— FOGSI FOCUS —

THE HEALTHY GENERATION X

FOGSI Perinatology Committee
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PREGNANCY IN HIGH RISK PATIENT
Minimal access
Maximal care

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President's message for FOGSI FOCUS

Dear Fogsians,

During an exceptional tenure as FOGSI President with FOGSI 2015 team, we had most outstanding events in all corners of India. We also had PCPNDT and ART proposed bills handled well at Government level. Skill, Knowledge and Enhancement has been our main focus, with great fellowship.

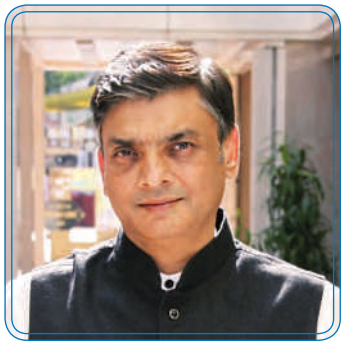
It is truly encouraging to write few words on **FOGSI FOCUS – The Healthy Generation X** jointly brought to reality by Dr. Reena Wani and Dr. Uday Thanawala. They had organized a unique event on 14th June for Obstetricians and Pediatricians with NMOGS on perinatal issues. A joint venture – having a scientific discussion with neonatologists as partners; which they always are! This Perinatology Workshop is being replicated in other societies as well. The focus of these meets and this Fogsi Focus is to deliver a healthy baby.

My theme for the Presidential year 2015 included Pregnancy in High Risk Mothers, hence, I am especially delighted by the coverage of maternal and neonatal health in this issue with inputs from experts in the field. A lot of issues related to perinatal care receive negligible importance by Gynaecologists and Obstetricians plus Family Practitioners.

A few committed workers like Dr. Reena Wani, Dr. Uday Thanawala, Dr. Sujata Misra, Dr. Karthik Bhagat, Dr. Saurabh Dani, and others in FOGSI have really worked hard to put their concern and thoughts, backed by latest scientific evidence in a well formed book which will be useful for all FOGSI members in their clinical practice.

We wish this FOGSI FOCUS a great success by truly enlightening all members to actively play their role in this subject on clarifying myths and focus on having healthy mothers and healthy babies.

Best regards,
Dr. Prakash Trivedi
President FOGSI 2015



Vice President's message
It starts with a healthy pregnancy

This FOGSI FOCUS focuses on delivering a healthy neonate – Focus on Gen X.

Fetal origin of adult disease is a reality- if the fetus is exposed to harsh or unfavorable conditions inutero – like placental insufficiency, IUGR, not only can it have immediate complications but could be the cause of disorders in adult life.

This FOGSI FOCUS is an attempt to address issues which we Obstetricians can try and improve the antenatal, intranatal and immediate postnatal care, so that the generation next is a healthy one.

Today, every expectant couple comes to an Obstetrician with the ultimate aim of having a healthy neonate. Born healthy and one which grows up to be a healthy individual. We monitor the pregnancy so as to keep the mother and the baby safe from disorders, which can jeopardize the health of either of them. The way we manage (screen and treat) disorders of pregnancy and delivery, has an impact on the future life of the neonate. Cardiovascular disorders and diabetes can have their origins inutero, and we as Obstetricians are the ones who, by treating a pregnancy well, can help in reducing these problems in the next generation.

Our job goes beyond giving the couple a live neonate. We need to focus on giving a healthy neonate

Dr. Uday Thanawala
Vice President FOGSI (2015)

Chairperson's message
Perinatology – An Indian Perspective

Perinatology is not a new word but awareness of the scope of its meaning is changing and evolving. This is primarily a cause for concern for all Obstetricians as we need to deal with 2 patients – mother and fetus. We may be having the help of Neonatologists, Physicians and other specialists but as Obstetricians we are finally responsible for the pregnant patients. Hence, our approach should be systematic and evidence based to have a healthy mother and newborn at the end of the long journey of 9 months. We need to work hand in hand so that in case of adverse outcome (which is sometimes not avoidable) we are not playing a "blame-game" but sharing responsibility.

The evaluation and management of perinatal issues in pregnancy is sometimes complicated by the difficulty in interpreting symptoms, concerns about performing certain tests and about the complications of therapy in both the mother and the fetus. Decision making is the most important activity in patient care. The theme for the year 2015 by our FOGSI President was "Management of High Risk Pregnancy". We have National experts covering various aspects of perinatology in this handbook with special focus on achieving healthy mothers and newborns. This should help us in decision making for perinatal health.

We need to know not only the preventive aspects but also the long-term issues due a particular disorder to counsel, treat and manage a case. For e.g., thyroid dysfunction in pregnancy and need for screening all newborns for congenital hypothyroidism includes mental retardation or the issues related to preterm births including consequences like retinopathy of prematurity. We are having consensus meetings and drawing up plans with inputs from experts in the field to have national guidelines, FOGSI Recommendations and hope for Government involvement in the form of White papers proposed for thyroid disorders, influenza in pregnancy and retinopathy of prematurity.

Obstetric decisions during perinatal period are challenging considering the fact that they can affect the mother, fetus, the pregnancy outcome as well as the long-term health of the mother and child. Early medical advice, up-to-date and timely treatment of various problems can prevent morbidity and mortality in pregnancy and neonatal period.

Robert Frost has said:

"The woods are lovely, dark and deep
But I have promises to keep
And miles to go before I sleep
Miles to go before I sleep….."

There is much to be done by us my friends and each one of us can make a difference in perinatal health!

Dr. Reena Wani
CHAIRPERSON PERINATOLOGY COMMITTEE FOGSI 2015-2017

Contents

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Antenatal care for healthy neonates

Postnatal care

Eat right –importance of correcting nutritional deficiencies (iron and vitamin D)

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Eating right!

Nutrition in pregnancy refers to the nutrient intake, and dietary planning that is undertaken before, during and after pregnancy. Nutrition of the fetus begins at conception. For this reason, the nutrition of the mother is important from before conception (probably several months before) as well as throughout pregnancy and breastfeeding.

An ever-increasing number of studies have shown that the nutrition of the mother will have an effect on the child, upto and including the risk for cancer, cardiovascular disease, hypertension and diabetes throughout life.

An inadequate or excessive amount of some nutrients may cause malformations or medical problems in the fetus, and neurological disorders. 23.8% of babies worldwide are estimated to be born with lower than optimal weight due to lack of proper nutrition.

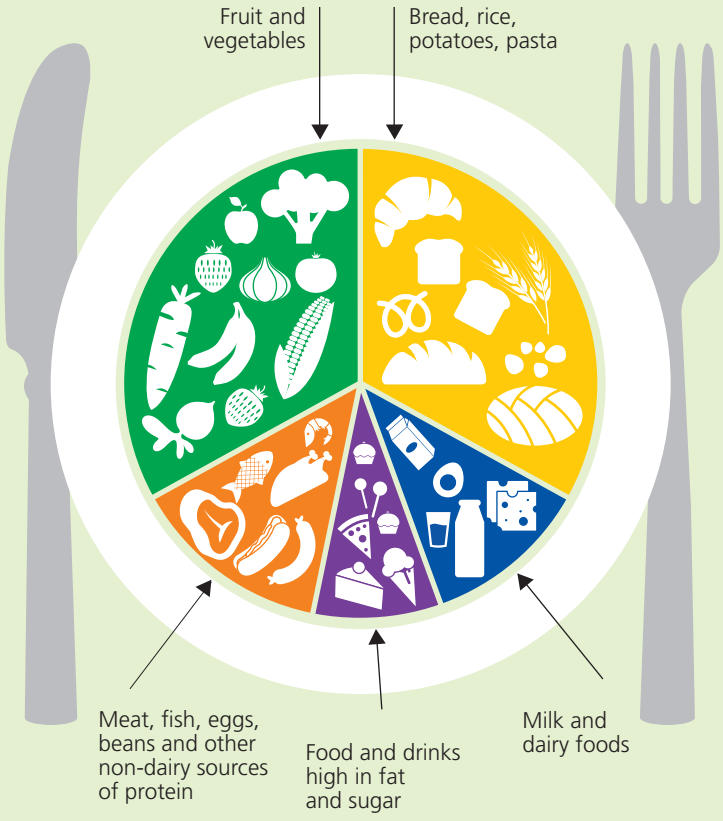
Personal habits such as smoking, alcohol, caffeine, using certain medications and street drugs can negatively and irreversibly affect the development of the baby, which happens in the early stages of pregnancy.

About 60% of the women have hemoglobin <10g/dl. They are not always from low socio economic status. It is also prevalent in middle and high socio-economic status due to poor knowledge about nutrition.

Fig. 1 Food pyramid

Fig. 2 Eat well plate

Use the eat well plate to help you get the balance right. It shows how much of what you eat should come from each food group.



Causes of poor nutrition[1,2]

1. Lack of information regarding the balanced diet.
2. Stereotype menu – same quality of food day after day.
3. Eating wrong type of food, what is known as junk food, aerated cold drinks, white flour preparations, sweet and sugar coated food items. Such kind of food is habit forming and will eventually kill the appetite.
4. In early months of pregnancy women develop anemia due to vomiting which causes loss of nutritional products.

There should be a balanced diet. Variety of food is the key to get all the ingredients.

Chronic deficiency of hemoglobin leads to poor vitality and fatigue[2,3]. Essential ingredients required in preventing anemia are:-

1. Iron
2. Folic acid
3. Vitamin B12
4. Vitamin C
5. Trace elements – zinc, chromium, selenium

The modern diet is deficient in folic acid because it is destroyed in cooking. Therefore, fresh green raw vegetables will be desirable – e.g. - lettuce and sprouted beans. In addition folic acid supplementation is also necessary.

Vitamin B12 is found in non-vegetarian diet. Lot of people in India are vegetarians, hence require supplementation.

Vitamin C promotes iron absorption. Citrus fruits and *amla* are good sources. Unpeeled potatoes are good sources.

This cause of maternal mortality and morbidity can be easily prevented by proper nutrition and supplementation. Aim is to have every woman with hemoglobin 12g%.

Table 1 - Nutrient requirements in women

Nutrient	Normal RDA	RDA in pregnancy	Risk of deficiencies in mother and fetus	Sources
Zinc	12mg/day	15mg/day	IUGR, premature and post mature baby, LBW, perinatal death, abnormal delivery with dystocia and placental abruption	Red meat, sea food, yogurt, lentils, milk, peas, baked potatoes
Iron	15mg/day	30mg/day	Maternal anemia, fetal anemia, LBW and preterm delivery	Apple, jaggery, dry fruits
Copper	1.5-3mg/day	1.5-3mg/day	Placental insufficiency and intrauterine death	Cooking in copper vessel
Chromium	50-200mcg/day	50-200mcg/day	Gestational diabetes and hyperglycemia	Onions, tomatoes, broccoli, white meat, grape juice, red meat, green beans
Selenium	55mcg/day	65mcg/day	Neural tube defects, sudden infant death syndrome and first trimester miscarriage	Asparagus, mushroom, garlic, red meat and sea food
Iodine	150mcg/day	175mcg/day	Miscarriage, still births, congenital anomalies, goiter, cretinism, impaired brain function and hypothyroidism	Iodized salt and sea food
Folic acid		15mcg/day	Neural tube defects	Meat, liver, chicken kidney, egg yolk, lentils, beetroot, almonds, banana, whole wheat grain

	Pregnant		Lactating	
Age (years)	14-18	19-50	14-18	19-50
Fat-soluble vitamins				
Vitamin A	750µg	770µg	1200µg	1300µg
Vitamin D[a]	5µg	5µg	5µg	5µg
Vitamin E	15mg	15mg	19mg	19mg
Vitamin K[a]	75µg	90µg	75µg	90µg
Water-soluble vitamins				
Vitamin C	80mg	85mg	115mg	120mg
Thiamin	1.4mg	1.4mg	1.4mg	1.4mg
Riboflavin	1.4mg	1.4mg	1.6mg	1.6mg
Niacin	18mg	18mg	17mg	17mg
Vitamin B6	1.9mg	1.9mg	2mg	2mg
Folate	600µg	600µg	500µg	500µg
Vitamin B12	2.6µg	2.6µg	2.8µg	2.8µg
Minerals				
Calcium[a]	1300mg	1000mg	1300mg	1000mg
Sodium[a]	1.5g	1.5g	1.5g	1.5g
Potassium[a]	4.7g	4.7g	5.1g	5.1g
Iron	27mg	27mg	10mg	9mg

Table 2 - Recommended dietary intake for Indians (ICMR)

	Adult women			Additional in pregnancy	
Food items	**Sedentary work**	**Moderate work**	**Heavy work**	**Grams**	**Kcal**
Cereals	410	440	575	35	118
Pulses	40	45	50	15	52
Milk	100	150	200	100	83
Fat	20	25	40		
Sugar	20	20	40		
Leafy vegetables	100	100	50		
Other vegetables	40	40	100		
Roots and tubers	50	50	60		
Total	**1875**	**2225**	**2925**	**160**	**293**

Importance of iron

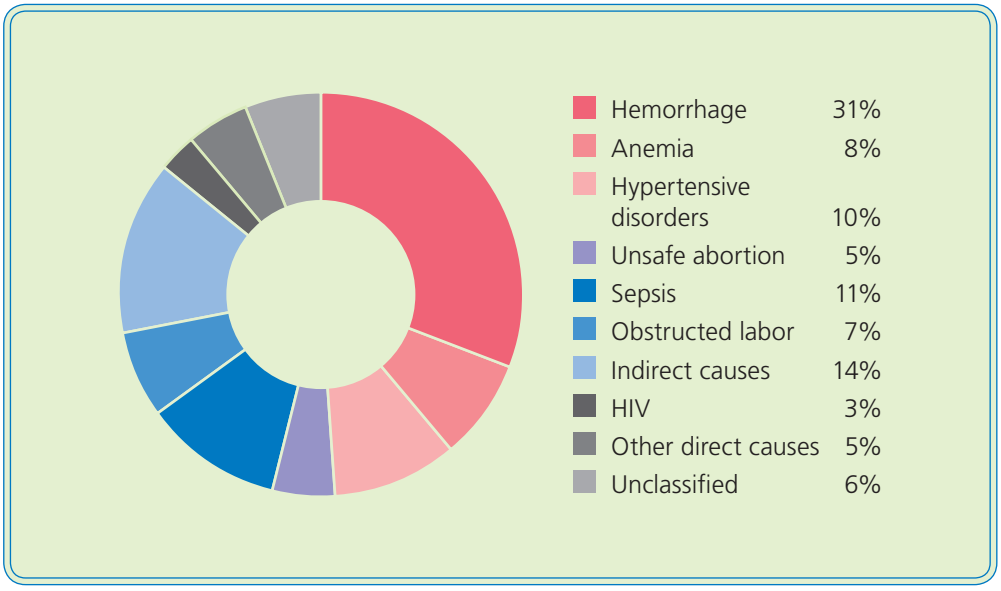
WHO lists iron deficiency as the major cause of anemia. Anemia is the direct cause of 3-7% of maternal deaths[1,2,3].

Incidence – According to WHO

- 40% of world's population suffers from anemia.
- Pregnant and elderly constitute 50%.
- Non pregnant women constitute 35%.
- 35% of women worldwide suffer from nutritional anemia and upto 80% of these are in Southeast Asia.
- Current estimates suggest that 13 million women during pregnancy suffer from anemia, of which 13% are severely anemic.
- Incidence in India is about 40-60%.

ICMR reports Indian incidence as 62%.

Table 3 - Causes of maternal death and contribution of iron deficiency anemia[7]



At birth the hemoglobin level and iron stores depend on the nutrient inputs from mother. A normal weight full term baby born to a healthy mother manages enough iron from its stores and breast milk. This stored iron is exhausted in 6 months. Infants and children who don't obtain adequate iron will suffer cognitive impairment that will affect the ability to learn and perform income earning tasks later in life. Anemic children are apathetic and anorexic, don't have energy to play and have trouble learning[4].

Causes of increased prevalence of anemia

Daily dietary intake of 15mg of iron can replenish loss of about 1.5mg assuming absorption rate of 10%. Daily requirement is more in pregnancy because[5,6]:

- Faulty diet – rich in carbohydrates, increased phosphates and phytates make iron insoluble
- Faulty absorption – intestinal infestation, intestinal hurry and hypochlorhydria
- Iron loss – sweat about 0.5mg/day, repeated pregnancy with lactation, excessive blood loss during menstruation, hook worm infestation and chronic malaria
- Increased demand during pregnancy
- Decreased intake – loss of appetite/vomiting
- Decreased absorption – antacids, H2 blockers and proton pump inhibitors
- Disturbed metabolism
- Prepregnancy health status – starts pregnancy with anemia
- Excessive demand – multiple pregnancy
- Recurrent pregnancy

Table 4 - Food factors influencing absorption

Enhancers	Inhibitors
Ascorbic acid	Oxalate in vegetables
Organic acids – citrus	Tannin in tea
Sprouted and fermented food	Phosphates in egg yolk
Meats and fishes	Proteins

Dietary sources rich in iron

- Vegetables – spinach, mustard and fenugreek
- Cereals – whole wheat, *bajra* and *jowar*
- Pulses – green peas and ground nuts
- Fruits – apple and banana
- Dates and jaggery
- Liver, meat, fishes and egg

General measures to reduce the incidence of anemia

1. Health education – to create and enhance anemia awareness amongst women, children and health workers.
2. Hookworm prevention – Albendazole 400mg stat and Malaria – chloroquine 300mg 2 tablets weekly from 2nd trimester in endemic areas.
3. Periodic iron and folic acid supplementation for pubertal, adolescent girls and women of all child bearing age.
4. Dietary modifications:
   a) Consumption of high iron bioavailability diets.
   b) Increasing consumption of vitamin C rich food with iron supplements.
   c) Encouraging common household processing methods – germination, fermentation and malting which increase vitamin C and decrease tannins and phytic acid content e.g. bioavailability of iron from germinated grain is almost 2 fold.
   d) Fortification of food – iron 30-35mgiron/kg of wheat flour.
   e) Fortification of common salt.

In infancy and childhood

1. Delayed cord clamping in newborns (by at least 1 min) has shown to increase iron stores.
2. Exclusive breastfeeding for at least 6 months of age.
3. Inculcating good eating habits from tender age.
4. Introducing fortified food.
5. Deworming for school children.

In pregnancy

1. Providing at least 100mg of iron for 100 days during pregnancy and continuing 3 months postpartum[8].
2. Routine de-worming in second and third trimester or postpartum period.
3. Making deliveries safe by reducing blood loss. Active management of third stage of labor.
4. Providing safe blood transfusion for woman with severe anemia.

In postpartum period

1. Exclusive breastfeeding. Minimizes postpartum blood loss. Lactational amenorrhea which saves on menstrual loss.
2. For those taking oral contraceptives, taking iron in blank weeks should be emphasized.
3. Injectable progesterone contraceptives like DMPA should be promoted, for added benefit of amenorrhea which reduces anemia.
4. Monitoring blood loss in IUCD users is important, or using LNG-IUCD which has lesser blood loss.

Table 5 - Treatment of iron deficiency anemia[8]

Population	Therapy
Non pregnant adolescent girls	Oral iron 60-120mg/day
Pregnant women	Oral iron 60-120mg/day
Refractory patients	Ferric gluconate complex in iron sucrose – 1gm total dose of elemental iron is infused in 6 sessions. Erythropoietin 150IU/Kg three times per week, combined with 100mg/day parenteral elemental iron.

Counseling regarding diet high in iron and correct all other dietary deficiencies. Monitor hemoglobin at 4 weeks and if it rises by >1g/dl diagnosis is confirmed, hence treat for additional 2 months, re-evaluate at 6 months[9]. Re-evaluate if anemia persists.

New supplementation practices

1. Development of gastric release system that improves iron absorption by prolonging the period of iron prescription to the gut and reduce side effects. A single 50mg tablet is as effective as two of ferrous sulphate tablets that provide 60mg of iron each[12].
2. The new developmental schemes which provide relatively higher dose of iron on a weekly basis. This new approach is safe and effective in pre-school children. Supplementation of pregnant women with once weekly 120mg of iron as ferrous sulphate is found to have same hemoglobin concentration at term compared to those taking 60mg iron daily[10].
3. Single weekly dose of 60mg iron to cover menstrual losses in majority of women. Women would enter pregnancy with an improved nutritional status. As soon as pregnancy is detected weekly dose would be doubled[11].

Table 6 - Effect of anemia on pregnancy

During pregnancy	During labour	During puerperium
1. Abortion and preterm labour. 2. Small for gestational age and have increased incidence of stillbirths and neonatal deaths. 3. Behavioral and cognitive defects. 4. Infancy anemia due to decreased iron stores in the neonate. 5. Pre-eclampsia. 6. Abruptio placenta. 7. Intercurrent infection.	1. Postpartum hemorrhage. 2. Cardiac failure.	1. Puerperal sepsis. 2. Subinvolution of uterus. 3. Lactational failure. 4. Deep vein thrombosis and pulmonary embolism. 5. Poor wound healing capacity.

Fetal effects

1. PROM
2. IUGR
3. IUFD
4. Prematurity
5. Abnormal trophoblast invasion
6. Fetal programming and disease of newborn: behavioral abnormalities, poor performance, decreased cognitive function
7. Neonatal anemia
8. Adult height associated with low birth weight and high ratio of placenta to birth weight

Pathophysiology of fetal effects

If maternal oxygenation is 98-100%, the fetus gets around 70% of O2, with fetal Hb. Fetus can compensate.

As the maternal Hb drops, fetal hypoxia develops, which leads to stimulation of fetal erythropoiesis.

↓

Increased viscosity of blood due to raised PCV sluggish circulation

↓

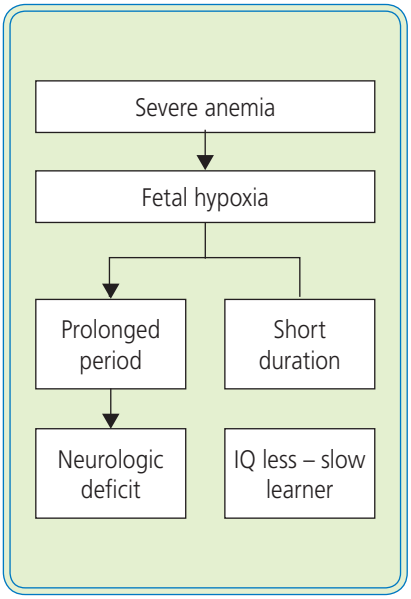
End artery thrombosis

↓

Failure of the organs supplied by these vessels

↓

Increased PCV causes
1. Brain damage
2. Necrotising enterocolitis
3. Hypoglycemia
4. Hypocalcemia
5. Hyperbilirubinimia
6. RDS



Importance of vitamin D

Vitamin D can be synthesized in the skin through exposure to ultraviolet light or can be obtained through dietary intake. Sunlight exposure is influenced by skin color, latitude, season, life style and cultural practice. It has important actions such as promoting insulin action and secretion, immune modulation and lung development. It therefore, has the potential to influence many factors in the developing fetus. This paper investigates the effects of vitamin D on the placento-fetal unit and the mother, in terms of calcium metabolism (classical actions) and non calcium effects (non classical actions). There is little information on vitamin D intake in pregnancy and lactation.

Requirements of vitamin D

Recommended daily allowance of vitamin D is 600IU per day. This is based on the amount of intake necessary to sustain blood levels of 25(OH)D above 50nmol/L for population with minimal sunlight exposure. Safe upper limits – 4000IU/ day for children more than 9 years, adults, pregnant and lactating women.

Definition

Pregnant women with serum levels of 25 OH vitamin D <75nmol/L.

Fig. 3 **Assessment of Vitamin D status**

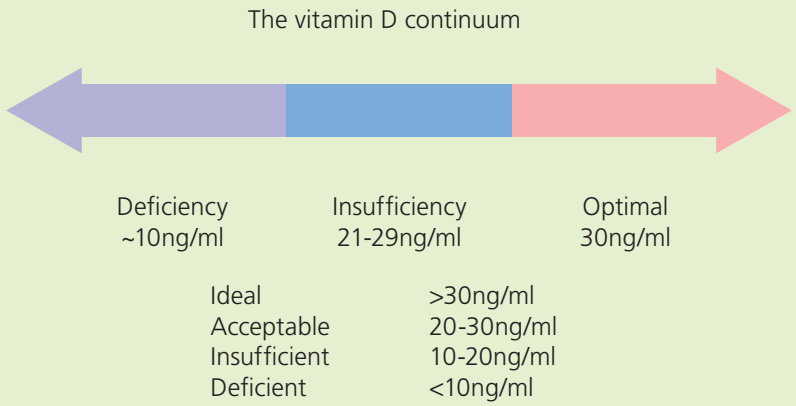
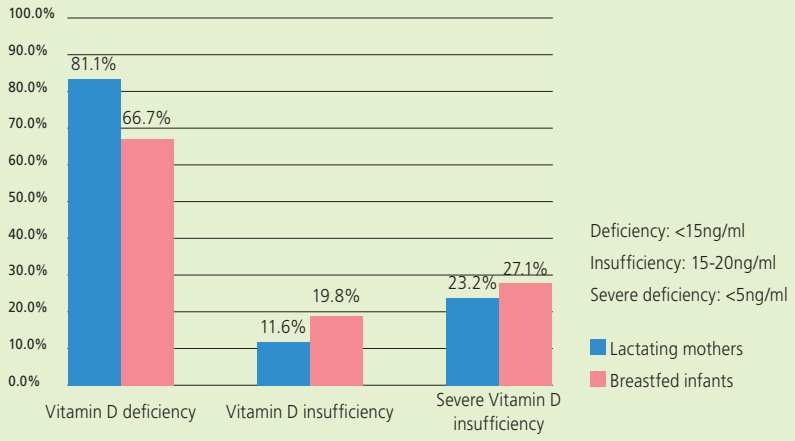


Fig. 4 **Vitamin D deficiency in lactating and breast fed infants[34]**

84% of the Indian women have 25 OH vitamin D <22.5ng/ml[33].



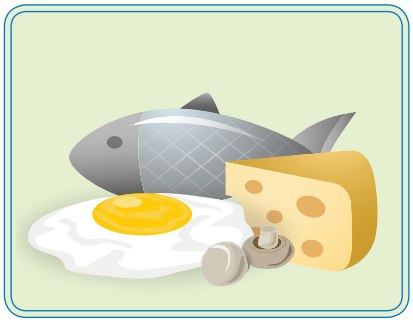
Functions of vitamin D

- Role is to maintain a normal level of calcium and phosphate in blood, which in turn facilitate other essential processes such as bone mineralization, contraction of muscles, nervous system activities and cellular function.
- Adequate vitamin D status is important for neonate, if not, it may develop neonatal hypocalcemia and rickets. Breast milk is poor source of vitamin D, thus vitamin D status during pregnancy is important for vitamin D status during early infancy.
- Vitamin D helps in establishing a proper maternal immune response of placenta.
- Vitamin D has a direct role in production of antimicrobial peptides such as cathelicidin, which play an important role preventing infection during pregnancy or early childhood.
- Vitamin D regulates expression of human chorionic gonadotrophin in syncytiotrophoblast and stimulates production of sex steroids[15].
- Vitamin D also influences musculo-skeletal growth.

Sources of vitamin D

- Fish oils, fatty fish, oysters, butter, mushrooms, beef, liver, cheese and egg yolks.

10-15 minutes sunshine, 3 times a week is enough to produce the body's requirement of vitamin D.



Maternal and fetal complications[19]

Pre-eclampsia

Low levels in the first half of pregnancy were related to the risk of developing pre-eclampsia and the neonates of these mothers had a two-fold increased risk of having vitamin D levels <37.5nmol/l (vitamin D deficient). Women with early-onset severe pre-eclampsia and a small-for-gestational-age (SGA) infant had significantly lower vitamin D levels than those with early-onset severe pre-eclampsia but non-SGA infants.

Low birth weight

In a study from Holland, women with vitamin D deficiency had a 2.4-fold increased risk of having an SGA baby. Another study found that maternal vitamin D levels of <37.5nmol/l in the first half of pregnancy were associated with an adjusted odds ratio of 7.5 for SGA infants in white women, but not in black women. Other studies demonstrated that low vitamin D levels in late pregnancy were associated with reduced intrauterine long bone growth and lower gestational age at delivery.

Impaired glucose tolerance in pregnancy

Hypovitaminosis D is associated with impaired glucose tolerance and diabetes in the general population[18]. However, the evidence for an association between low vitamin D levels and gestational diabetes Mellitus (GDM) is conflicting. Low concentrations of 25(OH)D have been related to the risk of developing type II diabetes mellitus (T2DM) through effects on insulin secretion and insulin sensitivity.

Other complications

Vitamin D deficiency (<37.5nmol/l) has been associated with a four-fold increased risk of primary caesarean section (caesarean section performed for the first time) although this has not been demonstrated in all studies[13]. Vitamin D deficiency is also associated with bacterial vaginosis in pregnant women.

Neonatal hypocalcaemic seizures

Neonatal vitamin D levels are correlated with those of their mother, with maternal vitamin D deficiency increasing the risk of neonatal vitamin D deficiency. Vitamin D deficiency is a major cause of hypocalcaemic seizures in neonates and infants.

Skeletal development and growth

Hypovitaminosis D is associated with impaired growth and bone development in the fetus.

Evidence is accruing to show that less profound maternal 25(OH) D insufficiency may lead to suboptimal bone size and density after birth without overt rachitic change. This is likely to lead to an increased risk of osteoporotic fracture in later life.

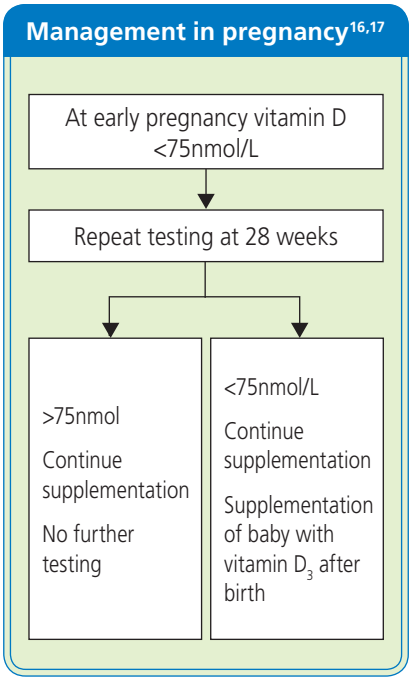
Fetal lung development and childhood immune disorders

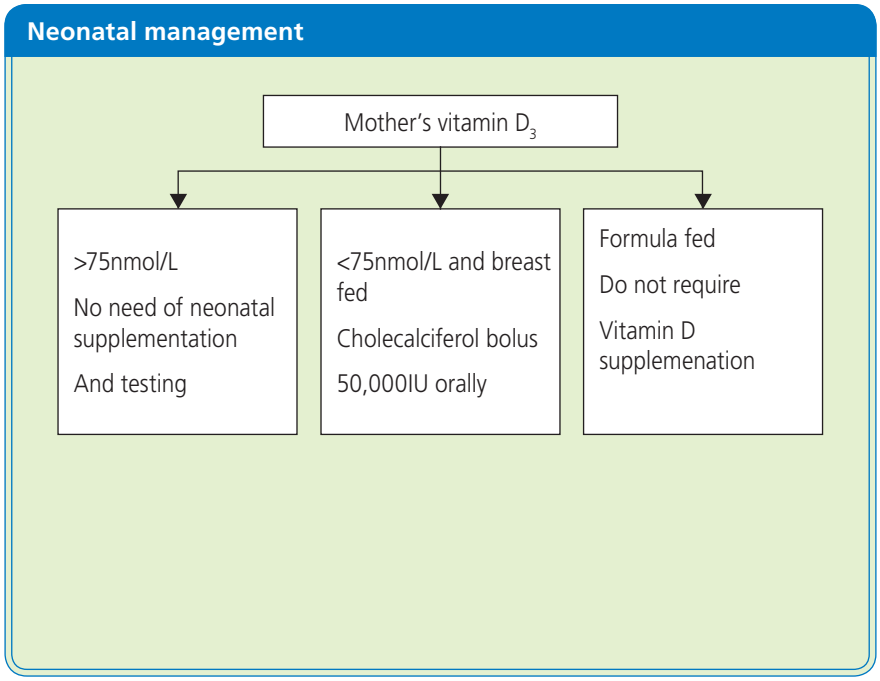
Low maternal vitamin D intake in pregnancy is associated with wheeze and asthma in the offspring. Low cord blood 25(OH)D concentrations have been associated with respiratory syncytial virus bronchiolitis and respiratory infections[14]. There are plausible physiological mechanisms for an association between prenatal vitamin D status and immune development. The metabolite 1,25(OH)2D has been shown in animal and in vitro models to have an immune-modulatory role and low levels of neonatal vitamin D have been linked to childhood asthma. Maternal vitamin D supplementation is associated with cord blood gene expression of tolerogenic immunoglobulin such as immunoglobulin-like transcripts 3 and 4 (ILT3 and ILT4). Cord blood 25(OH)D is correlated with mononuclear cell release of IFN-γ and hence Th1 cell development.

More research is needed on the potential association between maternal vitamin D in fetal lung development and childhood allergy; there are ongoing studies investigating long-term neonatal putative benefits of adequate maternal vitamin D.

Normal Values and recommended Supplementation

Levels >75nmol/L need no further testing.
Levels <75nmol/L – dietary intake of 1gm calcium per day.
Vitamin D supplementation – 1000IU combined with 1gm calcium.





Single dose of vitamin D syrup provides 4 months of vitamin D stores.

Vitamin D and pregnancy

Pregnancy is a known risk factor for vitamin D deficiency.

Vitamin D deficiency during pregnancy may lead to gestational diabetes, increased risk of infections, cesarean section and low birth weight.

Vitamin D deficiency is linked to 40% increased risk of pre-eclampsia in early pregnancy.

ACOG guidelines

Circulating 25 OH vitamin D3 <32ng/ml or <80nmol/L.

Insufficient evidence to support a recommendation for screening of all pregnant women for vitamin D deficiency.

For pregnant women thought to be at increased risk, maternal 25 OH vitamin D levels should be checked.

Most expert agree with 1000-2000IU per day is safe.

Higher dose regimen used for treatment of vitamin D deficiency has not been studied.

At this time, there is insufficient evidence to recommend vitamin D supplementation for prevention of preterm birth or pre-eclampsia.

Vitamin D deficiency and iron deficiency anemia is there any link!

Pregnant women with low serum 25 OH vitamin D levels had 46% higher risk of developing anemia[20].

Fig. 5 - Link between vitamin D deficiency and iron deficiency anemia

	Low	Adequate
Outcome	% (N)[2]	% (N)[2]
Severe Anemia (Hb <85g/L)	38.7 (212)	31.0 (339)
Anemia (Hb <110g/L)	92.5 (40)	83.0 (94)

>50% infants with iron deficiency anemia had low 25 OH vitamin D levels[20,21].

20% of Asian children had both vitamin D and iron deficiency anemia.

Children with vitamin D deficiency had low Hb and serum iron[22].

Studies have showed signs of both deficiencies and during the winter 50% of children with low vitamin D had low haemoglobin compared with normal vitamin D.

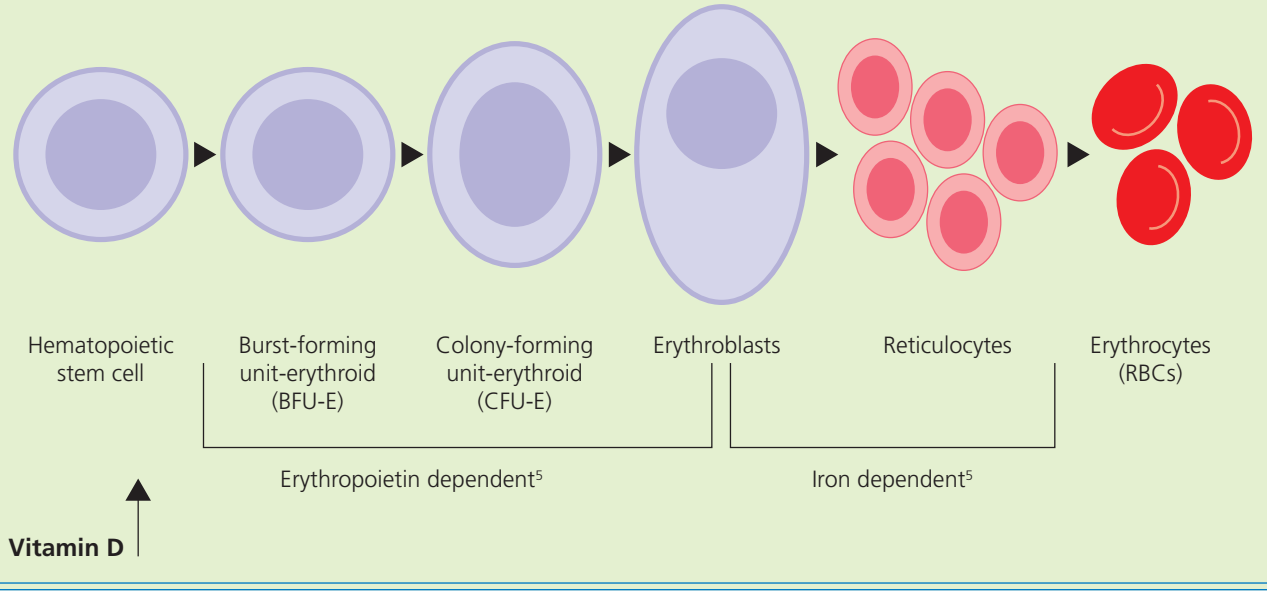
Mechanisms

Can Vitamin D deficiency cause anemia!

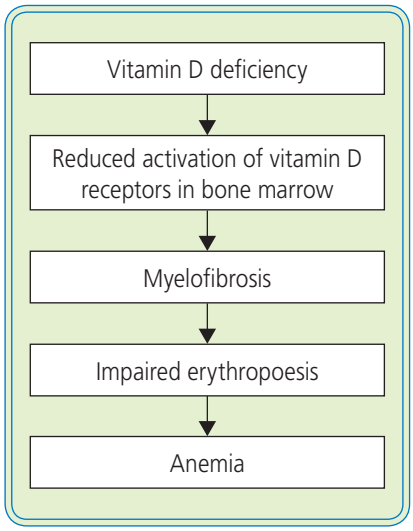
Vitamin D receptors are present in bone marrow.

Buffy coat of bone marrow containing erythroid precursors shown to have high concentration of 25 and 1, 25 hydroxy vitamin D[23].

Fig. 6 **Role of vitamin D in erythropoesis**



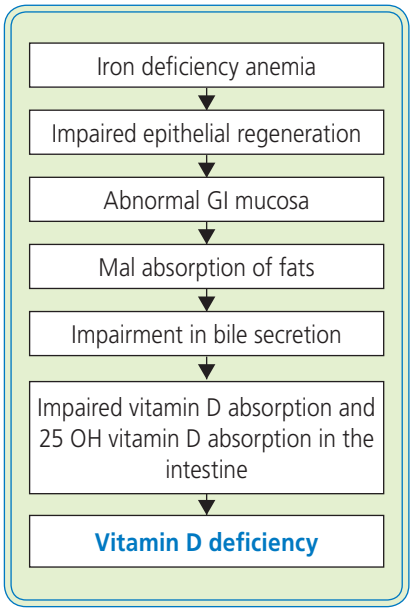
Vitamin D deficiency could result in reduced activation of eryhtroid precursors, causing anemia[24].



Vitamin D supplementation will help in initial phase of erythropoesis.

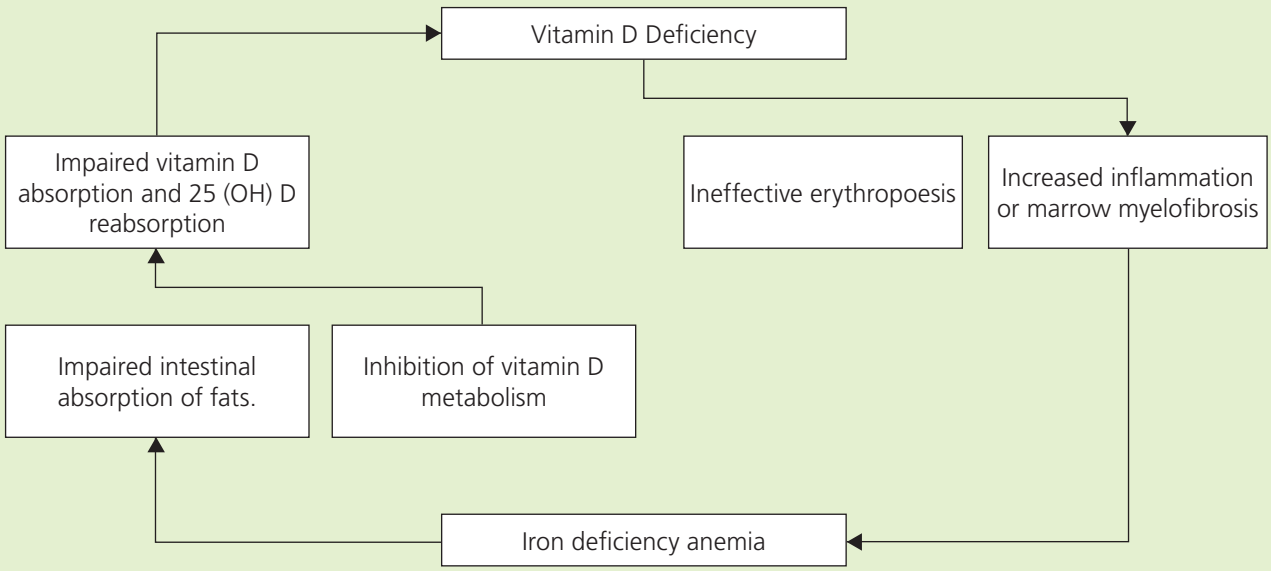
Iron supplementation would be required for later phase. Myelofibrosis was observed in children with vitamin D deficiency induced rickets[25,26,27].

Can Iron deficiency anemia cause Vitamin D deficiency!



Dietary/supplementary vitamin D absorbed from the intestine, is converted to 25 OH vitamin D in liver. Some of the 25 OH vitamin D is secreted into the bile and is reabsorbed by entero-hepatic circulation[28.29.30].

Fig. 7 **Iron deficiency anemia causing vitamin D deficiency**



Summary

- Multiple micronutrients are often taken by pregnant women in developed countries, but their benefits are limited, except for prophylactic folic acid taken during the periconceptional period.
- Women in developing countries may benefit from multiple-micronutrient prophylaxis in pregnancy, but the underlying basis and rationale for changing from supplementation with iron and folate to supplementation with multiple micronutrients is in research.
- Micronutrients may affect fertility, embryogenesis and placentation, and the prophylactic use of some micronutrients may be useful in preventing several adverse pregnancy outcomes.
- Efforts to increase awareness of a healthy diet should be strengthened not only throughout pregnancy but also before.
- Vitamin D deficiency with iron deficiency is prevalent in all age groups.
- Mechanism of iron deficiency anemia leading to vitamin D deficiency is not fully established[31,32].
- The above available data indicates a vicious cycle.
- Supplementation with 1000IU Vitamin D and 100mg iron daily would improve the status.

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Effect of endocrine disorders on the neonate

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Pregnancy is associated with hormonal and metabolic changes, and blood levels of glucose as well as thyroid hormones have a significant impact on maternal metabolism and fetal development. The fetus relies primarily on maternal substrates for its development and disordered maternal glucose levels as well as thyroid profile is known to have adverse effects.

Both these disorders are known to cause complications – early in the gestational period, and late in adolescence and adulthood. In order to ensure that the burden of this disease is curbed in the coming years, it is mandatory to offer screening programmes to all women during preconception counseling sessions. For the women who have not being screened earlier, it is of utmost importance to screen them in their first antenatal check up.

Thyroid disorders in pregnancy

Screening for and management of hypothyroidism in pregnancy

In the fetal development process, infant's thyroid gland develops around seven weeks of gestation and by the 12th week, the fetal thyroid hormones are produced. Supplementation of maternal thyroid hormones nurtures the fetus and plays an important role in the development of fetal neurological systems. Without proper thyroid levels, pregnancy outcome is not only at risk for abnormal fetal growth and development, but also at risk for various pregnancy complications.

Overt maternal hypothyroidism in the first trimester is associated with pregnancy complications like pre-eclampsia, placental abruption, preterm birth, low birth weight, and fetal death and intellectual impairment during childhood. The effects of mild maternal thyroid deficiency with a normally functioning fetal thyroid gland are less clear and less studied. This is important because the spectrum of thyroid deficiency begins with subclinical hypothyroidism characterized by an elevated serum thyrotropin (TSH) concentration but a normal serum free thyroxine level till overt hypothyroidism.

During pregnancy there is a increased need of thyroid hormones due to:

1. Increased levels of TBG result in lowering free T4 concentrations
2. Increased demand for iodine
3. Thyroid stimulation by Chorionic Gonadotropin (a subunit mimicry)

There is a substantial risk that a previously unnoticed subclinical hypothyroidism will turn into overt hypothyroidism. Previous studies show that subclinical maternal hypothyroidism is also associated with poor pregnancy outcomes

such as placental abruption, preterm birth, and low birth weight infants. The deleterious effect of thyroid dysfunction also affects neurointellectual development in infancy and childhood. It is recommended that S.TSH should be mantained below 2.5mU/ml in early trimester and below 3mU/ml in late trimester to avoid subclinical hypothyroidism.

Thyroid function tests in pregnancy

Measurement of serum Thyroid Stimulating Hormone (TSH) is the most simple, practical and economic screening test for thyroid dysfunction. A value of 2.5mU/L is presently accepted as the upper limit of serum TSH for the first trimester of pregnancy. In the presence of an abnormal serum TSH value, the determination of Free Thyroxine (FT4) or its equivalent Free Thyroxine Index (FT4I) may be done. A suppressed TSH value and high concentrations of FT4 or FT4I are diagnostic of hyperthyroidism.

The determination of TSH receptor antibodies (TSHRBab or TRAb) are indicated only in special circumstances in order to predict the possibility of fetal or neonatal thyroid dysfunction (e.g. in Grave's disease; Fetal/Neonatal hypothyroidism in previous pregnancies; active disease on treatment with anti thyroid drugs).

The values of thyroid hormones during pregnancy is trimester specific

Test	Non Pregnant	First Trimester	Second Trimester	Third Trimester
Free T4 (pmol/L)	11-23	10-24	9-19	7-17
Free T3 (pmol/L)	4-9	4-8	4-7	3-5
TSH (pmol/L)	<4	0-1.6	1-1.8	7-7.5

Maternal placental fetal interactions:

It is important to note that:

- Maternal TSH and TRH do not cross the placental barrier.
- Maternal thyroxine crosses the placenta in the first half of pregnancy and this has a positive effect on the intellectual development of the fetus.
- Methimazole (MM) and Propylthiouracil (PPU) used for treatment of hyperthyroidism cross the placental barrier.

Hypothyroidism in pregnancy

Subclinical Hypothyroidism

Subclinical hypothyroidism is a form of mild thyroid dysfunction where there is an elevated levels of Thyroid Stimulating Hormone (TSH) accompanied with normal free thyroxine levels. This entity indicates the inability of the thyroid gland to increase its output in response to increased demand such as pregnancy. Serum TSH is one of the most sensitive tools in the diagnosis of thyroid disorders. It is also the most economical and hence, is most frequently employed for screening and follow-up in subclinical hypothyroidism.

Screen or not to screen?

The cost effectiveness of routine screening of all pregnant women was evaluated by Thung et al. from New Haven and he concluded that screening for subclinical hypothyroidism in pregnancy will be a cost-effective strategy under a wide range of circumstances.

The American College of Obstetricians and Gynecologists has stated that routine screening and treatment of subclinical hypothyroidism cannot be recommended. However, other authors have stated that screening of all pregnant patients is a cost effective strategy. Pregnant women should be screened at booking visit.

Indian data

Odisha study

A prospective study on Prevalence of Subclinical Hypothyroidism in Pregnancy and Its Impact on Feto-Maternal Outcome done in O&G department of SCB Medical College Cuttack, ODISHA by A. Misra, Sujata Misra et al. They have reported a 5.3% prevalence of SCH. Out of total 566 cases screened, 30 cases had subclinical hypothyroidism. Both euthyroid and hypothyroid group were compared in terms of their age, parity, gestational age, socio-economics status geographical area distribution and pregnancy outcomes. The mean age for SCH in pregnancy was 28 years. 60% of SCH patients belong to rural area and 23% cases were more than 30 years of age. Abruptio placentae was present in 17% of cases of SCH which was 2% in euthyroid group ($p < 0.001$, odds ratio 9). 20% of SCH cases had preterm delivery ($p<0.001$, odd ratio 6). Low birth weight was prevalent in 17.5% cases of SCH which was 2.5% in euthyroid control group. 30% cases of SCH were delivered by LSCS and most common indication being fetal distress. 43% APGAR score was ≤3 in 5 min in 6% cases of SCH. Similarly, admission to NICU was 30% in SCH which was 3.5% in euthyroid group. Cord blood TSH was >20mIU/dl in 6% cases of SCH.

This strongly supports the need for screening for SCH in pregnancy.

Both overt and subclinical hypothyroidism were associated with increased risk of eclampsia, pre-eclampsia, and pregnancy induced hypertension. The incidence of postpartum depression may also be increased in these patients, necessitating the need for initiating therapy with selective serotonin uptake inhibitors. Delayed neurological problems are seen in the affected fetus.

Management

Levothyroxine sodium is the drug of choice for treatment of subclinical hypothyroidism and is started in an initial dose of 25-50µg daily, empty stomach prior to breakfast. Usually, the dose required is 1.5µg/lb body weight. Dosage may be increased in steps of 25-50µg at intervals of 4 weeks till the TSH levels fall in the lower half of the normal range.

Evaluation of Therapy

The goal of therapy is to maintain the TSH levels in the lower half of the lower range 0.3-2.0mU/L. The full response of TSH to T4 therapy is relatively slow. A minimum of 8 weeks are necessary between changes in dosage and assessment of therapy.

Once the dose is stabilized, follow-up should be yearly with ultrasensitive TSH assay.

Overt hypothyroidism

Overt hypothyroidism during pregnancy is uncommon because many women are anovulatory leading to subsequent infertility, and an increased rate of early spontaneous abortion, if conception occurs. The two most common etiologies of primary hypothyroidism are autoimmune thyroiditis (Hashimoto's thyroiditis) and post thyroid ablation therapy, either surgical or Iodine 131 induced.

Pregnant women with pre-existing hypothyroidism carry an increased risk of abortion, anemia, gestation hypertension (including severe forms of eclampsia and pre-eclampsia), abruptio placentae, and postpartum hemorrhage have been described. The likelihood of complications depends upon the severity of the hypothyroidism and the adequacy of maternal treatment.

Diagnosis

The diagnosis of hypothyroidism is confirmed by the determination of serum TSH and FT4 or FT4I. Regardless of etiology, primary hypothyroidism is classified into subclinical hypothyroidism (normal FT4 and elevated TSH) and overt hypothyroidism (low FT4 and elevated TSH).

Those with positive anti TPO antibodies and a serum TSH >2.5mU/L should be treated with L-thyroxine, to keep the serum level between 0.3 and 2.0mU/L.

Patients on thyroid therapy before conception should have their TSH checked at 4-6 weeks of gestation and dose of L-thyroxine should be adjusted accordingly. Routine increase in thyroxine dose is not indicated.

The serum TSH should be repeated every 4-6 weeks during the first 20 weeks, at 24-28 weeks and at 32-34 weeks gestation.

Immediately after delivery, they should return to prepregnancy dose.

If hypothyroidism has been diagnosed before pregnancy, it is recommend to adjust the preconception L-T4 dose to reach a TSH level not higher than 2.5mU/L (ideally lower than 2.0) prior to conception.

The L-T4 dose usually needs to be increased by 4-6 weeks gestation and may require a 20-50% increase in dosage (or even more).

Patients should separate L-T4 ingestion and the ingestion of iron supplements vitamins containing iron, calcium supplements, and soy-based food by at least 4 hours.

After delivery, most hypothyroid women need the L-T4 dosage they received during pregnancy to be decreased to the preconception dosage. TSH level should be rechecked at 6 weeks postpartum, and it is important to continue monitoring TFTs for at least 6 months after delivery.

Hyperthyroidism in pregnancy

Hyperthyroidism affects 0.2% of all pregnant women. Inappropriate production of Human Chorionic Gonadotropin (hCG) is a leading cause of hyperthyroidism during first trimester of pregnancy.

1. **Transient hyperthyroidism** is the most common cause of hyperthyroxinemia in pregnancy and is caused due to high or inappropriate levels of hCG. It is also known as gestational thyrotoxicosis. This condition is suspected in women who present in 4-8 weeks of gestation with sudden onset of severe nausea and vomiting and the thyroid tests are in the hyperthyroid range. However, they have no clinical manifestations of Grave's Disease. Common findings are weight loss of at least 5kg, ketonuria, abnormal liver function tests, and hypokalemia.

   The FT4 levels are elevated up to 4 to 6 times. FT3 too is elevated in 40% of patients. The T4/T3 ratio is less than 20 in HG while it is higher than 20 in Grave's hyperthyroidism. This disorder resolves spontaneously between 14-20 weeks and anti thyroid drugs are usually not needed.

2. **Subclinical Hyperthyroidism**
   Subclinical hyperthyroidism is characterized by normal FT4 and suppressed TSH. It is associated with the following:
   - Normal pregnancy (up to 15%)
   - Mild nausea/vomiting
   - Multiple gestation
   - Hyperreactioluteinalis – luteoma of pregnancy (later in pregnancy) – a rare condition in which hCG levels are higher than in normal pregnancy and hyperthyroidism in second trimester of pregnancy and resolution after delivery

3. **Hyperthyroid**
   The diagnostic clinical clues in favour of hyperthyroidism are: presence of goiter, ophthalmopathy, proximal muscle weakness, tachycardia (>100 beats per minute), hyperdynamic circulation with a loud systolic murmur and weight loss or inability to gain weight inspite of a good appetite.

   A suppressed TSH value in presence of a high FT4 or FT4 index confirms the diagnosis. Thyroid peroxidase antibodies (anti-TPO) are indicated in cases where the etiology of hyperthyroidism is in doubt.

   The goal of treatment is normalization of thyroid tests as soon as possible and to

maintain euthyroidism with the minimal amount of anti thyroid medication. The initial recommended dose of PTU (Propylthiouracil) is 100-450mg/day in divided doses (half life is 8 hours) and for MM (Methimazole), 10-40mg/day divided in 2 daily doses. In patients with minimal symptoms, an initial dose of 10mg MM daily or PTU 50mg 2 to 3 times per day is initiated.

Clinical improvement is evident in 2-6 weeks and improvement in the thyroid function tests are seen within the first 2 weeks of therapy, with normalization to chemical euthyroidism in 3-7 weeks.

The dose is adjusted every few weeks according to the clinical response and the result of thyroid function tests. Common side effects of anti thyroid drugs are pruritus and skin rash. Very few cases of "Methimazoleembryopathy" have been reported in infants of mothers treated with MM in the first trimester. This includes choanal atresia, esophageal atresia and minor developmental delay. This is not seen with the use of PTU.

Beta adrenergic blocking agents (propranolol 20-40mg 6 hourly or atenolol 25-50mg/day) are very effective in controlling the hyperdynamic patients and may be used in the first few weeks in symptomatic patients. Used in patients with symptoms like tremors, tachycardia, palpitations. Dose is adjusted to keep resting pulse within 70-90 bpm.

Iodine 131 therapy is contraindicated in pregnancy.

Surgery is indicated in a few selected cases like those with allergy to ATDs, non-responders to ATDs or unusually large goiter needing high dose of ATD. Surgery is best done in the second trimester of pregnancy.

Breastfeeding is permitted if the daily dose of PTU or MM is less than 200 or 20mg/day, respectively. The total dose should be distributed in divided doses after each feeding. The infant should be screened for neonatal thyrotoxicosis on days 3-4 and 7-10 days of delivery if the TSH receptor antibody titre is high late in pregnancy (III/B).

4. Thyroid storm

Thyroid crisis or "storm" is a rapid worsening of the thyrotoxicosis brought about by stress, e.g., infection, labor, or surgery. This usually occurs in uncontrolled thyrotoxicosis. Fever is a prominent feature and may exceed 40°C. Mental status is altered, ranging from extreme nervousness and restlessness, confusion to psychosis, seizures and coma. There may be diarrhea, nausea and vomiting and non specific abdominal pain. Tachycardia and atrial fibrillation may be present. As thyroid storm is a life threatening condition, with mortality rates as high as 10%, immediate treatment should be instituted. The goals of treatment are to decrease the production of thyroid hormone, decrease the effect of circulating hormone, provide supportive therapy and treat the underlying cause. Propylthiouracil 300-400mg every 8 hours orally, by nasogastrictube or rectally, is the drug of choice. It inhibits thyroid hormone synthesis and helps in restoring the electrolyte balance. Aspirin should not be used as an antipyretic agent since it displaces thyroid hormone from TBG and thus increases the free-hormone concentrations. Heart failure due to rapid atrial fibrillation should be treated with digoxin and diuretics, though the dose of digoxin needs to be higher than normal in the thyrotoxic patient, since the rate of degradation is increased.

Postpartum thyroid dysfunction

Thyroid dysfunction, either hyper or hypothyroidism, has been recognized with increasing frequency in the first 13 months following delivery and after abortions. Postpartum thyroiditis is prevalent in 1.1-16.7% of all women and is the most common cause of thyroid dysfunction in the postpartum period.

The symptoms are usually non-specific and include tiredness, fatigue, depressions, palpitations and irritability.

Two forms of PPT are generally encountered:

1. An autoimmune form, which is more common and eventually develops into chronic hypothyroidism.
2. A non-autoimmune form, without antibodies, that appears to be transient without progressing to permanent hypothyroidism.

The clinical course is not uniform. It may be present in four forms:

1. An episode of hyperthyroidism (2-4 months), followed by hypothyroidism (4-6 months) and reverting to euthyroidism after the seventh month.
2. An episode of hyperthyroidism (3 to 4 months) reverting to euthyroidism.
3. An episode of hypothyroidism (4 to 6 months) reverting to euthyroid state.
4. Permanent hypothyroidism after the hypothyroid phase.

Management

Most recover spontaneously. For hypothyroid symptoms, small dose of L thyroxine (0.050mg/day) will control symptoms allowing for a spontaneous recovery of thyroid function following the discontinuation of the drug.

In the presence of hyperthyroid symptoms, ß-adrenergic blocking agents (propranolol 20-40mg 6 hours or atenolol 25-50mg/day) are very effective in controlling the symptoms. Anti thyroid medications are not effective as the hyperthyroxinemia is secondary to release of thyroid hormones due to acute injury of the gland (destructive hypothyroidism).

Contraception

The thyroid status essentially remains normal in women taking oral contraceptive pills. As the conventional thyroid tests may be misleading when patients are taking steroidal contraceptives, the free thyroxine level should be measured in women with thyroid dysfunction and desirous of using oral contraceptives. The non-hormonal contraceptive methods like IUCD, barrier methods, spermicidal creams, etc. do not influence the thyroid status.

Gestational diabetes mellitus is defined as carbohydrate intolerance of variable severity with onset or first recognition during the present pregnancy. It does not exclude the possibility that the glucose intolerance may have antedated the pregnancy.

The reported prevalence of GDM is around 2-5%, but it can be as high as 14% depending on the population described and the criteria used for diagnosis. Prevalence of GDM in women with defined low risk factors such as being of white ethnic origin, younger than 24 years and having a body mass index of less than 25kg/m2, ranges from 1.4 to 2.8%. The prevalence in women with defined high-risk factors such as being older than 25 years, being obese or having a family history of diabetes ranges from 3.3% to 6.1%. Women diagnosed as GDM are at an increased risk of developing type 2 diabetes in approximately 50% of cases in later life.

Diabetic mothers are also at an increased risk of hypertension in late pregnancy. Other obstetric complications such as polyhydramnios, preterm labour and abortions are also commonly encountered in pregnant diabetics. Infants of diabetic mothers are prone to respiratory distress syndrome, hypoglycemia, cardiomyopathy, neonatal jaundice, impaired calcium and magnesium homeostasis and sudden intrauterine death.

The screening and treatment guidelines broadly enfold:

- Preconception information
- Diagnosis and management of GDM
- Glycaemic control in the preconception period, antenatal and intrapartum periods
- Appropriate medications for controlling diabetes and its complications
- Management of diabetic emergencies (for e.g., hypoglycemia and ketoacidosis)
- The timetable of antenatal appointments to be offered to women with diabetes
- Timing and mode of birth (this is inclusive of induction of labour, caesarean section, analgesia and anaesthesia, and the use of steroids for fetal lung maturation)
- Initial care of the newborn baby
- Management of diabetes and its complications during the postnatal period

The screening procedure should be simple, safe, precise and validated. It should also be acceptable to the population with well defined cut off levels.

A number of screening procedures and diagnostic criteria (ADA, WHO, CDA, NDDG and Australian criteria) have been advocated.

Most recent and accepted method is suggested by IADPG- International Association of Diabetes and Pregnancy Study Groups Recommendations on the Diagnosis and Classification of Hyperglycemia in Pregnancy (March 2010) based on HAPO study suggested the following:

Glucose	measuremmol/l	mg/dl
FPG	5.1	92
1-h plasma glucose	10.0	180
2-h plasma glucose	8.5	153

This also implies that if one follows the ADA criteria of 2 step test, women will have to visit the antenatal clinic on two occasions – (a) screening and (b) for diagnostic procedure. If we follow the IADPGS criteria, the number of blood samples drawn are multiple (3 blood samples).

This becomes difficult to implement in a country like ours where there are logistic difficulties for so many tests and difficult for the patients to come fasting from long distances. Recognizing these shortcomings DIPSI has suggested a practical and pragmatic test for Indian setting, based on the WHO test, except a fasting glucose test is not done at all. Only a 2 hour reading after ingestion of 75gms of glucose is taken and if above 140mg/dl the patient is diagnosed with Gestational diabetes. This has been validated in many studies and endorsed by WHO (2013) for resource poor settings.

A single test procedure to diagnose gestational diabetes mellitus in the community (suggested by DIPSI)

This refers to a test that detects glucose intolerance without the woman necessarily undergoing a test in the fasting state and the diagnostic test too if performed at the first visit itself.

As glucose concentrations are not affected much by the time since the last meal in a normal glucose tolerant woman, performing this test procedure in the non-fasting state is rational. This single step procedure serves both as screening and diagnostic test for GDM, is simple, economical and feasible. The pregnant woman need not be fasting and in a single visit bit serves as a screening and diagnostic test.

With 75 gm OGTT (WHO criteria)

Plasma Glucose	In Pregnancy	Outside Pregnancy
2 hours ≥200mg/dl	Diabetes	Diabetes
2 hours ≥140mg/dl and ≤199mg/dl	GDM	IGT
2 hours ≥120mg/dl and ≤139mg/dl	GGI	-
2 hours <120mg/dl	Normal	Normal

In the antenatal clinic, a pregnant woman after undergoing preliminary clinical examination, has to be given a 75g oral glucose load, without regard to the time of the last meal. A venous blood sample is collected at 2 hours for estimating plasma glucose by the GOD-POD method. GDM is diagnosed if 2 hours plasma glucose is ≥140mg/dl.
DIPSI

Gestational weeks at which screening is recommended

Insulin is detectable in the fetal pancreas by as early as 9 weeks post-conception. By following the usual recommendation for screening between 24 and 28 weeks of gestation, the chance of detecting unrecognized type 2 diabetes before pregnancy (pre- GDM) is likely to be missed. If the 2 – h PG is >200mg/dl in the early weeks of pregnancy, she may be a pre-GDM and A1c of >6 is confirmatory. A pregnant woman found to have normal glucose tolerance [NGT], in the first trimester, should be tested for GDM again around 24th-28th week and finally around 32nd-34th week.

Management of GDM

A team approach is ideal for managing GDM. It should ideally comprise of an obstetrician, diabetologist, dietitian, midwife and pediatrician.

Patient Education

The compliance with the treatment plan depends on the patient's understanding of:

- The implications of GDM for her baby and herself
- The dietary and exercise recommendations
- Self monitoring of blood glucose at home
- Self administration of insulin and adjustment of insulin doses where necessary
- Identification and treatment of hypoglycemia (patient and family members)
- Incorporate safe physical activity (walking at usual pace/arm exercise)
- Development of techniques to reduce stress

Treatment

Target Blood Glucose Levels

In normal pregnancy, the mean plasma glucose (MPG) + 1 SD value for fasting is 89mg/dl, and 2 hour is 122mg/dl, hence maintenance of Mean Plasma Glucose (MPG) level ~105 to 110mg/dl is desirable for a good fetal outcome. This is possible if FPG and 2 hour post prandial peaks are ~90mg/dl and ~120mg/dl respectively.

Medical Nutrition Therapy (MNT)

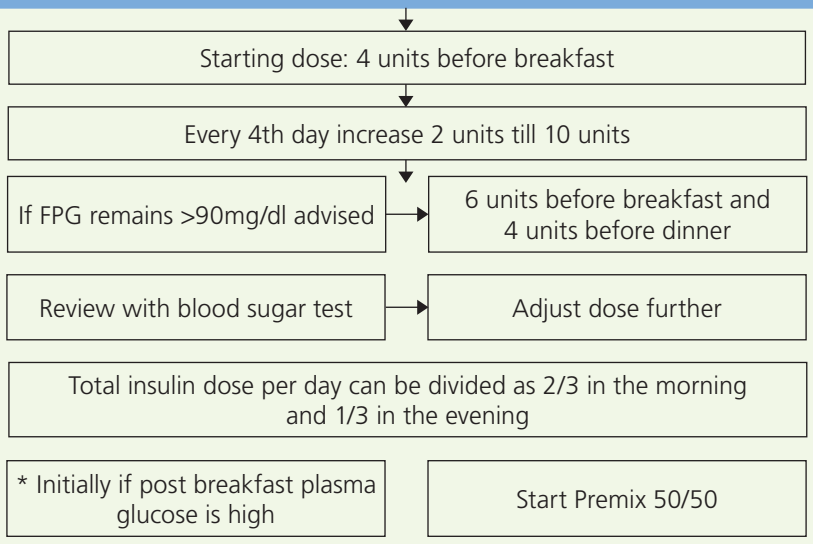
a) **General Principles:** All women with GDM should receive nutritional counseling. The meal pattern should provide adequate calories and nutrients to meet the needs of pregnancy. The meal plan aims to provide sufficient calories to sustain adequate nutrition for the mother and fetus and to avoid excess weight gain and post prandial hyperglycemia. Approximately 30-40kcal/kg ideal body weight or an increment of 300 kcal/day above the basal requirement is needed in 2nd and 3rd trimesters.

b) Calorie Counting: This implies splitting the usual breakfast into 2 equal halves and consuming the portions with a two hour gap in between. By this the undue peak in plasma glucose levels after ingestion of the total quantity of breakfast at one time is avoided. More than 90% of GDM can be managed by MNT (Observation from the Diabetes in Pregnancy Awareness and Prevention [DIPAP] Project, supported by the Government of Tamil Nadu and World Diabetes Foundation [WDF]).

Initiating Insulin Therapy

Once diagnosis is made, Medical Nutritional Therapy (MNT) is advised initially for two weeks. If MNT fails to achieve control i.e., FPG ~90mg/dl and post meal glucose ~120mg/dl, insulin may be initiated.

A. Preferable to start with Premix insulin 30/70 of any brand *.



B. If GDM is diagnosed in the third trimester, MNT is advised for a week. Insulin is initiated if MNT fails.

C. If 2- hour PG >200mg/dl at diagnosis, a starting dose of 8 units of premixed insulin could be administered straightaway before breakfast and the dose has to be titrated on follow-up. Along with insulin therapy, MNT is also advised.

Note:

1. Usually women with gestational diabetes do not require >20 units of insulin per day for glycemic control [40], in comparison to type 1 and type 2 pregnant women whose daily requirement of insulin may be high.
2. Pre-gestational diabetic women during pregnancy may require high dose of insulin. A few may require Multiple-Daily Injections (MDIs), usually given as short acting insulin before breakfast and lunch and intermediate-acting insulin or premix before dinner.
3. Insulin dose is always individualized and has to be adjusted on follow-up.
4. If insulin requirement drops, placental insufficiency or fetal jeopardy has to be suspected (may also be due to increased utilization of maternal glucose by the supercharged beta cell mass of the macrosomic fetus [40] – "fetal handling of maternal glucose").

Monitoring glycemic control

The success of the treatment for a woman with GDM depends on the glycemic control maintained with meal plan or pharmacological intervention. Studies suggest 1, 1 ½ and 2 hours post meal for monitoring glycemic control [56-63]. 2 hours post meal monitoring is preferred as the diagnosis of GDM is also based on 2 hours plasma glucose. It is easier to remember this timing, as the time for diagnosis and also for monitoring is the same i.e. 2 hours.

They should be advised to perform Self Monitoring of Blood Glucose (SMBG) on a daily basis, failing which, at least weekly monitoring should be encouraged. If self-monitoring is not possible, laboratory venous plasma glucose has to be estimated for adjusting the dose of insulin.

Oral Antidiabetic Drugs

Insulin secretagogue [Glybenclamide]

A randomized unblinded clinical trial compared the use of insulin and glyburide in women with GDM who were not able to meet glycemic goals on meal plan. Treatment with either agent resulted in similar perinatal outcomes. All these patients were beyond the first trimester of pregnancy at the initiation of therapy and publications on other drugs belonging to this group are dismal.

Metformin

In women with gestational diabetes mellitus, metformin (alone or with supplemental insulin) was not associated with increased perinatal complications as compared with insulin. Metformin has been found to be useful in women with Polycystic Ovarian Disease (PCOD) who failed to conceive. Continuing this drug after conception is still a controversy, but there are a few studies favoring continuation of metformin throughout pregnancy in these women. More studies are required before routinely recommending oral anti-diabetic drugs during pregnancy.

Measuring Other Parameters

Maternal

A1c level will be helpful to differentiate between a pregestational diabetic and GDM. If the A1c level is more than 6%, she is likely to be a pre GDM. A1c is useful in monitoring the glucose control during pregnancy, but not for the day to day management. A1c level may serve as a prognostic value.

The blood pressure has to be monitored during every visit. If blood pressure is found to be more than 130/80, advise alpha-methyldopa 125mg and dose to be adjusted on follow-up. Examination of the fundus and estimation of microalbuminuria, every trimester is recommended particularly in women with pregestational diabetes.

Fetal

Fetal Surveillance

Ultrasound Fetal Measurement: Ultrasound monitoring is recommended in each trimester. A fetal echo is a must at 24 weeks, especially in prediabetics to rule out cardiac defects. In addition, documenting fetal biophysical profile in the late trimester is advisable. Doppler umbilical blood flow measurement or cardiotocograph [CTG] may be performed around 36 weeks of gestation in GDM with other pregnancy complications such as pre-eclampsia, hypertension, antepartum hemorrhage and intrauterine growth retardation.

Timing of Delivery

Delivery before full term is not indicated unless there is evidence of macrosomia, ployhydramnios, poor metabolic control or other obstetric indications (e.g. pre-elampsia or intrauterine growth retardation). Inducing at 38 weeks is preferable over 39 weeks of gestational age.

Delivery

During labour, it is essential to maintain good glycemic control yet avoiding hypoglycemia. Lower insulin requirements are common during labour (often no insulin is necessary). Maternal blood glucose level should be monitored after delivery, 24 hours postpartum and if found to be high, checked again on follow-up. A neonatologist's presence at the time of delivery is ideal, more so if significant neonatal morbidity is suspected.

Plasma Glucose and Insulin IV Fluid

Plasma glucose at time of onset of labour	Insulin/IV Fluids
<70mg/dl	5% GNS - 100ml/hr
90-120mg/dl	NS - 100ml/hr
120-140mg/dl	NS - 100ml/hr plus *4 units of Reg. insulin added with IV fluid*
140-180mg/dl	NS - 100ml/hr plus *6 units of Reg. insulin added with IV fluid*
>180mg/dl	NS - 100ml/hr plus *8 units of Reg. insulin added with IV fluid*

Drip rate: 16 to 20 drops per minute. Maternal Capillary blood glucose to be checked by glucometer every 1 hour and drip rate adjusted.

Neonatal management

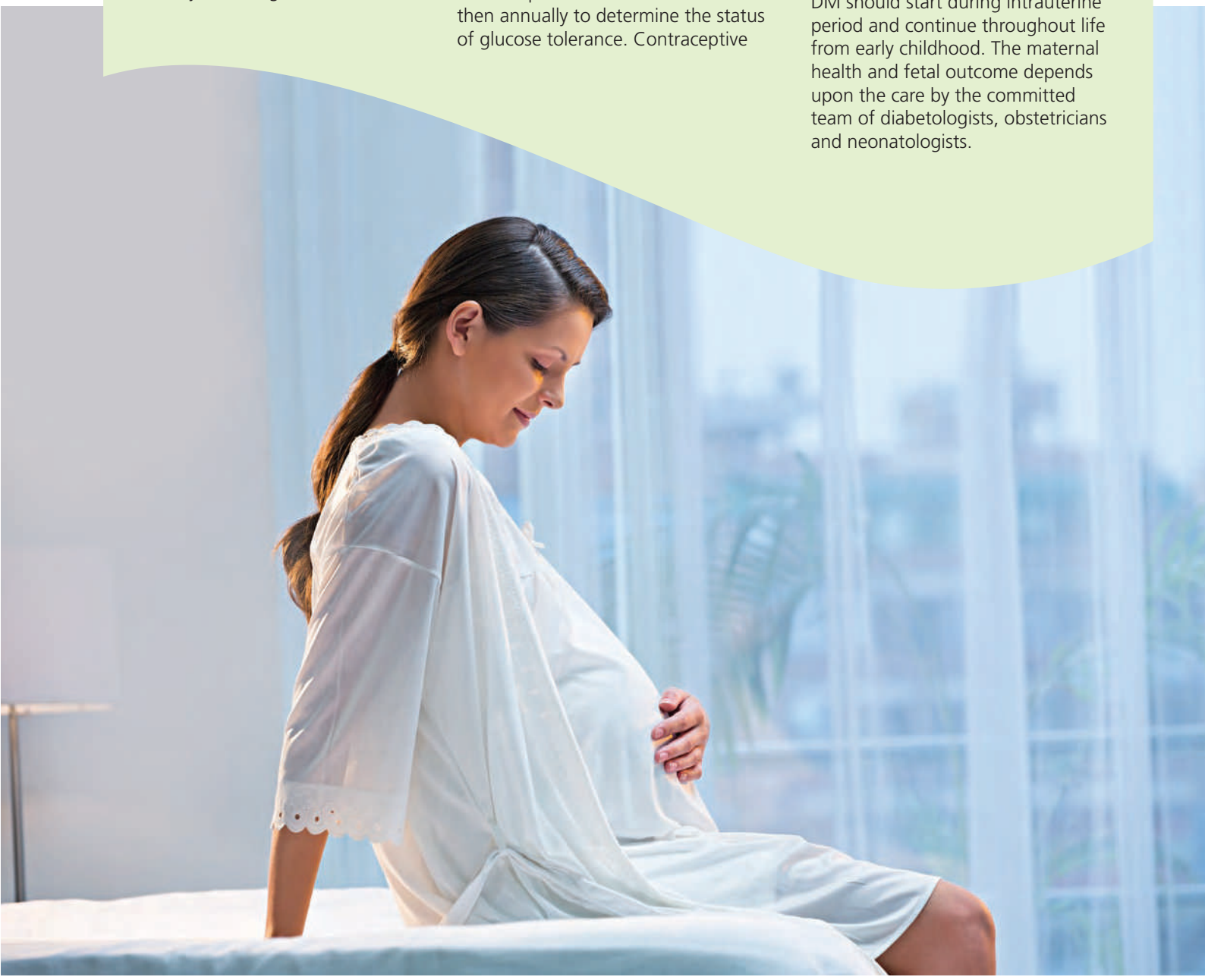
The neonates of mothers with GDM are also at risk of all complications similar to the infants born to mothers with overt diabetes, particularly those infants born macrosomic. In the Indian population, the normal birth weight of new born babies is between 2.5-3.5kg. Neonates should be monitored closely after delivery for respiratory distress. Capillary blood glucose (cut-off of 44mg/dl i.e. 2.6mmol) should be monitored at 1, 2 and 4 hours after birth and then again before feeding. Early breastfeeding is actively encouraged.

Follow up of GDM

It is important that women with GDM be counseled with regard to their increased risk of developing permanent diabetes. Indian women with GDM have a high-risk of developing diabetes (especially type 2 diabetes mellitus), and metabolic syndrome at a comparatively young age. They should be made aware of the symptoms of hyperglycemia and advised regarding healthy eating and exercise patterns.

Gestational diabetic women should undergo OGTT with 75g oral glucose, using WHO criteria for the non-pregnant population at 6-8 weeks postpartum. If found normal, GTT is repeated after 6 months and then annually to determine the status of glucose tolerance. Contraceptive advice and counseling regarding planning future pregnancies should be given. To avoid occurrence of neural tube defect in an unplanned pregnancy, 0.4mg dose of folic acid is recommended on a daily basis by Centre for Diabetes Control for all women of child bearing age. The daily requirement of Vitamin B12 during pregnancy is 2.6mcg which may not be available in a vegan diet. Hence, multi-vitamin tablets containing the required amount of B12 in addition to other vitamins maybe recommended. Medical review by a family physician before conception i.e. a pre-conception OGTT should be considered.

Preventive measures against Type 2 DM should start during intrauterine period and continue throughout life from early childhood. The maternal health and fetal outcome depends upon the care by the committed team of diabetologists, obstetricians and neonatologists.



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Ensuring healthy outcome in small fetus (SGA-PIH, IUGR)

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SGA birth is defined as an Estimated Fetal Weight (EFW) or Abdominal Circumference (AC) less than the **10th centile** and **severe SGA** is defined as an EFW or AC less than the **3rd centile**[1].

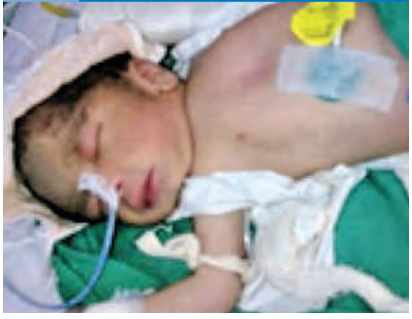
Fetal Growth Restriction (FGR) is not synonymous with SGA. This diagnosis does not necessarily imply pathologic growth abnormalities, and may simply describe a fetus at the lower end of the normal range. Some, but not all, SGA are growth restricted while 50-70% of SGA fetuses are constitutionally small, with fetal growth appropriate for maternal size and ethnicity. Growth restriction implies a pathological restriction of the genetic growth potential. As a result, growth restricted fetuses may manifest evidence of fetal compromise (abnormal Doppler studies, reduced liquor volume).

Low Birth Weight (LBW) refers to an infant with a birth weight <2500 g. This includes 2 broad categories, Preterm (Appropriate for Gestational Age – AGA) and SGA (as above). However, there may be an overlap and mixed picture too. Preterm labor is covered in chapter 4 in more detail.

Small for Gestation Age (SGA) fetuses are divided into:

- Normal (constitutionally) small: small women will have small babies
- Factors related to fetus:
  - Birth defects
  - Chromosomal anomaly
  - Inborn errors of metabolism
  - Fetal infection
  - Multi fetal gestation

Fig 1 **Newborn SGA of eclamptic mother**



- Placentea mediated growth restriction
  - Maternal factors can affect placental transfer of nutrients, for e.g.; low pre-pregnancy weight, under nutrition, substance abuse or severe anemia.
  - Medical conditions can affect placental implantation and vasculature and hence transfer, for e.g.: pre-eclampsia, autoimmune disease, thrombophilias, renal disease, diabetes and essential hypertension.

SGA birth, particularly when severe (birth weight <3rd centile) or necessitating delivery <36 weeks of gestation, is characterized by failure of trophoblast invasion of the myometrial uterine spiral arteries and reduced uteroplacental blood flow.

As a group, structurally normal SGA fetuses are at increased risk of perinatal mortality and morbidity but most adverse outcomes are concentrated in the growth restricted group.

Identification

Effective screening for intrauterine growth restriction requires accurate dating and includes a review of the mother's menstrual history, relevant assisted reproductive technology information, and either a first trimester or early second trimester dating ultrasound.

Methods that can be employed to predict the likelihood of a SGA fetus/neonate include:

1st & 2nd trimester	2nd & 3rd trimester
Medical and obstetric history and examination	Maternal weight gain
Maternal serum screening	Abdominal palpation and measurement of symphysis fundal height (SFH)
Uterine artery Doppler	USG biometry and Doppler indices

All women should be assessed at booking for risk factors for a SGA fetus/neonate to identify those who require increased surveillance. Women that have previously had a SGA neonate have at least a twofold increased risk of a subsequent SGA neonate[2].

Medical and obstetric history

Maternal medical conditions associated with an increased risk of a SGA neonate are:

- Diabetes with vascular disease
- Chronic hypertension
- Renal impairment (especially when associated with hypertension)
- Antiphospholipid syndrome
- Congenital heart disease, in particular cyanotic congenital heart disease

Maternal risk factors associated with an increased risk of a SGA neonate are:

- Maternal age ≥35 years
- Indian/Asian or African American ethnicity
- Moderate alcohol intake, drug use (cocaine use), tobacco chewing (*masheri*) and cigarette smoking
- Nulliparity
- Social deprivation, low socio-economic status
- Unmarried status, unwanted pregnancy
- Body mass index (BMI) <20, BMI >25
- Daily vigorous exercise
- A short (<6 months) or long (>60 months) inter-pregnancy interval
- Heavy vaginal bleeding during the first trimester.
- Singleton pregnancies following IVF

Clinical examination

Low **maternal weight gain** has been shown to be associated with a SGA infant in a preterm population.

Serial Measurement of Symphysis Fundal Height (SFH) is of limited value in routine obstetrical care, but continues to be the only physical examination screening test available.

SFH should be measured from the fundus (variable point) to the symphysis pubis (fixed point) with the cm values hidden from the examiner from 24 weeks of gestation.

Women with a single SFH which plots below the 10th centile or serial measurements which demonstrate slow or static growth should be referred for further investigation. SFH is associated with significant intra and inter-observer variation and serial measurement may improve predictive accuracy[3].

Maternal obesity, abnormal fetal lie, large fibroids, hydramnios and fetal head engagement contribute to the limited predictive accuracy of SFH measurement.

Biochemical markers

A low level (<0.415 MoM) of the first trimester marker PAPP–A is considered a major risk factor for delivery of a SGA neonate.

USG biometry

Fetal abdominal circumference (AC) or estimated fetal weight (EFW) <10th centile can be used to diagnose a SGA fetus. When using two measurements of AC or EFW to estimate growth velocity, they should be at least 3 weeks apart to minimize false-positive rates for diagnosing FGR. Where the fetal AC or EFW is <10th centile or there is evidence of reduced growth velocity, women should be offered serial assessment of fetal size and umbilical artery Doppler.

Uterine artery Doppler

In high-risk populations uterine artery Doppler at 20-24 weeks of pregnancy has a moderate predictive value for a severely SGA neonate. In women with an abnormal uterine artery Doppler (defined as a pulsatility index [PI] >95th centile) and/or notching at 20-24 weeks of pregnancy, subsequent normalization of flow velocity indices is still associated with an increased risk of

a SGA neonate. Repeating uterine artery Doppler is therefore of limited value.

- Women with an **abnormal uterine artery Doppler** at 20-24 weeks should be referred for serial ultrasound measurement of fetal size and assessment of well-being with umbilical artery Doppler commencing at 26-28 weeks of pregnancy.
- Women with a **normal** uterine artery Doppler do not require serial measurement of fetal size and serial assessment of well-being with umbilical artery Doppler unless they develop specific pregnancy complications, for e.g., antepartum haemorrhage or hypertension. However, they should be offered a scan for fetal size and umbilical artery Doppler during the third trimester.

Serial ultrasound measurement of fetal size and assessment of well-being with umbilical artery Doppler should be offered in cases of fetal echogenic bowel.

Investigations

Offer a referral for a **detailed fetal anatomical survey and uterine artery Doppler** if severe SGA is identified at the 18-20 weeks scan.

Karyotyping should be offered in severely SGA fetuses with structural anomalies and in those detected before 23 weeks of gestation, especially if uterine artery Doppler is normal. In severe SGA, the incidence of chromosomal abnormalities has been reported to be as high as 19%. Serological screening for congenital cytomegalovirus (CMV) and toxoplasmosis infection should be offered in severe SGA.

DIPSI Test of 75gms glucose load as suggested by FOGSI GDM screening cum diagnostic test is useful to identify gestational diabetes using 140mg/dl cut off at 2 hours.

Testing for syphilis and malaria should be considered in **high-risk** populations.

Interventions

Bed rest

Rationale behind bed rest is the idea that blood flow to the placenta will increase if activities of other organs is decreased. However, randomized trials have shown no benefit.

Nutritional supplements

There is no consistent evidence that dietary modification, progesterone or calcium prevent birth of a SGA infant. These interventions should not be used for this indication. However, for calcium deficient populations WHO in 2011 has included calcium supplementation of 2gms per day as an essential intervention which may help in prevention of pre-eclampsia.

Antenatal Corticosteroids

This is a simple intervention which should always be given to promote lung maturation when possibility of early delivery is anticipated. Recent evidence suggests that the fetal outcomes are better even in late preterms and steroids should be used until 38 weeks when elective delivery/induction is to be done.

Antiplatelet agents

Antiplatelet agents may be effective in preventing SGA birth in women at high-risk of pre-eclampsia[4]. In such women, antiplatelet agents should be commenced at, or before, 16 weeks of pregnancy. Fertility clinics may be using these peri-conceptionally also and often continue the same.

Treatment of pre-eclampsia

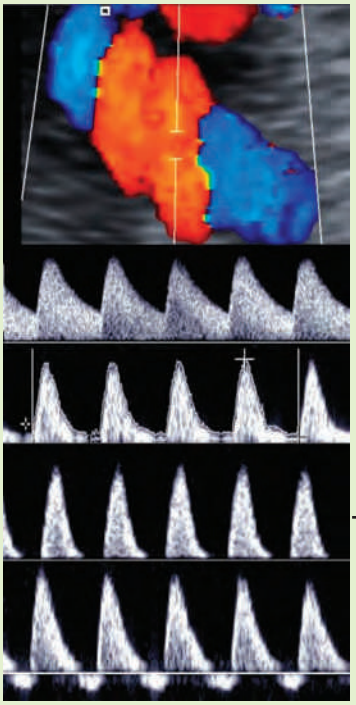
Antihypertensive drug therapy for mild to moderate hypertension in pregnancy does not seem to increase the risk of delivering a SGA neonate[5] but treatment with oral beta-blockers was associated with an increased risk of a SGA neonate partly dependent on one small outlying trial involving atenolol. Alpha methyldopa is the most commonly used drug, but Labetalol is being used more often now. FOGSI-HDP Gestosis program has suggested guidelines and dosages for appropriate treatment. ACOG Task Force guidelines have also suggested that Labetalol, Nifedipine, Methyldopa or Hydralazine can be used to achieve reduction of blood pressure to below 160/110mm Hg when expectant management is being done[6].

Interventions to promote smoking cessation may prevent delivery of a SGA infant. The health benefits of smoking cessation indicate that these interventions should be offered to all women who are pregnant and smoke.

Antithrombotic therapy appears to be a promising therapy for preventing delivery of a SGA infant in high-risk women. However, there is insufficient evidence, especially concerning serious adverse effects, to recommend its use.

The optimal method and frequency of fetal surveillance in SGA infant [7,8]

Fig 2 **Insonation of the umbilical artery Doppler**



Umbilical artery Doppler

Umbilical artery Doppler should be the primary surveillance tool in the SGA fetus. When umbilical artery Doppler flow indices are normal it is reasonable to repeat surveillance every 14 days. More frequent Doppler surveillance may be appropriate in a severely SGA fetus.

When umbilical artery Doppler flow indices are abnormal (pulsatility or resistance index >+2 SDs above mean for gestational age) and delivery is not indicated, repeat surveillance twice weekly in fetuses with end-diastolic velocities present and daily in fetuses with absent/ reversed end-diastolic frequencies.

Cardiotocography (CTG)

When IUGR is detected, FHR monitoring will show a sequence of changes that correlates with worsening of fetal condition: lack of accelerations f/b decreased variability and then onset of spontaneous decelerations. These parameters are not only dependant on the severity of fetal compromise but also on the gestational age at the time of assessment. Usual frequency of FHR monitoring for IUGR fetuses is twice a week.

Amniotic fluid volume

Interpretation of amniotic fluid volume should be based on single deepest vertical pocket (at least 2cms). The presence of oligohydramnios suggests fetal compromise in IUGR pregnancies, but is itself not an indication of delivery. The evaluation should be performed every week and the frequency of non stress testing should be increased if the AFI is low. The possibility of severe congenital fetal malformation should be considered when severe oligohydramnios is found in the initial evaluation of IUGR.

Biophysical Profile (BPP)

The Biophysical Profile (BPP) includes four acute fetal variables (breathing movement, gross body movement, tone and CTG, and amniotic fluid volume; each assigned a score of 2 (if normal) or 0 (if abnormal). Vintzileos et al demonstrated that components of BPP follow a sequential order in their disappearance related to the severity of acidosis – reactivity of FHR followed by breathing movements, f/b fetal movements and f/b fetal tone. Reducing BPP score is associated with lower antepartum umbilical venous pH and increasing perinatal mortality.

Middle Cerebral Artery (MCA) Doppler

In the preterm SGA fetus, Middle Cerebral Artery (MCA) Doppler has limited accuracy to predict acidaemia and adverse outcome and should not be used to time delivery.

In the term SGA fetus with normal umbilical artery Doppler, an abnormal middle cerebral artery Doppler (PI <5th centile) has moderate predictive value for acidosis at birth and should be used to time delivery.

Cerebral vasodilatation is a manifestation of the increase in diastolic flow, a sign of the 'brain-sparing effect of chronic hypoxia, and results in decreases in Doppler indices of the Middle Cerebral Artery (MCA) such as the PI. Reduced MCA PI or MCA PI/umbilical artery PI **(cerebroplacental ratio)** is therefore, an early sign of fetal hypoxia in SGA fetuses.

Ductus Venosus (DV) and Umbilical Vein (UV) Doppler

Ductus venosus Doppler has moderate predictive value for acidaemia and adverse outcome. It should be used for surveillance in the preterm SGA fetus with abnormal umbilical artery Doppler and can be used to time delivery.

Making sense of Doppler US in Obstetrics[7]

- Indices should be measured only after 23 weeks
- Primarily useful in placental insufficiency IUGR
- Cerebroplacental ratio (MCA PI/ UA PI) appears to be a more sensitive index to predict poor outcome
- Need to separate constitutionally small versus pathologically small fetus (normal indices, AF)

Timing of delivery[7,8]

At present there is no effective intervention to alter the course of FGR except delivery. Timing delivery is therefore, a critical issue in order to balance the risks of prematurity against those of continued intrauterine stay; death and organ damage due to inadequate tissue perfusion.

Critical determinants in decision-making

- Gestational age
- Interpretation of surveillance tests which should accurately predict perinatal outcomes of importance (death, major morbidity and neurodevelopmental delay)
- The neonatal setup available

Preterm SGA fetus prior to 32 weeks with:

- **Umbilical artery AREDV detected**, delivery is recommended when DV Doppler becomes abnormal or UV pulsations appear, provided the fetus is considered viable and after completion of steroids.
- **Even when venous Doppler is normal,** delivery is recommended by 32 weeks of gestation and should be considered between 30-32 weeks of gestation.
- **If MCA Doppler is abnormal,** delivery should be recommended no later than 37 weeks of gestation.

SGA fetus detected after 32 weeks of gestation

- With an abnormal umbilical artery Doppler, delivery no later than 37 weeks of gestation is recommended.
- With normal umbilical artery Doppler, a senior obstetrician should be involved in determining the timing and mode of birth of these pregnancies.
- Delivery should be offered at 37 weeks of gestation.

Mode of delivery[8]

- **Umbilical artery AREDV:** delivery by caesarean section is recommended.
- **Normal umbilical artery Doppler or with abnormal umbilical artery PI but end-diastolic velocities present:** offer induction of labour but rates of emergency caesarean section are increased and continuous fetal heart rate monitoring is recommended from the onset of uterine contractions.

Early admission is recommended in women in spontaneous labour with a SGA fetus in order to initiate continuous fetal heart rate monitoring.

A lot depends on the neonatal setup available – a small baby with a birth weight of 700g may survive especially if SGA is in a good setup. Small babies may have a better chance in a good NICU if delivered by LSCS.

Compared to appropriate for gestational age fetuses, term and near term SGA fetuses are at increased risk of FHR decelerations in labour, emergency caesarean section for suspected fetal compromise and metabolic acidaemia at delivery. This reflects a lower prelabour pO2 and pH, greater cord compression secondary to oligohydramnios and a greater fall in pH and higher lactate levels when FHR decelerations are present.

Summary: approach for intrauterine growth restriction in clinical practice

Screening for intrauterine growth restriction.

History: maternal, fetal and placental risk factors; establish dates by first trimester ultrasound and last menstrual period.

Physical: SFH measurement

Diagnosis of intrauterine growth restriction: EFW or AC <10th percentile.

Early onset and late onset FGR represent two distinct clinical phenotypes of placental dysfunction.

Investigations to consider:

- Biochemical screening tests for Trisomy 21 as a test of placental insufficiency.
- First trimester ultrasound for dating and nuchal translucency.
- Uterine artery Doppler at 19-23 weeks if biochemical markers are abnormal.
- If SFH (in centimetres) is less than gestational age (in weeks) by >3, arrange ultrasound for EFW, AFV or DVP, biophysical profile, and/or umbilical Doppler studies.

Management of intrauterine growth restriction

Investigations	Maternal management	Fetal management
• Offer amniocentesis if there is high-risk of aneuploidy. • Consider TORCH screen.	• Conduct ongoing monitoring for pre-eclampsia. • Corticosteroids for lung maturity. • Consider adding low-dose aspirin early in the pregnancy if patient fulfills the criteria for its use.	• If pre-viable (<500g ± <24 weeks): offer counseling by multi-disciplinary health care team regarding fetal monitoring and obstetrical intervention until viability. • If viable (>500g and >24 weeks): conduct initial ultrasound assessment: EFW, AFV, umbilical Doppler; in third trimester (~26 weeks) consider weekly BPP and growth every 2 weeks. • If growth continues along growth curve: conduct weekly biophysical profile and umbilical artery. • Antenatal surveillance requires adjustment of monitoring intervals based on signs of disease acceleration or changes in maternal condition (especially PIH), when delivery is not yet indicated. • Offer delivery at 37 weeks.

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Prediction and prevention of preterm birth

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Background

Preterm Labor (PTL) complicates 5-10% of pregnancies and is a leading cause of neonatal morbidity and mortality worldwide.

It is a major public health problem in terms of loss of life, long-term disability (cerebral palsy, blindness, deafness, chronic lung disease) and health care costs both in the developing and the developed world[2]. Preterm births are the most important single determinant of adverse infant outcome, in terms of both survival and quality of life.

The incidence of preterm labor has remained almost static since last 40 years. There are no consistent data that any intervention (including hydration, antibiotics, or tocolytic therapy) can delay delivery in women for longer than 24 to 48 hours once they have presented in preterm labor[3]. For this reason, preventative strategies for PTL have been used and evaluated through many clinical trials.

As such, most of the mothers with PTL do not perceive typical symptoms and majority of them have no currently identifiable risk factor. It has been suggested that premature cervical shortening or ripening might be the primary mechanism preceding onset of actual PTL.

Upto 75% of preterm labor which occurs either spontaneously or following PPROM can be predicted by various methods[2]. Clinical predictors of PTL in 2012 ACOG guidelines are similar to those mentioned in the 2001 practice bulletin.

The goal of all attempts to predict and prevent preterm labor is to improve preterm infants' chances of surviving with as few complications as possible. The methods discussed here can be used to identify pregnancies at risk for preterm labor so to take appropriate measures to reduce perinatal morbidity and mortality.

Preterm births are the most important single determinant of adverse infant outcome, in terms of both survival and quality of life.

Risk factors (ACOG)

1. **Prior Preterm Birth (PTB)**
   Prior PTB is one of the strongest risk factors for subsequent PTB. The number of prior preterm births and the gestational age at the prior delivery significantly affect the recurrence risk of preterm birth.

2. **Short cervical length**
   Short cervical length is most commonly defined as less than 25mm, usually before 24 weeks of gestation, but can be considered up to 28 weeks of gestation as measured by Transvaginal ultrasonography. It is associated with higher risk of PTL.

3. **A history of cervical surgery**
   Surgeries like conization and loop electrosurgical excision procedure, traditionally has been thought to be a risk factor for preterm birth but this link has not been established.

4. **Uterine instrumentation**
   The proposed mechanism is intrauterine microbial colonization, injury to the endometrium, or both. It has been associated with an increased risk of preterm birth in some studies.

5. **Other factors**
   Pregnancy associated with vaginal bleeding, urinary tract infections (UTIs), genital tract infections, and periodontal disease are considered potential risk factors. However, treatments for any of these have not been definitively demonstrated to result in a decreased risk of preterm birth.

6. **Behavioral risk factors**
   Low maternal prepregnancy weight, smoking, substance abuse, and short interpregnancy interval.

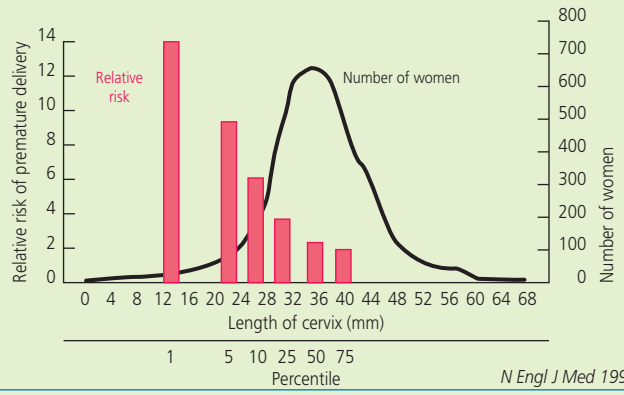
These risk factors can be classified into either non-modifiable or potentially modifiable. Prior preterm birth, cervical injury or anomaly, uterine anomaly, low prepregnancy weight and absent prenatal care are some of the important non-modifiable risk factors. While lower genital tract infections and urinary tract infections in a mother are factors which are modifiable or treatable[3].

Research has focused on combined risk scoring systems that use multiple serum markers, ultrasound, and maternal demographic factors, but these have not been fully validated in large scale studies[4].

Screening methods

The goal of screening is the early identification of pregnant women at an elevated risk of going into labor prematurely, so that these women can be helped to carry their pregnancies to term

Fig 1 Relative risk of PTL according to cervical length



N Engl J Med 1996; 334:567–72

1. Cervical length screening

Cervical length remains relatively constant in pregnancy. In women with PTL, the rate of cervical length change may be predictive of preterm birth. The rate of cervical shortening is faster in women who deliver preterm than in those who deliver at term. In a review of 39,284 cases of preterm birth (<37 weeks), short cervix was most important single predictor of preterm birth[5]. A strong inverse correlation exists between residual cervical length as measured by transvaginal ultrasound and preterm birth[3].

Both Transperineal (TP) and Transvaginal (TV) cervical assessments have been studied for measuring cervical length, but most of the studies have evaluated TV assessment. Transvaginal cervical ultrasonography has been shown to be a reliable and reproducible way to assess the length of the cervix. It is not affected by maternal obesity, position of the cervix, and shadowing from the fetal presenting part[1].

For measuring cervical length, a faint line of echo density between internal and external os needs to be identified after placing transvaginal probe in the anterior fornix. The cervical length is the shortest of three measurements taken between calipers placed at the internal os and external os. If funneling is present, measurement should be taken from the funnel tip to the external os. Undue pressure over cervix during the procedure may cause false increase in the cervical length. Cervical funneling does not increase risk of PTL associated with a shortened cervical length[1].

Because of poor positive predictive values and sensitivities and lack of proven effective interventions, routine transvaginal cervical length assessment is not recommended in women at low risk[4].

2. Other specific tests and monitoring modalities

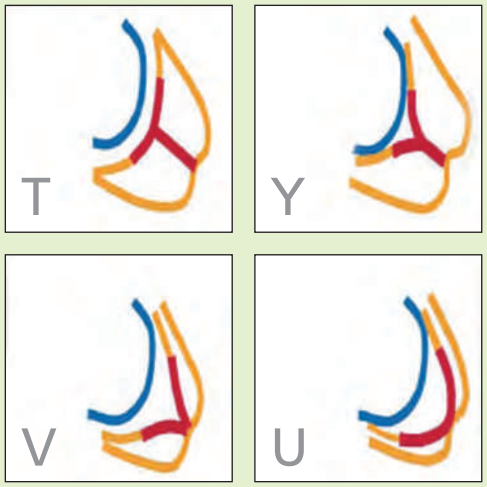
Salivary Estriol, bacterial vaginosis testing, home uterine activity monitoring (HUAM) and Fetal fibronectin measurement have been proposed to assess a woman's risk of preterm delivery.

HUAM is based on the principle of tocodynamometry. Earlier studies showed that HUAM was effective in predicting the onset of PTL, but recently it has showed no benefit in predicting PTL[2].

Salivary Estriol has very poor sensitivity and specificity and has a very high false positive rate when used for prediction of PTL. It may also increase the cost of prenatal care[2].

Bacterial Vaginosis (BV) has been found to increase the risk of preterm labor by two-fold in earlier studies. However, results have been largely inconclusive and the benefit of screening for BV in low risk population is still unclear[2].

Fig 2 Cervical changes in transvaginal ultrasound



Iams. Early Detection of Prematurity. Obstet Gynecol 2003.

Ultrasonographic cervical length assessment and fetal fibronectin appear to be similar in predictive ability, and the combination of both in a high-risk population maybe of value. However, further research is needed in this area[4].

Largely, these modalities are no longer recommended as screening strategies as they do not improve perinatal outcomes in asymptomatic women[1].

Interventions

1. Role of progesterone supplement

The most important single advance of the past decade has been the introduction of progesterone supplementation for the prevention of premature labor. In 2011, the US Food and Drug Administration (FDA) for the first time has approved the use of progesterone supplementation (hydroxyprogesterone caproate) during pregnancy to reduce the risk of recurrent preterm birth in women with a history of at least one prior spontaneous preterm delivery[3].

Preventive treatment with progesterone can lower the rate of preterm birth in high-risk groups by more than 30%[6]. The optimal progesterone formulation, route of delivery, and dose for the prevention of preterm birth has not yet been determined[3].

Vaginal progesterone has been studied as a management option to reduce the risk of preterm birth in asymptomatic women with singleton gestations without prior preterm birth with a very short cervical length[1]. It reduces the risk of preterm birth and neonatal morbidity and mortality[7].

No evidence exists to support the addition of an alternative form of progesterone to the current progesterone treatment (e.g., adding a vaginal form to an intramuscular form), who is already receiving preventive progesterone therapy. Also, there is no evidence to suggest that switching from treatment with intramuscular progesterone to treatment with vaginal progesterone is beneficial if a short cervix is identified[1].

Progesterone can also be used beneficially for secondary prevention after tocolysis, although no benefit has been demonstrated in twin pregnancies. The available evidence supports the recommendation that all pregnant women who have either a prior history indicating increased risk or current, asymptomatic cervical insufficiency should receive progesterone supplementation until 34 completed weeks of gestation[6]. Progesterone supplementation can prevent only up to one-third of recurrent preterm births, and the long-term benefits of progesterone supplementation are not yet clear[3].

Recommendations for progesterone supplement

a) **Progesterone Supplementation in Women with a History of Spontaneous Preterm Birth**
There is increasing evidence that progesterone supplementation can reduce the rate of spontaneous preterm birth in this group of women[3].

A woman with a singleton gestation and a prior spontaneous preterm singleton birth should be offered progesterone supplementation starting at 16-24 weeks of gestation, regardless of transvaginal ultrasound cervical length, to reduce the risk of recurrent spontaneous preterm birth[1].

b) **Progesterone Supplementation in Women with Cervical Shortening**
Cervical shortening is a known risk factor for preterm birth in both low and high-risk populations. Progesterone administration significantly reduced the rate of spontaneous preterm birth before 34 weeks. Whether progesterone acts by attenuating further cervical shortening is not yet clear[3].

Vaginal progesterone is recommended as a management option to reduce the risk of preterm birth in asymptomatic women with a singleton gestation without a prior preterm birth with an incidentally identified very short cervical length less than or equal to 20mm before or at 24 weeks of gestation[1].

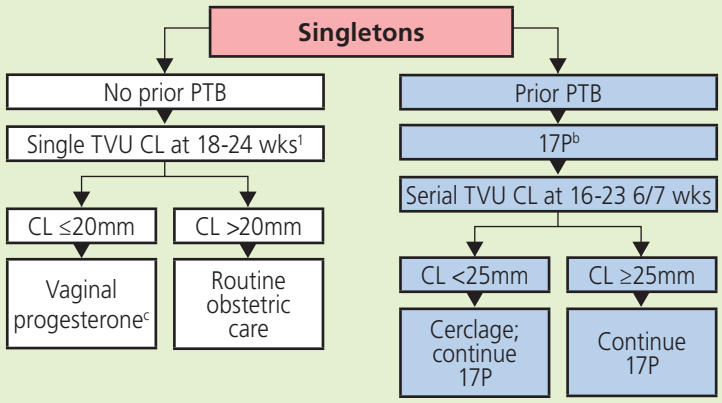
c) **Women with a Cerclage**
It is not clear whether progesterone provides additional benefit to women with a cervical cerclage in place[3].

d) **To treat women in preterm labor**
Several studies have investigated use of progesterone in women who remained undelivered after an episode of preterm labor. Women who received 17P experienced less shortening of the cervix and a reduced rate of preterm delivery. However, there was no difference in the overall rate of preterm birth, admissions for recurrent preterm labor, or admissions to the neonatal intensive care unit[3].

e) **Multiple Gestation**
Progesterone supplementation does not prolong gestation or improve perinatal outcome in women with multiple gestations as the mechanism leading to preterm labor and delivery in multiples is different from that in singletons[3].

Progesterone treatment does not reduce the incidence of preterm birth in women with twin or triplet gestations and, therefore, is not recommended as an intervention to prevent preterm birth in women with multiple gestations[1].

Fig 3 **Algorithm for use of progestogens in prevention of PTB in clinical care**



[a]If TVU CL screening is performed; [b]17P 250mg intramuscularly every week from 16-20 weeks to 36 weeks; [c]eg, daily 200-mg suppository or 90-mg gel from time of diagnosis of short CL to 36 weeks. a, cervical length; *PTB,* preterm birth; *17P,* 17-alpha-hydroxy-progesterone caporate; TVU, transvaginal ultrasound. *SMFM. Progesterone and preterm birth prevention. Am J obstete Gynecol 2012.*

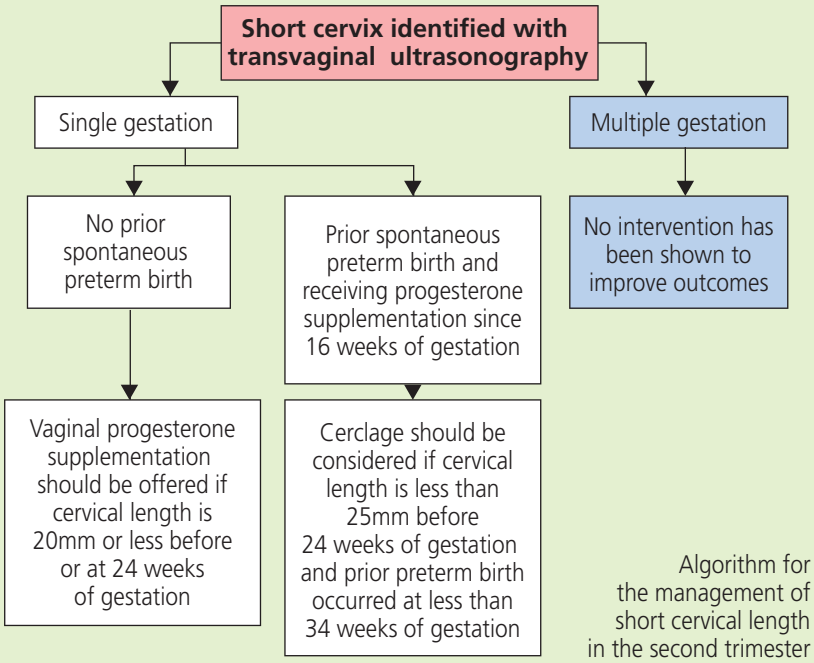
2. Role of cervical encerclage

Available evidence suggests that, in women with a current singleton pregnancy, prior spontaneous preterm birth at less than 34 weeks of gestation and short cervical length (less than 25mm) before 24 weeks of gestation, cerclage placement is associated with significant decrease in preterm birth outcomes[1].

Cerclage for cervical length less than 15mm was associated with a significant decrease in preterm birth at less than 35 weeks of gestation, while, when cervical length is less than 25mm, it has not been associated with a significant reduction in preterm birth[1].

In asymptomatic women with a history of spontaneous preterm birth and an ultrasonographically diagnosed short cervical length (<25mm) prior to 24 weeks of gestation, cervical cerclage should be considered to reduce the risk of preterm birth[4].

Fig 4 **Flow chart for management of women with short cervical length**



Algorithm for the management of short cervical length in the second trimester

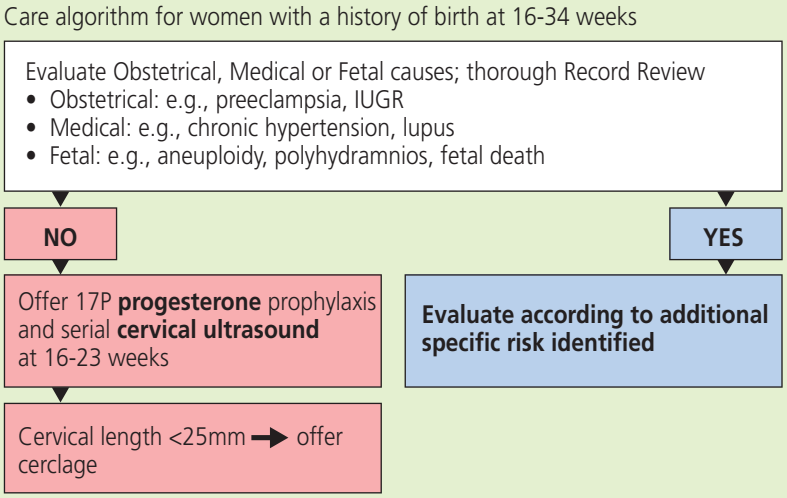
Acog practice bulletin 130. Obstet Gynecol. 2012;120(4):964-973

ACOG level B recommendation mentions that cerclage may increase the risk of preterm birth in women with a twin pregnancy and an ultrasonographically detected cervical length less than 25mm and is not recommended[1].

In all asymptomatic women, who present with membranes at or protruding past the external cervical os, an emergency cerclage should be considered to reduce the risk of preterm delivery[4].

Insufficient evidence exists to assess whether progesterone and cerclage together have an additive effect in reducing the risk of preterm birth in women at high-risk for preterm birth[1].

Fig 5 **Algorithm for management of women with history of prior preterm birth**



Iams. Care for women with prior preterm birth. Am J Obstet Gynecol 2010.

3. Other interventions

Other interventions, such as pharmacotherapy with indomethacin or antibiotics, activity restriction, or supplementation with omega-3 fatty acids are not recommended as clinical interventions for women with an incidentally diagnosed short cervical length[1].

No specific randomized trials have evaluated any interventions in asymptomatic women at >24 weeks gestation who are at increased risk of preterm birth and having a short cervical length. Management of these women includes reduction of activity level, work, or travel, relocation, increased surveillance, and administration of corticosteroids[4].

Key Points for Clinical Practice

- Routine transvaginal cervical length assessment is not recommended in women at low risk.
- Salivary Estriol, bacterial vaginosis testing, Home Uterine Activity Monitoring (HUAM) and fetal fibronectin measurement are no longer recommended as screening strategies as they do not improve perinatal outcomes in asymptomatic women.
- In asymptomatic women with a history of spontaneous preterm birth and having short cervical length (<25mm) prior to 24 weeks of gestation, cervical cerclage should be considered to reduce the risk of preterm birth.
- Vaginal progesterone is recommended as a management option to reduce the risk of preterm birth in asymptomatic women with a singleton gestation without a prior preterm birth with an incidentally identified very short cervical length less than or equal to 20mm before or at 24 weeks of gestation.
- Insufficient evidence exists to assess whether progesterone and cerclage together have an additive effect in reducing the risk of preterm birth in women at high-risk for preterm birth.
- In women admitted for suspected preterm birth or where there is possible early delivery anticipated for any reason, it is essential to give antenatal corticosteroids for lung maturity.
- **The most cost effective intervention is giving antenatal steroids- Betamethasone 12mg -2 doses 24 hours apart, or Dexamethasone 8mg-4 doses 12 hours apart. In high risk cases such as previous history of preterm birth, multiple pregnancy, or any condition like IUGR-which may entail a preterm delivery-one must remember to give steroids as early as 24-26 weeks. They take a week to take effect and repeated doses are not required.**
- In case of inevitable preterm labor, it is essential to consider inutero transfer to a centre equipped to handle the premature newborn.

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Editorial note

Best practices and newer concepts – Dr. Reena Wani

As Chairperson Perinatology Committee, there has been much feedback from neonatologists that obstetric practices need to be optimized for better outcomes and decreasing problems of prematurity once preterm birth is imminent and unavoidable. The authors have covered prediction and prevention beautifully. However, I would like to emphasize the following clinical practice points which are now being implemented in many feto-maternal medicine units in our country also.

- Two essential interventions all basic obstetric units can offer which reduce perinatal mortality are:
  - Administration of antenatal corticosteroids (combined with tocolysis for at least 2 days)
  - Inutero transfer to appropriate neonatal care facility in this time
- Antepartum administration of magnesium sulphate for neuro protection:
  - Given if preterm delivery is imminent, between 24-32 weeks
  - Usually given as 6gms load over half an hour, followed by 2g/h for a maximum of 12 hours; stop if delivery is no longer considered imminent
- Cesarean delivery offers survival advantage in non-vertex presentations
- Delayed cord clamping (by at least 1 minute) reduces the risk of many neonatal morbidities and mortality (<32 weeks)

Reference

Preterm Labor. Locatelli A, Consonni S, Ghidini A. In: SimpsonL (Ed): Best Practices in High Risk Pregnancy. Obstet Gynecol Clin N Am 2015; 42: 255-274.

Prevention of Retinopathy of Prematurity (ROP) – National ROP Task Force Guidelines, GOI 2015

Preventing Blindness due to Retinopathy of Prematurity
Roles and Responsibilities of Obstetricians

Message from ROP Task Force, Ministry of Health, Govt. of India
The advancement and wider availability of obstetric and neonatal care in our country has led to an impressively increasing survival of preterm newborns. However, this has also resulted in an unwanted 'third' epidemic of Retinopathy of Prematurity (ROP).

ROP refers to an abnormal proliferation of the retinal blood vessels seen in sick preterm neonates. This can result in retinal detachment and irreversible blindness. However, with high quality obstetric and neonatal care, most of ROP can be prevented. Even in those who develop ROP, a timely diagnosis and timely treatment by LASER can prevent visual loss. The risk of sight-threatening ROP increases with decreasing gestational age at birth, unregulated exposure of the neonate to oxygen, blood transfusion and sepsis.

ROP does not manifest any external signs except in very late irreversible stage. Diagnosis of ROP is currently dependent on the examination of retina by indirect ophthalmoscopy by an ophthalmologist trained in its diagnosis and handling of preterm infant, or by retinal imaging with help of very expensive RetCAM system.

What all can obstetricians do to prevent visual loss due to ROP?

- **Prevent prematurity:** Prevent multiple pregnancies of high order during management of infertility, prevent teenage pregnancies, identify and manage pregnant woman at high-risk of preterm birth, treat preterm premature rupture of membranes by appropriate antibiotics, administration of calcium for prevention of hypertensive disease of pregnancy, use of tocolytic agents and judiciously timed delivery.
- **Use antenatal steroids in women at risk of preterm delivery:** Antenatal steroids prevent respiratory distress and intraventricular hemorrhage, two important risk factors of ROP.
- **Judicious and controlled oxygen therapy:** Each birthing unit should have provision for compressed air, blended oxygen and pulse oximetry during resuscitation at birth. If newly born infant needs positive pressure ventilation, it should be started with room air. If there is no response with room air, blended oxygen should be administered and increased gradually to keep oxygen saturation within target range prescribed during resuscitation (70% at 3 minute and 80% at 5 minute after birth).
- **Promoting delivery of a preterm infant in a hospital** with well equipped neonatal resuscitation corner (as described above) and special care newborn unit.
- **Promoting and facilitating exclusive use of expressed breast milk:** during antenatal as well as postnatal period.
- **Counseling and facilitating families** for timely screening, follow-up and treatment of ROP by the ophthalmologist.

Which babies should be screened for ROP and when?

ROP Task Force/ RBSK Operational Guidelines 2015

In view of several reports of large babies of relatively higher gestations developing Aggressive Posterior ROP (AP-ROP) in our country, the criteria suggested for ROP screening have been moved upwards as follows:

- All infants admitted to a special care newborn unit (SCNU) or NICU and having any 1 of the following:
  - Gestation ≤34 weeks
  - Birth weight ≤2000g (if gestation is unknown or unreliable)
  - Gestation >34 weeks PLUS risk factors
  - Considered at risk by pediatrician, irrespective of gestation or weight
- The first examination should be performed **not later than 4 weeks of age or 30 days life** in infants born ≥28 weeks of gestational age. Infants born <28 weeks or <1200gms birth weight should be screened early, by 2-3 weeks of age, to enable early identification of AP-ROP.

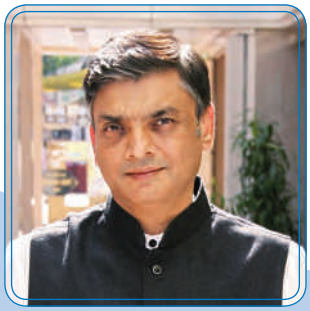
For further details contact ashokdeorari_56@hotmail.com

सत्यमेव जयते

National consensus meeting in AIIMS

National consensus meeting in AIIMS

Screening for detection of fetal Aneuploidies



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Joint Secretary FOGSI (2005)
Chairperson Medical Disorders in Pregnancy Committee (2006-2008),
Founder Secretary and Past President Navi Mumbai OBGY Society

Is my baby normal?

One thing no expectant mother wants is a defect in her baby.
Today, we are in an age where imaging sciences have made it easy for us to pick up structural defects and that too relatively early in pregnancy so as to offer a safe termination. But imaging sciences may not always pick up a chromosomal defect particularly T21.

Trisomy 21 is the most common trisomy at the time of birth. Also called Down syndrome, it is associated with moderate to severe intellectual disabilities and may also lead to digestive disease, congenital heart defects and other malformations. Incidence is about 1 per 1000 babies born each year. It is named after **John Langdon Down,** the British doctor who fully described the syndrome in 1866. The genetic cause of Down syndrome is an extra copy of chromosome 21. Other chromosomal defects, which we can screen for are **Trisomy 18 (Edwards syndrome) and Trisomy 13 (Patau syndrome)** are associated with a high rate of miscarriage. These babies are born with severe brain abnormalities and often have congenital heart defects as well as other birth defects. Most affected individuals die before or soon after birth and very few survive beyond the first year of life. Most often these fetuses either abort or show a major defect on USG.

However, Downs can be elusive, and at times does not show up on a normal sonogram. Thus, we have sophisticated screening methods to offer.

Should we be offering Downs screening to all women Or selective to elderly women?

Though incidence is higher as age advances, but since younger women generally have more children, about **75-80%** of children with Down syndrome are born to younger women. But Universal Screening is as yet not a standard of care.

One has to decide what one will do in one's practice. Consider the following points:

1) You must once listen to a mother who has a Downs child – the trouble and sacrifices she gives to bring up this child so that he/she can have some place in society. The average IQ of a young adult with Down syndrome is 50, similar to the mental age of an 8 or 9 year old child, but this varies widely. Some children with Down syndrome are educated in typical school classes while others require more specialized education. In adulthood about 20% in the United States do paid work in some capacity. Life expectancy is around 50-60 years

in the developed world with proper health care.

We must bring all these facts before a couple and let them decide if they want to take the screening tests. I have had 40 year olds who in spite of a high NT have declined the screening or invasive testing since they were open to having a Downs baby. In fact, many countries (e.g. Australia) feel that a Downs individual can have a fulfilling life and thus one should not be biased about aborting a Downs baby.

2) Generally, we in India opt to offer it to the educated and financially well off patients, but we must consider the fact that a Downs baby is a bigger burden for the economically weak, and the cost of the tests may be more affordable than bringing up a Downs baby.

3) Lastly, we must take into account the medico-legal climate of the country.

Our job is to make the couple aware of this disorder, and that screening tests are available. Results should be explained and information must be provided through non-directive counseling.

They should go in for the testing only if they are sure they want to abort the fetus if proved to be Downs (and this may entail invasive testing). I personally don't subscribe to the view that the woman should be offered an invasive test, even if she has decided NOT to abort and continue the pregnancy, just for her knowledge. One can always then wait for her to deliver and test the child.

Our job is to make the couple aware of this disorder, and that screening tests are available. Results should be explained and information must be provided through non-directive counseling.

When and how to screen?

K. H. NICOLAIDES

Table 1 - Performance of different methods of screening for Trisomy 21

Method of screening	Detection rate (%)	False positive rate (%)
MA	30	5
First trimester		
MA + fetal NT	75-80	5
MA + serum free ß - hCG and PAPP-A	60-70	5
MA + NT + free ß - hCG and PAPP- A (combined test)	85-95	5
Combined test + nasal bone or tricuspid flow or ductus venous flow	93-96	2.5
Second trimester		
MA + serum AFP, hCG (double test)	55-60	5
MA + serum AFP, free ß - hCG (double test)	60-65	5
MA + serum AFP, hCG, uE3 (triple test)	60-65	5
MA + serum AFP, free ß-hCG, uE3 (triple test)	65-70	5
MA + serum AFP, hCG, uE3, inhibin A (quadruple test)	65-70	5
MA + serum AFP, free ß-hCG, uE3, inhibin A (quadruple test)	70-75	5
MA + NT + PAPP-A (11-13 weeks) + quadruple test	90-94	5

MA - maternal age, NT - nuchal translucency ; ß-hCG - ß-chorionic gonadotrophin, PAPP-A - pregnancy-associated plasma protein- A.

If we look at the above table[1], maternal age has only a 30% detection rate. Adding NT value to maternal age the detection rate goes up to 80%.

Maternal age + NT + double marker test gives us upto 95% detection rate for a false positive of 5%. A small increase is there if we add nasal bone and Doppler studies.

Thus, today, screening is offered at the time of the 11- 13.4 weeks scan. The double marker test is offered for the biochemical markers of PAPP-A and Serum Beta HCG. These values with the value of NT, maternal age, gestational age and weight are taken into account to give the patient a personalized risk of having T21, 13 and 18. Correction is made for factors like maternal diabetes and smoking.

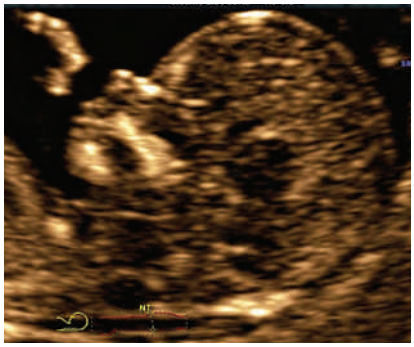
Only second trimester biochemistry (triple and quadruple) have a much lower – 70% detection rate and should be offered if the patient presents late.

Nuchal Translucency

Measured between 11-13.5 weeks on USG. There are strict criteria to be observed while doing a NT, some of which are:

- Proper mid sagittal plane
- 75% magnification
- Neutral position of head
- Proper placement of calipers

It is advisable to have a FMF certified person doing the NT scan. Besides measuring the NT, gross structural anomalies can be ruled out. Please look at the images of NT in the report (it should look like this).



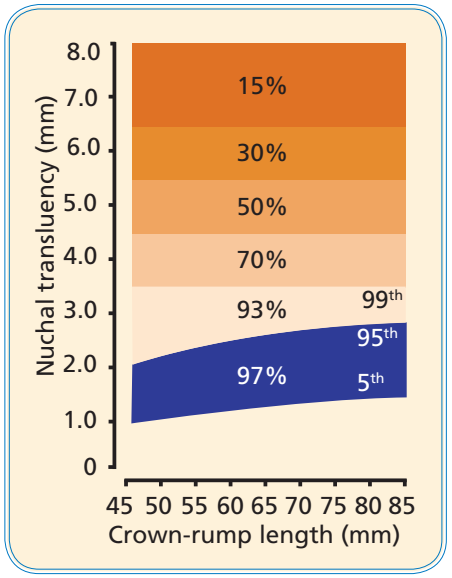
What if the NT is high of say 3.5?

What prognosis to give to the patient?

This is an example taken from the FMF website.

E.g.: fetus with NT of 3.5-4.4mm

In 100 fetuses with NT of 3.5-4.4mm diagnosed at 12 weeks, 20 would have a chromosomal abnormality and 80 would be euploid.



In the 80 euploid fetuses there would be 2 (2.5%) that would die in the subsequent few weeks.

In an additional 8 of the 80 euploid fetuses (10%), there would be a major defect.

The remaining 70 euploid fetuses with no major defects would be live born and healthy.

Only a high NT does not call for a termination. Although increased fetal NT thickness is associated with abnormalities and fetal death, majority of babies survive and develop normally. After the diagnosis of increased NT the aim must be to distinguish as accurately and quickly as possible between those that are likely to have problems from those where the baby is likely to be normal.

What is a positive screen?

Each laboratory gives a value – generally 1:250 is the cut off. If the risk is 1:90 means out of 90 similar women screened only 1 will have Downs. But this is above the cut off and an invasive test either CVS or Amniocentesis is indicated.
What if the risk comes to 1:260? Well, one can do one of the following:

1) Let cut offs be cut offs and not do anything further.
2) FMF has a defined a Intermediate risk 1:51 – 1:1000 as per FMF guidelines and look for additional markers:
   - HR
   - Nasal bone
   - DV
   - Facial angle
3) Do Integrated Screen – First trimester biochemistry + NT + Triple Test all are integrated and given a risk. For this, the laboratory must have the software to integrate all the values.
4) Offer Non Invasive Prenatal Testing

Is screening for Downs in multiple pregnancies different?

More than twins – no biochemical screening as LRs are derived yet and lack of evidence; hence only NT and anomaly scans.

Twins with a vanishing twin – if there is a measurable CRL, again biochemical screening not reliable as not known how much is being secreted from the live one and how much already secreted from the dead one.

Live DC twins – assumed that the hormonal sharing is 50-50 and so can do biochem screening but using correction factor as in the FMF and the life cycle softwares; after the NT scan. If one baby has markers or defects suggestive of chromosomal abnormalities, then again directly offer invasive testing.

Live MC twins – the placenta is shared. However, it's not clear how much is shared by which twin. One would get average risk for pregnancy. (pregnancy specific risk) and special FMF correction factors need to be applied. If your laboratory cannot give this, it is better to do only a good NT.

Non Invasive Prenatal testing (NIPT) – is it the holy grail?

DNA from the fetus circulates in the mother's blood. This Cell-free DNA (cfDNA) results from the natural breakdown of fetal cells (presumed to be mostly placental) and clears from the maternal system within hours of giving birth.

Testing maternal blood for this DNA is a Non Invasive Prenatal Testing (NIPT). Though it is not a diagnostic test – because it is 99.5% specificity, 99.9% sensitivity, and not 100% – it is still a expensive screening modality.

Understanding NIPT:

Katie Stoll is a genetic counselor in Washington State. On the blog, The DNA Exchange, she examines the role of the incidence rate for Down syndrome and a test's Positive Predictive Value (PPV)[3].

- In population of 100,000, 35 year old women who have an incidence rate of 1-in-250, 400 will be pregnant with a child with Down syndrome (100,000 X 1/250 = 400).
- NIPS labs report a sensitivity rate of 99.5%, meaning 99.5% of those actually carrying a child with Down syndrome will be detected by NIPS.
- Therefore, of the 400, 35 year old moms, 398 will receive a

"positive" NIPS result (400 X 99.5% = 398). Note as well that 2 will receive a "negative" NIPS report a false negative, since they are carrying a child with Down syndrome.

- NIPS labs also report a 99.9% specificity rate (the percentage of those pregnancies not carrying a child with Down syndrome that will receive a negative NIPS report).
- In Stoll's example, there are 99,600 moms not carrying a child with Down syndrome (100,000 moms – the 400 carrying a child with Down syndrome = 99,600).
- Of those 99,600 moms, 99,500 will receive a negative report (99,600 X 99.9% = 99,500).
- This then means 100 will receive a "positive" NIPS result (99,600 - 99,500 = 100) making these 100 false positives.
- So, in this example, there were 400 pregnancies actually carrying a child with Down syndrome. Of these, 398 would receive a positive NIPS result, but 100 false positives would also be reported, making for a total of 498 positive NIPS reports when only 400 pregnancies were actually carrying a child with Down syndrome.
- This means that a positive NIPS report means the mother has a 1-in-5 chance of a having a false positive (100 false positives / 498 = 20%, or 1-in-5). And, this false positive rate goes up; the lower the incidence rate. Current testing, however, can only provide a highly accurate recalculation of the probability that the fetus has Down syndrome.

As a result, what had been hoped to be Noninvasive Prenatal Diagnosis (NIPD) can only be called Noninvasive Prenatal Testing (NIPT).

So when to use NIPT?
Indications for considering the use of Cell Free Fetal DNA

- Maternal age 35 years or older at delivery.
- Fetal ultrasonographic findings indicating an increased risk of aneuploidy.
- History of a prior pregnancy with a trisomy.
- Positive test result for aneuploidy, including first trimester, sequential, or integrated screen, or a quadruple screen.
- Parental balanced robertsonian translocation with increased risk of fetal Trisomy 13 or Trisomy 21.

ACOG Recommendations for use of NIPT[2]

- Cell free fetal DNA testing should be an informed patient choice after pretest counseling and should not be part of routine prenatal laboratory assessment.
- Cell free fetal DNA testing should not be offered to low-risk women or women with multiple gestations because it has not been sufficiently evaluated in these groups.
- A negative cell free fetal DNA test result does not ensure an unaffected pregnancy.
- A patient with a positive test result should be referred for genetic counseling and should be offered invasive prenatal diagnosis for confirmation of test results.

Thus, on screening for Downs the ISPD Position Statement (4 April 2013) states:

1. Ultrasound nuchal translucency at 11-13 completed weeks combined with serum markers at 10-13 weeks.
2. Extending option (1) to include other first trimester sonographic markers, provided ultrasound performance has been prospectively validated by the center where the screening is to be performed.
3. A 'contingent' test whereby women with borderline risks from option (1) have option (2) at a specialist center and risk is subsequently modified.
4. Four maternal serum markers (quadruple test) at 15-19 weeks, for women who first attend after 13 weeks 6 days.

   (Integrated screening can be offered when CVS is not available. A serum integrated test when NT measurement is unavailable.)
6. Contingent second trimester ultrasound to modify risks for aneuploidy for women having options (1), (4) or (5).
7. cfDNA screening for women classified as high-risk by any of the above options (1-6). Or those with maternal age; presence of an ultrasound abnormality suggestive of Trisomy 21, 18 or 13; family history of a chromosome abnormality that could result in full Trisomy 21, 18 or 13; and history of a previous pregnancy /live birth with Trisomy 21, 18 or 13.

Conclusion

When we talk of aneuploidies T21, 18 and 13 are the most common ones. While offering a screening, one must remember that these are all screening tests and not definite tests. The only definite test is tissue sampling. Thus, decision of termination should never be based on screening tests. Biochemical testing and USG help us to narrow and shrink the number of women who will require tissue sampling.

A Downs baby can be social and financial burden. Today, we have technology to help us screen for it in the antenatal period. We as obstetricians should make our patients aware of this and offer screening to all who demand it.

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2. The American College of Obstetricians and Gynecologists Committee on Genetics The Society for Maternal-Fetal Medicine Publications Committee Number 545 • December 2012
3. How accurate is the new blood test for Down syndromeMARK LEACHJULY 30, 2013; DOWNSSYNDROMEPARENTING.COM

Neonatal resuscitation: updated guidelines

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With every newborn baby a little sun rises.

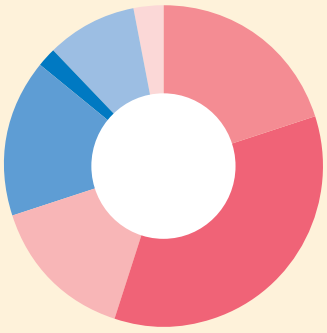
Birth asphyxia accounts for about 20% of total neonatal deaths each year. For India to achieve Millennium Development Goals of Infant Mortality rate of less than 29 per 1000 live births, reduction in the number of neonates suffering asphyxia is essential.

Approximately 10% of newborns need some form of assistance to begin breathing at birth, less than 1% neonates require extensive resuscitation at birth, rest 90% of neonates make smooth transition from intra-uterine to extra-uterine life.

Causes of Neonatal Deaths

The major causes of newborn deaths in India are pre-maturity/preterm (35%); neonatal infections (33%); intrapartum related complications/ birth asphyxia (20%); and congenital malformations (9%).

Causes of Neonatal Deaths



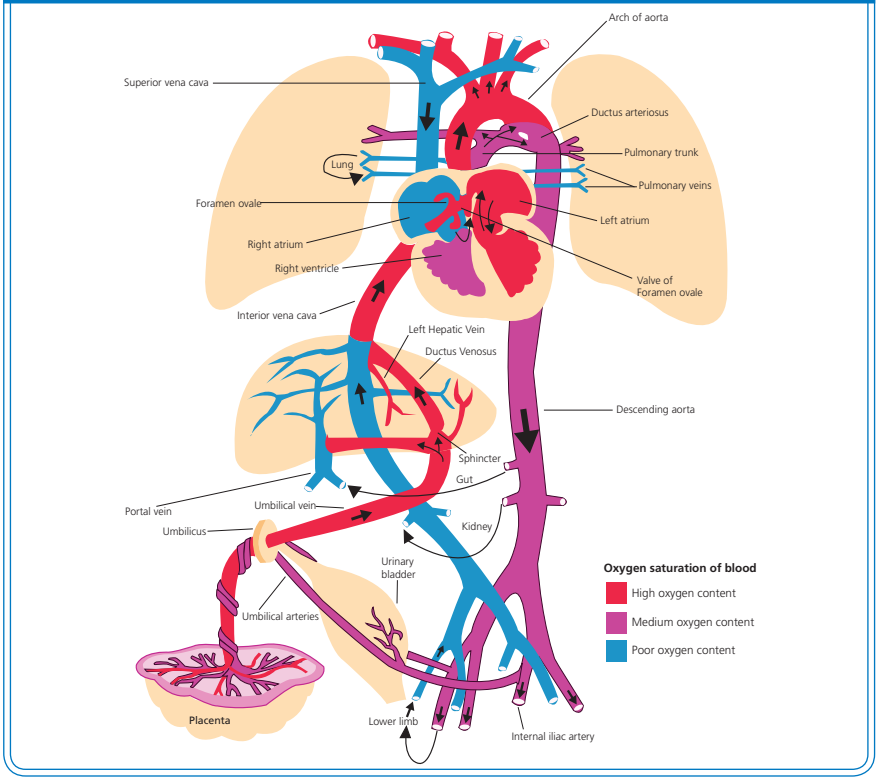
Birth asphyxia	20%
Preterm	35%
Sepsis	15%
Pneumonia	16%
Diarrhea	2%
Malformations	9%
Other	3%

Source: Liu et al, Lancet 2012 Statistical Report

Transitional changes at birth

Before birth, the placenta is the source of oxygen and other nutrients for the fetus. The fetal lungs show breathing movements as early as 20 weeks, but are fluid filled and do not serve as a source for oxygen. Less than 15% of the fetal cardiac output passes through the lungs due to high resistance of the pulmonary vessels. As a result, most of the blood flows through the lower resistance pathway, the ductus arteriosus into the aorta.

Fetal Circulation



After birth, removal of the placenta results in shift of site for gas exchange from placenta to the lungs. Clamping of the cord results in a cessation of blood flow in the umbilical vein and an increase in the systemic vascular resistance. Current evidence suggests that cord clamping should be delayed for at least 30-60 seconds for most vigorous term and preterm newborns. If placental circulation is not intact, such as after a placental abruption, bleeding placenta previa, bleeding vasa previa, or cord avulsion, the cord should be clamped immediately after birth. There is insufficient evidence to recommend an approach to cord clamping for newborns who require resuscitation at birth.

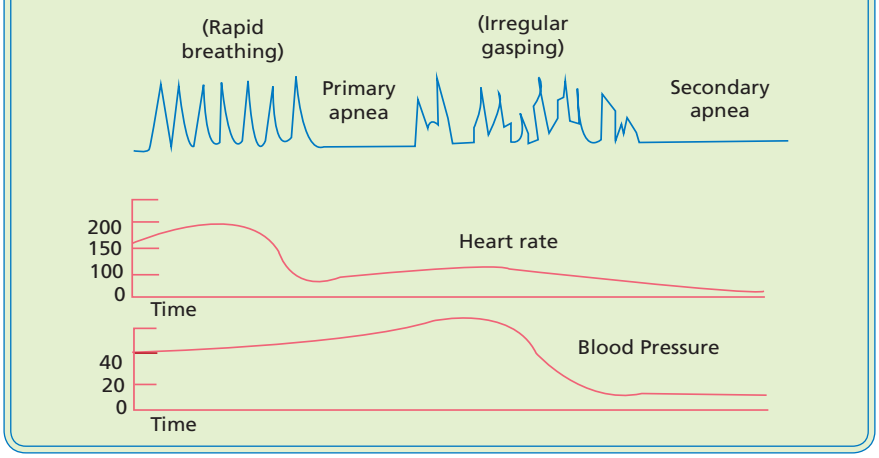
Expansion of the lungs with the cry of the newborn results in absorption of the fluid in the alveoli by the pulmonary lymphatics and a decrease in the pulmonary vascular resistance with an increase in the pulmonary blood flow, thus establishing the lungs as a source of gas exchange. This decrease in pulmonary resistance coupled with increase in the systemic vascular resistance and increase in the oxygen saturation (from a Po2 of 25mm Hg to 50mm Hg postnatally) serves as a stimulus for constriction of the ductal smooth muscle leading to closure of the ductus arteriosus. Blood earlier passing through the ductus, bypassing the lungs, now flows through the lungs. Functional closure of the ductus arteriosus occurs within 12-24 hours after birth, anatomical closure takes upto 2-3 weeks.

At the end of a normal transition, the neonate is breathing air and using his lungs for gas exchange. The normal transition occurs within a few minutes of birth, the process may be completed over several hours to days postnatal. A normal newborn takes upto 10 minutes to achieve an oxygen saturation of 90% or greater.

Difficulties maybe encountered before labor, during labor, or after birth. Problems occurring before or during labor are commonly due to compromise in placental or uterine blood flow, manifesting as fetal tachycardia followed by bradycardia, exaggerated fetal movements and visceral overactivity. Difficulties after birth are mostly due to problems such as airway obstruction or failure of reabsorption of the lung fluid.

A number of experimental studies in animals has shown that perinatal stress results in a specific sequence of events. There is an initial period of rapid and labored breathing followed by gasping and primary apnea. The heart rate begins to fall, stimulation such as drying or flicking of the soles helps in the resumption of breathing at this stage. If hypoxia persists, the newborn enters a period of secondary apnea. At this stage assisted ventilation becomes necessary.

Sequence of events of respiratory failure in experimental animals



Immediately after birth the newborn makes vigorous efforts to inhale air into the lungs. As the alveoli expand and fill with air, the increased pressure promotes the resorption of the lung fluid, delivers oxygen to the pulmonary vessels decreasing the pulmonary vascular resistance and increasing the pulmonary blood flow. Any interruption in this transition causes the lung to remain filled with fluid and pulmonary resistance remains elevated and lungs are poorly perfused. As a consequence, oxygen supply to the tissues and organs of the body is compromised. This activates a protective compensatory mechanism known as "diving sea reflex", which redistributes the blood flow to maintain the function of the vital organs, perfusing the brain, heart and adrenals at the expense of the other organs, lungs, kidneys, gastrointestinal tract, liver, spleen, skeletal muscles and skin.

Approximately 10% of newborns need some assistance at birth to begin breathing. The presence of risk factors can help identify those who may need resuscitation, but we must be always prepared to resuscitate, as some newborns with no risk factors may require resuscitation. Every birth should be attended by someone who had been trained in initiating neonatal resuscitation.

Risk factors

Antepartum Risk Factors

- Maternal infections
- Placental insufficiency – Toxemia, hypertension, diabetes mellitus
- Polyhydramnios
- Oligo-Hydramnios
- Multiple gestation
- Post-term gestation
- Malformations in fetus
- Bad obstretical history

Intrapartum Risk Factors

- Premature labor
- Antepartum hemorrhage
- Meconium stained liquor
- Prolonged labor (>24 hours)
- Premature rupture of membranes (>12 hours)
- Cord prolapse

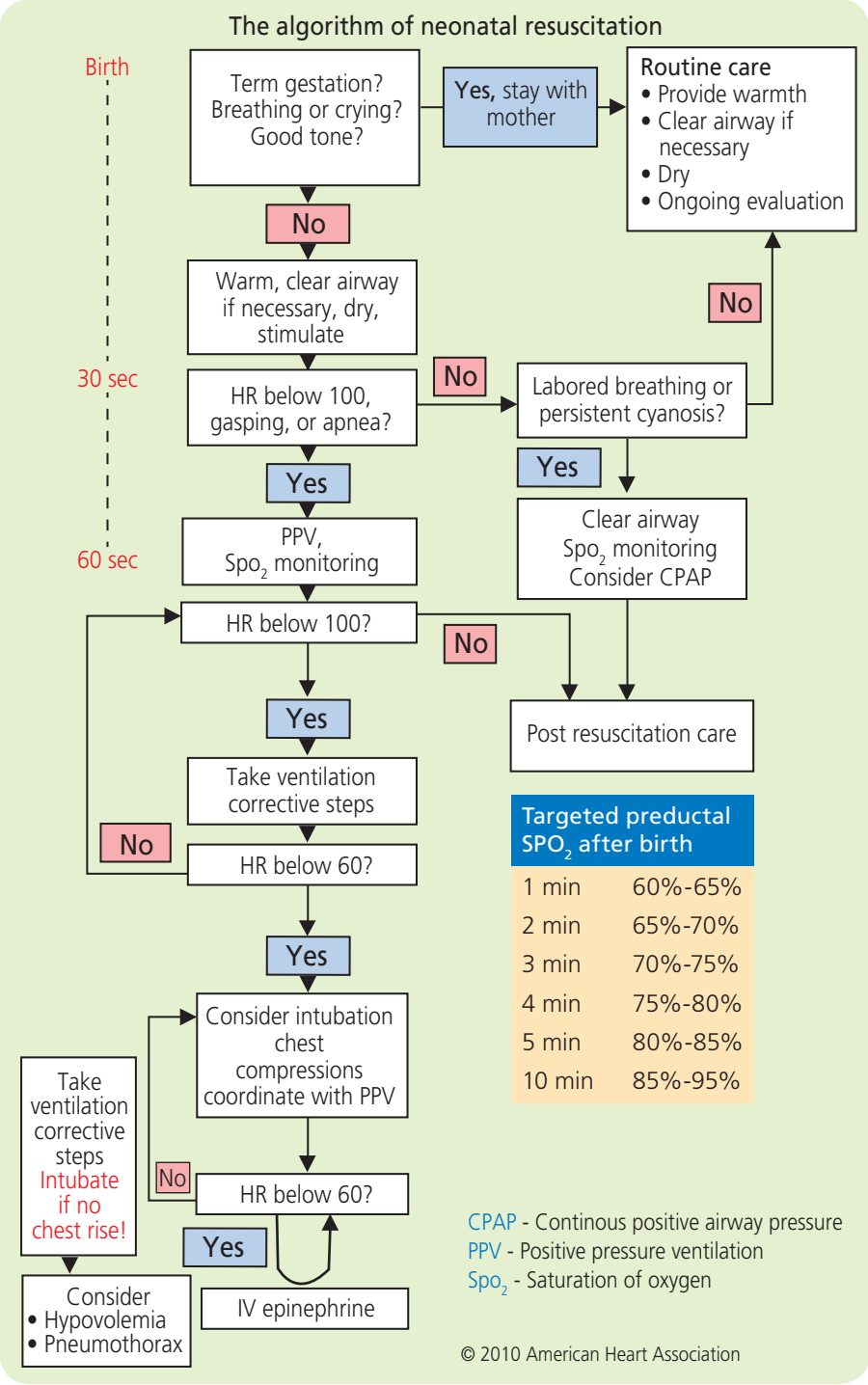
Birth asphyxia

There are a number of different definitions of birth asphyxia.

Asphyxia refers to a combination of hypoxia, hypercarbia and metabolic acidosis. The National Neonatology Forum (NNF) of India describes asphyxia as "baby has gasping and inadequate breathing or no breathing at 1 minute". It corresponds to an Apgar score of 3 or less. The American Academy of Pediatrics uses the term perinatal asphyxia to be present when a newborn manifests all of the following features:

- Cord umbilical artery pH<7.0 with a base deficit of >10mEq/l.
- Neonatal neurologic manifestations suggestive of hypoxic-ischemic encephalopathy.
- Evidence of multisystem organ damage (e.g. renal, cardiovascular, gastrointestinal, or pulmonary).

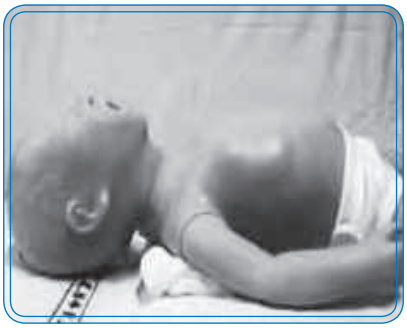
The flow diagram below describes the steps for resuscitation.



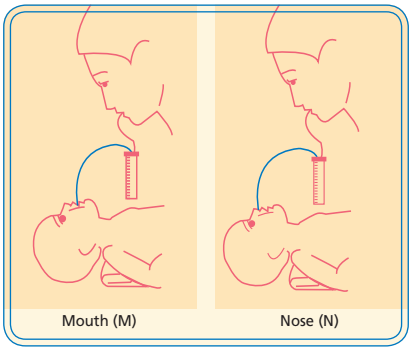
The resuscitation efforts are directed at the first minute of life also called **"Golden minute".** The components of resuscitation in newborns can be remembered by the pneumonic: TABC

T-Temperature: Ensure a warm delivery room which is draught free and has a room temperature of 25 degree Celsius or more. Place the newborn on the mother's abdomen, dry the baby and remove wet linen. Provide warmth by skin-to-skin contact with mother. If resuscitation is required, place the baby under the radiant warmer, on prewarmed clean dry linen.

A-Airway: Position the head in sniffing position to open the airway using a shoulder roll. Clear the airway of secretions, mouth and nose (M before N)

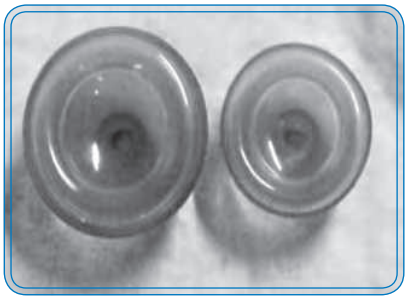


Sniffing position



B-Breathing: Tactile stimulation, by flicking of soles or rubbing back. Inappropriate and vigorous stimulation is not helpful and can cause serious injury. Shaking the baby or keeping the baby upside down should be strictly avoided.

If a baby remains apneic despite tactile stimulation, positive pressure ventilation should be immediately initiated with bag and mask. Position the baby in sniffing position. Use a

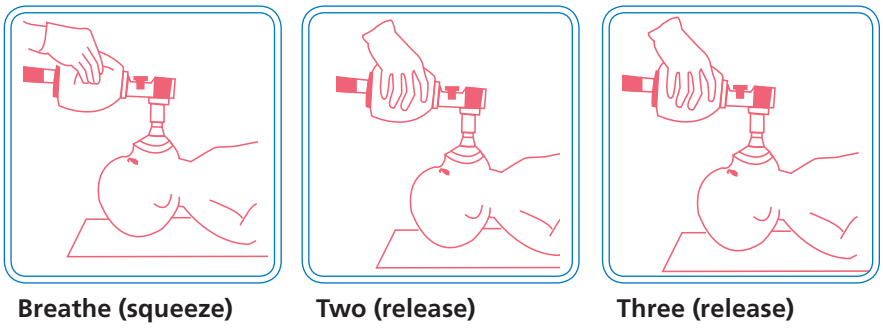


proper size mask as per the gestation of the newborn 0 for preterm and 1 for a term baby.

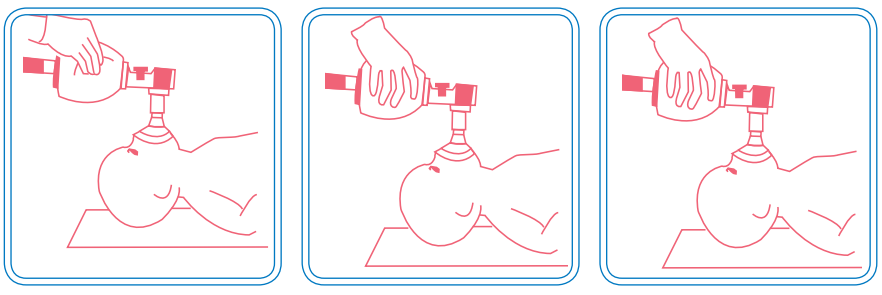
Resuscitation bags to be used in newborns need to have a volume between 250-750ml. Term newborns have a tidal volume of 4-6ml/kg. Bags larger than 750ml cannot deliver such small volumes and bags smaller than 250ml will not adequately re-inflate between breaths when 40-60 breaths/min are used. Commonly self inflating bags are used for resuscitation, deliver a rate of 40-60 breaths per minute – call loudly "squeeze, two, three". Deliver a breath when you call squeeze and allow the bag to recoil during calling "two-three".

If a baby remains apneic despite tactile stimulation, positive pressure ventilation should be immediately initiated with bag and mask. Position the baby in sniffing position. Use a proper size mask as per the gestation of the newborn 0 for preterm and 1 for a term baby.

Delivering 40-60 breaths using self-inflating bag



Breathe (squeeze) **Two (release)** **Three (release)**



Breathe (squeeze) **Two (release)** **Three (release)**

For babies born at term, it is best to begin PPV with room air rather than 100% oxygen. Provide up to 5 -10 manual breaths looking for chest rise, check for heart rate. If there is no chest rise or there is no rise in heart rate take ventilation corrective measures

Actions	
M	Adjust **Mask** to assure good seal on the face
R	**Reposition** airway by adjusting head to sniffing position
S	**Suction** mouth and nose of secretions, if present
O	**Open** mouth slightly and move jaw forward
P	Increase **Pressure** to achieve chest rise
A	Consider **Airway** alternative (endotracheal intubation or laryngeal mask airway)

If the heart rate is more than 60 bpm but less than 100 bpm, continue PPV as long as the baby is showing improvement. Ensure effective ventilation, and re-assess respiratory effort, heart rate every 30 secs (oxygen saturations may be monitored continuously if available). PPV can be discontinued when, the heart rate is above 100 bpm and there is sustained spontaneous breathing.

Babies with known or suspected diaphragmatic hernia should not receive PPV by mask during resuscitation; intubate the baby as soon as possible.

If the baby's heart rate is below 60 bpm despite 30 seconds of effective PPV (chest rise with ventilation), next step will be to initiate chest compression. Increase oxygen concentration to 100% when initiating chest compressions. During a neonatal resuscitation, it is recommended that the oximeter probe be placed on the newborn's right hand or wrist to detect preductal saturation.

C-Circulation

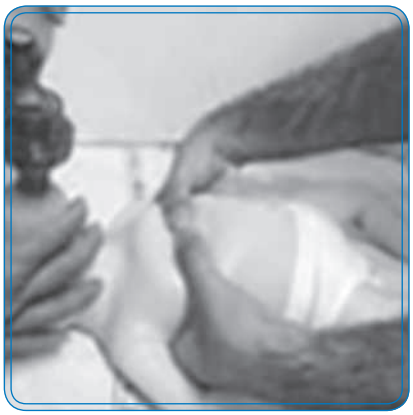
Stimulate and maintain circulation with chest compressions. Chest compressions are required to ensure that heart is able to pump the blood being oxygenated in the lung by mechanical ventilation. Chest compressions are indicated when the heart rate remains less than 60 beats/min after at least 30 seconds of PPV that inflates the lungs, as evidenced by chest movement with ventilation. In most cases, you should have given at least 30 seconds of ventilation through a properly inserted endotracheal tube or laryngeal mask. In babies with heart rate of below 60 bpm despite PPV, the oxygen level drops to cause acidosis and significant myocardial dysfunction. Chest compressions are performed to supplement the mechanical ability of the heart to maintain circulation till the time myocardium is oxygenated to provide adequate function and deliver oxygen to the brain. Ventilation is provided by bag and mask. To make it more effective intubation should be carried out. It compresses the heart. between the sternum and spine to cause the intrathoracic pressure to rise, and pump the blood into the circulatory system. Blood enters the heart from the veins when pressure from sternum is released

If the heart rate is more than 60 bpm but less than 100 bpm, continue PPV as long as the baby is showing improvement. Ensure effective ventilation, and reassess respiratory effort, heart rate every 30 secs (oxygen saturations may be monitored continuously if available. PPV can be discontinued when, the heart rate is above 100 bpm and there is sustained spontaneous breathing.

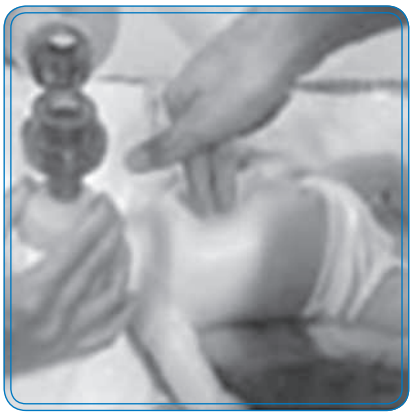
Methods of Chest Compressions

- 2- Thumb method – Sternum is depressed by 2 thumbs while the chest is encircled by hands, and spine is supported by fingers.
- 2- Finger method – In this method the tips of 2 fingers (middle finger and index or ring finger) are used to depress the sternum. The spine is supported by other hand or by placing the baby on a hard surface.

The 2- thumb method is preferred since it is able to provide more constant pressure, and the depth of compression is more controlled.

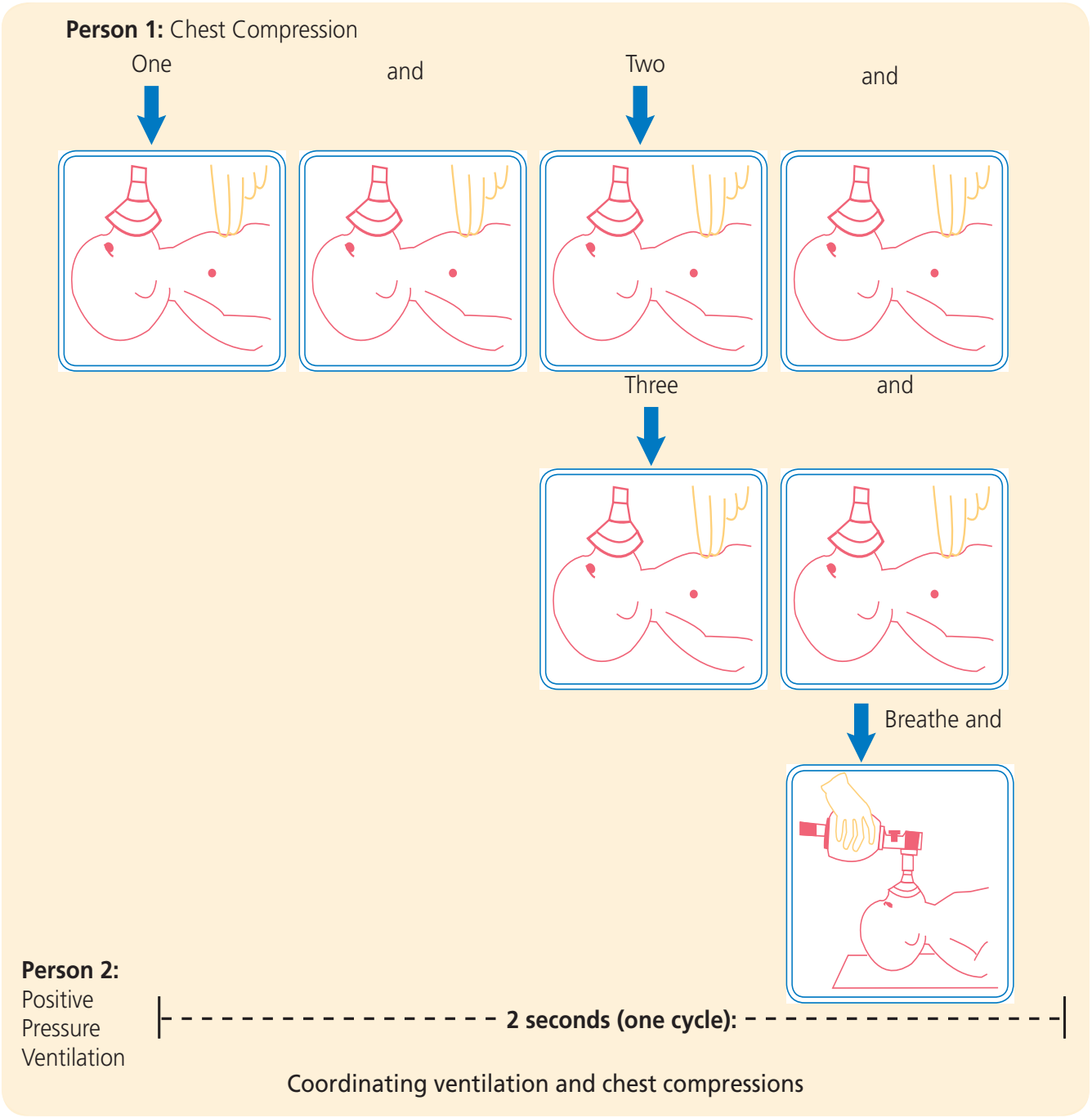


2-Thumb technique



2-Finger technique

The depth of compression of sternum should be approximately one third the anterior-posterior diameter of the chest.
For every 3 compressions 1 breath is delivered (hence, in a minute, 90 compressions and 30 breaths are given)



Coordinating ventilation and chest compressions

Discontinue chest compressions when heart rate is above 60 bpm but the PPV is continued. After stopping the chest compression effective ventilation is delivered at 40-60 breaths/minute. Then ventilation is gradually stopped after heart rate goes above 100 bpm and the baby begins to breathe spontaneously. The baby is then shifted to NICU/SCNU for post resuscitation care.

In the event baby does not show signs of improvement, check if PPV is effective; if the baby is not intubated then perform endotracheal intubation. ET tubes of different sizes e.g. 2.5, 3.0, 3.5 and 4.0mm internal diameter are available, the size of the ET tube will depend on the weight and gestation of the neonate.

Medications

Very few newborns will require medications during resuscitation. Insert the umbilical catheter if heart rate remains below 60 bpm, to provide medication. Commonly used drugs are Epinephrine. Babies who have a heart rate of less than 60 bpm despite adequate resuscitation for 90 seconds are likely to have low cardiac output to meet the oxygen requirement of vital organs. Epinephrine improves cardiac contractility, thus, the cardiac output which improves blood supply and oxygen to these organs. It is available in 1:1000 and 1:10000 concentration, given as 0.1-0.3ml/kg 1:10000 IV, 0.5-1ml/kg 1:1000 concentration can be used by endotracheal route if no IV access. Check the baby's heart rate, 60 seconds after administering epinephrine, as you continue positive-pressure ventilation and chest

compressions. The heart rate should increase to more than 60 bpm within 60 seconds after giving epinephrine. If this does not happen, you can repeat the dose every 3-5 minutes. However, any repeat doses should be given intravenously if possible.

Babies in shock appear pale, have delayed capillary refill and have weak pulses. They may have a persistently low heart rate, and circulatory status often does not improve in response to effective ventilation, chest compressions, and epinephrine. If the baby appears to be in shock and is not responding to resuscitation, administer a volume expander 10ml/kg of normal saline, Ringer's lactate or O Rh-negative packed red blood. If still there is no improvement one should consider airway malformations, pneumothorax, diaphragmatic hernia, congenital heart disease or extreme prematurity. In a newly born baby with no detectable heart rate, it is appropriate to consider stopping resuscitation if the heart rate remains undetectable for 10 minutes.

When resuscitation is performed effectively each step takes 30-45 secs.

APGAR scores earlier widely used are no more useful as it is an objective method of evaluating the newborn, performed at 1 minute and 5 minutes. As we have seen resuscitation is aimed at the First minute of life, Apgar score are assessed at 1 minute. Hence, Apgar score is not used to guide resuscitation.

Apgar Score

Sign	Score = 0	Score = 1	Score = 2
Heart Rate	Absent	Below 100 per minute	Above 100 per minute
Respiratory Effort	Absent	Weak, irregular, or gasping	Good, crying
Muscle Tone	Flaccid	Some flexion of arms and legs	Well flexed, or active movements of extremities
Reflex / Irritability	No response	Grimace or weak cry	Good cry
Color	Blue all over, or pale	Body pink, hands and feet blue	Pink all over

Post resuscitation care

Newborns who required resuscitation, but responded to the initial steps, need to be closely observed and do not need to be separated from their mother. Ongoing observation of breathing, color, temperature and activity can be carried out with the newborn on the mother's chest.

Those newborns who required greater resuscitative efforts need to be admitted to the newborn care unit and close cardiopulmonary monitoring should be done as they are at greater risk of developing complications. Careful monitoring of oxygen saturation, heart rate, glucose levels, treat shock and seizures as per protocol.

There are no laws in India that mandates that all babies at birth should not be resuscitated nor who should/may not be resuscitated. In most situations, it is generally acceptable, if parents and health care providers agree that withholding or withdrawing resuscitation is futile, would prolong dying and would not offer sufficient benefit to justify the burden that it would impose. If the mother is a minor, then the legal guardian would have to make the informed choice about the baby's treatment. Babies born between 25-28 weeks has been increasing in the developed countries, it may still not be true for most parts of our country. Non-initiation of resuscitation may be considered appropriate in confirmed gestation below 25 weeks, anencephaly, and confirmed lethal genetic malformation/disorder.

Babies in shock appear pale, have delayed capillary refill and have weak pulses. They may have a persistently low heart rate, and circulatory status often does not improve in response to effective ventilation, chest compressions and epinephrine.

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CHECK LIST: Equipment for Neonatal Resuscitation in Delivery Room

Temperature → Airway → Breathing → Circulation/ Clean hands → Dextrose

Temperature

- Designated resuscitation area
- Radiant warmer or 200w bulbs (50 cm)
- Warmed linen (3) and shoulder roll

Clean hands and help

- Gloves
- Watch with seconds hand
- Stethoscope
- Helper

Airway

- Shoulder roll
- Suction apparatus – 80-100mmHg with 10F (12,14) suction catheter, 5 or 6F and 8F for ET suction
- Mucus extractor
- Meconium aspirator

Breathing

- Self inflating ambu bag (250-750ml) with mask size 0 and 1
- Oxygen supply-source, tubings, reservoir
- T piece resuscitator
- Laryngoscope with straight blades 0, 1 and 00 (optional) and extra set of batteries
- Endotracheal tube with inner diameter of 2.5, 3, 3.5, 4
- Endotracheal tube stylet (optional)
- Scissors and adhesive tape for fixing Endotracheal tube
- 8F feeding tube

Circulation

- Umbilical catheters 3.5, 5 F.
- Three way stop cock
- Syringes 1, 2, 5, 10, 20ml
- Sterile gloves
- Medications: Epinephrine, NS, RL.
- ECG and SPO2 monitor with ECG leads

Dextrose

- Glucometer with glucose strips
- Dextrose 10% solution

Suggested list of equipment as per availability by FOGSI Perinatology Committee

Breastfeeding
importance and implementation

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Breastfeeding is a natural consequence of childbirth. Infact, we consider the duration of pregnancy to be 15 months: 9 months till delivery plus 6 months of exclusive breastfeeding. But how often do you see it happen? All animals (mammals) are sensible since they do not question breastfeeding, but are we?

The breastfeeding culture has eroded in recent times due to many reasons: social, economical, political and individual. Since breastfeeding is not instinctive knowledge, it needs to be taught and learnt and needs a lot of support from the family and the society/community.

Someone conducted an interesting experiment. Two chimpanzees gave birth in the zoo: One was born in captivity and the other was brought in from the wild. They observed that the one brought from the wild had no problems but the one born in captivity couldn't feed her baby because she had never seen it being done. This illustrates the importance of exposing our young ones to 'breastfeeding' as a norm in the family and community/society and importance of the maternity services in promoting breastfeeding.

Let us make a controversial statement here: we believe, Maternity service is responsible for the baby, from the time it takes the first breath till the time breastfeeding is established and the Obstetrician heading the Maternity Service is the key person. Responsibility of the Maternity Service does not end with a safe childbirth and resuscitation; it ofcourse starts with the first breath but ends only when lactation is successfully established. Let's look at the typical scene in the Labour Room – Once the baby delivers and cries, the Obstetrician sutures the episiotomy and washes his hands off. The Paediatrician congratulates the mother and leaves with a few words of encouragement. The baby is left at the mercy of the Staff Nurse. **BREASTFEEDING IS NOT GIVEN THE DUE IMPORTANCE IT DESERVES**. Someone has to take responsibility of the baby – that is the job of the Maternity Service.

A lot of work has been done by the WHO and UNICEF on this subject and a great deal of thought has gone in this issue. The only way to promote **exclusive breastfeeding** is to implement the "Ten Steps to Exclusive Breastfeeding" described by the WHO. Implementing each step by itself is useful, but implementing all the Ten Steps together is the key to success. Once lactation is successfully established, the duration of breastfeeding depends on not only the Paediatrician and the Health Workers but more so, on the attitudes of the mother, the family and the community/society at large. In our experience, the growth of the baby is 'proper' (according to the WHO Growth Charts) till the time the baby is exclusively breastfed but it falters later because of improper complementary food and diminished duration of breastfeeding.

Do's and Don'ts in implementing the Ten steps to Successful Breastfeeding

Every facility providing maternity services and care for newborn infants should:

1. **Have a written breastfeeding policy that is routinely communicated to all health care staff and displayed prominently in all strategic positions. It would be ideal to display the policy in local languages too.**

Guidelines for Mothers on Breastfeeding based on the 'TEN STEPS TO SUCCESSFUL BREASTFEEDING' by WHO and UNICEF

[Family members are requested to help mothers to follow the guidelines]

1. This maternity service is committed to help mothers for successful breastfeeding by following policy.
2. Hospital staff has been trained to help you to breastfeed successfully.
3. Guidance for appropriate successful breastfeeding and baby care is given before and after delivery (Pre-Delivery and Post-Delivery Counseling).
4. Soon after delivery, hold your baby close to give skin-to-skin contact (in about 5 minutes) to facilitate the baby to start breastfeeding within an hour of delivery (Early Contact and Breastfeeding).
5. a) Learn to attach and position the baby properly and comfortably while breastfeeding. This will help to prevent pain, soreness and cracked nipples. Also learn to express and store breast milk.
   b) Do not apply any cream on sore or cracked nipples.
6. a) Do not give glucose/ jaggery/ sugar/ plain water or honey before the first breastfeed (No Prelacteal feeds).
   b) The breast milk during the first 3-5 days (colostrum) after delivery, though scanty, is highly nutritious, protective and also sufficient for the baby.
   c) Give only breast milk (Exclusive Breastfeeding) till the baby has completed 6 months of age. Water, top milk, honey, vitamins and almonds should not be given during this period and continue breastfeeding at least till second birthday.
   d) Do not give your baby gripe water, *balkadu*, glucose water or tonics for teething.
7. Always keep your baby with you in the same bed (Bedding In).
8. a) Breastfeed whenever your baby is hungry and without any restriction of time (Demand Feeding). However, breastfeed at least 10 times/24 hours till breastfeeding is established (First 1-2 weeks).
   b) Establishment of breastfeeding is indicated by baby starting to urinate frequently (at least 6-7 times/24 hours) and gaining weight to cross birth weight latest by fifteenth day. After this period adequacy of feeding in an exclusive breastfeed baby is indicated by baby urinating at least 6-7 times in 24 hours and gaining at least 500gms/month.
   c) Mother should feed on one side as long as possible because the milk which comes initially is rich in water and sugar (foremilk), while the milk in the later part is rich in fats (hind milk).
9. Do not use bottles, pacifiers, animal milk (formula powder/ ready) or baby food. Free or subsidised samples of these items are not accepted in this maternity home. Their advertisement in any form is also prohibited here.
10. For any breastfeeding problem we recommend an expert. Kindly consult the doctor or our Mother Support Counsellor even after discharge. You are requested to note their phone numbers from the receptionist / nurses.
11. Do not put restrictions on mother's diet and fluid intake
12. Introduce appropriate, hygienically prepared, homemade, mashed complementary food in adequate quantities at the end of six months and continue to breastfeed till the second birthday and beyond.

2. Train all health care staff in skills necessary to implement this policy.

   This involves educating not only the staff nurses but also the '*Mausis*' and the '*Ayahbais*'. Everyone in the Maternity Service should be talking the same 'lingo' and give standard advice.

Training session for maternity service staff conducted by BPNI

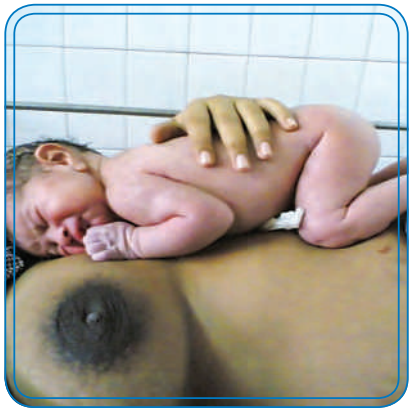
3. Inform all pregnant women about the benefits and management of breastfeeding.

   It is best to initiate the discussion on breastfeeding with the mother-to-be at the earliest opportunity. However, the women are more amenable to suggestions in the third trimester, when they start thinking about how to manage the baby. At our facility, we invite mothers-to-be for a group discussion at around 28th week where the concept of breastfeeding is introduced and information is given about the advantages of breastfeeding and disadvantages of Formula Feeds. Involvement of the mother-in-law and the husband in this discussion helps.

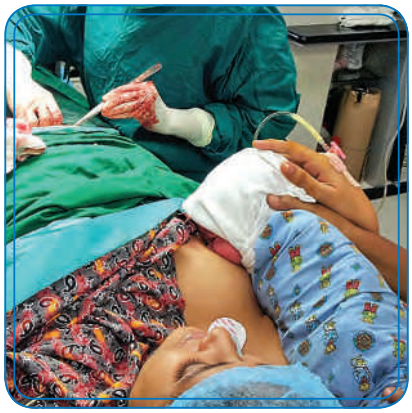
Antenatal counseling session

4. **Help mothers initiate breastfeeding within a half-hour of birth.**

This depends essentially on the conviction of the Obstetrician and his ability to educate and involve the staff. Most of the times, breastfeeding is delayed because of unnecessary labour room routines like weighing, washing/ bathing the baby, giving vitamin K injection and wrapping it before presenting to the mother who is cleaned and shifted to the wards. Some of these routines can wait, some unnecessary and some wrong. The maternity service has to be geared up, especially the Staff Nurses and *Mausis*, to be able to initiate breastfeeding at the earliest, within an hour of birth. The best method of initiation of breastfeeding is the **"Breast Crawl"** where once after birth if baby cries and breathes well, it is placed on the mother's abdomen where he / she will crawl to the breast on its own and take the first feed. Please check the details and see the video on http//www.breastcrawl.org



Breast Crawl



Breast Crawl during LSCS

5. **Show mothers how to breastfeed and how to maintain lactation even if they should be separated from their Infants.**

Breastfeeding is not instinctive. It needs to be taught and learnt. Young mothers should be encouraged to breastfeed their infants in front of their siblings. Only when the young ones see infants being breastfed will they accept it as a norm. This was amply illustrated by the Chimpanzee story. The media should also promote breastfeeding at every possible opportunity.

The young mother is most amenable to suggestions especially from the health workers during pregnancy. We prefer to open discussion with the mother about their feeding preferences at around 28 weeks. We believe it is best discussed in a group meeting. We conduct an antenatal class at 28 weeks of gestation. In this group meeting, advantages of breastfeeding and disadvantages of Formula feeds are discussed and the mother to be is actually made to practice how to hold the baby and taught different positions for breastfeeding. Involvement of the family, especially the mother, the mother-in-law and the father-to-be makes a huge difference not only in the initiation but also duration of breastfeeding.

After delivery, the lactation Counsellor visits every mother, reinforces the key messages, teaches the correct position for breastfeeding, confirms proper latching and demonstrates expression techniques. Each mother is taught how to express milk before discharge. In fact, if the baby is transferred to the neonatal unit, the mother is taught and encouraged to express milk every two hours soon after birth or the earliest opportunity after a traumatic difficult labour. This becomes easier if the mother is counselled earlier in the antenatal period.

6. **Give newborn infants no food or drink other than breast milk, unless medically indicated.**

Exclusive breastfeeding is advocated for the first six months of life. It is easier to promote and practice Exclusive breastfeeding by following all the 'Ten Steps to successful breastfeeding' in the Maternity Facility. However, in practice, quite a number of babies get 'Top' feeds or Formula feeds because of a perceived fear of hypoglycemia. Most Maternity Services believe that if the baby doesn't feed every two hours, it will go into hypoglycemia and resort to Supplementary Formula Feeds.

7. **Practice rooming in allows mothers and infants to remain together 24 hours a day.**

It has been amply proved that the baby kept in close contact with the mother immediately after birth maintains the temperature, maintains the sugar levels, doesn't have gross metabolic disturbances, cries less and has better neuropsychiatric development later in life. Please do not underestimate the tremendous power of skin-to-skin contact not only immediately after birth but even later.

Kangaroo Mother Care (KMC)

Bedding in: baby sleeps in the same bed with the mother

The 'Kangaroo Care' concept where extremely premature babies are nursed in continuous skin-to-skin contact works equally well for term infants as well, with equally astonishing results. Continuous skin-to-skin contact is possible with 'bedding in' rather than just 'rooming in' where the baby is kept in the same bed as the mother all the time. The concept of keeping the babies in a nursery is obsolete and the cribs have no place in the maternity unit. The incidence of SIDS also reduces by keeping the baby next to the mother in the same bed.

8. Encourage breastfeeding on demand.

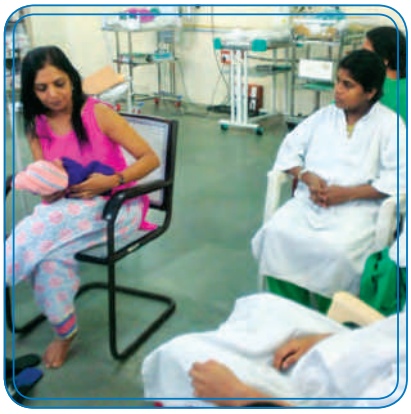
Breastfeeding on demand is the norm. However, in our opinion, it is possible to practice Demand Feeding successfully only after lactation is established. Initiation of breastfeeding should be by 'Breast Crawl' where the baby who has cried and breathes well is kept on the mother's abdomen soon after birth – she crawls to the breast and takes the first feed. The baby should be fed at least 10-12 times in 24 hours for the first couple of days till lactation is established. This translates into breastfeeding every 2 hours, practically. We call this 'Proactive Feeding'. Proactive Feeding helps not only initiation and maintenance but also hastens the establishment of lactation and smoothly progresses to Demand Feeding. It is difficult to continue breastfeeding without support from the family, Maternity Services and the society. The antenatal counseling works very well here, especially an interactive group meeting. Detailed discussion on the fear of hypoglycemia and Proactive Feeding can be found in 'Breastfeeding: a guide for the medical profession by Ruth Lawrence, 6th edition, Elsivier Mosby, 2005' and the 'Manual for Obstetrics and Gynaecology practitioners, edited by Dr. Suchitra Pandit and Dr. Reena Wani, a FOGSI publication, Jaypee 2014'.

9. Give no artificial treats or pacifiers (also called dummies or soothers) to breastfeeding infants.

There are no controversies on this issue. The IMS Act should be adhered to by every facility in true spirit

10. Foster the establishment of breastfeeding support groups and refer mothers to them on discharge from the hospital or clinic.

This is one place where the Western suburbs of North Mumbai score. Most Maternity Services, even when they follow all the Baby Friendly Practices, do not have a Mother Support Group. The first Mother Support Group in Mumbai was established by the Breastfeeding Promotion Network of India (Maharashtra) (BPNI) in 1995. BPNI has trained more than 59 Lactation Counsellors over years and offers services of 27 qualified Lactation Counsellors who are active and 8 Lactation Consultants (IBCLCs) to mothers in Mumbai. The activities of the group involve conducting Antenatal Counseling Sessions, post delivery visit to every mother in the facility to teach and confirm proper position, attachment on the breast and expression



Mother Support Group (MSG) leader counseling mothers in NICU

of milk before discharge. The MSG covers 3 Major Municipal Hospitals, 10 Tertiary Care Private Hospitals and 50 Nursing Homes. These counsellors are always available to the mothers even after discharge from the hospital. Their activities are monitored and knowledge/ skills updated by the BPNI Maharashtra. The BPNI Maharashtra has printed a booklet on baby care written by 28 Paediatricians in 4 different languages, extremely useful to the new mother. You may reach the MSG at Dr. Gangal's Clinic on 02228809698.

To conclude, well-being of the baby is the responsibility of the Maternity Service, right from the time of birth till lactation is established. Exclusive breastfeeding is possible not only by implementing all the 'Ten steps to successful breastfeeding' and all the 'Baby Friendly Hospital Initiative' practices but also from involvement of the mother, the family and the society at large. The initiation of breastfeeding depends primarily on the attitudes and organisation of the Maternity Service but duration of breastfeeding depends on the attitudes of the mother, support from the family members and of course timely help from the Mother Support Group. This requires antenatal counseling of the whole family and awareness of the importance of breastfeeding in the society.

Key messages

- Exclusive breastfeeding for 6 months
- To start proper complementary food after 6 months
- To continue breastfeeding at least till the 2nd birthday

How to wake up a sleepy baby

- Remove any blankets
- Change the infant's diaper
- Place the infant skin-to-skin
- Massage the infant's back, abdomen, arms and legs

Early feeding cues

- Sucking movements
- Sucking sounds
- Hand-to-mouth movements
- Rapid eye movements
- Soft cooing or sighing sounds
- Restlessness
- Crying is a late feeding cue and may interfere with effective breastfeeding

How does human milk facilitate euglycemia/ maintain sugar levels?

- Gluconeogenic amino acid precursors (alanine)
- Long chain FA: Initiate transcription of carnitine palmitoyl transferase: enzyme for ketogenesis
- Lactose: minimizes insulin secretion

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Multisensory stimulation for healthy happy baby development

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GDBP 2014 -2015

"If a drop of water falls in ocean it has no identity but if it falls on a leaf it shines like a diamond."

Anonymous

If baby gets multisensory stimulation baby will get healthy and happy development.

A strong body of foundational and emerging research suggests that multisensory stimulation—touch, smell, sound, and/or visual stimuli—benefits the social, emotional, cognitive and physical development of babies.

Stimulation is essential early in development; within the first 3 years of life, there is rapid development of most of the brain's neural pathways [around 85%] supporting communication, understanding, social development, and emotional well-being[1].

Stimulating multiple senses sends signals to the brain that strengthen the neural processes for learning. Through consistent multisensory experiences, research shows that babies gain healthy developmental benefit such as reduced stress in healthy and preterm infants[2, 3] and better quality and quantity of sleep in healthy babies[4], discharge in preterm infants[5].

A considerable number of cognitive processes depend on the integration of multisensory information. The brain integrates this information, providing a complete representation of our surrounding world and giving us the ability to react optimally to the environment. Infancy is a period of great changes in brain structure and function that are reflected by the increase of processing capacities of the developing child.

The four major sensory modalities recommended for neonatal developmental intervention include:

Visual stimulation (decoration of surroundings with brightly colored objects)

Auditory stimulation (talking, singing, music boxes, recorded mother's voice, recorded heartbeat)

Tactile stimulation (non nutritive sucking, stroking, flexing, massaging, rubbing, handling, positioning)

Vestibular-Kinesthetic stimulation (rocking, oscillating beds, e.g. waterbeds)

Dramatic growth in a child's physical, motor, cognitive and social-emotional development is very much dependent on the stimulation a parent provides in the first several years of a child's life. Touch is a powerful tool to maintain alert state in babies, to calm them or as an attention-getting stimulus. Touch is also a good reinforce for positive infant behavior and learning.

Development depends on the maturation of the nervous system and sensory motor abilities to interpret, and use stimuli to change behavior patterns for more effective functioning in the in the environment. Combination of biological inheritance and environmental stimulation stimulate the child to gradually achieve independence in all areas, let him make his own decisions and take his own time.

The promptness and warmth with which the mother feeds her baby contributes a great deal towards development of security and trust in the baby, and thus, leads to the beginning of social bonding.

In the case of young birds and mammals, there exist sensitive and critical periods during which there is a heightened sensitivity to stimulation or deprivation which may have a lasting and irreversible effect.

Each child needs an experientially rich environment for his / her optimum development. Richness is not merely the richness reflected by costly clothes, good food, expensive toys or a concrete house but is richness of experience in terms of parent child interaction and parental aspiration. A home in which the child gets an opportunity to listen to good stories, to play with varieties of objects and to sing with adults, is perhaps the richest home as far as the young child is concerned. A home which believes in the capacity of the child and has high hopes for him / her is the best stimulator.

Each parent is in a position to provide stimulation to one's own child and it should be done right from early infancy. Synapses if not neurons are renewable. The concept of synapse sculpturing indicates that neurotransmission can be improved by selectively stabilizing one type of impulse at the expense of others.

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Everyday experiences in a baby's life can develop and stimulate his or her senses and provide parents an opportunity to nurture their baby's ability to learn, think, love and grow. A simple ritual of bath time and massage is an ideal opportunity to create a multisensory experience. Bath time provides an opportunity for increased skin-to-skin contact (touch stimulation)[6] and direct eye contact[7] as well as the introduction of new textures, sights, sounds and smells that can stimulate a baby's tactile, visual, olfactory and auditory senses.

The sense of smell, in particular, is directly linked to emotional memory[8], A mother's scent can help soothe a crying baby[9] while a pleasant scent during bath time is shown to promote relaxation in both baby and parent[6]. A ritual that includes a warm bath followed by massage with a gentle skin moisturizer and quiet

activities is a scientifically supported and simple behavioral intervention for improved quality and quantity of sleep in babies[4].

By encouraging parents to view everyday rituals, such as bath time and massage, as opportunities for multisensory stimulation, experiences can be created that can contribute to a lifetime of healthy development.

Home is the place where the child starts to enrich his experiences. For an infant his whole environment is his/her home and hence, an optimal home environment will go a long way in promoting normal child development. The child's early environment is constituted by the mother, father, siblings, and maybe uncles and aunts. The home should be one that provides a stimulating environment to the child and that too at no extra cost. If the biological make-up is adequate and the psycho-social environment is congenial, the child will develop into a healthy personality.

He/she will be well adjusted, productive; will have the zest for life and the capacity to form intimate relationships with others.

The parental attitudes especially that of the mother has the greatest influence on child's development. Mother influence her child's psychological growth and behavior; as traditionally in India, it is considered the privilege and responsibility of the mother. The maximum influence is exerted by the mother /mother substitute in the first 3 years of life[11].

A loving relationship means that the infant experiences a strong physical and emotional intimacy with someone who holds him or her in high esteem, who is delighted with the infant, and who gives the infant a warm feeling.

A great deal of attention to the child, feeds the child, talks with the child, plays with the child (especially), and responds regularly and readily to the child's needs signaled by say, crying. The parent who recognize and responds to the different signals of a child is one to whom the child is likely to become strongly attached.

All need to be cuddled, spoken to gently, stimulated and loved. Development depends upon the biological inheritance and environmental stimulation or

A loving relationship means that the infant experiences a strong physical and emotional intimacy with someone who holds him or her in high esteem, who is delighted with the infant, and who gives the infant a warm feeling.

learning. Thus, stimulations play an important part in child development. Various easily available age appropriate toys are advised and the optimum time for stimulation is when the child is most active and playful[10].

Different types of home environment[12]

Physical home environment

- Toys
- Learning materials
- Level of visual and auditory input

Cognitive home environment

- Quality and quantity of language used in the home
- The variety of sensory and social experiences available
- The extent to which parents actually encourage achievement

Social home environment

- The degree of parental responsiveness
- The amount of warmth and nurturance available
- The level of encouragement provided for independence of maturity
- The extent to which parents restrict child behavior
- The type of discipline used

Supportive home environment

- Strong social support networks
- Stimulating, nurturing and predictable environment needed for good development

A major benefit of social support is that it provides a buffer against the negative consequences of stressful circumstances.

Child development and home environment

Child's early environment is constituted by the mother, father, siblings and grandparents

Try to recognize and respond to the different signals of the child

Social skills are developed when more time is spent with the child

Age appropriate toys enhance optimal child development

Multisensory Environments The Benefits

Motivation to be involved in one's daily activities depends largely on the senses (Kristen Meyer). Cognitive psychologists suggest that the main ingredient of the intellectual phenomenon is sensory stimulation that allows a human being to apprehend through its senses its environment and respond towards it.

Multisensory Environments improve the development of thought, intelligence and social skills.

Multisensory Environments offer people with cognitive impairments and other challenging conditions the opportunity to enjoy and control a variety of sensory experiences.

Multisensory Environments can open up a whole new world for individuals with cognitive and physical impairments.

Providing a stimulating environment can:

- Increase concentration and focus attention
- Develop or reactivate senses of hearing, sight, smell, touch and taste
- Heighten awareness and improve alertness
- Improve coordination and motor development
- Promote cognitive development by increased brain function
- Lead participants to explore their environment
- Provide security
- Be in an unrestrained atmosphere where participants feel able to enjoy themselves
- Improve creativity
- Stimulate the sensory building blocks
- Develop of a sense of cause and effect
- Develop language – more vocalization
- Promote social interactions
- Promote mental and physical relaxation – stress levels drop dramatically
- Result in more calmness and lower aggressive behaviors
- Increase opportunity for choice and self-determination
- Improve communication and sharing
- Lead to non-responsive patients becoming communicative
- Provide relief from pain and painful physiotherapy

Last but not least, participants are happier and have fun.

The simple pleasures and joys that children experience running, playing and enjoying a sunny day are sometimes not available for children with special needs. Due to limitations, they don't experience or are unable to interact with their surroundings, limiting their sensory experiences.

Multisensory stimulation is as necessary for survival as food and water.

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Kangaroo Mother Care
practical aspects

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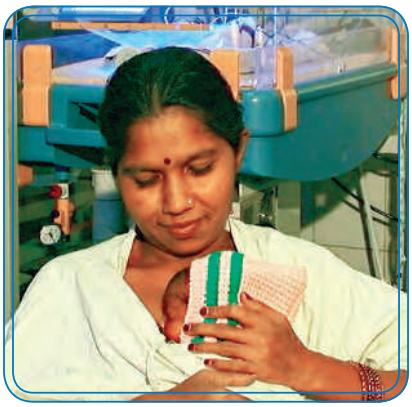
What is Kangaroo Mother Care?

Kangaroo Mother Care is a low cost, comprehensive method of care of stable Low Birth Weight Infants. The baby is placed between mother's breasts in direct skin-to-skin contact and breastfed exclusively.



Benefits of KMC

Research has proved beyond doubts benefits of KMC to baby, mother, family and community.

- Facilitates physiological stability and thus, fosters baby's health and wellbeing
- Provides effective thermal control with a reduced risk of hypothermia
- Promotes lactation and facilitates the feeding interaction
- Increases rate and duration of breastfeeding
- Decreases incidence of hypoglycemia, apnea and sepsis
- Attains better weight gain, reduces hospital stay and achieves better follow up rates
- Alleviates pain in preterms
- Reduces maternal stress
- Empowers parents: stronger bonding, increased confidence, and deep satisfaction due to active involvement in care of the baby
- Reduces the health care cost significantly as it saves money on equipment, medicines, artificial feeds, and prolonged hospital stay required during conventional care

Components of KMC

1. **Kangaroo Position:** Skin-to-skin contact
2. **Kangaroo Feeding:** Exclusive breastfeeding
3. **Early discharge and follow up**

Kangaroo Position: Early, continuous and prolonged skin-to-skin contact between the mother and her baby is the basic component of KMC. Baby is placed in a vertical position between the breasts of mother. Mother acts as a source of warmth, nutrition and multimodal stimulation.

Exclusive breastfeeding: Importance of feeding breast milk to LBW baby cannot be overemphasized. In fact skin-to-skin contact is described as the first step to navigate the course from birth to breast in ELBW infants.

Eligibility criteria

Mother: All mothers can provide KMC, irrespective of age, parity, education, culture and religion. If mother is not available, any other family member can provide KMC to the baby after proper counseling.

Baby: All stable LBW babies are eligible for KMC. However, very sick

babies needing special care should be cared under radiant warmer initially. KMC should be started after the baby is hemo-dynamically stable. Guidelines for practicing KMC are as given:

- **Birth weight >1800g:** These babies are generally stable at birth. Therefore, in most of them KMC can be initiated soon after birth.
- **Birth weight 1200-1799g:** Many babies of this group have significant problems in neonatal period. It might take a few days before KMC can be initiated.
- **Birth weight<1200g:** It may take days to weeks before baby's condition allows initiation of KMC. However, every attempt should be made to initiate KMC as soon as possible.

KMC implementation or in house adaptation

KMC training of nurses, physicians and other staff involved in the care of the mother and the baby is the first step of implementation. KMC adaptation is a process of physical, emotional and social adjustment of the mother and the family of the preterm baby to the methodology of KMC. This is accomplished through a process of targeted education, training, and emotional support. It is advisable to sensitize and educate pregnant mothers in antenatal period and to identify women at high-risk for delivering preterm / low birth weight babies.

Preparing for KMC

KMC nurse plays a pivotal role in successful implementation of KMC. Healthcare providers should counsel and motivate mother. Once the mother realizes the benefits of KMC for her baby, she will learn and undertake KMC. The first few sessions are important and require extended interaction. Presence of husband and other family members during these sessions helps in building positive attitude of the family and ensuring family support to the mother which is particularly crucial for post-discharge home-based KMC.

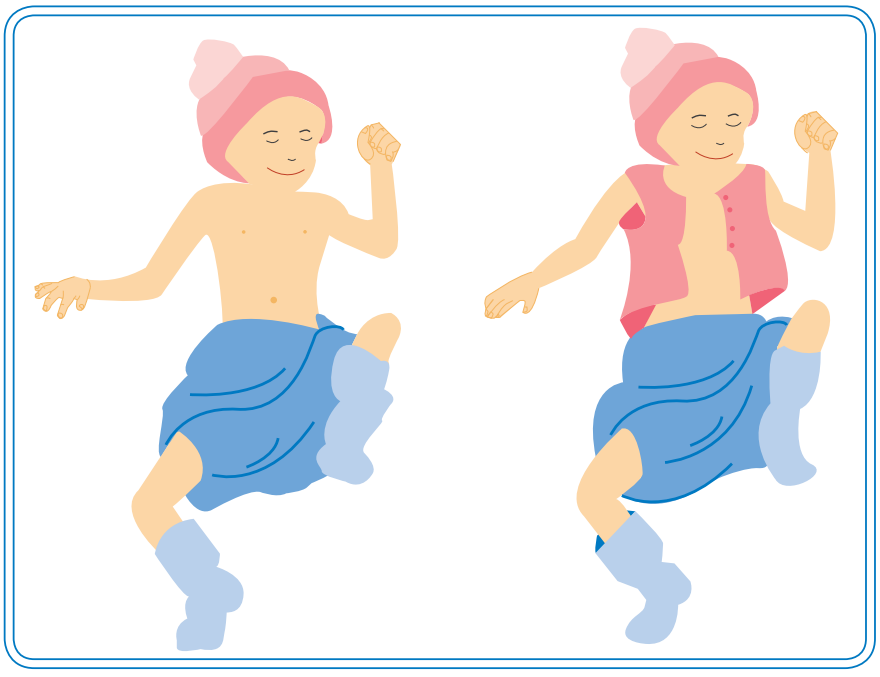
The following points must be taken into consideration while providing KMC:

- The mother should be free from serious illness to be able to provide KMC.
- She should receive adequate diet and supplements recommended by her physician.
- The mother should maintain good hygiene: daily bath/sponge, change of clothes, hand washing, short and clean finger nails.
- The mother should be explained how to breastfeed or express milk while the baby is in KMC position. The baby could be fed with *paladai,* spoon or tube, depending on the condition of the baby.
- Family members should also be encouraged to provide KMC when mother wishes to take rest or do some work.

Mother: KMC can use any front-open gown, shirt, light dress or blouse and sari as per the local culture. Suitable apparel that can secure the baby for extended period of time can be adapted locally. KEM kangaroo bag works very well with our mothers.

Baby: Baby is suitably dressed with cap, socks, nappy, and front-open sleeveless shirt or *'Jhabala'*. The baby's chest is not covered to allow skin-to-skin contact.

The first few sessions are important and require extended interaction. Presence of husband and other family members during these sessions helps in building positive attitude of the family and ensuring family support to the mother which is particularly crucial for post-discharge home-based KMC.



The KMC Procedure

Kangaroo positioning

- The baby should be placed between the mother's breasts in an upright position.
- The head should be turned to one side and in a slightly extended position which helps to keep the airway open and allows eye-to-eye contact between the mother and her baby.
- The hips should be flexed and abducted in a "frog" position; the arms should also be flexed.
- Baby's abdomen should be at the level of the mother's epigastrium. Mother's heartbeats and breathing stimulate the baby, thus, reducing the occurrence of apnea.
- Support the baby's bottom with a kangaroo bag, sling/binder.
- Baby should receive most of the necessary care including feeding while in Kangaroo position. The baby needs to be removed from skin-to-skin contact only for changing diapers and clinical assessment.
- A comfortable chair with adjustable back may be useful to provide KMC during sleep and rest. In the KMC ward or at home, the mother can sleep with the baby in kangaroo position in a reclined or semirecumbent position, about 15-30 degrees from above the ground. This can be achieved with an adjustable bed or with several pillows on an ordinary bed. This position may decrease the risk of apnea in a baby.

Alleviation of maternal fear is crucial for success of KMC. Mother can be taught physical exercises to relax as well as stimulation and massage therapy for baby while baby in KMC position. This helps to boost mother's confidence and empowers her in care of her fragile baby.

It is helpful when KMC mother interacts with someone already practicing KMC for her baby.

Time of initiation

KMC can be started as soon as the baby is stable. Short KMC sessions can be initiated during recovery with ongoing medical treatment (IV fluids, oxygen therapy). KMC can be provided while the baby is being fed via orogastric tube or on oxygen therapy.

Duration of KMC

- Skin-to-skin contact should start in the nursery, with a smooth transition from conventional care to continuous KMC.
- Sessions that last less than one hour should be avoided because frequent handling may be stressful for the baby.
- The length of skin-to-skin contacts should be gradually increased up to 24 hours a day, interrupted only for changing diapers.

Monitoring

Monitoring attains special significance in KMC. Mother should be involved in observing the baby during KMC so that she herself can continue monitoring at home. She should check that

- Baby's neck position is neither too flexed nor too extended
- Breathing is regular
- Temperature is maintained i.e. baby's hands and feet are warm to touch
- Color is pink
- Breastfeeding well

Monitoring growth is mandatory. Mother should be educated to recognize danger signs and to report to health care facility immediately.

Discharge criteria

The standard policy of the unit for discharge from the hospital should be followed, generally the following criteria is accepted at most centres:

- Baby's general health is good and no evidence of infection
- Feeding well and receiving exclusively breast milk
- Gaining weight (at least 15-20gm/kg/day for at least 3 consecutive days)
- Maintaining body temperature satisfactorily in room temperature
- The mother and family members are confident to take care of the baby in KMC and are motivated to come for follow-up visits regularly

When should KMC be discontinued?

KMC should be continued till baby reaches 40 weeks post conceptional age or attains weight of 2500gms. The baby starts wriggling to indicate that she is uncomfortable, pulls her limbs out, cries and fusses every time the mother tries to put her back in skin-to-skin contact. This is the time to wean the baby from KMC.

Post- discharge follow up

Close follow up is a fundamental pre-requisite of KMC practice. Each unit should formulate its own policy of follow up. In general, a baby is followed twice weekly till weight gain is satisfactory: 15-20gms/kg/day and subsequently weekly till 37-40 weeks of gestation or till the bay reaches 2.5-3kg of weight. Thereafter, a follow up once in 2 weeks may be enough till 3 months of corrected age. Later, the baby should be seen at an interval of 1-2 months during first year of life.

The baby starts wriggling to indicate that she is uncomfortable, pulls her limbs out, cries and fusses every time the mother tries to put her back in skin-to-skin contact. This is the time to wean the baby from KMC.

More frequent visits should be made if the baby is not growing well or his condition demands. Monitoring of growth and nutrition as well as neuromotor, neurodevelopmental, neurosensory, neurophysiological assessments and provision of early intervention treatment whenever indicated are integral components of follow up.

KMC in different settings

KMC should be practiced at all levels of neonatal care. It is important to realize that KMC is not a poor man's choice but ideal way of humanizing sophisticated care imparted at tertiary level units. Where neonatal care services are inadequate, the baby should be transferred to a proper facility immediately after birth, along with the mother/ family member. Transfer should take place after initial stabilization and appropriate management. One of the best ways of stabilizing and transporting small babies is by keeping them in continuous skin-to-skin contact with the mother/ family member before and during transport. If referral is not possible, KMC may be the only option of care. Community awareness about the benefits of KMC is the need of the hour.

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Neonatal jaundice and hyperbilirubinemia

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Introduction

Jaundice is the visible manifestation of bilirubinemia, caused by the accumulation of bilirubin in the skin and mucous membranes. It is a common problem in neonates with an incidence of 70-80%.

Most of these neonates develop pathological hyperbilirubinemia during the first week of life. Premature babies have much higher incidence of neonatal jaundice requiring therapeutic intervention than term babies. Although most jaundice in neonates is physiologically normal. It is a cause of concern for the physician and a source of anxiety for the parents. It is important to detect pathological causes of jaundice and those babies at risk of significant hyperbilirubinaemia with the aim of preventing bilirubin encephalopathy.

Types of jaundice

Physiological

This is attributable to physiological immaturity of neonates to handle increased bilirubin production. Other attributing factors could be higher concentration of red blood cells, shorter life span of newborn red blood cells, slower metabolism, circulation and excretion of bilirubin. Usually appears 2 to 4 days after birth, resolving after 1 to 2 weeks. No treatment is required but baby should be observed closely for signs of worsening jaundice.

Breastfeeding failure jaundice

This increased frequency of jaundice is not related to characteristics of breast milk but rather to the pattern of breastfeeding. Decreased frequency of breastfeeding is associated with exaggeration of physiological jaundice. Encouraging a mother to breastfeed her baby at least 10-12 times per day would be helpful.

Breast milk jaundice

Develops 5-7 days after birth and peaks at 14 days. A suggested cause is an increased concentration of β-glucuronidase and other unidentified factors in breast milk which inhibits conjugation or enhances intestinal absorption. These babies with TSB (Total Serum Bilirubin) beyond 10mg/dl after third week of life should be investigated for prolonged jaundice.

Mother should be advised to continue breastfeeding in frequent intervals. TSB levels usually decline over a period of time.

Pathological (Non-physiological)

TSB concentrations have been defined as non-physiologic if concentration exceeds 5mg/dl on first day of life in term neonates, 10mg/dl on second day, or 12-13 thereafter. Treatment is required in the form of phototherapy or exchange blood transfusion. One should investigate to find the cause of pathological jaundice.

Presence of any of the following signs denotes that the jaundice is pathological.

- Clinical jaundice detected before 24 hours of age
- Serum bilirubin more than 15mg/ dl
- Clinical jaundice persisting beyond 14 days of life
- Clay/white colour stool and/or dark urine staining the clothes yellow
- Direct bilirubin >2mg/ dl at any time

Risk factors of jaundice

A simple pneumonic for risk factors is JAUNDICE

J - Jaundice within first 24 hours of life

A - A sibling who was jaundiced as neonate

U - Unrecognized haemolysis

N - Non-optimal sucking/nursing

D - Deficiency of G6PD

I - Infection

C - Cephalhematoma /bruising

E - East Asian/North Indian

Assessment

Jaundice may be a sign of serious illness.

Review the history

1. Family history of significant haemolysis
2. Clinical examination for following physical findings:
   - Weight (Small for Gestational Age)
   - Prematurity
   - Hydration including elimination (number of wet nappies and stools)
   - Dark urine and light stools
   - Microcephaly
   - Pallor/ Petechae
   - Cephalohematoma
   - Hepatosplenomegaly
   - Evidence of Hypothyroidism

Look for risk factors or precipitating factors

- Preterm birth
- Asphyxia
- Acidosis

Visual inspection of skin

Kramer's dermal staining may be used as a clinical guide to the level of jaundice (Table 1).

Table No 1: Guide to Dermal staining with level of Bilirubin (Modified from Kramer's original article)

Area of body	Level of Bilirubin
Face	4-6mg/dl
Chest, upper abdomen	8-10mg/dl
Lower abdomen, thighs	12-14mg/dl
Arms, lower legs	15-18mg/dl
Palms, soles	15-20mg/dl

Newborn should be examined in good light. Dermal staining in newborn progresses in a cephalo-caudal direction. The skin should be blanched with digital pressure and the underlying colour of skin and subcutaneous tissue should be noted. Newborns detected to have yellow discoloration of the skin beyond the legs should have an urgent laboratory confirmation for level of Total Serum Bilirubin (TSB).

Bilirubin encephalopathy

Bilirubin enters the brain as free (unbound) bilirubin or as bound to albumin in the presence of disrupted blood-brain barriers.

Acute bilirubin Encephalopathy:

Refers to the clinical manifestations of bilirubin toxicity seen in the first few weeks after birth.

Clinically it can be divided into three phases:

a. Early phase
Lethargy, hypotonia, poor feeding and high-pitched cry.

b. Intermediate phase
Irritability, hypertonia of extensor muscles, seizures, fever. All infant who survive, this phase develop **chronic bilirubin encephalopathy** (clinical diagnosis of **Kernicterus**).

c. Advanced phase
Pronounced opisthotonus, high-frequency hearing loss, shrill cry.

Investigations

Bilirubin measurement

a. **Total Serum Bilirubin (TSB)**
Must do for all jaundice infants to determine exact value, which will help to decide treatment options.

b. **Transcutaneous Bilirubin (TcB)**
This method is non-invasive and based on reflectance data of multiple wavelengths from bilirubin stained skin. TcB has a linear correction to TSB and may be useful as a screening device to detect significant jaundice and decrease the need for frequent TSB levels.

c. **Other relevant investigations routine**
- CBC with peripheral smear examination
- Blood group (maternal and baby)
- DCT (Direct Coomb's Test)

Consider in special cases

A. Microbiological cultures
B. TSH
C. G6PD deficiency
D. Hb Electrophoresis
E. Metabolic work up

Differential diagnosis

Jaundice visible at <24 hours – a medical emergency:
- Measure serum bilirubin within 2 hours of identifying obvious or suspected jaundice
- Commence phototherapy while awaiting serum bilirubin results
- Urgent neonatology/paediatric reference
- To exclude pathological causes of jaundice
- Organise transfer to nearest referral service

Jaundice first visible at 24 hours to 10 days

Most commonly benign physiological jaundice
- Dehydration
- Sepsis
- Haemolysis
- Polycythemia
- Breakdown of extravagated blood (e.g. bruising)
- Increased entero-hepatic circulation
- Metabolic diseases

Onset of jaundice after 10 days of age and prolonged jaundice
- Hypothyroidism
- Haemolytic anemia
- Hereditary Spherocytosis
- Pyloric stenosis or gastrointestinal obstruction

Differential diagnosis for conjugated hyperbilirubinemia
- Congenital obstruction and malformations of the biliary system
- Idiopathic neonatal hepatitis
- Infections
- Metabolic disorders
- Prolonged parenteral nutrition
- Requires urgent referral to a neonatologist/ paediatrician

Management

Management of jaundice is directed towards reducing the level of bilirubin and preventing CNS toxicity.

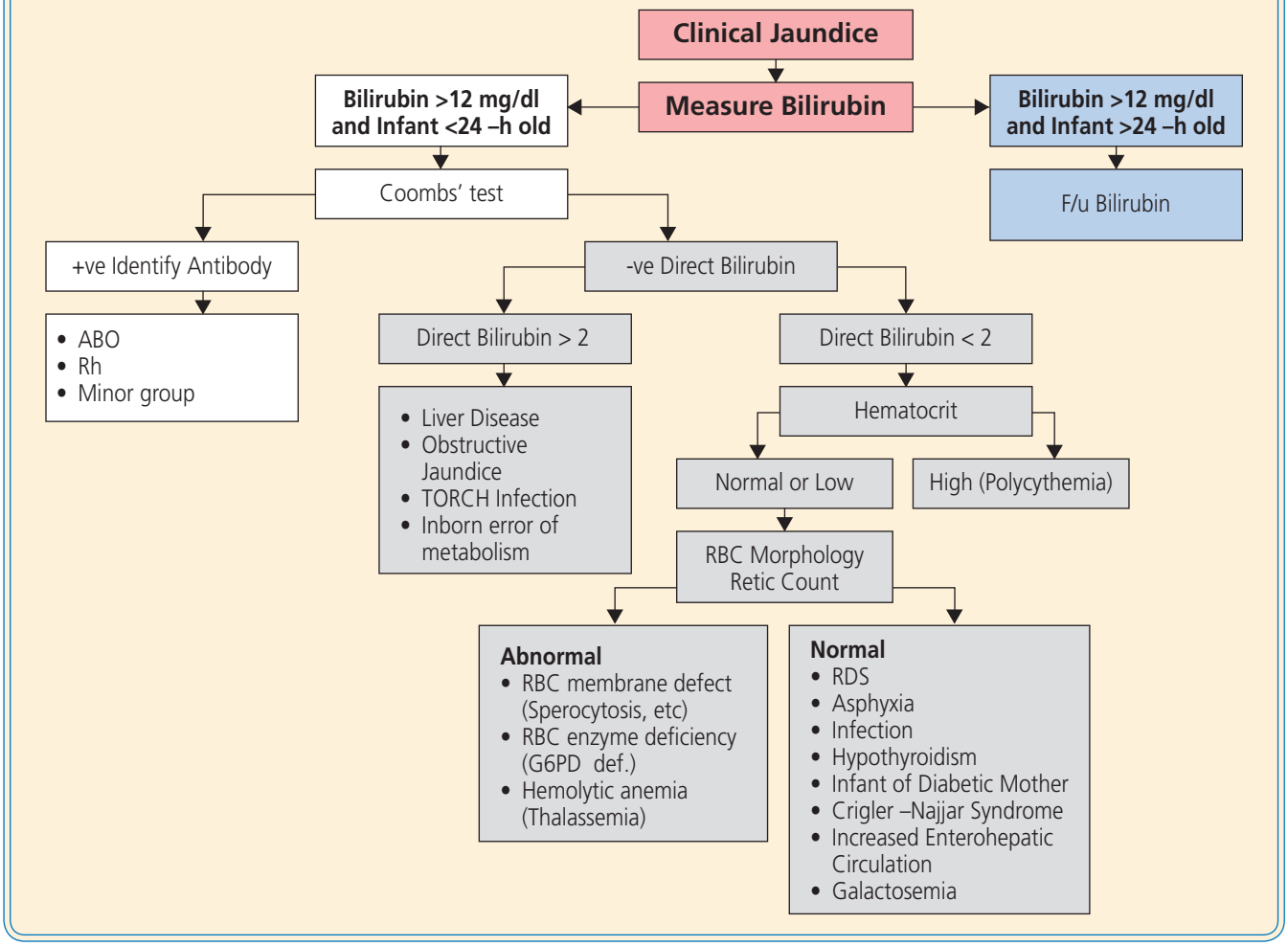
A. Prevention

1. Maternal and labour history significance

Table No 2: Significance of maternal and labour information

Information	Significance
Unexplained illness during pregnancy	Consider congenital infection (TORCH)
Diabetes mellitus	Increased incidence of jaundice
Drug ingestion during pregnancy	Sulfonamides, nitrofurantoins, antimalarials may increase hemolysis in G6PD- deficient infants
Vacuum extraction	Increased incidence of jaundice and Cephalohematoma
Oxytocin-induced labour	Increased incidence of jaundice
Delayed cord clamping	Increased incidence of jaundice among polycythemic infants
Apgar score	Increased incidence of jaundice among asphyxiated infants

Algorithm: Approach to Neonatal Jaundice



2. Pregnancy, labour and birth

Test all pregnant women for ABO, Rh (D) blood types during pregnancy:

A. If maternal red blood cell antibodies noted antenatal, test cord blood:
   1. Blood group1 including Rh type
   2. Direct antiglobulin test (Coombs test)
   3. CBC for haemoglobin and haematocrit
   4. Discuss with neonatologist

B. If the mother has not had antenatal blood tests send:
   1. Maternal blood for blood group (ABO/Rh)
   2. Baby's cord blood for blood group, Rh type and Coomb's test

3. Breastfeeding

- Support all women for breastfeed
- Encourage demand feeding or at least 3-4 hourly or as age appropriate
- Consider referral to Lactation Consultant / Lactation Support group to provide the mother with feeding support
- Promote the ingestion of colostrum to increase stooling to prevent reabsorption of bilirubin
- (EBM – Expressed Breast Milk) is the feed of choice even in sick infant too

B. Treatment

Hyperbilirubinemia can be treated with phototherapy, exchange transfusion and pharmacological agents. Adequate hydration is also an important consideration. It is important to also treat the underlying illnesses that may be causing jaundice.

Table No 3: Treatment Modalities to Reduce Serum Bilirubin Concentration[5]

Hydration
Phototherapy
Exchange transfusion
Others (Immunoglobulin, Phenobarbitone, metaloprotoporphyrins)

Table No 4: Guidelines for management of hyperbilirubinemia in the healthy term Newborn (TSB mg/dl)

	Serum Total Bilirubin level (mg/dl)			
Age (h)	Consider Phototherapy	Phototherapy	Exchange Transfusion if Intensive Phototherapy* fail	Exchange Transfusion and Phototherapy
25-48	≥12	≥15	≥20	≥25
49-72	≥15	≥18	≥25	≥30
>72	≥17	≥20	≥25	≥30

**Intensive PT should produce a decline in STB of 1-2mg/dl within 4-6 hours and should continue to decline below the threshold for exchange transfusion*

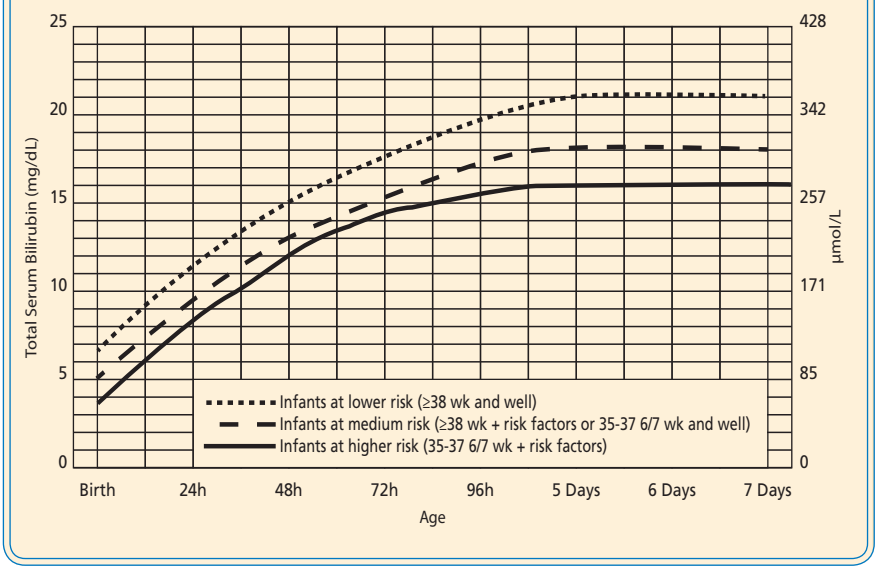
Phototherapy

Special blue lamps with a peak output at 425 to 475nm are the most efficient for phototherapy.

Effective phototherapy depends on:

1. Light spectrum. Blue green spectrum is most effective
2. Irradiance (Energy output) Special blue tubes 10-15cm above the infant will produce an irradiance of at least 35Uw/cm2 per nm
3. Distance from the infant
4. Extent of skin area exposure
5. TSB level at start of PT higher the TSB, the more rapid decline in TSB with PT
6. Cause of jaundice. Jaundice due to hemolysis or obstructive cause

Fig 1 **Guideline for phototherapy in hospitalized infants >35 weeks**



Side effects of Phototherapy

1. Insensible water loss
2. Watery diarrhea
3. Low calcium
4. Retinal damage
5. Mutations, DNA breaks have been described in cell culture

- Use total bilirubin. Do not subtract direct (conjugated) bilirubin.
- **Risk factors = isoimmune hemolytic disease, G6PD deficiency, asphyxia, significant lethargy, temperature instability, sepsis, acidosis, or albumin <3g/dL.**
- For well infants 35-37 6/7 weeks, can adjust TSB levels for intervention around the medium risk line. It is an option to intervene at lower TSB levels for infants closer to 35 weeks and at higher TSB levels for those closer to 37 weeks.
- It is an option to provide conventional phototherapy in hospital at TSB levels 2-3mg/dl below those shown.

Phototherapy for neonates born at <35 weeks of gestation

- It is generally recommended to treat hyperbilirubinemia at lower levels in Low Birth Weight (LBW) infants in comparison to term infants.

Exchange Transfusion
Based on the above mention chart (Figure 1), when phototherapy fails to bring down bilirubin level below cut off range, excess transfusion is recommended.

Discharge planning

- Reassure that neonatal jaundice is common and usually transient
- Parents and carers should also seek advice from a healthcare professional if their baby:
  - Has worsening jaundice
  - Has jaundice persisting beyond 14 days
  - Is passing pale chalky stools or dark urine
  - Is not feeding well
  - Shows signs of dehydration

Recommended follow-up

- Within the first 24 hours of life – **do not discharge** a baby with visible jaundice.
- Follow up can be planned as per table given below.

Follow-up Assessment

Let Neonatologist / Pediatrician evaluate the baby.

Where there is lack of speciality care, follow-up assessment must include:

- Baby's weight and percentage change from birth weight
- Review of feeding history to determine adequacy of intake
- Voiding and stooling pattern
- Presence or absence of jaundice
- Clinical judgement to determine the need for total serum bilirubin level measurement
- Overall look the infant (Sick look, or alert and awake, or drowsy) to rule out sepsis and overt jaundice

Table 5: Suggested follow-up policy

Scenario	Age at Discharge	Follow up
None of risk factors* present	24-72 h	48 hours after discharge
Any risk factor* present	>72 h	F/U Optional
	24-48 h	24 hours after discharge**
	49-72 h	48 hours after discharge**
	73-120 h	48 hours after discharge**

**Risk factors: History of jaundice treatment in previous sibling, setting of blood group incompatibility, visible jaundice at discharge, gestation <38 completed weeks, high prevalence of G6PD deficiency, primipara mother, weight loss at discharge >3% per day or >7% cumulative weight loss. **may need a repeat visit depending on physician's assessment.*

Key points

- Promote and support successful breastfeeding.
- All neonates should be monitored clinically for appearance of jaundice during first postnatal week.
- In cases of discharge before 72-96 hours from the hospital, a thorough assessment of risk factors for severe jaundice should be done in all babies.
- In neonates with significant jaundice, investigations should include blood groups of mother and baby, a Coomb's test, evidence for hemolysis and G6PD assay in areas known to have high prevalence of G6PD deficiency.
- We need to assess jaundice risks the way we assess other risks, refer to paediatrician/neonatologist.

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Neonatal screening importance and implementation

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History

Newborn Screening (NBS) started in 1960 with the pioneering work of Dr. Robert Guthrie in the USA in screening Phenylketonuria (PKU). Today, NBS is recognized internationally as an essential, preventive public health program for early identification of disorders in newborns that can affect their long-term health.

NBS has expanded from single disorder screening in 1960 to multiple disorders screening, today. With the introduction of system of collection and transportation of blood samples on filter paper, wide scale screening was made possible.

With the introduction of Tandem Mass Spectrometry (TMS) in 1990 there was a move from one test per disorder to one test for multiple disorders. Today in several parts of the world screening is performed universally for as many as 50-60 treatable disorders.

Disorders

NBS includes several disorders and new disorders are being evaluated for inclusion. The list of disorders that are screened in any population depends on the principles of the Wilson and Jugners classical screening criteria[2] which has now been updated by WHO as laid down in Table 1. Most countries always start with a small list and expand as time goes by. As per guidelines[3] issued by the National Neonatal Forum of India (NNF India), every baby in India should be screened for Congenital Hypothyroidism (CH), Congenital Adrenal Hyperplasia (CAH) and G6PD Deficiency. It also states that in urban or resource rich settings the babies should be screened for the expanded panel of over 50 treatable disorders. The list of treatable disorders is published by the American College on Medical Genetics[4] (ACMG). All disorders were grouped in three categories based on the screening criteria. Only disorders that fulfilled the screening criteria were included in the list i.e., 32 in the Core and 26 in the Secondary Panels. Disorders that were not treatable or did not fulfill the screening criteria were excluded.

Since India does not have any universal screening programs or guidelines, healthcare providers can choose what panels to offer to the parents. It would be a good practice, though, to include a minimum of 3 disorders as advised by NNF to the maximum described in the current guideline by the U.S. Department of Health and Human Services[5]. Anything outside this list would be inappropriate, for now.

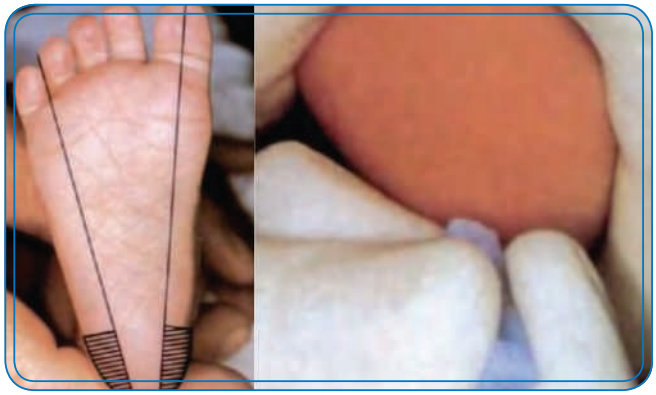
Table 1. Screening criteria[1]

- The screening programme should respond to a recognized need.
- The objectives of screening should be defined at the outset.
- There should be a defined target population.
- There should be scientific evidence of screening programme effectiveness.
- The programme should integrate education, testing, clinical services and programme management.
- There should be quality assurance, with mechanisms to minimize potential risks of screening.
- The programme should ensure informed choice, confidentiality and respect for autonomy.
- The programme should promote equity and access to screening for the entire target population.
- Programme evaluation should be planned from the outset.
- The overall benefits of screening should outweigh the harm.

Methods

The process of screening newborns has been refined over the years to perfection. The salient features are: Collection, Transportation, Technology and Reporting.

- **Collection:** The sample is collected by heel prick using an auto-lancet from the sides as shown by the shaded area in figure 1 and 2. Blood should not be collected within 24 hours of birth. The sample is directly collected on a CLSI (Clinical and Laboratory Standards Institute) approved filterpaper[6]. Umbilical cord blood should not be used for screening as it has limited value and not recommended for comprehensive screening programs.
- **Transportation:** Once the sample has been collected allow it to dry for 4 hours. Once dried it can be shipped to the Newborn Screening Laboratory by post or courier.
- **Technology:** NBS tests are performed using different technologies for different disorders. For CH, CAH, G6PD, Galactosemia, Biotinidase Deficiency and Cystic Fibrosis, Biochemical Enzyme Assay is the preferred. For hemoglobin variants HPLC (High-performance liquid chromatography) is one of the techniques. For Amino Acid Disorders, Organic Acid Disorders and Fatty Oxidation Disorders, Tandem Mass Spectrometry (TMS) is the norm.
- **Reporting:** The results of NBS will mention the following possibilities: Normal, Presumptive Positive, Deficient or Request Repeat. Repeat may be requested by the screening lab to reanalyze those samples which are not conclusive or sample is insufficient. Presumptive Positive/ Deficient means that the baby has a high likelihood of a certain disorder and more definitive tests should be done to confirm or disprove the same.



Umbilical cord blood should not be used for screening as it has limited value and not recommended for comprehensive screening programs.

Incidence

Individually these disorders may be rare but collectively they are not uncommon. In several studies over the years we consistently observe that the incidence in India[7,8] is much higher as compared to international statistics[9,10,11,12]. One probable reason could be number of marriages in India among close relatives, unlike the western counterparts. The incidence of CH is comparable to the incidence of Down's Syndrome and Syphilis – two very common disorders for which we screen in pregnancy.

Disorder	World	India
CH	1:3,000	1:900
CAH	1:7,000	1:2,000
ACMG Panel	1:1,350	1:650 ~1:1,100

Disorder	Incidence
Syphilis	1:1000
Down's Syndrome	1:820
CH	1:900

Counseling

Counseling plays a very crucial role for NBS due to the absence of any nationwide NBS program and, also, since there is not much awareness of the benefits of NBS. Antenatal Care Giver or an Obstetrician has to play this very important role of counseling the parents. NHS[13] of United Kingdom and ACOG[14] (American College of Obstetricians and Gynecologists) recommend that obstetricians should counsel parents about NBS during the antenatal period. Even in the USA and UK, where NBS is mandatory, obstetricians play a very crucial role. In a study done on focus groups of parents it was suggested that information on NBS should be incorporated into the prenatal care[15].

Implementation

NBS is not a diagnostic test. It is a screening program. Like any screening test, we need to identify the target population, which in this case is **every newborn**. There are no absolute contraindications to NBS. Relative contraindication is severe prematurity. But, in that situation also NBS may be performed after birth and repeated again after the baby attains maturity. Since there are no government guidelines on NBS it will be at the discretion of the individual hospital/doctor to make it mandatory or optional. If mandatory, the question is "Which Screening Panel?" The choice of panel would mainly depend on the financial status of the parents. It would be wise to make a small basic (inexpensive) panel mandatory for all and offer an option to parents to opt-in for a complete ACMG panel.

It would save time if all parents are counseled together somewhere in the early third trimester. Counseling aids could be used in form of Powerpoint presentation, videos or other communication channels.

There are plenty of instruments available for patient education in various languages since NBS is a popular public health program in many countries:

- Ontario NBS program (Hindi) https://youtu.be/WFWl6HqBvIM
- Save Babies Through Screening Foundation (English) https://youtu.be/G_qjpjO3gFE

Choosing a NBS Laboratory is very important. Choose a laboratory which participates regularly in CDC's NSQAP. NSQAP (Newborn Screening Quality Assurance Program) is a voluntary, non-regulatory program of Centers for Disease Control and Prevention, Atlanta, to help laboratories maintain and enhance the quality of test results. The program provides services to newborn screening laboratories in 67 countries. NSQAP has been the only comprehensive source of essential quality assurance services for dried blood spot testing for more than 33 years. An accreditation like CAP or NABL would be a desirable addition.

Laboratory report for newborn screening test	
Acylcarnitine Profile Fatty acid Oxidation and Organic Acid Disorders	Within Normal Limits
Amino Acid Profile Amino Acid Disorders, Urea Cycle Disorders	Within Normal Limits
Gluoces-6-Phosphate Dehydrogenase (G6PD) Deficiency Gluocose-6-Phosphate Dehydrogenase (G6PD)	Within Normal Limits
Congential Adrenal Hyperpiasia (CAH) 17-hydroxylprogesterone (17-OHP)	Within Normal Limits
Cystic Fibrosis (CF) Immunoreactive Trypsinogen (IRT) *Not valid after 2 months of age	Within Normal Limits
Galactosemia (GAL) Total Galactose (TGAL)	Within Normal Limits
Congenital Hypothyroidism (CH) Thyroid Stimulating Hormone (TSH)	Within Normal Limits
Biotinidase Deficiency (BIOT) Biotinidase	Within Normal Limits
Haemoglobinopathies Sickle Cell and other Haemolglobinopathies *Not valid after 3 months of age	Within Normal Limits

QNS-Quantity Not Sufficient; **NA**-Not Applicable; **DBS**-Specimen Dried Blood Spot; **Panel** Hb+ Fs+

It is generally very easy to read and understand a NBS report. The report clearly mentions normal, positive/ deficient or repeat. For a normal report nothing needs to be done. For a positive report, a confirmatory test may be needed to confirm the screening test result. For a repeat test, you would be asked to send a second sample to the laboratory. Generally, no expertise is required to decipher the report. In case of a normal report, an obstetrician need not seek help of any other specialist.

Conclusion

Every baby should be screened for basic disorders. All parents should be educated and counseled during the antenatal period, preferably in the early third trimester. All parents should be offered NBS after delivery. An opt-out form may be used for parents refusing a NBS test. Heel prick should be done after 24 hours of birth (not before).

A complete ACMG panel should be offered to all patients that can afford it. There is no contraindication of performing a Newborn Screening Test.

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