 1,25 D3	
4	Hypomagnesemia	High : PTH	
		Low : Phosphate, Mg,1,25 D3	
5	VDDR1	High : SAP, PTH	
		Low : Phosphate, 1,25 D3	
6	VDDR II	High : SAP, 1, 25 D3, PTH	
		Low : Phosphate	

(VDDR: vitamin D dependent rickets)

Learning Objectives:

1-Definitions LGA SGA Hypocalcemia ,Hypoglycemia IUGR
2- Identify the Causes & risk factors for these problems
3-What are the Problems encountered
4- Describe clinical presentations of these problems
5-Outline management.
6-Conduct an ongoing program to monitor the progress of such children.
7-Appropriately utilize hospitalization, consultation with other health professionals & community resources