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Figure 1. Abnormalities of the newborn (1)

GENERAL AND EPIDEMIOLOGICAL DATA

From the time of the Assyrian and Babylonian astrologists, as well as physicians and philosophers of the Hippocratic era, congenital illnesses or abnormalities have been reported. They were once thought to be supernatural occurrences known as terata, from which the term teratology was derived (2). Teratology was born in the 1930s with the publishing of a series of experiments in which pregnant pigs were fed a vitamin A-deficient diet. All of these piglets had various abnormalities, most notably an absence of eyes. Josef Warkany, a physician, is regarded as the founder of experimental teratology. In the 1930s and 1940s of the previous century, he was the first to demonstrate that external stimuli can also generate CDDs in mammals. In a series of investigations on experimental animals with congeners of physiologically active compounds, such as amino acid imitating azaserine, the sensitivity of mammalian embryos to harm from xenobiotic agents was revealed. Human equivalent of these experiments was described in the 1950s, when aminopterin has been used to induce abortion in female pregnancies. Thalidomid was widely used as a sedative and to relieve morning nausea during pregnancy in Europe, Australia, Canada, Japan, and Brazil throughout the 1950s and 1960s (3). The early 1960s thalidomide incident advanced our understanding of developmental toxicology by offering a clear example of a chemical with moderate adult toxicity but substantial embryotoxicity. The mild sedative-hypnotic drug thalidomide (used for nausea and vomiting and beneficial against influenza) was suspected of causing limb reduction abnormalities ranging from hypoplasia of one or more digits to the complete disappearance of all limbs. Phocomelia (the structures of the hand and feet may be reduced to a single little digit, or may appear almost normal but extend directly from the trunk, like the flippers of a seal-phoca) is an example of thalidomide embryopathy. Proof was provided by the independent discoveries of Lenz (1961) and McBride (1961), which sparked global interest in clinical teratology (4).

Even though teratogenic exposures only account for a very small percentage of all birth defects, there are approximately 3 million people in the United States who are currently living with the consequences of developmental defects that were caused by exposure to teratogens while they were still in the womb. It is essential to keep in mind that the vast majority of birth malformations caused by teratogens can be avoided by having a solid understanding of teratology's six fundamental principles (5).

On a daily basis, humans are exposed to millions of potentially harmful substances and hazardous circumstances. However, only a small percentage of these compounds have been studied in animals, and even fewer have been proven as teratogenic in humans, because teratogenicity studies in humans are prohibited for ethical reasons (3).

Definition

Teratology is the study of aberrant development's causes, mechanisms, and patterns. Teratology began as a descriptive discipline, originating from a range of supernatural and scientific hypotheses explaining the cause of congenital deformities, such as maternal impact, the location of the stars, and hybridization. While myths and imaginative explanations of congenital (1)developmental disorders (CDDs) were popular, there were also medical explanations that appear reasonable now (1).

Teratogenesis is the process of a fetus developing abnormalities. Such a defect is caused by a teratogenic substance. In most cases, the term teratogen refers to a substance that causes anatomical abnormalities in an embryo that was previously differentiating normally. Irradiation, chemicals (drugs), and pathogenic pathogens are all teratogens agents (6). Teratology (from the Greek teratos, "monster") is the study of birth abnormalities, congenital deformities, and developmental diseases (CDDs). Due to the combined effects of internal and environmental stimuli during fetal developmental processes, these abnormalities may be visible or latent at birth (2). The etiology factors may be identified as internal causes (genetics, which account for roughly 30% of the etiology of these anomalies in humans), external or environmental variables (15%), and the combination of environmental conditions and genetic susceptibility, which accounts for the majority of the etiology of these defects in humans (2).

SIX FUNDAMENTAL PRINCIPLES FOR THE NOTION OF TERATOLOGY

Wilson proposed six fundamental principles for the notion of teratology in 1973:

1. The genotype of the conceptus and the way in which it communicates with its environment both have a role in the susceptibility of the conceptus to teratogenic effects.

2. The stage of development at which an individual is exposed to a teratogen determines their level of susceptibility to that substance;

3. Teratogenic agents operate on developing cells and tissues in specific ways (mechanisms) to start aberrant developmental events (pathogenesis);

4. Death, malformation, growth retardation, and reduced function are the four manifestations of aberrant development.

5. The ability of harmful impacts to reach developing tissues is determined by the nature of the influence.

6. Manifestations of Deviant Development Increase in Frequency and Degree as Dosage Increases(7).

Depending on the gestation period during which these factors occur, these anomalies cause organ or tissue development to be disrupted. Before the initial consultation or even the detection of the pregnancy, the key developmental phase for mal-formations is the first weeks of gestation (in humans, the first 8 weeks) (2). The three germ layers (endoderm, mesoderm, and ectoderm) develop into tissues and organs during the embryonic phase (blastogenesis and organogenesis). During the next stage (the fetal period), the neural tissues and sensory organs continue to develop until birth (2).

First principle:

When taking into consideration what is already known about the effects of exposure to established human teratogens, it is evident that two of the most defining characteristics of teratogens are that they produce a variable phenotype in the exposed and affected infants and that not all exposed infants are affected by the teratogen. There is a wide variety of phenotypic expressions that can occur in newborns who have been exposed to teratogens. The easiest way to demonstrate variable susceptibility to a teratogen is to establish a correlation between the levels of teratogenic exposure and the rates of birth defects that have been documented in clinical practice. For illustrate, the percentage of infants born with congenital problems after being exposed in utero to hydantoins, the anticonvulsant medicine that is most frequently used, is less than 10 percent. In a similar vein, just a small percentage of the infants who were exposed to thalidomide experienced negative effects. The same can be said for the condition known as fetal alcohol syndrome. It appears that some moms can drink alcohol frequently during their pregnancies without causing any harm to their children, while other mothers can consume very little alcohol and still find themselves in serious danger (5).

Second principle:

It is a fundamental principle of biology that organisms that are still in the process of growing and developing are more susceptible to the effects of change than organisms that have already reached their complete maturity. This suggests that increased vulnerability persists throughout the developmental period of the embryo, albeit not necessarily at a constant rate. However, this does not imply that the rate of progression remains the same (5).

The pre-implantation period occurs after fertilization but before implantation, during which the zygote splits but does not get larger. Because all of the embryo's cells are totipotent (meaning they have the ability to develop into any tissue) at this point, the death of a few cells will not cause any defects. The embryo implants as a blastocyst in the uterus, with two layers of inner cell mass. Some cells will help to grow the embryo itself, while others will help to develop the extraembryonic membranes. Neurulation, which occurs between weeks 3 and 5, is a significant developmental milestone. The growth of the neural tube and its eventual closure do not take

place in a vacuum but rather in conjunction with the development of other systems. After the neural tube has fused together, it goes through a process called vesiculation and eventually gives rise to the five distinct regions that make up the brain and spinal cord. The period of organogenesis, which occurs between weeks 3 and 8, is defined by the separation of cell groups into primordia that will go on to create the future organs. Histogenesis starts before organogenesis is finished and continues on for a significant amount of time after parturition. When a developing fetus is subjected to a teratogenic insult during a stage of gestation other than the first trimester, a variety of distinct malformation patterns are produced. When contemplating the use of prospective medication therapy during a specific stage of gestation, it is essential to have a solid understanding of the developmental time frames involved. It's possible that there are times when one medicine, rather than another, is the best option to utilize given the suspected target tissues and mechanisms of action (5).

Third principle:

The term mechanism refers to the first, and frequently only, occurrence in a chain of events that connects cause and effect. The first event is possibly the most essential of the sequence, not only because it serves as a link between the cause and the subsequent physiologic changes, but also because it has the potential to impact the nature of these latter changes. Teratogenic exposures cause alterations that are not always specific to the causative variables. Another route by which teratogens might cause harm is through altering the integrity or function of nucleic acids. Congenital deformities can be caused by changes in nucleic acid integrity or function during critical times of development. This pathway could be important in the development of phenytoin-induced teratogenesis (5).

The Forth principle:

The repercussions of aberrant development are not equally likely to occur and are most likely linked to the time of exposure relative to prenatal development. Although any one, or even all, of these outcomes may occur if enough embryotoxic agents were administered at high sensitivity times, specific manifestations are more likely to occur at specific stages. Malformations are unaffected in the pre-implantation embryo. If the dosage is high enough, the embryo will die before the pregnancy can be detected. After organogenesis begins, abnormalities of a particular organ or system reflect the particular sensitivity and requirements of rapidly differentiating and expanding tissues. This general increase in sensitivity during organogenesis renders the embryo vulnerable to die. Teratogenic injury during histogenesis and functional maturation throughout the fetal period is anticipated to result in tissue-level structural abnormalities, functional loss, or both. The data collected from Accutane-exposed pregnancies demonstrate the fourth principle of teratology quite effectively. Exposure to Accutane results in a spontaneous abortion rate of 40 percent among exposed embryos. Of the remaining 60%, there is a 25% chance of a significant deformity and an additional 52% chance of a cognitive or developmental impairment (5).

The Fifth principle:

Not every teratogen reaches its intended target (the embryo) in the same manner. Physical agents including x-rays, microwaves and ultrasound travel through the material unchanged and access the fetus directly trough mother to the uterus. Important considerations for assessing whether a chemical will reach the fetus include maternal dose, route of entry, physical qualities (solid, liquid, or gas), and absorption rate. The importance of placental transfer cannot be overstated. Because practically all unbound small molecules in the maternal plasma gain access to the conceptus across the placenta, the placenta is not an absolute barrier. The overall dose of a chemical reaching the conceptus is determined by the interaction of several factors, for example, maternal functional capability, compound chemical nature, and placental transport (5).

The Sixth principle:

Teratogens and teratogenic activity have a dose-response connection, just like medications and therapeutic effect. It is essential to keep in mind this idea in relation to thresholds for a variety of toxicologic consequences (5).

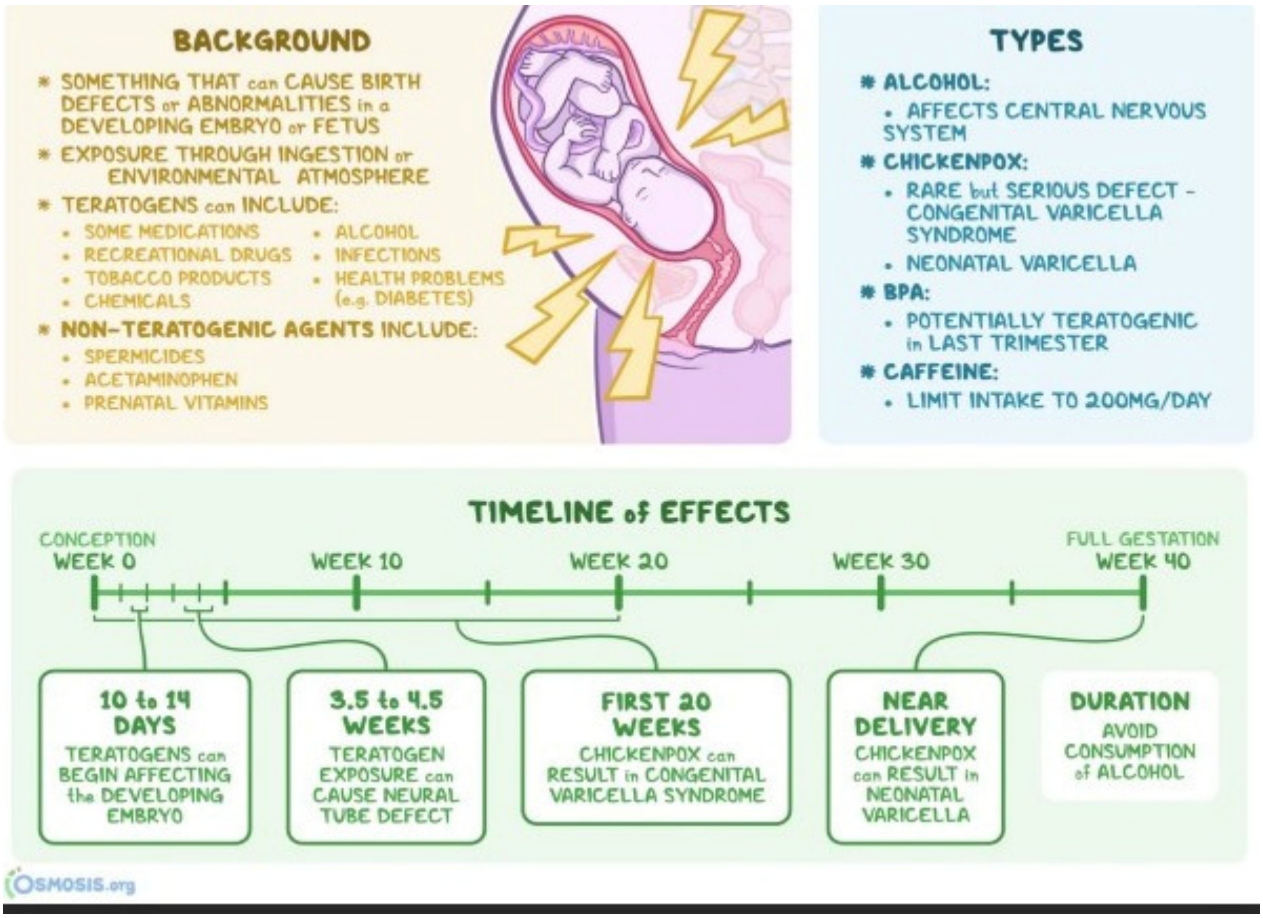

Figure 2. Teratogenesis. (8)

RISK FACTORS

It is possible to divide the risk factors for developing abnormalities into four categories:

- hereditary,
- environmental,
- modifiable (such as obesity in the mother before pregnancy and smoking),
- and nonmodifiable (genetic polymorphisms) (9).

Important in determining the cause of any etiological problem is both the developmental stage of the conceptus and its genetic status (10).

There are many factors that can play a role in the development of birth abnormalities. Sixty-five to seventy percent of all birth abnormalities are considered to have a cause that cannot be determined. There are chromosomal or cytogenetic anomalies responsible for between 3 and 5 percent of all congenital malformations. Genetic causes account for approximately 20 percent of all congenital malformations. Two to three percent of all developmental problems can be traced back to a mother's infection with a virus like HIV, rubella, or CMV. Unbalances in the mother's metabolism, such as those produced by diabetes, are responsible for a very small fraction of the cases of congenital malformations. Teratogens are responsible for between 2 and 3 percent of all abnormalities that are considered to be birth defects. During pregnancy, these are thought to have been caused by exposures to either the environment or to iatrogenic factors (5).

Congenital abnormalities can take several forms, including the following:

1. Structural describes a condition in which the outward shape or structure is aberrant.

2. Functional: When the normal operation of the organ is disrupted in some way. A functional anomaly can have a malfunction at the cellular level, which means that a particular enzyme might not be generated appropriately. For instance, in hemophilia, a specific factor that is needed for clotting is missing.

3. Metabolic: A condition in which there may be a problem with a patient's metabolism due to the lack of or a problem with one or more enzymes (11).

Table 1. Teratogenic agent classification (5)

Causes of birth defect
Teratogen-induced malformations
Maternal infection with viral agents
Chromosomal defects
Genetic factors
Unknown

DRUGS AS TERATOGENIC AGENTS

The clinical implications of pharmacological teratogens must be considered in the context of human developmental abnormalities. Almost any substance taken by the mother during pregnancy has the potential to harm the fetus, resulting in an anatomical abnormality (teratogenic). Almost all lipid-soluble substances pass through the placenta without difficulty. Water-soluble compounds with a lower molecular weight pass through more easily. The amount of medication that is free to pass the placenta is influenced by the degree to which it is bound to plasma protein. With the exception of big organic ions like heparin (both fractionated and unfractionated) and insulin, most medicines pass the placenta to some extent (6).

The Particulars of the Agent

There are some agents that are more likely to cause birth defects than others. The premise that a substance can only be teratogenic in a subset of species is somewhat less self-evident. Primate species, for instance, are more likely to develop phocomelia as a result of exposure to thalidomide than rodent species. However, a single teratogen can have several effects on different organ systems within a single species. Certain organ systems are more severely damaged than others, but the pattern of anomalies also reflects how the organ systems were varying at the time the agent was given. For instance, giving thalidomide to a pregnant woman between days 35 and 37 results in ear deformities; giving the drug to a pregnant woman between days 41 and 44 results in amelia or phocomelia (12).

Dosage

Even if it is generally the case that higher doses of a known teratogen are more harmful than lower ones, this is not always the case. An embryo has the potential to respond to a teratogen in one of three distinct ways at any given time:

1. At a low dose, there is no effect;

2. At an intermediate dose, a pattern of organ-specific malformations may occur;

3. At a high dose, the embryo may be killed, causing the organ-specific teratogenic action to go unrecognized (7).

The effect is also determined by the stage of development that the medicine is delivered in when it is being studied. That example, a teratogenic substance might only be harmful at a higher or lower dose during a particular stage of development. In a similar vein, a substance may be lethal but not teratogenic at a particular dose level, but at a higher dose it may be either fatal or teratogenic depending on the circumstances (6).

Phase of development in the embryo

The period of time during embryogenesis in which the developing fetus is exposed to a substance that might cause birth defects is a significant one. There are three stages of susceptibility that can be identified, with the periods between each step varied depending on the organ system:

1) During the first few weeks of life, roughly 2 weeks following conception in humans, the embryo is relatively resistant to teratogenic insults. Although a significant injury might kill an embryo, surviving embryos usually show no organ-specific abnormalities. The rationale is most likely that early embryonic cells have not irreversibly differentiated. If one cell dies, another cell may be able to take over its function (7).

2) Organ differentiation occurs between embryonic weeks 3 and 8 (menstrual weeks 5–10) in most human organ systems; however, differentiating occurs later in the brain and gonads. During organogenesis, teratogen susceptibility is at its peak. Teratogens have organ-specific effects; for example, a teratogen may impact one organ system at one stage of development but another at another. Not only does the particular period at which the insult occurs decide whether or not a malformation will arise, but it also dictates the specific spectrum of defects that will emerge. For example, in the rat, 100 rad of radiation causes no anomalies on days 8 or 11, but several anomalies on day 9 (eye, brain, spinal cord, heart, aortic arch, and urinary system) and day 10 (eye, brain, spinal cord, heart, aortic arch, and urine system) (eye, brain, and urinary system) (13).

Embryonic development is defined by increased organ size after organogenesis. This stage begins 8 to 10 embryonic weeks for most human organ systems. A teratogen can impact the embryo's general growth or the size of a specific organ at this time. Visible abnormalities, on the other hand, are unlikely. Administration of androgens to a pregnant woman beyond the 12th week may result in clitoral enlargement of her female fetus but no displacement of the urethral opening or fusion of the labioscrotal folds. In general, a substance that has a negative effect on a newborn has a similar effect on an older fetus. Anomalies can also be caused by secondary consequences. Cocaine usage, for example, can cause vasoconstriction and subsequent atrophy of a distant organ (6).

In the second and third trimesters of pregnancy, the brain and gonadal tissues continue to develop. As a result, drug use during pregnancy is a problem, even if the consequences may not be apparent only till later in life. Some of the uterine malformations caused by diethylstilbestrol occurred as late as 20 weeks after exposure, but were not noticed until after puberty. During pregnancy and the neonatal era, the brain is developing. Chronic alcohol intake in the course of pregnancy can lead to fetal alcohol syndrome (6).

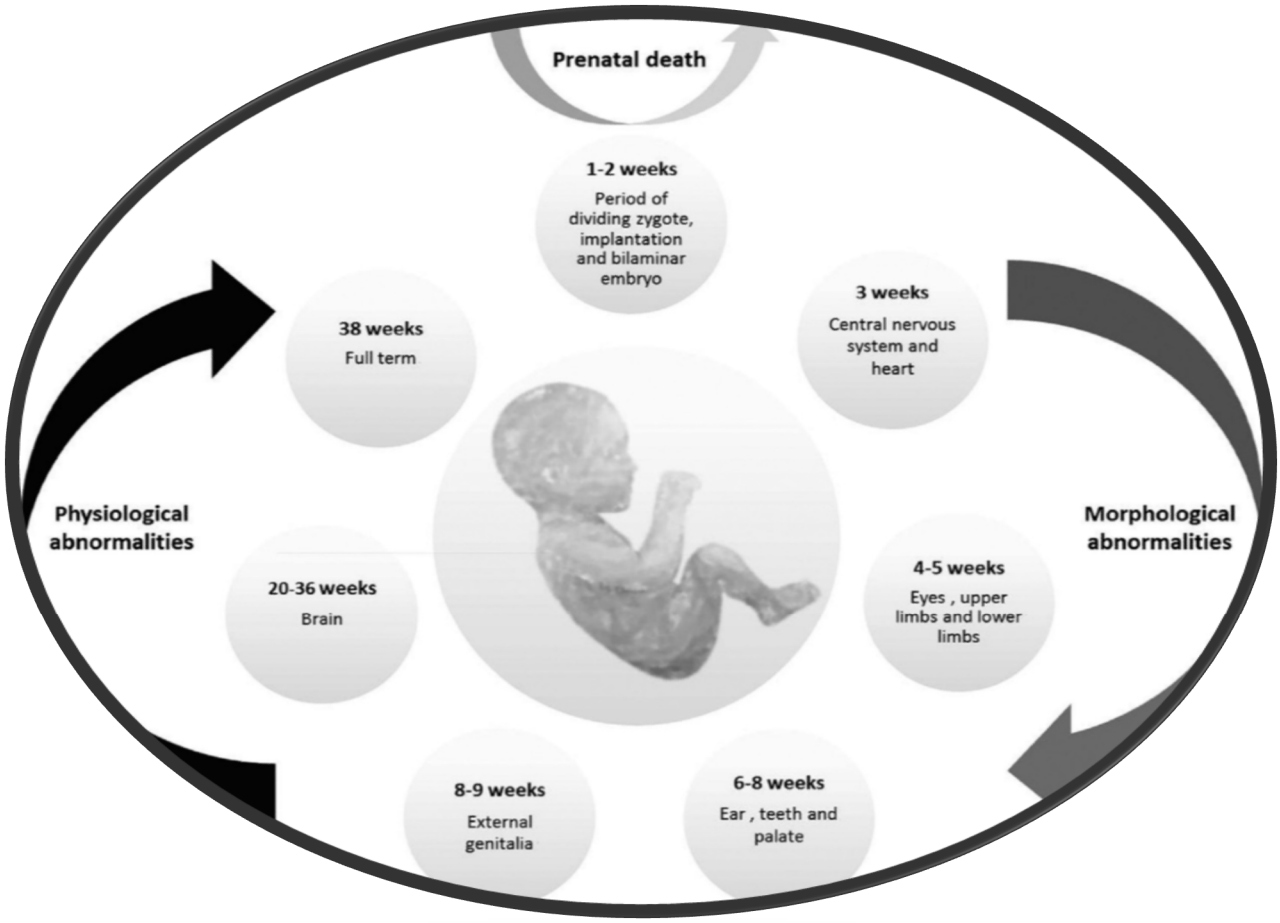

Figure 3. The fetus growth and teratogen impact above it (3)

Genotype

The efficiency of a teratogen is influenced by the mother's and fetus' genotypes. Inbred strains of mice whose women are given glucocorticoid during gestation, for example, genotype dictates the likelihood of cleft palate (14). A primary goal of the pharmaceutical sector is to be able to identify people who are more likely to experience negative side effects. Single nucleotide polymorphisms (SNPs) giving such features are the focus of current attempts (6).

Drug Interactions

When two teratogens are given at the same time, they may have a different effect than when they are given individually. Folic acid, for example, inhibits cortisol-induced teratogenesis in mice, probably due to the activation of enzyme systems that catabolize the teratogen or compete for binding sites (15). On the other hand, one substance may increase the teratogenic potential of another (6).

Other Factors

Other environmental or morphologic factors, such as maternal or fetal weight, in utero position of the fetus, closeness to other affected litter mates, uterine vasculature, and food, can all influence teratogenic response. However, further examination usually finds that these elements are linked to the previously mentioned issues. For example, the inverse relationship between maternal weight and fetus sensitivity to cortisol-induced cleft palate is due to dose per unit mass rather than weight per se (6)**.**

ACTION OF A TERATOGEN ON CELLS

A teratogen can influence embryogenesis by provoking gene mutations, chromosome breakage or nondisjunction, depletion or inhibition of precursors or substrates, depletion or inhibition of energy sources, inhibition of enzymes, or changes in the intracellular milieu as a result of changes in membrane integrity (7). These conditions result in cell mortality, decreased cell division, failure of predicted cell contact, interruption of cellular proliferation, or mechanical disruption (6). Despite of the starting cause or intermediate consequence, the end result is typically an organ with an insufficient number of cells. Lacking the critical mass required for

induction or maintenance of differentiation, the particular organ system fails to develop (16). Certainly, a few anomalies (e.g., polydactyly or labioscrotal fusion) may occur from either enhanced cell proliferation or failure of localized cell degeneration (6).

TERATOGENICITY PROOF

Teratogens are frequently discovered by observant clinicians. Regretfully, many agents are mistakenly accused, necessitating a thorough review of case files. As a result, retrospective case-control designs are frequently used. Because recall and memory biases make control and subject (mothers of afflicted infants) in incentive unequal, such an experimental design is effective in finding teratogens but sensitive to false-positive outcomes. Normal controls, on the other hand, have less incentive to recall events than women who have abnormal infants (an "anomaly control," a woman who has an aberrant outcome but not the one being examined, can be employed to mitigate this difficulty). However, conclusive cohort (prospective) studies are costly and difficult to conduct. As a result, there is no perfect method for evaluating teratogens. A variety of methodologies can be applied, with the end result usually being a scientific agreement. Any investigation is complicated by the fact that comparable congenital defects can develop in women who have not been exposed to teratogens (6).

TERATOGENIC RISK

The US Food and Drug Administration (FDA) divides drug labeling into five categories for use during pregnancy:

(A) The US Food and Drug Administration (FDA) divides drug labeling into five categories for use during pregnancy: (A) controlled studies in women have failed to show a risk to the fetus in the first trimester, and fetal injury looks unlikely;

(B) Animal studies show no risk to the fetus; no controlled human studies or animal studies show a harmful effect on the fetus; well-controlled studies in pregnant women have failed to establish a risk to the fetus;

(C) Research indicate the medicine has teratogenic or embryocidal effects in animals, but there are no controlled trials in women, or there are no studies in either animals or women;

(D) Positive proof of human fetal risk exists, yet advantages in some circumstances (such as life-threatening situations or serious conditions for which safer medications cannot be used or are ineffective) may make the drug's usage tolerable despite its risks;

(E) Fetal abnormalities have been shown in animal or human studies, or evidence of fetal risk based on human experience, or both, and the risk obviously surpasses any potential benefit (6).

The FDA deleted the pregnancy letter categories (A, B, C, D, and X) and published a new final rule, the "Pregnancy and Lactation Labeling Rule" (PLLR), for classification based on a narrative framework rather than a category system, which gives a clearer representation of potential dangers of drug exposure during pregnancy(3). These labeling amendments took effect on June 30, 2015, and all prescription medications and biological products must comply with them (17).

THERAPEUTIC DRUGS AND THEIR EFFECTS

Table 2. Teratogenic drugs (18)

1. ACE (angiotensin converting enzyme) inhibitors such as: • benazepril • captopril • enalapril • fosinopril sodium • lisinopril • quinapril • ramipril
2. Acne medication isotretinoin (Accutane, Retin-A).
3. Alcohol ingested chronically or in binges.
4. Androgens (male hormones).
5. Antibiotics: tetracycline (Achromycin), and doxycycline (Vibramycin), and streptomycin.
6. Anticoagulant (blood-thinner): warfarin (Coumadin).
7. Anticonvulsants such as: • phenytoin (Dilatin),

• valproic acid (Depakene, Valprotate), • trimethadione (Tridione), • paramethadione (Paradione), and • carbamazepine (Tegretol).
8. Anti-depressant drug lithium (Eskalith, Lithob).
9. Antimetabolite/anticancer drugs: methotrexate (Rheumatrex) and aminopterin.
10. Antirheumatic agent and metal-binder (chelator) penicillamine (Ciprimene, Depen).
11. Antithyroid drugs such as: • thiouracil/propylthiouracil and • carbimazole/methimazole.
12. Cocaine.
13. Thalidomide (Thalomid) which was approved by the FDA for the treatment of a complication of leprosy (erythema nodosum leprosum).

Vitamin A: Isotretinoin (Accutane) is a known teratogen in humans. This medicine is intended to treat cystic acne, however it has been used inadvertently by women who were not attempting to become pregnant (19). It is classified as contraindicated in pregnancy, with relevant cautions that a negative pregnancy test must be obtained prior to treatment. In prospectively investigated patients, the probability of structural malformations is estimated to be around 25%. A further 25% suffer from mental retardation alone (20).

Although there is minimal experience with methotrexate, a folic acid antagonist, it appears to be a human teratogen. Multiple congenital malformations, including cranial deformities and

deformed extremities, were found in the infants of three women who had received methotrexate in the first trimester of pregnancy (21).

Phenytoin, Valproic Acid, Carbamazepine: Women with epilepsy who take anticonvulsants during pregnancy have a risk of abnormalities that is roughly double that of the general population. In comparison to the general risk of 2–3%, the chance of serious abnormalities in epileptic women taking anticonvulsants is around 5%, with cleft lip with or without cleft palate and congenital heart disease being the most common. Valproic acid (Depakene) and carbamazepine (Tegretol) both have a 1% chance of causing neural tube malformations and perhaps other abnormalities in children (22).

Fetal alcohol syndrome (FAS) is a condition that affects the children of alcoholic mothers and manifests as gross physical retardation that begins before birth and continues after birth (23).

https://www.osmosis.org/learn/Fetal_alcohol_syndrome?_ga=2.110203463.377918161.1654459104-1853866621.1654459103

Caffeine isn't regarded as a teratogen. It is, however, a stimulant and diuretic that might induce an increase in blood pressure and heart rate in some people. Caffeine can pass the placenta and have similar effects on the growing fetus's blood pressure and heart rate if eaten during pregnancy. Caffeine use during pregnancy is currently recommended to be limited to 200 mg per day (24).

BIOLOGICAL TERATOGEN AGENTS

Perinatal infections are responsible for approximately 2% to 3% of all congenital abnormalities (25). The congenital infections of toxoplasmosis, others (Syphilis, Hepatitis B), rubella, Cytomegalovirus (CMV), and herpes simplex are referred to as the TORCH complex or TORCHes infection. Toxoplasma gondii, Treponema pallidum, Hepatitis B virus, Rubella virus, cytomegalovirus, and herpes simplex (HSV) viruses are responsible for these infections. Human immunodeficiency virus (HIV), parvovirus, and varicella virus are some of the other pathogens linked to congenital illnesses. The intrauterine transmission of these illnesses to the fetus causes a variety of symptoms in the newborn. During pregnancy, lapsed vaccines, sexually transmitted illnesses, and animal exposures are all risk factors for mothers. Because fetal harm is largely dependent on gestational age, the timing of maternal infection is a critical epidemiologic determinant. Infections throughout the first trimester, with the exception of HSV, had the poorest prognosis (26).

Varicella can be teratogenic to a developing fetus. If a pregnant woman gets chickenpox within the first 20 weeks of her pregnancy, she runs the risk of congenital varicella syndrome, a rare but

dangerous birth condition. Skin scars, anomalies of the eyes, legs, limbs, and brain, as well as gastrointestinal difficulties, are all possible outcomes for a fetus with congenital varicella syndrome. If a pregnant woman contracts chickenpox around the time of delivery, the newborn may be at risk for neonatal varicella, a life-threatening condition that can cause serious or deadly sickness in the newborn within a few days after delivery (24).

CONCLUSIONS

Patients should be informed about non-drug options for dealing with stress, aches and pains, and virus infections during pregnancy. Any drug should be taken only if the risk-to-benefit ratio justifies it, and the lowest effective dose should be employed. Patients should be informed about the dangers of social drug use. Because the long-term consequences of medications in the uterus may not be known for many years, any drug usage during pregnancy should be approached with caution (6).

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DYNAMIC DYSTOCIA

Figure 4. Dynamic Dystocia (1)

EPIDEMIOLOGICAL AND GENERAL INFORMATION

Dystocia is frequent in nulliparous women, accounting for more than half of all primary cesarean deliveries. It is important for doctors who provide maternity care to be knowledgeable in the diagnosis, treatment, and prevention of dystocia. This is because the rate of cesarean deliveries is continuing to climb. In the event that labor does not advance, inadequate uterine contractions, fetal malposition, or cephalopelvic disproportion may be to blame. It's possible that the problem is with the proportions. Before resorting to operational delivery for patients with arrested labor, doctors should make sure that the patient has had adequate uterine contractions for a period of at least four hours. Administering an infusion of oxytocin for augmentation purposes as required.

For women who have never given birth, high-dose Oxytocin-infusion techniques for labor augmentation result in a shorter total labor time compared to other labor induction methods. Low-dose treatments can be used safely without creating side effects (2).

The second stage of labor can be any of the following:

- If fetal monitoring is favorable, the procedure may be extended beyond typical time restrictions. In addition, there is improvement in the decline. Encourage the use of trained people to help with dystocia prevention.
- In addition, there is improvement in the decline. Encourage the use of trained people to help with dystocia prevention.
- Labor support partners, postponing admittance to the hospital until the active phase of labor.
- If at all feasible, avoid elective labor induction until 41 weeks of pregnancy, and use epidural analgesia sparingly (2).

In the United States, a cesarean section is performed on one in three pregnant women, making it the most common major surgery in the country (3). For decades, labor dystocia ("slow or difficult labor or delivery") has been the most often cited reason for cesarean sections among women attempting vaginal birth. This condition accounts for almost fifty percent of all primary cesarean births (4). However, labor dystocia is not a definite criterion for cesarean delivery. When identifying dystocia, doctors have greater subjectivity than when diagnosing other criteria for cesarean delivery. Because labor dystocia is so poorly defined, there is a big concern that many women with a normal labor progression may be subjected to a needless cesarean birth. Unnecessary surgery undermines birth safety and outcomes, increases short- and long-term morbidity, raises health care costs, and fails the women who rely on maternity care providers to provide safe, evidence-based treatment (5).

The definition of the labor

The process through which the viable products of conception (the fetus, the placenta, and the membranes) are expelled from the uterus through the vagina and into the outside world is referred to as labor. Labor is a series of events that take place in the genital organs. It is known as preterm labor when it occurs before the 37th week of pregnancy. The identical technique is used to expel a viable live fetus, but it is called mini-labor. The occurrence of regular uterine contractions, as well as effacement and dilation of the cervix and fetal descent, characterizes labor. A parturient is a pregnant woman who is in the process of giving birth. A viable fetus is expelled or extracted from the uterus during delivery. Delivery is not synonymous with labor; in the case of an elective cesarean section, delivery can occur without labor. Vaginal delivery, either spontaneous or assisted, or abdominal delivery are both options (6).

NORMAL LABOR (EUTOCIA):

Labor is considered normal if it satisfies the requirements listed below:

1. Initiated and completed spontaneously.

2. with the presentation of the vertex.

3. without unnecessary delay.

4. Natural termination with only minor assistance.

5. Without any difficulties impacting the mother's and/or children's safety (6).

DYSTOCIA (ABNORMAL LABOR)

Definition of dystocia

Abnormal labor is defined as any divergence from the concept of normal labor. Abnormal labor is defined as labor with a presentation other than the vertex or with complications even when the vertex is present, influencing the course of labor, changing the manner of termination, or negatively affecting the maternal and/or fetal prognosis (6). The term labor dystocia refers to prolonged or arrested cervical dilatation during the active phase of labor, as well as prolonged or arrested descent during the second stage (7). In maternity care, caring for mothers with dystocia is a significant concern. Dystocia is a term that describes a condition that lasts for a long amount of time. Labor is moving slowly. It is prevalent in nulliparous women, as evidenced by the fact that the number of women who need augmentation, vaginal birth, or a cesarean section.

RISK FACTORS

There are four major etiologic factors for abnormal labor (dystocia):

1. The "passage," which refers to pelvic architecture;

2. The "passenger," which refers to fetal size, presentation, and position;

3. The "powers," which refers to uterine activity and cervical resistance;

4. The "patient" and "provider" (8).

Factors that may contribute to a slow progress during labor:

- Premature rupture of membranes
- Nulliparity
- Labor induction
- Maternal age 35+
- Fetal weight 4kg+
- Hypertensive disorder
- Polyhydramnios
- Fertility treatments
- Ineffective uterine contractions
- Pelvic contractures
- Cephalopelvic disproportion
- Fetal malposition or malpresentation
- Early use of analgesics
- Nerve block anesthesia (click here for more information on problems associated with analgesia/anesthesia)
- Anxiety and stress disorders at the mother (9).

THE OBSTETRIC PELVIS PASSAGE

The fetus adopts positions and attitudes during labor that are influenced by the shape of the mother's pelvis. The inlet, midpelvis, and outflow make up the "real" pelvis. The anterior wall of the pubic symphysis is about 5 cm long, and the posterior wall is around 10 cm long.

The iliopectineal lines, which can be followed anteriorly along the pectineal eminence and pubic crest to the symphysis, border the pelvic inlet laterally. The sacrum at the level of the iliopectineal lines forms the posterior boundary. Between the sacral promontory and the pubic symphysis, the anteroposterior diameter (obstetric conjugate) is the smallest distance. If the obstetric conjugate is less than 10 cm or the maximum transverse diameter is less than 12 cm, the inlet is usually deemed constricted. Dystocia is far more common when both diameters are contracted than when only one diameter is contracted (8).

The posterior part of the symphysis and pubis limited the midpelvis anteriorly, while the sacrum at the level of S3 or S4 bounded the midpelvis posteriorly. The pelvic sidewalls and ischial spines form the lateral barrier. The gap between the ischial spines is the smallest diameter of the pelvis, measuring 10 cm or more in most cases. The midpelvis, which runs from the inferior aspect of the pubic symphysis to the sacral hollow at the level of the ischial spines, has an anteroposterior diameter of 11.5 cm or more. When the interspinous diameter is smaller than 10

cm, midpelvic contraction should be suspected. The midpelvis is considered definitely constricted when its diameter is less than 9 cm. Inlet contractions are less prevalent than midpelvic contractions (8).

The pelvic outlet is made up of two triangular regions with a common base but not in the same plane. The pubic arch forms the anterior triangle. The sacral sciatic ligaments and ischial tuberosities form the sides of the posterior triangle, which has the tip of the sacrum as its apex. From the inferior margin of the pubic symphysis to the tip of the sacrum, the anteroposterior diameter is normally around 11.5 cm. The distance between the inner borders of the ischial tuberosities, or transverse diameter, is roughly 10 cm. Outlet contraction without midplane contraction is uncommon (8).

Dystocia can be caused by soft tissue anomalies in the pelvis. The most frequent pelvic masses associated with dystocia are uterine myomas. They may restrict the delivery canal or cause the fetus to be mispresented. Ovarian tumors, bladder distention, a pelvic kidney, excess adipose tissue, uterine malposition, and cervical stenosis or neoplasm are all possible causes of upper genital tract dystocia. Partially vaginal or vulvar atresia, significant edema or inflammation, Bartholin's or Gartner's duct cysts, vaginal septum, massive condylomata, hematomas, and neoplasms can all induce lower genital tract dystocia (8).

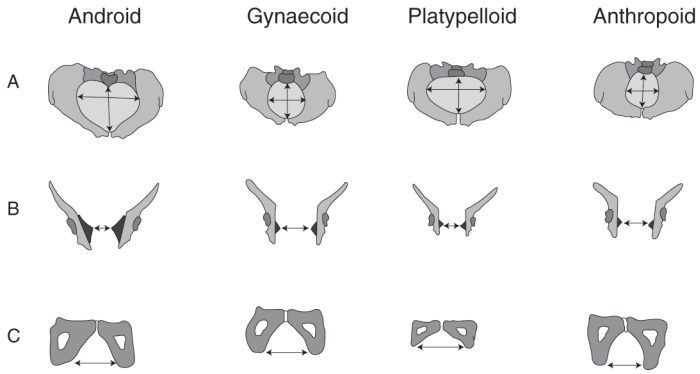

Figure 5. Anatomy of the pelvis in obstetrics (10)

Pelvimetry

A clinical assessment of the pelvic appropriateness can alert the clinician to the possibility of pelvic dystocia. A 2.5-fold increase in primary cesarean section is linked to a clinically small pelvis (11). The actual pelvic dimensions, rather than the shape and type of pelvis, determine the result of childbirth. The diagonal conjugate (measured from the inferior edge of the pubic symphysis to the sacral promontory), prominence of the ischial spines, convergence of pelvic sidewalls, angle of the subpubic arch, and sacral curvature are all clinically assessable pelvic dimensions (8).

Clinical indicators that raise the possibility of disproportion during labor are:

- Pelvic sidewalls are convergent
- Ischial spines are prominent
- Diagonal conjugate is <11.5 cm
- Subpubic arch angle is <90 degrees
- Sacrum is flat
- No descent of vertex with Valsalva or fundal pressure (Müller-Hillis maneuver) (8).

PASSENGER: THE UNBORN CHILD

The dimensions of the fetus, as well as its orientation and presentation, play significant roles in the progression of labor. The size and shape of the pelvis as well as an abundance of soft tissue can have an effect on the position and presentation of the fetus. Even though macrosomic infants have a higher chance of developing dystocia, the vast majority of occurrences of abnormal labor are seen in pregnancies that weigh less than 4,000 grams. In term pregnancies, the biparietal diameter (BPD), which is the smallest transverse dimension of the fetal skull, measures roughly 9.5–9.8 centimeters on average. The suboccipitobregmatic diameter, which is also roughly 9.5 centimeters in length on average, is the anteroposterior dimension that is the shortest. By shaping, the fetal head may be able to compensate for a moderate degree of pelvic rigidity. Because the bones of the skull overlap at key suture lines, the BPD can be reduced by 0.5 cm without causing any harm to the developing fetus. Mold growth of a severe enough severity can cause tears in the tentorium and even cause bleeding inside the skull. It is possible for prenatal scalp necrosis or skull fracture to occur if there is persistent and intense pressure between the fetus and the delivery canal. There is a possibility that the mother will develop a fistula of the vesicocervical, rectovaginal, or vesicoovaginal type. Other hazards associated with fetopelvic disproportion include: cord prolapse, extended labor leading to an increased risk of infections in both the mother and the baby, uterine rupture, postpartum hemorrhage, incorrect presentation or position, and trauma to both the mother and the newborn (8).

Malposition and Malpresentation

Dystocia could be the cause of fetal malpresentation, or it could be the effect of it. The likelihood of pelvic dystocia should be brought to the attention of the doctor by nonvertex manifestations. In the case of compound presentations, a mild pressure may be used to coax a fetal hand that is positioned next to the head to withdraw. It is more unusual to see the fetal foot alongside the head, but vaginal birth may still be an option provided that the pelvis is suitable. In all except the most extreme circumstances of premature birth, the delivery of a transverse lie must be

performed via cesarean section. The partially extended head of an average term fetus with a brow presentation has an occipitomental dimension of 13.5 cm when the fetus is presented in this position. Brow presentations are linked to pelvic contraction, small or large infants, and nuchal masses. Brow presentations can also occur in pregnancies with multiple fetuses. Two thirds of them will spontaneously change their presentation to either a facial or an occipital one. Conversion using manual methods or forceps is not recommended any longer. If the brow presentation continues after delivery, a cesarean section is typically advised, with the exception of situations in which the fetus is small. In a face presentation, the fetal head is totally hyperextended out of the body. The incidence rate is approximately one in every 600 births. Anencephaly and brow presentation are two characteristics that are associated with this condition. If the mentum (chin) continues to be located posteriorly, a cesarean delivery will be required since the fetal neck will not be able to hyperextend further to accommodate the curvature of the pelvis. When the mentum is in an anterior position, a vaginal birth may still be an option. Conversion of face presentations by manual methods or forceps is not recommended any longer (8).

In roughly ten to fifteen percent of active labors and twenty-five percent of early labors, the fetal occiput is presented in a posterior position. This position is more likely to occur in individuals with anthropoid-type pelvises. Enhanced maternal backache, a persistent anterior cervical lip, ineffective contractions, and a drawn-out second stage are some of the clinical indications associated with an occiput that is in a posterior position. When a diagnosis based on clinical examination is uncertain, the use of ultrasound to determine that the occiput is in a posterior position is extremely helpful. Regional anesthesia and a lack of voluntary effort can make it more difficult for the occiput to rotate on its own to an anterior position. The newborn may be able to deliver spontaneously from the occiput posterior position if there is sufficient space in the posterior triangle of the pelvic exit; however, an episiotomy may still be required. Other approaches include rotating the object manually or using forceps. The Kielland forceps are the best option because they do not have a pelvic curvature. The Scanzoni maneuver can be performed with traditional forceps in order to rotate the vertex. In today's clinical practice, forceps rotations are performed infrequently since they require specialized training and knowledge. Because of the higher risk of cesarean section and operational vaginal deliveries associated with persistent occiput posterior position, the rate of spontaneous vaginal delivery drops to below 25 percent for nulliparous women and above 57 percent for multiparous women (12). A lower 5-minute Apgar score, infant acidemia, birth trauma, admission to the critical care nursery, and lengthier neonatal hospitalization are some of the poor neonatal outcomes that have been linked to persistent occiput posterior posture (11). It is possible to manually rotate a fetus from an occiput posterior position to an occiput anterior position, which will result in a lower rate of cesarean section. The presence of multiple participants is the most important element linked to successful manual rotation attempts (13). Because of internal rotation, the occiput transverse posture is generally temporary. The anteroposterior diameters of platypelloid and android pelves are thin, preventing proper rotation. Cesarean delivery is required if the transverse

arrest is thought to be caused by a constricted pelvis. A forceps rotation may be attempted if the pelvis is judged to be adequate. Oxytocin may be beneficial in cases of transverse arrest, such as uterine inertia and pelvic floor muscular weakness. Asynclitism can arise if the pelvis has a pronounced sacral promontory and the vertex does not orient the sagittal suture in the midplane of descent. Small degrees of pelvic inlet constriction may be overcome by asynclitism of the fetal head. The outcome is better in anterior asynclitism, where the sagittal suture is closer to the sacrum, than in posterior asynclitism, where the sagittal suture is closer to the pubic symphysis. A deep transverse arrest occurs if the asynclitism does not overcome the contracted anteroposterior diameter (8).

Fetal Anomalies

Most abnormalities capable of causing disproportion are discovered before labor begins, thanks to the widespread use of ultrasonography. Hydrocephalus is a common developmental defect that results in dystocia. True cephalopelvic disproportion has been linked to a biparietal diameter higher than 120 mm. Cerebrospinal fluid can be withdrawn to allow a vaginal delivery if the fetus has a fatal condition; this is a rare treatment in modern obstetrics. Premature closure of the cranial sutures, known as cranial synostosis, can produce deformation but seldom leads to dystocia. Encephaloceles are usually delicate and might rupture during delivery, resulting in a disappointing prognosis. Cesarean section delivery is required for potentially viable conjoined twins. Hydrops fetalis, posterior urethral valves, Wilms' tumor, polycystic kidneys, ovarian and hepatic tumors, and ascites are all abdominal masses that can cause dystocia. In order to allow vaginal birth, ascitic fluid and other cystic masses can be drained percutaneously during labor. Ascitic fluid can quickly re-accumulate. Although meningomyeloceles, omphaloceles, and gastroschisis do not commonly hinder labor, the best obstetric care for these disorders is debatable. An untreated sacrococcygeal teratoma might cause a sudden inability to deliver the fetus beyond the abdomen. In such instances, flexing and delivering the legs may be possible to provide more area for the mass to deliver. Resuscitation and stabilization of the newborn on the perineum, followed by cesarean delivery, is another possibility (8).

Macrosomia fetus

In the literature, there is no agreed-upon definition of fetal macrosomia. The most common definition is a birth weight of over 4000 grams. The number of children born weighing more than 4000 grams has been rising (14). Shoulder dystocia, meconium aspiration, hypoxia, brachial plexus damage, placenta previa, traumatic midforceps, and fetopelvic disproportion are all risks they face. The head is larger than typical, but it is also more calcified, which means it has less

molding ability. The fetal trunk's size may potentially play a role in dystocia and mechanical issues during birth. Shoulder dystocia and arrest and protraction disorders are examples of labor anomalies (8).

Fetal Weight Estimation

The precise measurement of fetal weight (EFW) is a difficult task. An accurate EFW would be helpful in making clinical judgments about shoulder dystocia prevention, oxytocin augmentation in atypical labor, and the use of midforceps in the care of macrosomic fetuses. Abdominal palpation and fundal height measures are used in clinical EFW. Clinically estimated fetal weight is difficult to apply to individuals, but it may be most useful in choosing patients for ultrasonographic EFW (8).

STRENGTH—UTERINE CONTRACTION

The causes of solely dysfunctional dystocia, which occurs when uterine contractility is insufficient to promote dilatation and descent, are unknown. For abdominal palpation to detect uterine contractions, a pressure greater than 10 mmHg above resting pressure is required. A tocodynamometer is placed on the abdomen over the fundus for external electronic monitoring. It can indicate us how often contractions happen and how long they last, but it can't tell us how strong they are or how long they last. Internal pressure monitoring is done either the transcervical insertion of an open-ended plastic cannula filled with fluid and connected to a pressure transducer, or the introduction of a disposable pressure transducer into the amniotic cavity after the membranes have ruptured. Internal intrauterine pressure monitoring measures resting uterine tone as well as the length, frequency, and severity of contractions (8).

Contractions occur every 3–5 minutes in early labor, with a pressure of 20–30 mmHg over resting tone. Contractions are usually every 2–4 minutes in active labor, with pressures 30–50 mmHg above resting tone. The pressures might climb to 100–150 mmHg when pushing. Early in labor, the resting pressure rises from 5 to 10 mmHg to 12–14 mmHg later. Contraction duration increases from 30 to 60 seconds in early labor to 60–90 seconds in later labor, in addition to increased frequency and tone. The minimum effective uterine contractility has been defined as a minimum of 5 minutes of contractions with a pressure greater than 25 mmHg (15).

Direct monitoring with an intrauterine pressure catheter provides the most reliable information on the intensity and strength of uterine activity. A stiff catheter guide is inserted just below the fetal presenting portion. The catheter guide is withdrawn once the pressure catheter has been progressed into the uterine cavity. A mark on the catheter that should be at the level of the

introitus after insertion can be used to establish the proper depth of insertion. The catheter should be inserted behind the presenting region of the fetus (16). Many researchers have devised objective measurements of uterine contractility, but none have been widely used in clinical practice. The Montevideo unit is the easiest way to calculate uterine work. Caldeyro-Barcia created it (17). Two different forms of aberrant contraction patterns have been linked to functional dystocia. Elevated resting pressures, higher contraction frequency, and impaired coordination are all signs of a hypertonic pattern, as is a delayed return to normal uterine tone (18). With fetal malpresentation and uterine overdistention, this pattern is more common. Oxytocin is normally not suggested, but it has been demonstrated to transform this pattern to successful labor on rare occasions. Hypotonic uterine dysfunction is more common and reacts to oxytocin more frequently. The contractions are synchronized, yet they are feeble, infrequent, or both. It's thought that contractions were never established normally in those with primary dysfunction. Secondary dysfunction is defined as contractions that were previously adequate but got weaker as labor progressed, usually after 4 cm dilation (8).

THE PATIENT (woman)

Although absolute fetopelvic disproportion is very rare, cesarean delivery for the indication of fetopelvic disproportion is a relatively common procedure. When making a diagnosis of dystocia, it is common practice to believe that the physician's role plays a substantial role. The mindset of the patient, the time of day, the availability of anesthetic support, the current medicolegal context, as well as the physician's own training and experience can all have an impact. Both the nature of the labor and its length can be affected by the patient's anxiety level as well as their ability to withstand discomfort. It is possible for medications taken during labor to change the contractility of the uterus. In order to stop labor, medical professionals have turned to β -mimetics, calcium channel blockers, magnesium sulfate, and antiprostaglandins. In addition to having a direct depressive impact on smooth muscle, ethanol also suppresses the release of oxytocin. Caffeine and theophylline both have the potential to lengthen the labor process. The effects of barbiturates are proportional to the dose taken. In anesthetic doses, pentobarbital, thiopental, and phenobarbital may be able to stop labor, however phenobarbital has very little impact. Both atropine and scopolamine work to relax the lower region of the uterus, which in turn reduces the number of contractions that occur. Tranquilizers offer multiple impacts; normally, big dosages delay labor (19). It is possible for epidural anesthesia to create a temporary reduction in contractility that lasts for ten to thirty minutes. If the anesthetic is administered during the latent phase, or if there is fetopelvic disproportion or malposition, then the effect will be considerably more pronounced. There is a possibility that the voluntary muscle activity that corrects malposition will be compromised. Because epidural anesthesia is linked to a lengthening of the second stage of labor, medical intervention is not advised unless the second stage of labor lasts for more than three hours with a regional anesthetic in a nulliparous parturient

or two hours in a parous parturient (20). There is a strong correlation between the cervical score and the beginning of labor that is spontaneous. The sensitivity of the myometrium to oxytocin may be reflected in the condition of the cervix. There is a possibility that inducing cervical ripening will heighten myometrial sensitivity and cause the cervix to become more malleable. Numerous medications, such as estradiol and relaxin gels, Foley catheters, Laminaria tents, and prostaglandin E2 and F2 administered through a variety of methods, have been examined and found to induce cervical ripening with variable degrees of efficacy. These agents include: Other more recent induction drugs, such as misoprostol, which is an analogue of the prostaglandin E1 molecule, have the potential to promote cervical ripening in addition to inducing and stimulating labor (8).

Obesity

It is expected that obesity will become an increasingly prominent cause of labor dystocia as obesity rates continue to rise in developed countries like the United States and the rest of the developed world. There is a lot of data to suggest that obese females are more willing to have dystocia (21). In nulliparous women who are giving birth to a singleton at term, having an excessive amount of weight before to becoming pregnant has been proven to increase the rate of cesarean section, particularly in extremely obese women (22).

Maternal Age Advancement

As the parturient population ages, it's important to recognize that older women are more likely to have a cesarean section. The mechanism behind this increased risk is unknown, but older women appear to have longer labors and greater rates of primary cesarean section for both elective and non-elective reasons (23).

Oxytocin

Oxytocin is an octapeptide produced in the hypothalamus and delivered to the posterior pituitary gland's axonal terminals. The reported maternal plasma concentrations of oxytocin during pregnancy and spontaneous labor are highly variable. During normal labor, oxytocin is released in pulses at 3- to 5-minute intervals in addition to a tonic baseline release, and fetal transfer of oxytocin to the maternal side may be an essential physiologic source (24). The beginning of uterine contractions appears to be aided by human myometrial oxytocin receptors, which peak in early spontaneous labor. The concentration of oxytocin receptors in the uterus is most likely the most important factor influencing the uterine response to endogenous or exogenous oxytocin (8). Increased contraction strength, velocity, and frequency, as well as increased intrauterine resting

pressure, are all oxytocic effects on the myometrium. Further increases in oxytocin may result in excessive contraction frequency and increased baseline tone, leading in decreasing contraction efficacy and the development of fetal discomfort after maximal efficiency is attained. If the contraction pattern appears to be enough (one every 3–4 minutes), but cervical dilatation is insufficient, clinical experience suggests that lowering the oxytocin dose occasionally improves efficacy. The uterus contractile pattern may provide an early assessment of response, however uterine activity quantification is far from ideal for detecting hypocontractile labor, detecting excessive stimulation, or guiding oxytocin therapy. Other parameters for titrating oxytocin are also advised because uterine activity varies greatly within and between individuals during normal childbirth (25). Excess uterine activity or fetal distress during oxytocin induction or augmentation may not constitute a pathologic condition needing emergent cesarean delivery. Contractions may become more frequent but less strong while a patient is in the supine posture. This position can potentially raise the risk of fetal hypoxemia and slow down cervical dilation. For hyperstimulation and fetal discomfort, placing the patient in a left lateral posture may be the only solution. Starting oxygen and lowering or halting the oxytocin infusion are two other options. Rather than terminating oxytocin, lowering the dose may help to correct the aberrant pattern and avoid an unnecessary delay in delivery. When resuming oxytocin administration, we recommend halving the previous rate. When labor has been established, it may be possible to reduce the oxytocin dose. The use of oxytocin during labor and delivery may reduce the risk of postpartum uterine atony. Before and during oxytocin induction or augmentation, the fetal heart rate and uterine activity should be monitored. In the current medicolegal atmosphere, this monitoring is critical, and it may help determine the most effective oxytocin dose. It's also a good idea to keep record of heart beat tones, contraction frequency and duration, and oxytocin levels (8).

DYSTOCIA - FUNCTIONAL LABOR ABNORMALITY

Cervical dilatation and fetal descent are the only two fundamental aspects of labor from a functional standpoint. Caldeyro-Barcia was the first to assess labor on a functional rather than anatomic/physiologic basis (17).

Labor pattern	Nulliparous	Parous
Protraction disorders		
Dilation	<1.2 cm/h	<1.5 cm/h
Descent	<1.2 cm/h	<1.5 cm/h
Arrest disorders		
Dilation	>2 h	>2 h
Descent	>1 h	>1 h

Figure 6. A list of diagnostic criteria for atypical labor patterns *(26)*

The time of beginning of regular uterine contractions is regarded 0 time on the labor graph and is considered as the time of onset of labor. Because the patient is usually at home when contractions begin, the beginning of labor (latent phase) is estimated by her. The cervical dilation for nulliparas and multiparas is usually around 2 cm at the start of labor, though the cervix may be closed if the membranes rupture prematurely. However, some multiparas may start labor with cervical dilations of 4–5 cm. In nulliparas, the fetal presenting region is located lower in the pelvis than in multiparas. Although it is commonly assumed that nulliparas should have an engaged fetal head when labor begins, this is not always the case. At labor onset, the presenting component in the nullipara can be expected to be a -1 station on average, compared to -1 to -2, or possibly slightly higher, in the multipara. All that is required of the physician is for him or her to determine whether labor is latent or active, and to recall a few simple numerical guidelines. The patient should be classified in latent phase if the cervix is less than 4 cm and dilation is greater than 1 cm/h in the nullipara and 1.5 cm/h in the multipara. In the latent phase, the average slope of dilation is less than 0.6 cm/h. If cervical dilation is greater than 5 cm or the cervix is dilating at a rate of at least 1 cm/hr in the nullipara and 1.5 cm/h in the multipara, the patient is in active phase. Although the two definitions for latent and active phases are mutually exclusive, they are not mutually exclusive. Intermediate dilations (between 4 and 5 cm) and slopes give an ambiguous picture of the stage of labor. These patients are frequently transitioning from a dormant to an active state (i.e., they are in acceleration phase). The acceleration phase is followed by the maximum slope phase, during which fast cervical dilatation occurs. The deceleration phase begins when the dilation reaches 9–10 cm. The fetal presenting part's descent may be latent until 9 cm of dilatation is reached, at which point it should be actively continuing (8).

The six dysfunctional labor patterns are:

(1) prolonged latent phase,

(2) protracted active phase dilation,

(3) secondary arrest of dilation,

(4) prolonged deceleration phase,

(5) protracted descent,

(6) arrest of descent, according to traditional definitions (8).

FIRST STAGE OF LABOR

The Friedman curve separates the first stage of labor into two parts: the latent phase, which begins when regular uterine contractions begin and ends at the beginning of the active phase, and the active phase, which begins when rapid cervical dilation begins and ends when the mother's cervix is fully dilated. The latent phase begins when regular uterine contractions begin and ends at the beginning of the active phase. The active phase often begins when the mother is between 3 and 4 centimeters dilated, although there are some definitions that place the threshold at 6 cm (9).

Prolonged Latent Phase

Regular contractions efface and dilate the cervix start the latent period, which ends with the initiation of active labor. The length of the latent phase is determined by a number of factors. In general, cervical dilation at the time of labor beginning is negatively associated to the latent phase. Similarly, the shorter the latent period is, the lower the fetal presenting part is in the pelvis at the time of labor's commencement. It's important to remember that sedation has the ability to produce a protracted latent phase. When the sedation wears off, most drugged patients continue labor. Prolonged latent phase is diagnosed after 21 hours in the nullipara and 14 hours in the multipara, according to established criteria (27). Such long periods are unacceptably long for patients in the absence of sedation and analgesia, and can lead to maternal tiredness. As the 12-hour mark in the latent phase approaches, one strategy is to carefully assess the patient. If the patient has had interval cervical effacement and dilation or fetal descent (showing that the patient is not in false labor), starting oxytocin augmentation is a reasonable option (8). Long latent periods are linked to adverse outcomes for the newborn, including as anomalies in the ensuing labor, low Apgar scores, and the requirement for neonatal resuscitation. An abnormally extended latent period is connected with an increased risk of third- and fourth-degree lacerations, febrile lacerations, and intrapartum blood loss for the mother. Additionally, the risk of infection is increased (9).

Active phase

The transition from the latent to the active phase starts after the latent period. According to Friedman, the active phase lasts for an average of 2.5 hours; however, other rewritten and extremely contentious definitions extend this time frame all the way up to 5.5 hours. There may be a difficulty with labor if the active phase lasts for an exceptionally long time (9).

Protracted Active Phase Dilation

Prolonged active phase dilatation in nulliparas should be detected when the dilation rate is less than 1 cm/h. The lower limit of normal for the multipara is 1.5 cm/h. A typical dysfunctional labor pattern is prolonged active phase dilatation. It appears to be linked to a slight cephalopelvic disproportion. Many cases of prolonged active phase dilation may have historically been labeled primary uterine inertia or hypertonic uterine inertia, implying some form of uterine malfunction. There may also be an iatrogenic component to this labor anomaly, as supine position may reduce uterine contractility, resulting in slower cervical dilation. While active labor is relatively insensitive to analgesia, the use of narcotics has been linked to slow dilation in the active phase in some circumstances. Early epidural anesthesia, especially if the presenting part's station is greater than -1, is linked to an increased risk of this labor anomaly (28). Prolonged active phase dilatation should also be regarded a significant risk factor for later labor dysfunction. Although the etiology of protraction is unknown, a viable strategy comprises early recognition of atypical labor progression during the active phase, fetal monitoring, lateral positioning, and cautious oxytocin administration. Just as the causes of prolonged active phase dilatation are unknown, so too is the optimal treatment (8).

Secondary Arrest of Dilatation

Secondary arrest of dilation is identified when cervical dilation has not changed for at least two hours. This duration condition would be the same for nulliparas and multiparas and is partially depending on the certainty with which cervical dilation may be assessed via digital examination. Secondary arrest, which happens in 5–10% of labors in the majority of studies, is more common with term than with preterm and with larger than with smaller fetuses. This anomaly occurs more often than prolonged latent phase, but less often than prolonged active-phase dilatation. Due to its link with greater fetal morbidity and mortality and a significantly increased risk of cesarean birth, it has been deemed the most serious of dilation disorders (8).

It has been advised that the diagnosis should not be made unless labor is vigorous, the cervix is more than 4 centimeters dilated, and there has been no cervical change for 2 hours with 200 or more Montevideo units every 10-minute interval (26). The prevalence of prolonged malposition is statistically related to the occurrence of subsequent arrest (i.e., persistent occiput posterior and persistent occiput transverse). However, it is uncertain if the related malposition is a consequence or cause of the arrest disorder. The likelihood of secondary arrest of dilation increases fivefold in nulliparous labors complicated by prolonged active phase dilation, compared to an eightfold rise in multiparous labors. This increase shows that "uterine inertia" may play a causal effect (8). During active labor, patients should undergo cervical checks at least

every two hours so that secondary arrest can be diagnosed as quickly as feasible. Examination closer to each hour may be necessary to detect the onset of arrest (29).

In cases with secondary arrest disorders, electronic monitoring for evaluation of uterine contractions and fetal heart rate is required. During the active phase, augmentation of oxytocin is initiated, beginning at 1–2 mU/min and increased by 1 mU/min every 30 minutes, in an effort to simulate normal uterine contractility. Maternal and fetal status must be closely checked. In the first hour following augmentation, cervical dilatation may be minimal; but, in rare situations, cervical dilation may restart fast, resulting in spontaneous vaginal birth. However, fetal descent typically occurs within the first hour, with cervical dilatation restarting subsequently (30). If there are signs of fetal distress, the fetus may be biochemically tested, but surgical delivery is usually essential. If labor does not develop regularly within two to three hours following the initiation of oxytocin augmentation, a c - section may be necessary (31)**.**

Prolonged Deceleration Phase

Deceleration is the third phase of active labor, following maximum slope and acceleration. The beginning of deceleration phase for nulliparous and multiparous labor begins at 9 centimeters. Active descent should begin at the beginning of the deceleration phase, however in many labors it begins sooner. Engagement that does not occur in nulliparas at the beginning of the deceleration phase (i.e. 9 cm) and in multiparas by the conclusion of the deceleration phase is abnormal. In nulliparous labor, a prolonged deceleration phase of at least 3 hours is required for diagnosis, while in multiparous labor, a prolonged deceleration phase of at least 1 hour is required for diagnosis. Because descent should be active at this stage in normal labor and the intervals for diagnosing descent problems are shorter than those required for diagnosing extended deceleration phase, the clinician's attention should be focused on descent rather than dilation at this point in labor. The risk of a second-stage abnormality increases if engagement has not happened by 9 cm of dilation. Descent problems are significantly linked to prolonged deceleration phases. As a labor anomaly, extended deceleration phase appears to be most strongly linked to secondary arrest. Labor augmentation with oxytocin, as outlined in the protocol above, is frequently required. A prolonged deceleration phase is uncommon, occurring in about 1–3% of all labors. Such instances, according to clinical experience, are typically coupled with chronic occiput transverse or posterior or some other pelvic anomaly that can be seen on clinical pelvimetry. Cervical edema and significant molding of the fetal skull are common in patients with this condition. In this condition temptation to use forceps through a nearly dilated but still incompletely dilated cervix (8). Some medical personnel will try to get the baby's head through the cervix by having the woman push through a contraction while they are trying to deliver the baby. The difficulty with this strategy is that it ultimately results in a worsening of the edema in the cervical region. When the cervix is not fully dilated and the baby's

head is not in the position required for birth, this method can sometimes mislead medical personnel into believing that the cervix is entirely dilated when it is. This ultimately results in the labor process being prolonged, which is problematic given that a cesarean section would have been necessary anyhow (9).

SECOND STAGE OF LABOR

The delivery of the baby marks the finish of the second stage of labor, which begins when the cervix has completely dilated and continues until the baby is born (9). When the cervix is fully dilated, the second stage of labor begins. The unintervened second stage of labor is expected to last one hour in nulliparas and 15 minutes in multiparas on average. Clinical limitations" for second-stage lengths have been postulated, at which point the clinician should get concerned and anticipate delivery complications. This clinical limit is 2 hours for nulliparas and 1 hour for multiparas, but the clinician should be worried if the second stage lasts longer than 45 minutes (8).

Protracted Descent

When nulliparous labor progresses at less than 1 cm/h, and when multiparous labor progresses at less than 2 cm/h, protracted descent must be suspected. Even if it is true that it is more difficult to estimate properly the station of the fetal presenting part than it is to estimate the degree of dilatation, it is still possible to make this diagnosis within an hour for nullipara patients and within half an hour for multipara patients. Because therapy may include extensive intervention, a careful balance between overdiagnosis and failure to detect protracted fall as soon as feasible should be pursued. Malposition and relatively minor degrees of fetopelvic disproportion are common causes of delayed descent; total fetopelvic disproportion is uncommon. The administration of epidural anesthetic is typically accompanied with a slow descent. A long descent necessitates a high level of expertise and attention. Other abnormal labor patterns typically precede it, which could indicate severe disproportion, uterine dysfunction, or both. It's debatable whether oxytocin stimulation is reasonable under such circumstances. On a case-by-case basis, the response must be provided. If delayed descent occurs in a labor already exacerbated by previous dysfunctional labor patterns in the context of oxytocin augmentation, it is not unreasonable to argue that a cesarean birth is the best option. The existence of a persistent occiput posterior is typically related with prolonged descent. Earlier, forceps rotation was often used to treat occiput posterior. Direct occiput posterior delivery and manual rotation, on the other hand, are acceptable and potentially less damaging options. In around half of cases complicated by protracted descent, normal spontaneous vaginal delivery and low forceps interventions happen (8). When shoulder dystocia is present, the second stage of labor is frequently halted (9).

Arrest of Descent

When descent has been completely stopped for at least 1 hour in the nullipara and 0.5 hour in the multipara, the diagnosis of stoppage of descent is established. Prolonged descent is typically preceded by it, and it has the same causal elements. When there are no other problematic labor patterns before the arrest of descent, experience suggests that, like secondary arrest of dilatation, it is particularly susceptible to oxytocin augmentation. Low-dose intravenous oxytocin is usually linked to natural vaginal birth. Electronic monitoring is appropriate in the case of augmentation for other labor problems, as well. The scenario is comparable to that of extended descent when arrest of descent is preceded by other dysfunctional labor patterns. If the patient is already getting oxytocin augmentation or has not reached full dilation, a cesarean section is generally the best option (8).

Friedman advocates a C-section after 2 hours of labor arrest, whereas other experts advise waiting at least 4 hours with Pitocin (synthetic oxytocin) augmentation before proceeding. The four-hour recommendation, on the other hand, puts infants in danger. If the baby is unable to pass through the delivery canal, they will continue to have severe contractions from Pitocin augmentation during the four hours they are blocked. Oxitocin-related hyperstimulation (also known as uterine tachysystole) may cause oxygen deprivation-related damage when the placenta is unable to replace its oxygen supply, increasing the risk of severe cranial compression (9).

THIRD STAGE OF LABOR

When the placenta does not entirely or properly separate from the uterus during the third stage of labor, the woman is at danger of significant maternal hemorrhage. This can happen if the placenta isn't fully separated or if the female has placenta accreta or percreta (9). It's debatable if placentas should be manually removed or treated expectantly throughout the third stage of labor. According to life-tablele research, 90 percent of term placentas deliver spontaneously within 15 minutes, with only 2.2 percent remaining undelivered at 30 minutes (i.e., a "retained placenta") (32). The present management of the third stage of labor is influenced by a number of factors, including a presumed standard of care that term placentas should be delivered within 30 minutes and the risk of bleeding if the third stage is delayed. Although the aim to limit maternal bleeding and the necessity for transfusion is the most critical factor (33). Prophylactic oxytocin, controlled cord traction, fundal massage, and early cord clamping to aid placenta delivery have all been shown to reduce the risk of bleeding (34). Regardless of gestational age, the frequency of bleeding rises at 40 minutes. This increase could be due to the fact that manual placental removal was performed for patients with active uterine bleeding, despite the fact that manual removal may increase blood loss in some circumstances. On the basis of these findings, systematic manual removal of the placenta before 10 minutes for any gestational age would be difficult to justify (8).

DIAGNOSIS

Protraction disorders and arrest disorders are the two categories of anomalies that can occur during labor. The progression of labor can be tracked using a graph called a partogram, which depicts cervical dilation and station across time. This can help medical professionals make an accurate diagnosis (2).

When care for women who have dystocia, physicians need to take into consideration the following four issues:

(1) If the contractions are of sufficient intensity;

(2) If the fetal position is abnormal.

(3) In the event that there is a cephalopelvic disproportion due to the possibility of macrosomia or a contracted pelvis

(4) Whether there are other associated clinical concerns (such as chorioamnionitis or nonreassuring fetal monitoring) that would affect the therapy options available to the patient (2).

PREVENTION

Reduce the prevalence of dysfunctional labor in primiparous women by:

1. Provision of labor support;

2. Avoidance of hospital admission in the latent stage of labor;

3. Avoidance of elective induction with an unripe cervix;

4. Use of epidural analgesia with caution (2).

Those who exercise or remain upright throughout the first stage of delivery report more comfort and tolerance for labor than women who remain supine (35). Certain characteristics of physician behavior and health-care systems may help to avert dystocia and subsequent cesarean birth. These include maintaining caregiver continuity throughout the procesess (36).

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INTRAUTERINE GROWTH RESTRICTION. FETAL DISTRESS. FETAL DEATH.

FETAL GROWTH RESTRICTION

GENERAL AND EPIDEMIOLOGICAL DATA

IUGR/SGA is caused by a variety of factors, including maternal, paternal, and environmental factors. IUGR is caused by a combination of placental and fetal causes, as well as genetic variables that have recently been added (1). Every year, it is estimated that 13.7 million children are born at term with low birth weight (LBW), accounting for 11 percent of all neonates delivered in developing nations. When compared to developed nations, this rate is six times greater. IUGR accounts for 23.8 percent of all infants, or over 30 million every year. The higher estimations may be due to the fact that kids delivered at home are more likely to be LBW in poor nations (birth weight 2500 g). The prevalence of IUGR varies by country, population, and race, and it rises as gestational age decreases. Asia has most of the IUGR neonatal burden, representing for around three-quarters of all affected newborns, followed by Africa and Latin America. IUGR-LBW rates may be classified as low (55 percent), moderate (5–10 percent), high (10–15 percent), or extremely high (10–15 percent) and very high (415 percent) for all births in each country. South Central Asia has the greatest occurrences of LBW and IUGR-LBW (2).

Definition

Intrauterine growth restriction (IUGR) is a significant and often overlooked cause of fetal and neonatal morbidity and death. It is characterized as a fetal growth rate that is lower than normal for the infant's development potential. The phrases IUGR and small for gestational age (SGA) are being used generally. Although there are slight distinctions between both of them (3).

Intrauterine growth restriction (IUGR) is described as a fetal growth rate that is less than normal for a certain infant's development potential based on race and gender. SGA is characterized if a baby's birth weight is less than the population norms on the growth charts (less than the 10th percentile for that gestational age). SGA refers for birth weight without considering in-utero growth. IUGR infants may have a normal birth weight for their gestational age, but they may have had any in-utero growth retardation as a result of a perinatal injury; as a result, IUGR is a clinical definition that is used to neonates with clinical signs of malnutrition (4).

Infants born at term or late may weigh less than 2500 g, while a diabetic mother's baby may weigh significantly more than 2500 g even before 37 weeks. As a result, an infant's survival fate is determined by both gestational age and birth weight.

New-born classification based on gestational age and birth weight

The following terms are connected to gestational age and birth weight:

1. Small for gestational age – SGA- refers to a birth weight that is less than the 10th percentile for gestational age.

2. Appropriate for Gestational Age - AG - for gestational age, the birth weight falls between the 10th and 90th percentiles.

3. Large for gestational age – LGA- refers to an infant's birth weight that is greater than the 90th percentile for gestational age (3).

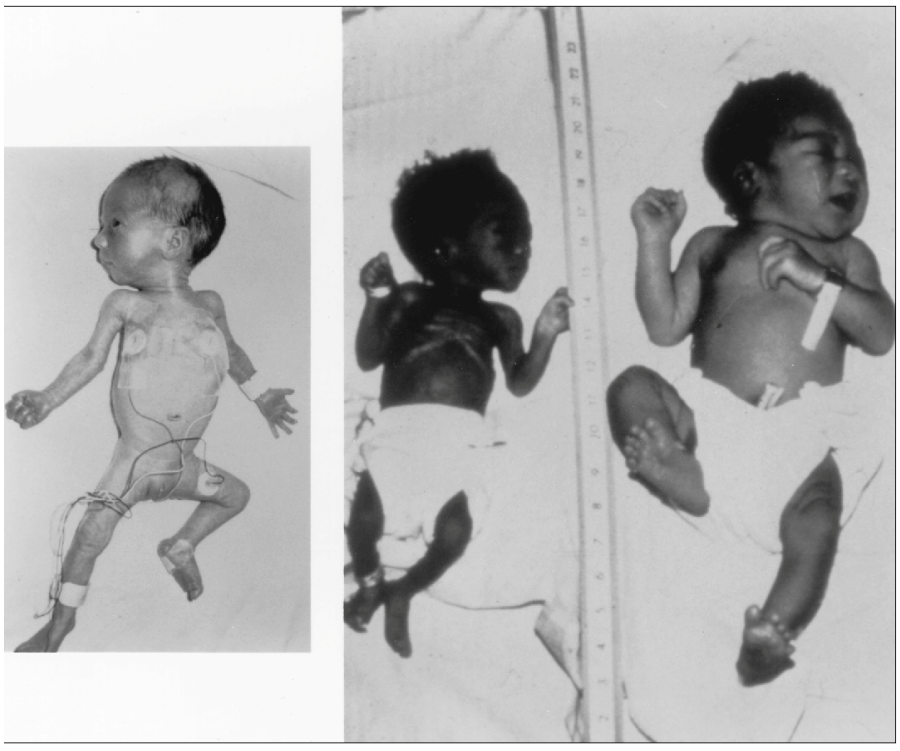

Figure 7. Comparison of infants of various gestational age (left - preterm infant, middle – SAG and right AGA) (5)

Preterm birth definition

Preterm birth is defined as a birth that happens before the completion of 37 menstrual weeks of pregnancy, regardless of birth weight. The growth potential (10th to 90th percentile) may be typical and suitable for the gestational period. SGA - About 70% of infants born with a fetal growth under the 10th percentile are found to be fully developed. They are modest by nature and have no elevated risk of negative outcomes. They exist at the extremes of the typical growth spectrum. The remaining 30% are severely hampered in their growth (3).

It's important to mention that a newborn with a birth weight below the tenth percentile might be SGA but not an IUGR, while a neonate with a birth weight above the tenth percentile could be an IUGR (4). About one-third of low-birth-weight babies have FGR. Its overall prevalence in developed countries is estimated to be between 2 and 8%. The incidence among term babies is around 5%, whereas the incidence among post-term babies is over 15% (3).

Fetal Growth Restriction (FGR) definition

Fetal Growth Restriction (FGR) is defined as a condition in which a baby's birth weight falls under the 10th percentile of the gestational age's average. Preterm, term, and post-term newborns can all have growth restriction (3).

Cellular hyperplasia is the first sign of normal fetal growth, followed by hyperplasia and hypertrophy, and finally hypertrophy alone. The majority of fetal weight gain (two-thirds) happens after the 24th week of pregnancy (3).

The small fetuses are split into two groups based on clinical evaluation and ultrasound inspection:

1. Small and healthy fetuses. For their gestational age, the birth weight is less than the 10th percentile. They have a healthy ponderal index and subcutaneous fat, and their neonatal history is usually unremarkable.

2. Fetuses whose growth is limited due to a diseased condition (true IUGR). The fetuses are categorized into two types based on the relative size of their head, abdomen, and femur:

(a) symmetrical or Type I - The harmful effect on the fetus occurs early in the phase of cellular hyperplasia. The overall number of cells is lower. The pathogenic process is unique to the fetus and affects all of its organs, including the brain.

(b) asymmetrical or Type II - During the phase of cellular hypertrophy, the fetus is affected later in the pregnancy. The total number of cells is the same, but the size is less than usual. Extrinsic

to the fetus maternal illnesses are the pathological conditions that frequently result in asymmetric growth retardation. These illnesses reduce uteroplacental blood flow, inhibit oxygen and nutrient transport, or reduce placental growth, all of which affect fetal size (3).

RISC FACTORS

Maternal, placental, fetal, or genetic factors may all contribute to IUGR. Genetic reasons contribute for around one-third of IUGRs, meanwhile the fetal environment contributes for the other two-thirds (6).

Maternal factor for IUGR

Table 3. Maternal causes for intrauterine growth restriction (1)

Age of the mother (<16 y or >35y)
Social and economic standing
Ethnicity or race
Drug addiction in the mother
Maternal medication
Maternal height and weight
Parity
Interval between pregnancies
A SGA infant's previous delivery
Assisted reproductive technologies
Failure to receive regular medical attention during pregnancy
Extreme malnutrition of the mother while she was carrying the baby.
Poor weight gain
Hematologic and immunologic disorders
Maternal medical disorders (nephropathy, collagen vascular disease)
Pathological conditions in pregnancy like preeclampsia and
diabetes associated with vasculopathy
Maternal infection and parasite infestations
Altitude

Living in a poor nation is connected with maternal anemia or malnutrition, which may lead to intrauterine growth restriction (IUGR). A low socioeconomic position may be related to the mother's nutrition as well as drug addiction (7).

Environmental tobacco exposure may be related with reduced birth weight, and smoking is connected with a reduction in birth weight of roughly 150–200 grams (8).

Excessive drinking during pregnancy is linked to fetal alcohol syndrome, whereas moderate drinking during pregnancy may be linked to intrauterine growth restriction (IUGR) (9).

IUGR may be caused by the mother's exposure to toxins as well as different drugs, such as warfarin, steroids, anticonvulsants, antineoplastic agents, anti-metabolite, and folic acid antagonists (10).

Women who stay at high elevations have limited placental blood flow due to lower blood volume, and they also have reduced oxygen carrying capacity, which may contribute to intrauterine growth retardation (11).

Placental factors for the IUGR

Any imbalance between the supply from the placenta and the requirements of the fetus in terms of nutrition or respiration will result in restricted fetal development. There are a variety of placental factors that might contribute to IUGR (1).

Table 4. Placental causes for intrauterine growth restriction (1)

Abnormal uteroplacental vasculature
Placental dysfunction (Pregnancy induced Hypertension (PIH), preeclampsia)
Thrombophilia-related uteroplacental pathology
Avascular villi
Decidual or spiral artery arteritis
Multiple infarctions
Partial molar pregnancy
Syncytial knots
Chronic inflammatory lesions
Single umbilical artery
Abruptio placenta
Velamentous umbilical cord insertion
Placental hemangioma
Placental infections
Infectious villitis
Multiple gestation
Chronic villitis of unknown etiology (CVUE)

The determination of intrauterine growth restriction (IUGR) is significantly impacted by placental weight. IUGR is associated with a low functional tissue mass in the placenta, which leads to a decrease in the area for exchange between the mother and the fetus. This occurs both at the surface area of the villous tissue and at the surface area of the fetal capillary tissue. As a result, the capacity to transport oxygen and nourishment from the mother to the fetus is diminished (12).

In a placenta with IUGR, there is a reduction in the number of terminal villi as well as a reduction in the surface area among those terminal villi. This reduction represents a dysfunction in the vascularization process that occurs in these pregnancies. In order to satisfy the needs of a developing baby, there must be sufficient invasion of trophoblast cells and an increase in the blood flow between the uterus and the placenta as the duration of pregnancy progresses. Doppler velocimetry methods of umbilical vessels and uterine arteries have demonstrated an increased vascular resistance in these vessels of an IUGR baby. This happens as a result of insufficient trophoblast invasion of the spiral arteries, which was shown to be the cause by these techniques (13).

IUGR patients are more likely to have complications such as placental abruption, velamentous cord insertion, single umbilical artery (SUA), true knot, and placental infarction. They cause a reduction in the transport of nutrients to the fetus, which ultimately results in IUGR (13).

One of the most common reasons for fetal development limitation is an infection of the placenta, such as placental malaria (PM). The levels of complement C5a and C5a receptors are elevated in patients with PM, which results in placental vascular insufficiency as a consequence of dysregulated angiogenic factors. These factors are necessary for placental vascular remodeling to take place during the course of fetal growth (14).

IUGR-related fetal risk factors

Table 5. IUGR-related fetal risk factors (1)

Chromosomal abnormalities
Genetic syndromes
Major congenital anomalies
Multiple gestation
Congenital infections
Metabolic disorders

It is estimated that between 7 and 19 percent of all children born with IUGR are caused by chromosomal abnormalities in the fetus (1).

The most prevalent types of chromosomal abnormalities are trisomies 13, 18, and 21. Trisomy 13 is also known as the Patau syndrome (Down syndrome) (15).

Bloom syndrome, Russell-Silver syndrome, Cornelia de Lange syndrome, Brachmann– de Lange syndrome, Mulibrey Nanism syndrome, Rubenstein–Taybi syndrome, Dubowitz syndrome, Seckel syndrome, Johanson–Blizzard syndrome, Fanconi syndrome, Roberts syndrome, and De Sanctis–Cacchione syndrome are some of the genetic syndromes that have been linked to IUGR (16).

Around 5% of all IUGR cases are caused by congenital infection. Toxoplasmosis and CMV are frequent infections in affluent nations, with rubella decrease due to vaccination, and the approach for regular TORCH screening has been questioned (17).

Malaria, congenital HIV infection, syphilis, and rubella are the most prevalent causes in developing countries. Malaria is the most common infectious disease in the poor world, such as Africa and Southeast Asia, accounting for 40% of cases in areas where it is prevalent (18).

Agenesis of the pancreas, congenital absence of islets of langerhans, congenital lipodystrophy, galactosemia, generalized gangliosidosis type I, hypophosphatasia, I-cell disease, Leprechanism, fetal phenylketonuria, and transient neonatal diabetes mellitus are some of the metabolic disorders that have been reported to result in IUGR in both the fetus and the infant (19).

It has been shown that multiple pregnancies are connected with around 3 percent of all occurrences of IUGR. This occurs more often in higher order pregnancies or in cases of monochorionic twin pregnancy. The growth rate of a fetus that is carrying twins is typical up to the 28th week of gestation, after which it begins to slow down physiologically. It is estimated that around 30 percent of all twin pregnancies will have a growth discordance of 15 percent or more. This phenomenon is said to be caused by "uterine overpopulation" (20).

Fetal growth limitation caused by a genetic factors

Researchers have discovered that polymorphisms in genes that code for proteins and hormones in the mother, the placenta, and the fetus may limit procreation (1).

Table 6. Fetal growth limitations caused by a genetic factors (1)

Placental genes
Homeobox Genes
SERPINA3 Genes
Cullin Genes
STOX1 gene
NEAT1 (Nuclear Paraspeckle Assembly Transcript 1) gene
Placental growth factor (PlGF)
Trophoblastic miRNAs (micro RNA)
Apoptosis Bcl-2 and Bax gene
Placental Insulin-like growth factor 1 (IGF1)
Placental Insulin-like growth factor 2 (IGF2)
Insulin like growth factor binding protein (IGFBP)-3 genes
Epidermal growth factor (EGF)
Maternal genes
Endothelin-1 (ET-1) and Leptin
Visfatin
Thrombophilia genes
Fetal genes
Protein S100B
N-terminal parathyroid hormone-related protein
Igf1 (Insulin Like growth factor 1) and SHOX gene
Insulin-like growth factors 1 receptor (IGF-1R) mutation

IUGR'S ENDOCRINE BASE

Insulin, thyroid, adrenal hormones, and pituitary hormones are among the hormones that have been linked to fetal development. These fetal hormones affect the metabolism and gene expression of fetal tissues, promoting growth and development in the womb (1).

Insulin regulates cell number by having direct mitogenic effects on cellular development. It stimulates glucose absorption and consumption by a variety of bodily tissues, mostly muscle, while also limiting protein breakdown. Insulin insufficiency causes embryonic development to be stunted because the fetal tissues' absorption and use of nutrients is reduced (21).

Insulin-Like Growth Factor-I: The amount of glucose that is available to the fetus has a favorable effect on IGF-I. IGF-1 has mitogenic capabilities, which induce somatic cell development and proliferation. It also has an effect on the transfer of glucose and amino acids through the placenta, which in turn affects the growth of the fetus. The findings of preclinical tests have

shown that significantly lower levels of IGF-I expression are associated with significantly lower rates of fetal growth (22). IGF-I promotes a rise in the number of oligodendrocytes and neurons, as well as neuronal outgrowth characterized by an expansion of dendritic arborization and axon terminal fields (23).

Deficiencies in fetal thyroid hormone may lead to developmental problems in a number of different organs. In most cases, fetal hypothyroidism reduces the amount of oxygen used and the amount of glucose that is oxidized, which in turn reduces the amount of fetal energy supplied for development. IGF-I concentrations both in the blood and in the tissues are reduced when hypothyroidism is present (24).

Glucocorticoids play a crucial role in the growth and maturation of fetal organs before birth, despite the fact that they do not have a significant impact on the rate at which fetal organs grow before birth. These include the accumulation of glycogen, the production of gluconeogenesis, the oxidation of fatty acids, the induction of the production and release of surfactant, the structural maturation of alveoli, the structural maturation of the gastrointestinal tract, the increased expression of digestive enzymes, the increased function of the adrenal glands, the transition from fetal to adult hemoglobin synthesis, and the maturation of the thymus, liver, and kidneys (25).

Despite its role as the primary hormonal regulator of postnatal growth, growth hormone has been shown to have no influence on the growth of developing fetuses (26).

PATHOPHYSIOLOGY

The primary cause of pathology in small for gestational age infants is a deficiency of nutrients in the mother or a failure of transfer from the placenta to the fetus. It could also be attributed to the fetus's diminished ultilization. The size of brain cells (asymmetric–SGA) and the number of cells (symmetric–SGA) are both lowered. The amount of glycogen in the liver has decreased. The renal and pulmonary contributions to amniotic fluid are reduced due to reduced blood supply to these organs, resulting in oligohydramnios. Intrauterine hypoxia and acidosis are risks for the SGA fetus, which can lead to intrauterine fetal death if severe.

DIAGNOSIS

Clinical

For screening purposes, clinical examination of the uterus to determine fundal height, liquid volume, and fetal mass may be performed. However, it has a lower sensitivity. After 24 weeks of pregnancy, a measurement known as symphysis fundal height (SFH) in cm has a strong correlation with gestational age. The presence of a lag of three centimeters or more is indicative of growth limitation. It is a parameter that takes up 30–80 percent of the total weight. Measurement in serial order is very crucial during the second part of pregnancy, the amount of weight gained by the mother either does not change or actually loses weight. A measurement of the abdominal circumference that reveals stable or declining values (3).

The objective of prenatal monitoring should be early discovery of IUGR, although the general prognosis of these IUGR hasn't altered significantly, despite the fact that monitoring may result in a change in delivery time or care. The kind and timing of prenatal monitoring are still a point of contention (27).

Standard testing methods include a detailed maternal and familial history for risk factors for intrauterine growth restriction (IUGR), a maternal physical examination including maternal pre-pregnancy weight and height, nutritional status, fundal height, and fetal palpation, as well as cardiotocography (CTG) and ultrasound with Doppler. The precise timing of the pregnancy and the measurement of the fetal weight are the first and most essential steps in making a diagnosis of IUGR. This is because both of these steps are required for monitoring the development of the fetus. In the first trimester, the appropriate gestational age should be estimated using both the last menstrual cycle and the crown-rump length. In the second trimester, fetal weight should be assessed using biometric measurements (abdominal circumference, head circumference, biparietal diameter, and femur length). To diagnose IUGR, use a specific fetal weight growth chart (28).

The biophysical profile (BPP), which measures fetal acid-base status, may be used to determine IUGR risk and monitor IUGR fetuses. BPP alterations in IUGR babies follow a predictable sequence, with responsiveness disappearing first, followed by fetal respiration, fetal movement, and tone, and finally a decline in amniotic fluid (29).

After identifying maternal risk factors and IUGR, the mother's karyotype is checked for aneuploidy, maternal infection with Toxoplasma and CMV, syphilis, and malaria, particularly in high-endemic areas. If severe SGA is detected during the 18–20 week scan, the mother should be assessed by a fetal medicine expert with a complete fetal anatomical assessment and uterine artery Doppler (30).

COMPLICATIONS

- **Fetal:**

a) Antenatal - Chronic fetal distress or fetal death.

b) Intranatal –Hypoxia and acidosis

- **Following birth**:

a) Immediate: - Asphyxia, bronchopulmonary dysplasia and RDS

- Hypoglycemia due to shortage of glycogen reserve in the liver
- Meconium aspiration syndrome
- DIC
- Hypothermia
- Pulmonary hemorrhage
- Polycythemia, anemia, thrombocytopenia.
- Hyperviscosity-thrombosis
- Necrotizing enterocolitis due to reduced intestinal blood flow.
- Intraventricular bleeding
- Electrolyte disorders
- Malfunction in multiple organs
- A rise in the incidence of maternal and infant illness and mortality.

b) Late: Babies born with asymmetrical IUGR typically make up the lost ground in their early infant years. Infancy is marked by a delay in neurological and intellectual development. IUGR caused by congenital infection, congenital defects, or chromosomal abnormality has the worst prognosis.

Further long-term consequences include:

- A higher risk of developing metabolic syndrome in adulthood, which includes obesity, hypertension, diabetes, and coronary heart disease (CHD).

- In LBW newborns, the orexigenic pathway is disrupted, resulting in increased hunger and decreased satiety.

- Renal vascular hypertension is caused by a decrease in the number of nephrons (3).

Per se, fetal growth restriction has no negative effects on the mother. However, underlying illness processes such as preeclampsia, heart disease, and starvation may be fatal. Unfortunately, a woman who has given birth to a child with growth retardation has a doubled risk of having another child. Instant neonatal mortality is approximately six times that of a typical newborn. However, it is less than that of preterm AGA newborns with the same birth weight. The majority of infants die within 24 hours. The mortality rate climbs to almost fifty percent. They are more likely to experience poor postnatal growth and negative cognitive outcomes (3).

IUGR FETUS MANAGEMENT

The treatment strategy is based on the results of a thorough diagnostic examination. Constitutionally small fetuses (70 percent) do not require intervention. Fetal abnormalities, infections, and genetic diseases should be explored in the 15% of fetuses who are symmetrically growth restricted. Unfortunately, there is no effective treatment available for this population. Finally, a fetus with a growth restriction due to placental illness or decreased placental blood flow (chronic placental insufficiency) may be treated. However, because there is no clear therapy in the majority of cases, assessing fetal health is more important in management (3).

Women who get IUGR early (before 34 weeks) have a poorer perinatal outcome than those who develop FGR later (after 34 weeks). Early delivery must be balanced against the danger of neonatal mortality owing to complications, as well as the chance of IUFD if delivery is delayed. After the 36th week of pregnancy, the majority of fetal deaths happen. As a result, accurate diagnosis and timely intervention are critical (3).

General measures

There is currently no recognized treatment for reversing growth limitation once it has occurred.

The following, on the other hand, might be worth a shot:

1. Appropriate bedrest, particularly in the left lateral decubitus position.

2. To correct malnutrition by balanced diet: 300 extra calories per day should be taken.

3. To begin treatment for the related aggravating conditions that are likely to cause growth limitation.

4. Smoking, tobacco, and alcohol abstinence.

5. Maternal hyperoxygenation by nasal prong at a rate of 2.5 L/min for short-term pregnancy prolongation;

6. In extremely specific situations with a history of thrombotic illness, hypertension, preeclampsia, or recurrent IUGR, low-dose aspirin (50 mg daily) may be beneficial.

7. If the fetal growth was stunted due to maternal malnutrition, maternal hyperalimentation with amino acids can help. When placental function is impaired, it is ineffective.

8. Improved placental perfusion may be aided by maternal volume expansion (3).

PLANNING AND SCHEDULING OF THE BIRTH

Planning and scheduling of the birth by following variables that includes:

(1) Presence of fetal abnormalities;

(2) Duration of pregnancy;

(3) Level of FGR;

(4) Related complicating condition;

(5) implicit pathology (3).

Depending on the presence of any extra risk factor, the optimal time of birth for a growth-restricted fetus can range between 34 and 37 weeks. When a pregnancy reaches 37 weeks or more, the delivery should take place. Pregnancy lasting less than 37 weeks - the majority of cases fall into this category. At least 37 weeks will be carried out with the pregnancy. After that, the delivery is finished (3).

The presence of phosphatidylglycerol and L: S ratio of 2 in the amniotic fluid research (amniocentesis) indicate that lung maturation has occurred. If lung maturation has not yet occurred, intrauterine transport to a facility with the necessary equipment is the best option. When the gestational age is fewer than 34 weeks, betamethasone medicationes used to speed up

pulmonary maturation. Corticosteroids lower the risk of HMD and intraventricular hemorrhage (IVH) in newborns. In situations of FGR with other risk factors for adverse perinatal outcome, delivery should be performed at 34 weeks of pregnancy (Preeclampsia, oligohydramnios, AREDV). When a preterm birth is required, prenatal corticosteroids should be administered. When a delivery is scheduled before 32 weeks, the mother should be given magnesium sulfate for fetal and newborn neuroprotection. Regardless of gestational age or birth time, fetuses with aneuploidy or congenital infection have a dismal prognosis (3).

The Royal College of Obstetricians and Gynecologists (RCOG) has issued recommendations for the care of IUGR fetuses, which include both monitoring and delivery. Where delivery is being contemplated, women with an SGA fetus between 24 + 0 and 35 + 6 weeks of pregnancy should receive a single course of prenatal corticosteroids. The umbilical artery is a blood vessel that runs through the abdomen. In the SGA fetus, Doppler should be used as the main monitoring method since it has been found to minimize perinatal morbidity and death in high-risk populations. Repeat Doppler monitoring will be based on past Doppler indices. In preterm SGA pregnancies, CTG and ultrasound measurement of amniotic fluid should not be utilized as the main criterion of monitoring, and BPP should not be done. The best gestation to birth the SGA fetus will be determined by the fetus' gestational age and a Doppler investigation of the umbilical artery. Delivery by cesarean section is suggested in the SGA fetus with umbilical artery. Women in spontaneous labor with an SGA fetus should be hospitalized immediately to provide for continuous fetal heart rate monitoring (30).

VARIOUS MODES OF DELIVERY

1. In certain circumstances, such as pregnancy lasting longer than 34 weeks with a healthy cervix and the baby's head being positioned low in the pelvis, a technique called "low rupture of the membranes" is used, which is then followed by oxytocin. When the cervix is unfavorable, one option for treatment is to utilize prostaglandin (PGE2) gel. The hue of the liquor could serve as a point of reference for future administration.

2. Because of the significant probability of intrapartum asphyxia, it is necessary to perform intrapartum surveillance using clinical, continuous electronic, and scalp blood collection.

3. When there is a higher risk of complications during vaginal birth (the presence of fetal acidemia, absent or reversed diastolic flow in the umbilical artery, or an unfavorable cervix), a cesarean delivery may be performed without first attempting labor (3).

The delivery should take place at a facility that is both well-equipped to do intense intranatal monitoring (both clinically and electronically) and that has the capacity to house a neonatal

intensive care unit. The measures to be taken during labor are those that are necessary for preventing premature delivery (3).

Instant and continuous care of the newborn infant after birth is important. It is important to have a pediatrician present during the delivery process. The exact same safety measures as in the section on premature birth must be observed. The newborn infant ought to be transported, if at all possible, to the neonatal critical care unit (3).

PREVENTION OF THE RISK OF IUGR

When compared to industrialized nations, the high prevalence of IUGR in underdeveloped countries is largely related to socioeconomic factors such as gender discrimination, and it does not seem to be reduced by treatments aimed just at pregnant women. In low and moderate income nations, adolescent and pre-pregnancy diet, pre-pregnancy weights, poverty, and the inter-pregnancy gap are all important predictors of fetal development. Interventions such as improving female nutrition, delaying the age of first pregnancy, preventing gender violence, treating chronic illness, and treating pregnancy-related disorders will all assist to reduce the prevalence of IUGR in underdeveloped nations. Despite the fact that many therapies have been tested all over the globe, certain evidence-based strategies have proved to lessen the prevalence of IUGR (31).

The following are examples of evidence-based proven interventions:

- Supplementation of balanced amounts of energy and protein
- Intermittent malaria prophylaxis during pregnancy
- Supplementing with a variety of micronutrients
- Entomophagous netting
- Anti-platelets can be used to treat preeclampsia
- Quitting tobacco.

RESPIRATORY DISTRESS IN THE NEWBORN

Fetal distress is a word that is often used but not well defined. The difficulty of getting an accurate diagnosis and commencing appropriate therapy is exacerbated by this definitional ambiguity (32).

DEFINITION

Though etymologically term is derived from the Greek word meaning pulseless, asphyxia has the pathologic connotation of inadequacy or lack of exchange of breathing gases. Acidosis, hypoxemia, and hypercarbia are used to define the severity of the condition. Anaerobic metabolism inside the body produces lactic acidemia in the presence of prolonged hypoxia, aggravating the acidosis (32). Although it is now recognized that the fraction of disabilities caused by birth asphyxia is quite minimal, maybe less than 10%, severe fetal hypoxia can induce cerebral palsy and lower degrees of neurologic impairment (33).

PATOPHYSIOLOGICAL MECHANISM OF THE RESPIRATORY DISTRESS

At the outset of asphyxia, the fetus responds with a remarkable sequence of reactions, the most notable of which is a complexly controlled redirection of blood flow that helps to reduce the harmful effects of oxygen deprivation in important organs. Unless the injury is severe or sustained, the fetus may survive asphyxia unharmed. Insufficiency of uterine blood flow, or insufficiency of umbilical blood flow, and rarely a reduction in uterine arterial oxygenation are the most prevalent asphyxial pressures placed on the fetus during childbirth. Late decelerations, varied decelerations, or extended bradycardia are all common fetal heart rate patterns in response to these stressors. The existence of normal fetal heart rate variability is thought to indicate good central nervous system integrity, including appropriate oxygenation. When the appearance of these patterns decreases or disappears, it means that the physiologic compensations have been overcome by the severity of the hypoxia. Knowledge of fetal reactions to asphyxia, as well as the known progression of fetal heart rate patterns during asphyxia, should allow for a more precise determination of the commencement of intolerable asphyxia, as well as more sensible intervention management and timing (32).

After severe hypoxia, the degree of harm to an individual fetus might vary considerably. Some fetuses may not survive the event in utero, others may have central damage that results in a baby with neurologic problems, while yet others may survive without obvious impairments (34).

PERINATAL ASPHYXIA

Definition and the diagnostic

Asphyxia neonatorum is a term that is commonly used in clinical settings to refer to the inability to establish adequate lung breathing during birth. The phrase "stopping of the pulse" is what it literally means. If left untreated, perinatal asphyxia can result in progressive hypoxemia, hypercapnia, and metabolic acidosis. Perinatal asphyxia is a disorder that impairs the blood's ability to exchange gases.

The following are the primary symptoms that must be present in order to make a diagnosis of prenatal asphyxia:

- Profound acidemia (pH 7.0) on umbilical cord arterial blood sample;
- Persistence of an Apgar score 0–3 for more than 5 minutes;
- Neurological manifestations (hypotonia, coma, seizures) in the immediate neonatal period;
- Evidence of multiorgan system dysfunction (3).

The majority of the time, it is the continuation of an antepartum or intrapartum occurrence. Asphyxia during pregnancy and delivery is a leading cause of death in newborns The risk of suffocation during pregnancy varies according to the gestational age of the mother (3).

At 11 weeks of intrauterine life, human fetal respiratory activity is observed. Initially, these are fast motions with a small amplitude (60–90 per minute). During periods of low-voltage electrocortical activity, such as rapid eye movement (REM) sleep, fetal breathing occurs. During high-voltage electrocortical activity (non-REM sleep), intermittent respiration is recorded. Increased fetal oxygen tension and hyperglycemia are associated with increased fetal respiration, while hypoxia has the opposite effect. The fluid-filled lung becomes the organ of gas exchange after birth (3).

The risk factors

Respiratory distress is caused by an increase in alveolar fluid content, insufficient clearance of lung fluid, absence or inhibition of surfactant activity, or decreased surface area for gas exchange. Important clinical reasons include:

- **Pulmonary factors**:
- Hyaline membrane disease
- Meconium aspiration

- Clear fluid aspiration
- Pulmonary hypoplasia
- Bronchopulmonary dysplasia
- Bronchopneumonia
- Airway obstruction
- Transient tachypnea
- Pneumothorax
- Pulmonary edema

- **Cardiovascular factors:**

- Congenital heart disease
- Aortic stenosis
- Coarctation of aorta
- Cyanotic—Transposition of great vessels
- Tetralogy of Fallot
- PDA
- VSD
- Heart failure
- Persistent pulmonary hypertension of newborn

- **Noncardiopulmonary factors:**

- Metabolic acidosis
- Hypo- or hyperthermia
- Hypoglycemia
- Asphyxia
- Drugs (Pethidine)
- Birth trauma
- Intracranial injury (3).

RESPIRATORY DISTRESS SYNDROME (RDS)

Syn: Hyaline Membrane Disease

Definition

Respiratory distress syndrome is characterized by arterial oxygen tension (PaO2) below 50 mm Hg and central cyanosis in room air (oxford network). Oxygen supplementation is necessary to maintain PaO2 > 50 mm Hg or pulse oximeter saturation > 85%. It ranges from 75 percent at 28

weeks gestation to 52 percent at 30 weeks gestation. The use of external surfactant has decreased the incidence of newborn mortality by 10% (3).

PATHOLOGY

The major cause is a deficiency in pulmonary surfactant. The lack of surfactant in the alveoli of the lungs causes an increase in alveolar surface tension. It is observed within the first twenty-four hours of birth. Surfactant is a substance with surface activity. At 24–28 weeks gestation, it is generated by alveolar epithelial cells termed Type II pneumocytes. Antenatal corticosteroids promotes but fetal hyperinsulinemia slows surfactant production. Additional factors that promote type II cell maturation include chronic stress, PIH, FGR, twins, and placental insufficiency. Poor lung compliance, decreased ventilation-perfusion ratio, and increasing atelectasis are seen. Hyaline membrane disease (HMD) is further worsened by the weakness of the newborn's breathing muscles. Extensive atelectasis is the resultant finding. There is a homogeneous eosinophilic membrane (hyaline membrane) that coats the alveolar ducts and terminal bronchioles. Both metabolic and respiratory acidosis are observed in the infant's blood (3).

DIAGNOSIS

There is a broad spectrum of severity ranging from extremely mild transient discomfort to fast progressing deadly sickness resulting in death within hours. Excessive negative pressures created to open obstructed airways result in chest wall contraction and distortion. Typically, clinical signs occur 4–6 hours after birth.

If two or more of the following characteristics are present at evaluations more than an hour apart, RDS can be diagnosed:

(1) Respiratory rate in excess of sixty breaths per minute;

(2) Nasal flaring;

(3) Rib retraction;

(4) Expiratory grunt;

(5) Central cyanosis.

Due to an extensive atelectatic process, a uniform reticulogranular pattern, also known as ground glass mottling, is visible on a chest X-ray (3).

DIFFERENTIAL DIAGNOSIS

Differential diagnosis includes:

(1) Aspiration pneumonia (liquor amnii or meconium);

(2) Pneumothorax;

(3) Diaphragmatic hernia;

(4) Congenital heart disease (3).

PREVENTION OF RSD

Prevention of RSD includes:

1. Before 34 weeks, give the mother two doses of betamethasone (12 mg) IM 24 hours apart. Cortisol stimulates phospholipid production in type II pneumocytes. The benefits start after 24 hours of therapy and last for 7 days. Cortisol activity is blocked by fetal hyperinsulinism.

2. Prevent fetal hypoxia in diabetic mothers by assessing lung maturity prior to premature induction of labor and delaying induction as much as possible without putting the fetus at risk.

3. Prevent fetal hypoxia in diabetic mothers by delaying induction as much as possible without putting the fetus at risk (3).

TREATMENT

Prevent hypoxia and acidosis; maintain fluid and electrolyte balance; avoid atelectasis and pulmonary edema; and avoid lung injury (barotrauma) and infection are the main management principles in RSD (3).

Treatment includes:

1. The baby should be admitted to a neonatal intensive care facility and nursed in a warm, humidified incubator (neutral thermal condition). Endotracheal suction is used to clean the airway on a regular basis.

2. To relieve hypoxia and acidosis, adequate warmed and humidified oxygen therapy at a concentration of 35–40% under positive pressure should be delivered using an endotracheal tube. Continuous positive airway pressure (CPAP) at 5–8 cm of water is recommended if arterial oxygen tension (PO2) cannot be maintained above 50 mm Hg.

3. Hypovolemia can be treated with albumin or another colloid solution.

4. Anemia must be treated, and any electrolyte imbalances must be corrected, as well as infection must be prevented.

5. To identify metabolic and respiratory acidosis, regular monitoring of arterial PO_2, PCO_2, pH, and base excess is required. FiO_2 levels that are higher than required can result in lung damage and preterm retinopathy.

6. Acidosis should be treated with intravenous sodium bicarbonate 4.2 percent (0.5 mEq/mL) in a 1: 1 dilution with distilled water and a minimum dose of 1 mEq/kg or 2 mL/kg body weight.

7. Continuous positive airway pressure (CPAP): Nasal (NCPAP) or nasopharyngeal (NPCPAP) administration is utilized early to avoid the need for mechanical breathing and tracheal intubation.

8. Surfactant replacement therapy has greatly enhanced the prognosis for RSD newborns. Surfactant is made primarily of phospholipids (80%) and protein (10%). It is manufactured and stored in the distinctive lamellar bodies of type II pneumocytes. Its primary role is to reduce surface tension and stabilize the alveolar air-water interface. Extremely premature infants receive preventative treatment (within 15 minutes of birth). Through a feeding tube, tracheal instillation is administered directly. During therapy, infant placement is modified to assist dispersion.

9. Indications for Mechanical Ventilation (Ventilator treatment) include: Respiratory acidosis with a $PaCO_2$ greater than 50 mm Hg and a PaO_2 less than 50 mm Hg, saturation <90 percent or severe apnea. Synchronized mechanical intermittent ventilation is desirable.

10. Hypocapnia increases the risk for BPD, CLD, and periventricular leukomalacia. It does need to be prevented.

11. Fluid and nutrition—If possible, intragastric feeding is the preferable route. Intravenous administration of 10 percent glucose in the amount of 60 mL/kg body weight per day may be administered to a term infant on the first day by a catheter put into the peripheral or umbilical vein if there is a danger of vomiting and aspiration.

12. Antibiotic treatment for common newborn infections should be initiated first (3).

COMPLICATIONS

- Acute complications of RDS include:
- Infection;
- Pneumothorax
- Pneumomediastinum;
- Persistent patent ductus arteriosus.

- Other complications are :

- intraventricular hemorrhage,
- chronic lung disease (CLD),
- bronchopulmonary dysplasia (BPD),
- intracranial bleeding,
- retionpathy of prematurity,
- pulmonary bleeding,
- barotrauma - pneumothorax,
- retrolental fibroplasia
- neurological abnormalities (3).

PROGNOSIS

Approximately one-third of infants are predicted to die. If acidity and biochemical abnormalities are adequately treated, a newborn with minor illness and good vitality may live. The long-term effects of birth weight and gestational age on the respiratory and neurological development of infants are depending on the infants' birth weight and gestational age. The incidence of the major morbidities (BPD, CLD, NEC, and IVH) is high among the tiniest newborns (3).

FETAL DEATH (STILBIRTH)

GENERAL AND EPIDEMIOLOGICAL DATA

Stillbirth affects approximately one in every 160 births, with about 24,000 newborns stillborn in the United States each year (35). Prenatal care (medical treatment throughout pregnancy) has improved as a result of developments in medical technology over the past 30 years, which has drastically decreased the rate of late and term stillbirths. 3 The rate of early stillbirth, on the other hand, has remained relatively constant throughout time (36). According to parent organizations, "stillbirth" has substituted "intrauterine fetal death" as the preferred expression. Attempts are now being made to include stillbirth in all scientific articles (37). There are less than 5 percent of stillbirths that are reported worldwide (38). In-utero fetal mortality is now rated as the fifth largest cause of death on a global scale. There is now only a partial understanding of the pathophysiology that is responsible for the death of a fetus. There are 76 percent of instances of stillbirth recorded worldwide that cannot be explained (38). There is a connection between intrapartum difficulties and half of the world's stillbirths; the majority of these fatalities could probably be avoided if there was more access to trained medical professionals (38).

Definition

A fetal death is defined by the United States Center for Health Statistics as the birth of a fetus with no signs of life, such as no breathing, heartbeats, umbilical cord pulsation, or distinct movements of voluntary muscles, regardless of the length of pregnancy. Stillbirth is the death of a fetus after a certain gestational age and/or weight, both of which have traditionally lacked consistency(39).

A stillbirth occurs when a baby passes away or is lost before to, during, or shortly after delivery. Both miscarriage and stillbirth describe the loss of a pregnancy, however the terms are used differently depending on when the event actually happens. A miscarriage is often defined in the United States as the loss of a baby before the 20th week of pregnancy, while a stillbirth is the death of a baby at or beyond 20 weeks of pregnancy (40). Intrauterine fetal death (IUFD) is a term that refers to all fetal deaths weighing 500 grams or more that occur during pregnancy (antepartum death) or labor (intrapartum). However, the death of a fetus weighing less than 500 g (before 22 weeks) has its own cause and is commonly referred to as abortion. Death during labor results in the delivery of a new stillborn baby and does not represent a management challenge. Thus, antepartum mortality that occurs after the period of viability is referred to as intrauterine death (3).

CLASSIFICATION OF THE STILLBIRTH

Stillbirth is further divided into early, late, and term categories.

Early stillbirth is the death of the fetus between 20 and 27 weeks of pregnancy.

A late stillbirth occurs between 28 and 36 weeks of gestation.

A term stillbirth happens between 37 or more completed weeks of pregnancy (40).

RISK FACTORS

There are various factors that might lead to a stillbirth:

- intrapartum problems
- high blood pressure
- diabetes
- infection
- genetic and congenital abnormalities
- placental failure
- and a pregnancy that lasts longer than forty weeks (38).

It is a terrible incident that will have repercussions for a long time throughout the whole society. We need to have a deeper understanding of the factors that lead to stillbirths in order to assist individuals who have been affected by this tragedy in dealing with their sorrow and, more significantly, to better equip ourselves to lower the chance of stillbirth in following pregnancies. This exercise discusses the role of the interdisciplinary team in assessing, managing, and enhancing the care provided to individuals who have been diagnosed with this condition (37).

Abnormalities of the Placenta

The most common findings in stillbirth are fetal growth restriction and placental abnormalities. 6% of stillbirths, placental factors such as a placental abruption are discovered (41). However, the majority of pregnancies with these results do not end in a stillbirth (42). Only the volume of the placenta, velamentous insertion, and the existence of a single umbilical artery may be determined prenatally at this stage. (37) It might be difficult to detect fetal growth limitation in the uterus. To assess the structure and function of the placenta in a noninvasive manner, novel approaches are required. Growth restriction is 30 percent more likely if the birth weight is less than the 10th percentile, and 70 percent more likely if the birth weight is less than the 3rd percentile (41). The risk of placental abruption and stillbirth is increased by cocaine usage, smoking, hypertension, and preeclampsia. In addition, uncommon placental abnormalities, such as choriocarcinoma and chorioangioma, improve the chances of stillbirth (43).

Diabetes

Up to five times greater, diabetes raises the chance of stillbirth (44). Diabetes may have an effect on the birth weight, and it's also been linked to having a correlation to the probability of stillbirth. When compared to pregnancies weighing in the 10th to 90th percentile, the chance of stillbirth is increased six times in women who have type 1 diabetes and three times in those who have type 2 diabetes if the birth weight is less than the 10th percentile. If the birth weight was over the 95th percentile and the mother had type 2 diabetes, the chance for stillbirth was increased by a factor of two. There is a statistically significant correlation between having type 2 diabetes and having a stillborn male child. At term, stillbirths caused by diabetes account for a third of all occurrences of the condition. When it comes to type 1 diabetes, the maximum risk of stillbirth occurs in the 38th week of pregnancy, whereas for type 2 diabetes, it occurs in the 39th week (45).

Race

When compared to women of other ethnic groups in the United States, black women who are not of Hispanic origin had a greater prevalence of stillbirth (11 per 1000 births). This population also has a greater prevalence of diabetes, hypertension, preterm membrane rupture, and abruption, all of which may be contributing factors to the increased chance of stillbirth (46).

Obesity

Even after correcting for other risk factors including diabetes, smoking, gestational diabetes, and preeclampsia, researchers found that obesity remained a significant independent risk factor for stillbirth. Obesity, which is defined as having a body mass index that is more than 30 kg/m2, is a serious public health issue that plagues industrialized nations. Women who are not obese have a stillbirth risk of 5.5 for every 1000 births (47).

Age

Because of an increased risk for aneuploidy and the medical difficulties that might arise during pregnancy, the chance of stillbirth increases with a mother's advanced age. Even after correcting for these other risk variables, maternal age above 35 is associated with an increased chance for stillbirth, which is further exacerbated by the fact that the mother did not have any previous children. When a woman reaches the age of 40, the chance is 1 in 116 for a nullipara and 1 in 304 for a multipara (48). Chromosomal abnormalities that are fatal to the fetus are more likely to occur in mothers older than 35, which is one of the possible causes of stillbirth (49). In addition, a father's age of 40 or older is associated with a greater risk of a stillbirth (50).

Substance Disorder

Tobacco use increases the incidence of both antepartum and intrapartum stillbirth (15/1000). Quitting smoking at the start of the second trimester decreases the probability to that of a non-smoker (51).

Although the actual cause of alcohol-related stillbirths has not been discovered, the risk is well-documented. 11.5 percent of pregnant women have at least one drink in a 30-day period, and 3.9% consume four or more drinks on at least one occasion during pregnancy (52).

Growth limitation is the most prevalent finding in pregnancies compromised by drug abuse. The increased risk of stillbirth linked with drug abuse is attributed to placental malfunction, vasoconstriction, hypoxia, and changes in endogenous hormones important for maintaining optimum well-being (53).

Gestational Age >38 weeks

Early and late-term gestational ages are associated with an increased risk of stillbirth. Inducing labor after 40 weeks of pregnancy may reduce the possibility of having a stillbirth or requiring a cesarean section (37).

Hypertension

Chronic hypertension triples the chance of stillbirth (42).

Birth Defects

Congenital malformations, which are characterized as physical or biochemical abnormalities, affect one out of every three pregnancies and are linked to an increased risk of stillbirth. Prenatal diagnosis of congenital abnormalities may influence antenatal monitoring policies in the hopes of lowering the incidence of stillbirth (37).

Polyhydramnios

Polyhydramnios is a condition that affects 1% to 2% of all pregnancies. It's defined as an amniotic fluid index of more than 24 cm or a deepest vertical fluid pocket of more than or equal to 8 cm as measured by abdominal ultrasonography. Polyhydramnios is caused by idiopathic causes 50% of the time. There is a link between these instances and an increased risk of fetal macrosomia as well as a two to fivefold higher relative chance of stillbirth (54). Polyhydramnios is linked to a greater risk of preterm birth, malpresentation, and cord prolapse, which might explain why it's linked to a higher chance of stillbirth. Pregnancies affected by unexplained polyhydramnios have a 3.2 percent incidence of aneuploidy, which is much greater than the overall population and may lead to a higher risk of stillbirth (55). Polyhydramnios has also been correlated to congenital abnormalities of the central nervous system, gastrointestinal system, cardiac system, hydrops, and aneuploidy, as well as maternal diseases including diabetes, infection, and diabetes insipidus due to lithium usage (56).

Oligohydramnios

An amniotic fluid index (AFI) that is less than or equal to 5 cm, or a maximum vertical pocket of less than 2 cm, is considered oligohydramnios. Because the AFI finds more instances of probable oligohydramnios and polyhydramnios, which leads to more inductions of labor with no difference in perinatal outcome, the deepest vertical pocket is the preferable measurement (57).

When no additional comorbidities are found, delivery for oligohydramnios may be recommended at 36-37 weeks of pregnancy, or sooner if fetal monitoring is unsatisfactory. Pregnancies with idiopathic oligohydramnios have comparable results to pregnancies with a normal amniotic fluid content at term when there is no additional risk factor (58).

Umbilical Cord

Although the umbilical cord has been linked to stillbirth, a nuchal cord may be seen in up to 30% of normal newborns. When determining the reason of a stillbirth, it's important to look for signs of cord blockage or circulatory restriction (37).

Late-onset Prenatal Care

Prior home birth and delayed initiation of prenatal care are statistically significant predictors for later unfavorable perinatal outcomes (59).

Multiple Gestations

The stillbirth rate quadruples for twin pregnancies (60). Possible contributory variables include growth restriction, premature delivery, fetal abnormalities, advanced mother age, and twin-twin transfusion syndrome. Due to the potential of cord entanglement, monochorionic twins have a greater chance of stillbirth (61).

Infection

Infection may be neglected as a cause of stillbirth because signs and symptoms of infection are often ignored and examination for infection is frequently not performed (62).

Antiphospholipid Syndrome

In addition to thrombotic events, antiphospholipid syndrome (APS) has been related to stillbirth since 1984 (63). One clinical and one laboratory criteria must be satisfied in order to identify antiphospholipid syndrome. Anticardiolipin antibodies, anti-beta2 glycoprotein 1 antibody, or lupus anticoagulant must be above the 99th percentile on at least 2 days separated by at least 12 weeks. Due to the limitations of existing techniques, these antibodies may not be detectable in some circumstances (64). Patients diagnosed with systemic lupus erythematosus have a risk of stillbirth ranging from 15 to 25 percent and need to have prenatal testing for antiphospholipid antibodies in addition to receiving therapy in order to minimize the possibility of unfavorable pregnancy outcomes (37).

Intrahepatic Cholestasis

There is a possibility that intrahepatic cholestasis may affect between 0.1 and 2 percent of pregnant women (65). There have been reports of fetal arrhythmias occurring in pregnancies that were complicated by cholestasis (66). The majority of these stillbirths show evidence of acute oxygen deprivation, but none of them show signs of development restriction or long-term uteroplacental damage (67).

PATHOPHYSIOLOGY

In utero survival of a fetus is contingent on a number of factors. These elements can be categorized as the health of the host in its surroundings, the function of the uteroplacental unit, the state of the environment in which the fetus resides, and the lack of fetal factors that are lethal. Stillbirth can be caused by a single insult or a combination of circumstances that disrupt the function of these life-sustaining mechanisms. Multiple physiological, hormonal, and anatomical adjustments are required for the maintenance and support of a pregnancy (68).

The integrity of the uteroplacental unit can be damaged by structural, functional, genetic, or exposures such as bleeding and infection. Placental discoveries may include 1) insertion of a single umbilical cord, 2) insertion of a velamentous umbilical cord, and 3) insertion of a furcate umbilical chord. 4) circummarginate placental membrane insertion, 5) circumvallate placental membrane insertion 8) terminal villous hyperplasia 10) acute chorioamnionitis of the chorionic plate 11) acute funisitis, 12) acute umbilical cord arteritis, 13) acute umbilical cord phlebitis, 14) acute vasculitis of the fetal blood arteries of the chorionic plate. 15) chorionic plate degenerative vascular alterations, 16) acute villitis, 17) chronic villitis, 18) avascular villi, 19) retroplacental

hematoma, 20) parenchymal infarction, 21) intraparenchymal (intervillous) thrombosis, and 22) perivillous fibrin deposition, 23) intervillous fibrin deposition, 24) placental weight, 25) placental weight/birth weight ratio (68).

Maceration is an aseptic degenerative process that occurs when a fetus dies. The epidermis is the first structure to be affected by the process, which results in blistering and skin peeling.It emerges 12 to 24 hours after death. The fetus swells and turns a dusky red color. Aseptic autolysis of the ligamentous framework occurs gradually, does liquefaction of the brain tissue and other viscera. The radiological signals are caused by these alterations, which vary in severity (3).

DIAGNOSES FOR STILLBIRTH

In order to confirm the diagnosis, it is generally necessary to perform many examinations**.** The patient reports that they have not observed any fetal movement since they last checked. After a varied period of time after the loss of the fetus, a reversal of the positive breast changes that occur during pregnancy will become apparent (3).

In the majority of cases, despite of the accessibility for autopsy, the history and data provided during standard prenatal and perinatal treatment will help determine the cause of stillbirth (69).

The patient's medical history should include information concerning gastrointestinal symptoms, vaginal bleeding or discharge, pelvic discomfort, and the last time fetal movement was detected. The maternal history contains of age, parity, and any history of hypertension, diabetes, hypercoagulability, autoimmune disease, or cancer: Recurrent miscarriages or stillbirths: father age and family medical history of inherited diseases. The history of the present pregnancy includes unexplained vaginal hemorrhage, trauma, fertility therapy, exposure to medications or radiotherapy, excess weight, infections, sexually transmitted illnesses, hypertension, preeclampsia, diabetes, anemia, fetal abnormalities, or growth limitation. Past obstetrical history includes preterm birth, stillbirth, or a fetus with growth restriction, along with any pregnancy complicated by preeclampsia, diabetes, deep venous thrombosis, pulmonary embolism, or a blood transfusion. Occupation, diet, drug and alcohol abuse, family abuse, traveling history, and animal exposures are included in the social history. Prenatal laboratory test findings include CBC, type and screen, HbsAg, syphilis, HIV, rubella, aneuploidy testing, urine toxicology, and diabetes screening (37).

PHYSICAL OBSERVATIONS

Physical examination before delivery:

Examine the patient whose fetal well-being is a cause for concern as quickly as feasible to assuage concerns and commence care promptly (37).

Per abdomen: Uterine tone is decreased, and the uterus feels flaccid, with gradual retrogression of the fundal height, which becomes less than the gestation duration. Braxton-Hicks contractions are difficult to detect. During palpation, there are no fetal movements and no fetal heart sound. The use of Doppler ultrasound is superior to the use of a stethoscope. CTG (cardiotocography) shows up that the fetal head has an egg-shell cracking feel to it, which is a late trait (3)

Proceed to auscultate fetal heart tones using a fetal doppler and, if necessary, commence electronic fetal monitoring. As soon as possible, perform an abdominal ultrasonography to establish the presence or absence of heart beat if doppler cannot detect it (37).

Physical examination after delivery:

Document observations, including measurements, from a medical evaluation of the umbilical cord and placenta. Take pictures of the placenta and cord. Swab between the chorionic and amniotic membranes using aerobic and anaerobic culture swabs to culture the placenta (37).

Evaluation of the death infant

Immediately following the baby's delivery, the birth attendant as well as a pathologist should do a comprehensive evaluation on the infant. The examiner should have access to a chart that will serve as a guide for them to note each of the preceding points (37).

The exam includes:

- Weight, height, diameter of the skull, and length of the foot (if less than 23 weeks, foot length may be used to estimate gestational age)
- Ears, eyes, mouth, mouth, nouse, and skull are all facial features.
- Cystic hygroma, spina bifida, and aberrant pigmentation may be found on the neck.
- Maceration, sloughing, and coloration of the skin.

- Insertion of the cord: central, marginal, and membranous
- Abdominal wall
- Gender of the infant: female, male, undetermined
- Palmar wrinkles, fingers, and extremities (37).

Take pictures of the head, face, entire body, hands, and feet. Take comprehensive images of the infant from all angles, including the front, back, and sides. Any irregularity should be photographed and recorded (37).

Examination of the Placenta

Aside from an autopsy, the placental examination is the most significant study. In 53% of cases, it may play a role in the diagnosis of stillbirth (70).

The birth attendant, a pathologist, or both may do the macroscopic placental assessment. With all photos, a ruler should be included to establish dimensions (71).

Autopsy

The remains must be handled with care, and an autopsy should be performed as soon as possible to provide confirmation to the family. The procedure for doing a stillbirth autopsy hasn't yet been defined. Though, such a documenting negative discoveries is just as vital as documenting favorable results. It may be difficult for some patients and families to bring up the subject of a stillborn autopsy. An autopsy can only be performed with written consent (37).

Imaging

To aid in the diagnosis of the etiology of stillbirth, a variety of imaging techniques can be used. A lateral and anterior-posterior X-ray of the entire fetus is called a Babygram. It may reveal signs of disease such as skeletal dysplasia, costovertebral deformities, ectopic calcifications, and gas collections (72).

Chromosomal Study

It is possible to identify chromosomal abnormalities in 5 percent of otherwise healthy-looking stillbirths (73).

LABORATOR TESTING

Amniocentesis should be provided to all patients if labor is not close, regardless of the results of any previous cell-free DNA screenings that may have been performed. Every patient needs a complete blood count, glucose level, and testing to determine their HIV and syphilis status. These aid in the screening for maternal hemoglobinopathy, infection, poor glycemic management, or undetected diabetes, as well as red cell alloimmunization. A test of the mother's urine for drugs should be considered, particularly a test for cocaine because of its association with gestational hypertension and placental abruption (37).

Screening for Infection

Because many women have positive serology from past infections, infection screening is complex. E. coli, group B Streptococcus, and Enterococcus species are the bacterial infections most frequently related with stillbirth. Most stillbirths caused by infections happened before 24 weeks of gestation (62). Clinically recommended testing may be performed for Cytomegalovirus (CMV) IgM and IgG, Toxoplasmosis IgM and IgG, and Parvovirus IgM. Histopathological examination will reveal evidence of viral infection in the fetoplacental tissues. Rarely are viral cultures necessary. CMV is the most common infection transmitted during pregnancy. There are typically no abnormal ultrasound findings; nevertheless, cerebral hemorrhage, cardiomegaly, hepatomegaly, minor ascites, and echogenic bowel may be recorded. On autopsy, thrombotic vasculopathy is observed. Histology may reveal CMV inclusions in epithelial cells of the kidney, which is the organ most commonly affected. The kidney, liver, brain, thyroid, lung, heart, pancreas, and placenta may have cytomegalovirus DNA. Herpes infections that start inside the uterus are extremely unusual. 95 percent of all infections in newborns are acquired during or just after pregnancy (37).

Evaluation for the Presence of Disseminated Intravascular Coagulation (DIC)

Today, due to early detection and therapy, disseminated intravascular coagulation is extremely rare in the context of stillbirth. DIC may need to be ruled out in situations of fetal death that has gone untreated for more than three weeks, or in stillbirths exacerbated by placental abruption or infection. There is no one lab or clinical test that can be used to diagnose DIC. DIC is treated with delivery of the stillborn and management of hemorrhage and or sepsis; supportive care with the provision of blood products as required; close clinical surveillance and repeat labs; and prompt response/specialist consultation if discovered in the context of a stillbirth (74).

TREATMENT AND MANAGEMENT

Transmission of the Diagnosis to Patients

If considered required, a second ultrasonographer may confirm a stillbirth. A health care provider conveys the diagnosis to the mother as soon as possible, making every effort to give privacy, understanding, and encouragement. How this develops depends on the circumstances. If the diagnosis has been made without prior warning, ultrasonographers typically contact a physician and arrange for an immediate consultation. If the diagnosis is made at the patient's bedside, it must be quickly confirmed and communicated to the patient. The patient may have the option of viewing ultrasound images with the physician. The patient will need compassionate assistance. Some patients may need to leave quickly as a coping method; if they are medically stable, they should be urged to do so. Some patients may find comfort in holding a hand until a family member arrives. Apologies and support are demonstrated by offering the patient the desired support and expressing regret. This may involve providing the patient with written instructions on how to contact you when necessary and how to make a follow-up session as soon as requested.

Management

The technique of delivery will be determined by the weeks of gestation of the stillborn, the patient's preferences, her physical condition, and her obstetrical/surgical history. Information is delivered concisely and clearly, and confirmation of comprehension must be received.

If the dead fetus is kept for several weeks, coagulation problems resulting from the discharge of tissue factor from the placenta could emerge (75). The risk is approximately 2%, and this diagnostic necessitates prompt treatment (76).

The mother/couple can return home if there is no disseminated intravascular coagulation, infection, or severe preeclampsia. If expectant management is desired, natural labor normally starts two weeks after the fetus has died (37).

DIFFERENTIAL DIAGNOSIS

- Pregnancy that is viable (In the case of a viable pregnancy, heart beats may go unnoticed by a fetoscope).
- Miscarriage
- Multifetal Pregnancy

In the case of a stillbirth accompanied by a live twin or triplet fetus, a multifetal pregnancy must be excluded.

- Existence of a Preexisting Maternal Illness
- Infection
- Violence against the person.

A fatal blow to the abdomen could be the cause of death for the fetus (37)

The following factors, although they are infrequently related with stillbirth, must be taken into consideration:

- Poisoning
- Abdominal Pregnancy
- Uterine Rupture
- Partial Molar Pregnancy (37).

PREVENTION STRATEGIES

The total risk of stillbirth recurrence ranges from 0% to 8% (3).

Stillbirth prevention screening and monitoring procedures are disputed. During antepartum care, it is appropriate to follow patients with disorders that enhance the risk of stillbirth using some sort of antenatal testing. However, clinicians should be aware that the majority of tests have a significant rate of false positives. In developed nations, the use of intrapartum cardiotocography

and the possibility to perform cesarean surgery for nonreassuring fetal heart tones has resulted in a reduction in stillbirth rates. This material should be made available in low- and middle-income nations, where stillbirths are the most common (37).

PROGNOSIS

Counseling on the possibility of recurrence is part of a woman's follow-up after a stillbirth is resolved. After a stillbirth, the chances of having another one are substantially doubled compared to women who have had a live birth. Multiple factors influence this risk, including parental factors, gestational age, and the cause(s) of the stillbirth (77). A woman may postpone future pregnancy until she feels emotionally and psychologically healed from the stillbirth. The average time between visits is 6 to 12 months (78).

COMPLICATIONS

Possible physical issues after a stillbirth are:

- Incomplete passage of the product of conception requiring medical or surgical managemen
- Infection
- Bleeding
- Disseminated intravascular coagulation
- A uterine injury requiring surgical repair, or hysterectomy
- In the future, there is an increased risk of recurrent stillbirth (37).

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NEWBORN CARE

"Any society, any nation, is judged on the basis of how it treats its weakest members—the last, the least, the littlest."

Cardinal Roger Mahony

INTRODUCTORY MATERIAL AND BACKGROUND DETAILS

A healthy newborn born at term (between 38 and 42 weeks) should have a birth weight that is above the national average (typically more than 2,500 g), cries immediately after birth, starts independent rhythmic respiration, and quickly adapts to the changing surroundings. The weight varies by country, although it is usually greater than 2,500 g. The length is 50–52 cm from crown to foot. The length of the baby is a more accurate indicator of gestational age than the weight. The biparietal diameter is about 9.5 cm and the occipito-frontal circumference is about 32–37 cm (1).

Figure 8. Newborn care

Within 24 hours of birth, the newborn must be thoroughly inspected. The crucial maternal and perinatal history should be reviewed before the actual examination (1).

EXAMINATIONS OF THE NEWBORN IN THE FIRST 24H

ROUTINE NURSERY CARE PROVIDED IMMEDIATELY AFTER THE BIRTH OF THE INFANT

The infant is properly inspected and the gestational age is determined.

The weight, front-occipital circumference (FOC), and length of the infant are all measured. The infant is classified as average for gestational age (AGA), small for gestational age (SGA), or large for gestational age (LGA) based on these factors (1).

The infant must be maintained in a temperature-neutral environment. This is the temperature range outside of the body when metabolic rate and oxygen consumption are at their lowest. The usual skin temperature of a newborn is 36.0–36.5 degrees Celsius (96.8–97.7 degrees Fahrenheit). The normal rectal temperature is 36.5–37.5°C (97.7–99.5°F). The temperature of the axillae may be 0.5–1.0°C lower. Radiation, conduction from the newborn to the surface in direct touch, convection from the infant to the surrounding environment, and evaporation of water from the skin are the mechanisms of heat loss. To prevent heat loss, take the following steps: Immediately after delivery, place the baby under a preheated (36.5°C) radiant warmer (servo-control), dry the baby immediately after birth, cover the baby (including the head) with a pre-warm towel, place the baby close to the mother's breast (Kangaroo method), wrap the mother and baby together, and begin early breastfeeding (1).

PHYSICAL EXAMINATION

Vital signs examination:

1. The temperature is measured and the site (e.g. rectal, oral, or axillary) is noted.

2. Respiratory rate: 30–60 breaths per minute. Pulse oximetry may be required (>95 percent and a 3% difference between the right hand and foot).

3. Heart rate: Normal, 100–160 beats per minute (bpm), and around 70–80 bpm when sleeping.

4. Blood pressure: 45–60/25–40 mm Hg is the normal range. Blood pressure is proportional to the infant's gestational age and birth weight. (1)

An examination of the body:

- **The skin tone**

The most essential parameter of cardiorespiratory function is skin tone. Anemia, birth asphyxia, or shock can all cause pallor. Cyanosis: Low oxygen saturation causes central cyanosis (bluish skin, including the tongue and lips). It could be caused by a congenital heart or lung condition. Hemoglobin desaturation should be greater than 3–5 g/dL. Drugs (nitrates or nitrites) or hereditary factors can cause peripheral cyanosis (bluish skin with pink lips and tongue). Methemoglobinemia (hemoglobin oxidizes from ferrous to ferric form) is frequently connected with it. Acrocyanosis (bluish hands and feet) may be common in the first few weeks after delivery. It could be the result of severe stress. Plethora is a common symptom of polycythemia in newborns. It can be seen in an infant who is overheated or underoxygenated. It important to measure the hematocrit value. Bilirubin levels > 5 mg/dL indicate jaundice. It's likely that significant bruising is the result of a difficult or traumatic birth. (1)

Most common skin rashes found on the newborn babies are:

-Milia;

-Mongolian spots;

-Erythema toxicum;

-Diaper rash (1).

- **Examination of the head**

Fontanels: Hypothyroidism, osteogenesis imperfecta, and chromosomal abnormalities are all linked to large fontanels (Down syndrome). Increased intracranial pressure, meningitis, or hydrocephalus may all cause a bulging fontanel. Fontanels that are depressed are a sign of dehydration. Hyperthyroidism, microcephaly, or craniosynostosis may all cause a short fontanel. Cephalhematoma should be distinguished from caput succedaneum. Mold may occur as a result of extended labor. Mold usually passes after 5 days. Subperiosteal bleeding caused by a violent delivery causes cephalhematoma. It is never longer than the suture line. To rule out a skull fracture, an X-ray and a CT scan should be performed. Estimate the hematocrit and bilirubin values. Hematomas rarely need aspiration since they usually disappear in 4–6 weeks. (1)

The following symptoms indicate raised intracranial pressure:

1. Enlarging anterior fontanel;

2. Separation of suture lines;

3. Immobility of upward gaze;

4. Visible scalp veins (1).

- **Neck:** Goiter, thyroglossal cysts, sternomastoid hematoma (sternomastoid tumor) or short neck, webbed neck (Turner's syndrome), movements of the neck are all examined (1)
- **Face and Mouth**: Hypertelorism (widely spaced eyes) or low-set ears (trisomy 9, 18, triploidy) or facial nerve injuries are checked for on the face. Clefts (palate, lips), natal teeth, lingual frenulum (tongue tie), macroglossia (Beckwith syndrome), and oral thrush are all evaluated in the mouth (1)
- **Eyes:** Congenital cataract, Brushfield's patches in the iris (Down's syndrome), subconjunctival hemorrhage (traumatic delivery), and conjunctivitis are all checked in the eyes (1).
- **Chest examination**: Asymmetry (tension pneumothorax), tachypnea, grunting, intercostal retractions (respiratory distress), pectus excavatum, and breath sounds are all checked on the chest. Due to maternal estrogen, the newborn's breasts may grow (normally 1 cm in diameter). "Witch's milk" refers to the white discharge from the nipple (1)
- **Heart:** The rate (typical 120–160 bpm), rhythm, quality of heart sounds, and existence of any murmur are also checked. VSD, PDA, ASD, transposition of major vessels, tetralogy of Fallot, coarctation of the aorta, and other conditions may all cause murmurs. Fetal echocardiography may be used to establish a prenatal diagnosis in the womb at 18–20 weeks of pregnancy (1).
- **Abdomen**: Any deformity, such as omphalocele , hepatomegaly (sepsis), splenomegaly (CMV, rubella infection), or any other tumor, is evaluated in the abdomen. Diaphragmatic hernia may cause a scaphoid abdomen (1).
- **Umbilicus** is examined for any discharge, redness or infection. A greenish-yellow colored cord suggests meconium staining (fetal distress). Single umbilical artery (more in twin births) indicates genetic (trisomy 18) and congenital anomalies (1).
- **Genitalia**: Before assigning a gender, genitalia should be thoroughly inspected. A male's penis (normal > 2 cm), testes inside the scrotum, any hydrocele, and hypospadias are all checked. Normally, the prepuce is lengthy and phimosis is present. Any clitorial enlargement (maternal drug) or united labia with clitorial enlargement is looked for in the female (adrenal hyperplasia). It's possible that blood-stained vaginal discharge is caused by maternal estrogen deficiency. Normally, the labia majora covers the clitoris and the labia minora (1).
- **Anus and Rectum**: Imperforation and the location of the Anus and Rectum are examined. Within 48 hours following birth, meconium should be passed (1).
- **The extremities, spine, and joints:** Syndactyly (digit fusion), polydactyly, simian crease (Down's syndrome), talipes equinovarus, and hip dislocation are all checked in the extremities, spine, and joints (Ortolani and Barlow maneuvers) (1).
- **Nervous system:** Irritability, aberrant muscular tone, reflexes, cranial and peripheral nerves (Erb's paralysis) are all evaluated. The gestational age influences neurological development. At birth, all reflexes, including the Moro reflex, are present (1).
- **Muscle tone:** Hypotonia (floppiness) and hypertonia (increased resistance) are examined (1).

BREATHING FOR THE FIRST TIME

The anatomical and physiological processes

involved in post-uterine breathing

Almost immediately after giving birth, a newborn is expected to make the transition from placental to pulmonary gas exchange. In order to differentiate between the two, the pulmonary vascular resistance needs to decrease, the pulmonary perfusion needs to rapidly increase, and the unique fetal vascular shunts need to start closing. Among these shunts are the patent ductus arteriosus and the patent foramen ovale. In addition to being essential for pulmonary gas exchange, lung ventilation is also very important. Recent research suggests that it is largely responsible for initiating changes in the cardiovascular system at birth (2). Amniotic fluid, which fills the fetal lungs while they are still in the uterus, must be rapidly expelled in order for the lungs to become ready for air breathing. This clearance happens via a variety of mechanisms, and the contributions of these mechanisms may vary according to the gestational age and mode of delivery of the individual. To begin, a large release of fetal adrenaline late in labor stimulates pulmonary epithelial cells to stop secreting and instead to start reabsorbing lung liquid as a result of sodium-channel activation. This happens as a result of the stimulation of pulmonary epithelial cells by the large release of fetal adrenaline. Blocking the receptors responsible for sodium channel activation can slow down or stop lung liquid clearance at birth, but it does not completely prevent it (3). During the labor process, the application of mechanical forces can assist in the clearance of lung fluid. Early reports described how the fetal thorax and abdomen were compressed as they passed through the birth canal, which ultimately resulted in liquid being expelled from the lungs (4). On the other hand, it's possible that uterine contractions coerce a change in the position of the fetus, which then causes compression of the thorax and higher pressures within the chest cavity. In contrast to the "vaginal squeeze" theory, this actually results in an earlier release of lung fluid during the labor process (5). A large proportion of lung fluids is eliminated after birth as a result of a third process. To be more specific, the pressure difference across the transpulmonary space that occurs during inspiration encourages the passage of fluid into the interstitial tissue. After this point, it is removed from the body gradually, most likely by the pulmonary circulation and the lymphatic vessles. It is possible for the pressure in the lung interstitial tissue to increase to the point that fluid can actually migrate back into the airspaces during expiration. This will only occur if the positive end-expiratory pressure does not prevent this from happening (6). It is possible that this has a role in the development of temporary tachypnea in the infant (5). As fluid is replaced by air, compression of the pulmonary vasculature decreases significantly, lowering resistance to blood flow. The ductus arteriosus normally closes as pulmonary arterial blood pressure falls. To allow air to enter the fluid-filled alveoli, high, negative intrathoracic pressures are required. Normally, residual air accumulates in the lung beginning with the first breath after birth. Lower pulmonary opening pressure is also

required with each subsequent breath. By the fifth breath of a normal mature newborn, the pressure-volume changes achieved with each respiration are very similar to those of an adult. As a result, the breathing pattern changes from shallow episodic inspirations typical of the fetus to regular, deeper inhalations. Surfactant, which is synthesized by type II pneumocytes, is a final mechanism that helps maintain lung inflation by preventing alveolar collapse. Inadequate surfactant, which is common in preterm neonates, results in 1368 respiratory distress syndrome. (5) By lowering the surface tension of the alveolar lining layer, which is the shallow pool of liquid that covers the cells of the distal airspaces, surfactant makes breathing and the exchange of gases easier. Exhalation causes the airspaces to become atelectatic if there is not a very low surface tension at the end of the exhalation phase. A lack of surfactant is at the root of respiratory distress syndrome (RDS), which manifests itself in infants who were born prematurely (7).

When risk indicators are present, medical professionals trained in neonatal resuscitation should be present during the birth. In order to stabilize the baby, this group prepares the necessary equipment, verifies that a suitable number of professionals are present, assigns roles and responsibilities, and discusses potential contingency plans. The projected gestational age, the color of the amniotic fluid, the number of fetuses present, and any additional dangers to the fetus are the topics of four questions that a neonatal practitioner will ask. A presentation that is not particularly vigorous is linked to a number of problems. Immaturity, hypoxemia or acidosis from any cause, sepsis syndrome, recent medicines delivered to the mother, and developmental anomalies of the central nervous system are examples of some of these conditions that may be present. Lung abnormalities, obstruction of the upper airway, pneumothorax, and meconium aspiration are some of the conditions that are associated with the respiratory tract (5).

CARE OF THE NEWBORN INFANT IN DELIVERY ROOM

Staff assigned for newborn assistance are responsible for urgent treatment and, if necessary, the beginning of emergency resuscitation (4).

Immediate care

Before and during birth, considerable consideration needs to be given to a number of factors that will ultimately determine how healthy the newborn will be.

These include:

(1) the health of the mother;

(2) prenatal complications, including any suspected fetal malformations;

(3) the gestational age of the mother;

(4) complications during labor;

(5) the length of labor and whether or not the membranes ruptured;

(6) the type of anesthesia used and its duration;

(7) the difficulty of the delivery;

(8) the medications taken during labor and their dosages, administration routes, and timing (4).

Umbilical Cord Clamping

Figure 9. Umbilical clamping (8)

In an ideal situation, obstetrical and pediatric teams will discuss ideas about the treatment of the umbilical chord. The newborn receives a transfusion of placental blood when the chord is not clamped immediately after birth. Delaying the act of clamping the umbilical cord by thirty to sixty seconds in term newborns elevates hemoglobin levels at delivery, improves iron storage during infancy, and enhances neurodevelopment at the age of four (9). Delaying the clipping of the umbilical chord can lower the risk of intraventricular hemorrhage, necrotizing enterocolitis, and the need for blood transfusions in premature neonates (5). It is best practice to do delayed cord clamping on babies, both preterm and term, who do not require resuscitation immediately after birth (10). In the event that a infant needs resuscitation or if the placental circulation is disturbed as a result of abruption, cord avulsion, bleeding placenta previa, or vasa previa, there should be no delay in providing treatment (5).

Newborn Resuscitation

The risk of death for newborns delivered at home is increased two- to thrice when compared with the risk of death for newborns delivered in hospitals (10).

When neonates are deprived of proper gas exchange before or after birth, a well-defined sequence of events leads to apneea. With oxygen deprivation and carbon dioxide (CO2) increase, there is a brief period of fast breathing, and if it continues, breathing stops, a condition known as primary apnea. This stage is marked by a decrease in heart rate and neuromuscular tone. Generally, simple stimulation will reverse primary apnea. If oxygen deprivation and hypoxia continue, the infant will have deep gasping respirations, followed by secondary apnea. This final phase is characterized by a further decrease in heart rate, a drop in blood pressure, and a loss of neuromuscular tone. Neonatal patients with secondary apnea will not respond to stimulation and will not resume breathing on their own. If assisted ventilation is not performed, death will occur. Because primary and secondary apneas are indistinguishable in the clinical setting, the presence of secondary apnea must be presumed. And in the event that there is a delay in the baby's response to the stimulation, prompt resuscitation with appropriate ventilation of the newborn who is unresponsive must be initiated (5).

Resuscitation Protocol

- **The Initial Evaluation**

The newborn is initially put in a warm environment to reduce heat loss, then the airway is cleared, and the infant is dried. The healthy infant will take a breath within seconds of delivery and cry within half a minute if stimulated, following which supportive care will be given (4). Evaluations of the newborn's tone, respiratory effort, and heart rate take place almost immediately after birth, typically during the delay that follows the clamping of the umbilical chord. The majority of term newborns are alert and active during the first ten to thirty seconds of their lives (11). Oral suctioning is not typically necessary for a newborn baby who is wailing very hard. Bulb suctioning, on the other hand, is most useful for those individuals who are unable to clear secretions on their own due to the presence of apnea or an excessive amount of secretions. Drying the newborn, providing light stimulation by caressing the back of the newborn, and continuing to observe the newborn throughout the transition period are additional normal care steps (5).

- **Assesment at 30 seconds of life**

Apnea, gasping respirations, or a heart rate of less than 100 beats per minute for more than 30 seconds after birth may require the use of positive-pressure ventilation with room air. The % of

oxygen is measured by pulse-oximetry, and assisted breathing rates of 30 to 60 breaths per minute are usually used. Supplemental oxygen may be provided in progressive levels within a normal range at this stage (4).

If the newborn is weak or was born prematurely, it is transferred to a radiant warmer that has been preheated in preparation for the first steps of newborn care. The moist birth covering that was used initially is taken away so that the newborn can dry off. The effects of cold stress have been linked to a variety of infant morbidities and fatalities. A warmer delivery room (greater than 25 degrees Celsius) should be provided for preterm infants, and additional measures should be taken to maintain euthermia. These additional measures include the application of polyethylene plastic "ponchos" or wraps to slow evaporative heat losses, the use of chemically activated thermal mattresses to reduce conductive heat loss, and the administration of warm, humidified respiratory gases during the process of respiratory stabilization. Preterm infants are especially susceptible to hypothermia (12).

- **Assesment at 60 seconds of life**

If the heart rate stays below 100 beats per minute, ventilation is insufficient. Check the position of your head, the secretions needs to be removed and, if required, increased inflation pressure (4). When using the radiant warmer, infants need to be positioned in a way that extends their necks just enough to fully expand their airways. It is possible to use a bulb syringe or a suction catheter to clear the infant's mouth and then the newborn's nose in the event that the newborn is apneic or has profuse secretions that it cannot clear. Intubation and suctioning of meconium-stained amniotic fluid on a routine basis are no longer suggested for newborns who are not actively breathing on their own (10). Intubation and suction are only used in cases where there is a suspicion of an obstruction in the airway (5).

A facemask is indicated for assisting ventilation at a pace of 40 to 60 breaths per minute. Pulse oximetry is used to measure oxygen saturation. Supplemental oxygen can be administered in graduated percentages to keep oxygen saturation levels in a normal range every minute of life. Improved heart rate is the best indicator of adequate ventilation.

Placed between the positive pressure device and the facemask, colorimetric end-tidal carbon dioxide (ETCO2) monitoring is a useful adjunct for detecting effective gas exchange during mask ventilatilation (13).

If the heart rate does not drop below 100 beats per minute after 5 to 10 positive pressure breaths, the attempted ventilation is insufficient, and corrective action is required. Mask leakage owing to an inadequate seal and airway malposition are the two most common issues. Intubation with an endotracheal tube or installation of a laryngeal mask airway is indicated if remedial efforts do not improve the heart rate (4).

An alternative airway is used if mask ventilation is unsuccessful or takes too long. A laryngoscope with a straight blade—size 0 for a preterm baby and size 1 for a term neonate—is used for tracheal intubation. It may be beneficial to apply gentle cricoid pressure. The basic means of confirming intubation of the trachea rather than the esophagus are an increase in heart rate and the measurement of $ETCO_2$ after several breaths. Look for symmetrical chest wall motion, equal breath sounds, especially in the axillae, and the absence of breath noises or gurgling over the stomach when auscultating. The tube is only used for tracheal suctioning if there is a suspected obstructed airway once it is in place. Otherwise, the endotracheal tube is fitted with a suitable positive-pressure device. Puffs of air are administered at a rate of 40 to 60 per minute, with a force sufficient to keep the heart rate stable. Opening pressures of 30 to 40 cm H2O enlarge the alveoli in term newborns without inducing barotrauma. After the lung has been expanded, less pressure is usually required (20 to 25 cm H_2O). Pressures of 20 to 25 cm H_2O are commonly utilized for premature newborns. A favorable response is indicated by an increase in heart rate and peripheral oxygen saturation (SpO_2) levels that are within acceptable values (5).

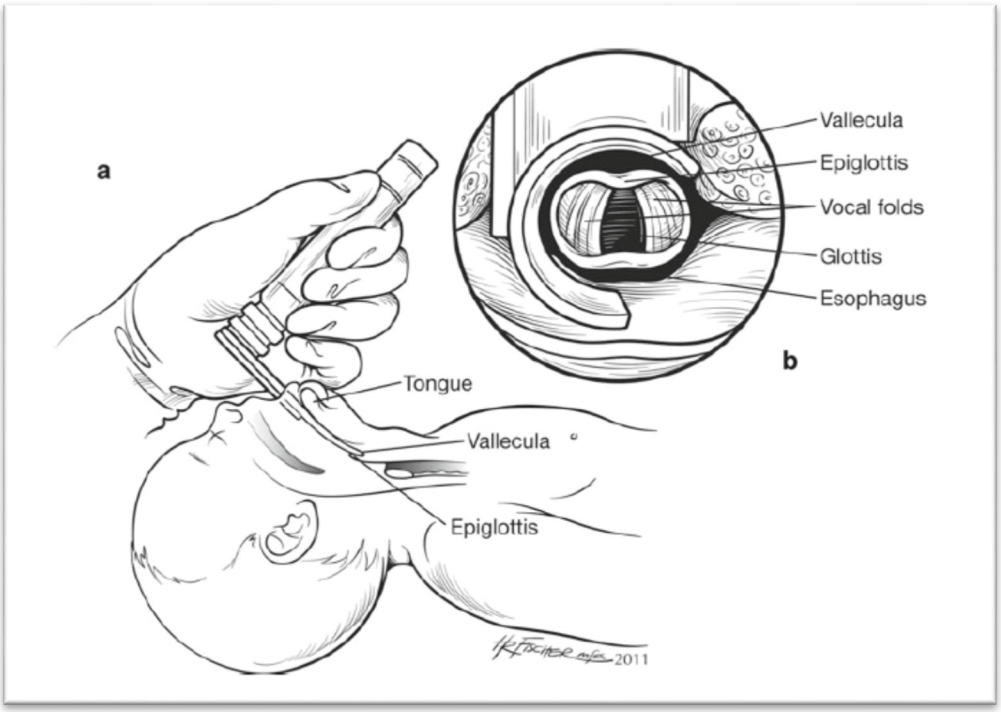

Figure 10. Endotracheal intubation (14)

- **Chest Compressions**

In most cases, all that is required to stabilize the newborn in the delivery room is sufficient ventilation. Chest compressions are started if the heart rate stays below 60 beats per minute after 30 seconds and despite corrective breathing measures, such as the installation of a tracheal tube. After the tracheal tube has been fitted, compressions are performed from the head of the bed rather than the side to allow for umbilical venous access by a provider. The oxygen concentration is boosted to 100% when compressions are started. Hands encircle the chest while thumbs depress the sternum in the two-thumb compression method. Compressions are applied to the bottom portion of the sternum, deep enough to produce a perceptible pulse. This is usually one-third of the chest's anterior-posterior diameter. This strategy, when compared to other procedures, results in reduced provider fatigue over time, greater produced perfusion pressures, and less hand malposition's, which can lead to traumatic injury (15).

It's recommended that you use a 3:1 compression-to-ventilation ratio, with 90 compressions and 30 breaths equaling 120 events every minute. Continue chest compressions and ventilations until the spontaneous heart is at least 60 beats per minute (4).

Figure 11. Chest compressions of the newborn (16)

- **Epinephrine**

At birth, approximately 10% of infants require some form of respiratory help in order to begin breathing on their own. If skilled positive-pressure breathing is started as soon as possible, the vast majority of these neonates will show signs of improvement without the requirement of cardiac compression or epinephrine. Epinephrine administration in the delivery room for the purpose of neonatal resuscitation is a rare occurrence because less than 0.1 percent of all babies have a need for the medication. There is a significant risk of death for newborns who require extended cardiopulmonary resuscitation (CPR), which may also involve the administration of epinephrine. Those who do make it through typically have compromised neurodevelopmental results in the long run (17).

If the heart rate stays below 60 beats per minute after adequate breathing and chest compressions, is recommended intravenously given of epinephrine. The intravenous dose ranges from 0.01 to 0.03 mg/kg. If venous access cannot be established, epinephrine can be given through the endotracheal tube, although its action is less efficient (17). When delivered through an endotracheal tube, greater doses—0.05 to 0.1 mg/kg—are used (5).

- **Interruption of Cardiopulmonary Resuscitation**

ILCOR has reached the conclusion that it is permissible to stop resuscitative attempts for a neonate that has not had a heartbeat despite at least ten minutes of continuous and adequate resuscitative efforts being performed on the baby. Furthermore, the choice of whether or not to continue with resuscitative efforts must be based on each individual's specific circumstances. (12)

EVALUATION OF NEWBORN CONDITION

- **Apgar score**

Dr. Virginia Apgar's scoring system, first developed in 1953, is still a helpful clinical tool for classifying newborn health shortly after birth and evaluating the efficiency of resuscitative efforts. Color, heart rate, reflexes, muscular tone, and respiration are all factors in the Apgar score. Apgar scoring is used to determine whether cyanosis, hypoperfusion, bradycardia, hypotonia, respiratory depression, or apnea are symptoms of hemodynamic compromise. Each element is given a score of 0 (zero), 1 (one), or 2 (two). All infants' scores are recorded at 1 minute and 5 minutes, with expanded recording at 5-minute intervals for infants who score seven or less at 5 minutes and those who require resuscitation as a way of response monitoring. Scores of seven to ten are regarded as acceptable. Apgar scores can change depending on gestational age, birth weight, maternal medicines, drug or anesthetic use, and congenital defects. Several aspects of the score are subjective and open to inter-rater variation. As a result, the Apgar score

has some limitations in that it provides somewhat subjective information about an infant's physiology at a specific point in time. It's beneficial for measuring resuscitation response, but it shouldn't be used to extrapolate results, especially at 1 minute, because it has no long-term clinical importance. While often reported, the Apgar score alone should not be taken as evidence of suffocation, and its use in outcome studies is typically incorrect. When it comes to determining a clinical score, resuscitation should always take precedence (18).

Table 7. Apgar Score Table (19)

Apgar Scoring System

Indicator		0 Points	1 Point	2 Points
A	Activity (muscle tone)	Absent	Flexed arms and legs	Active
P	Pulse	Absent	Below 100 bpm	Over 100 bpm
G	Grimace (reflex irritability)	Floppy	Minimal response to stimulation	Prompt response to stimulation
A	Appearance (skin color)	Blue; pale	Pink body, Blue extremities	Pink
R	Respiration	Absent	Slow and irregular	Vigorous cry

- **Umbilical Cord Blood Acid–Base Studies**

The fetus's intrapartum acid-base state is crucial in determining the relationship between intrapartum events and newborn condition. The examination of umbilical artery cord blood gases is found to be an excellent representation of the fetal acid-base state just before birth. The presence of harmful acidemia can be scientifically confirmed or excluded by blood gas analysis. Although numerous factors such as sampling, storage, and assessment might affect measurements, there is a large margin of error when fast examination is not possible. Because a substantial deviation from the standard procedure is required before a sample is alleged to be imprecise, it is unlikely that standard sampling methods would be ineligible in litigation (20).

Acid–base studies can be performed on blood obtained from umbilical veins to determine the neonate's metabolic condition. Following birth, blood is collected by clamping a 10- to 20-cm piece of cord with two clamps near the newborn and another two clamps near the placenta. After that, the chord is cut between the two proximal clamps, followed by the two distal clamps. (20)

Arterial blood is taken from the isolated cord section into a 1- to 2-mL plastic syringe containing lyophilized heparin or a similar syringe that has been flushed with a 1000 U/mL heparin solution. The needle is capped and the syringe is delivered to the laboratory on ice once the sampling is completed. Despite efforts to ensure fast conveyance, blood maintained at ambient temperature for up to 60 minutes shows no significant changes in pH or partial pressure of CO_2 (pCO_2) (21).

- **Fetal Acid–Base Physiology**

Both carbonic and organic acids are produced by the fetus. The oxidative metabolism of CO_2 produces carbonic acid (H_2CO_3). CO_2 is normally cleared quickly by the fetus through the placental circulation. Carbonic acid levels rise when CO_2 removal is reduced. This frequently occurs as a result of a disruption in placental exchange. Respiratory acidemia occurs when H_2CO_3 builds up in fetal blood without organic acids rising at the same time. Organic acids, on the other hand, largely contain lactic and hydroxybutyric acid. These are produced by anaerobic glycolysis and increase with prolonged placental exchange dysfunction. Organic acids are progressively excreted from fetal blood. Metabolic acidemia occurs when they accumulate without a corresponding increase in H_2CO_3. Bicarbonate (HCO_3) levels fall as metabolic acidemia progresses because it is utilized to buffer the organic acid. Mixed respiratory-metabolic acidemia is caused by a rise in H_2CO_3 concentrations accompanied by higher organic acid levels, as represented by lower HCO_3 levels. Respiratory and metabolic acidemia, as well as tissue acidosis, are almost certainly part of a progressively worsening continuum in the fetus. This is in contrast to adult pathophysiology, in which diverse illnesses result in either respiratory or metabolic acidosis, such as pulmonary disease or diabetes. A decrease in uteroplacental perfusion is one of the most common causes of fetal acidemia. This causes CO2 retention, or respiratory acidemia, which can progress to mixed or metabolic acidemia if left untreated (5).

- **Suggestions for Evaluating Cord Blood Gas**

Cord gas analysis is performed in all neonates at birth in some facilities. For intrapartum cesarean delivery cases with fetal compromise, aberrant fetal heart rate tracing, fever, and a low 5-minute Apgar score, it seems feasible to acquire cord blood gas tests. Multifetal gestation and severely stunted fetuses are two other examples.

Although acid–base blood tests on the umbilical cord are unreliable predictors of immediate or long-term unfavorable neurological outcomes, they do provide the most objective evidence of the fetus metabolic condition at delivery (5).

PREVENTIVE CARE

- **Prophylaxis for Eye Infections**

During the neonatal period, 1-12 percent of all infants have conjunctivitis. Ophthalmia neonatorum is a conjunctivitis with a mucopurulent disease that appears within the first month of life. It's basically an infection contracted during a vaginal delivery. Chlamydia trachomatis and Neisseria gonorrhoeae are the most common infectious pathogens involved with ophthalmia neonatorum. Topical ocular prophylaxis should be started as soon as possible after birth. A preventative regimen of 1% nitrate solution, 1% tetracycline solution, 1% erythromycin solution, 2.5 percent povidone-iodine solution, and fusidic acid is recommended (22).

- **Hepatitis B Immunization**

The neonate is passively immunized with hepatitis B specific antibodies if the mother is seropositive for hepatitis B surface antigen. All medically stable neonates with birthweights larger than 2000 g are routinely immunized with a thimerosal-free hepatitis B vaccination before being discharged from the hospital (23).

- **Zika Virus**

Mosquito bites are the most common way for this illness to spread. Most people are asymptomatic while they are infected, but it can lead to serious birth abnormalities. The screening process starts with a question about recent travel to endemic areas. Serological screening is then conducted for women who are at risk. Before being discharged from the hospital, all babies of women who tested positive for Zika virus during pregnancy should have a comprehensive checkup, a neurological assessment, a postnatal head ultrasound, a standard newborn hearing screen, and Zika virus laboratory testing (24).

- **Vitamin K**

Vitamin K injections will protect newborns against vitamin K-dependent hemorrhagic illness Within 1 hour of birth, a single intramuscular dosage of vitamin K ranging from 0.5 to 1 mg is administered (5).

ROUTINE NEWBORN CARE

- **Estimation of Gestational Age**

The gestational age of a newborn can be calculated shortly after delivery. The link between gestational age and birthweight can help doctors identify newborns who are at risk of problems.

For example, infants that are little or large for gestational age are more likely to develop hypoglycemia and polycythemia, and blood glucose and hematocrit tests are recommended (5).

- **Skin and Umbilical Cord Care**

After delivery, all excess vernix, blood, and meconium are gently cleaned away as the newborn is kept warm. Any vernix that remains is quickly absorbed and vanishes within 24 hours. The first bath will not be given until the neonate's temperature has stabilized. In the immediate care of the chord, aseptic precautions must be taken (5). Shortly after delivery, the umbilical cord begins to lose water from Wharton jelly. The cord stump loses its characteristic bluish-white, moist color within 24 hours and becomes dry. It quickly dries out and turns black. The stump sloughs and leaves a stump within a few days to weeks. The umbilicus is a tiny, granulating wound that heals to produce the umbilicus. Separation normally takes a long time. Within the first two weeks, the event will take place. The range is between 3 and 45 days (8). Despite precautions, a severe umbilical infection called omphalitis can occur. Staphylococcus aureus, Escherichia coli, and group B streptococcus are the most likely causes. Typical cellulitis symptoms, such as stump discharge, are usually helpful in determining the diagnosis. Moderate erythema and occasional bleeding at the scar site are also frequent with cord detachment, but other patients have no visible symptoms (5).

- **Feeding and Weight Loss**

Breastfeeding often begins in the delivery room in many hospitals. Most term infants grow when they are fed 8 to 12 times per day for 15 minutes each time. Until the baby is six months old, breast feading should be done exclusively (4).

- **Stools and Urine**

The colon contains mushy, brown-green meconium for the first 2 or 3 days after delivery. Desquamated intestinal epithelial cells, mucus, epidermal cells, and lanugo (fetal hair) that have been eaten with amniotic fluid make up this substance. Bile pigments are responsible for the distinctive color. The intestinal contents are sterile during fetal life and for a few hours after delivery, but microorganisms quickly invade the bowel contents. 90% of babies have meconium stooling during the first 24 hours, and the majority within 36 hours. Newborns usually clear quickly after delivery, however this might take up to two days. The passage of meconium and urine suggests that the gastrointestinal and urinary tracts are both functional. A congenital abnormality, such as Hirschprung disease, imperforate anus, or a posterior urethral valve, is indicated if the newborn fails to defecate or urine after these timeframes. Meconium is replaced with light-yellow, softer, homogeneous excrement after the third or fourth day as a result of milk consumption (5).

- **Neonatal Hyperbilirubinemia**

Approximately one-third of all newborns develop physiological jaundice between the second and fifth days of life. It's especially significant because most hospitals have early discharge policies. Treatment recommendations are based on gestational age, hour of life, and risk factors, as well as standard phototherapy equipment and monitoring guidelines (24).

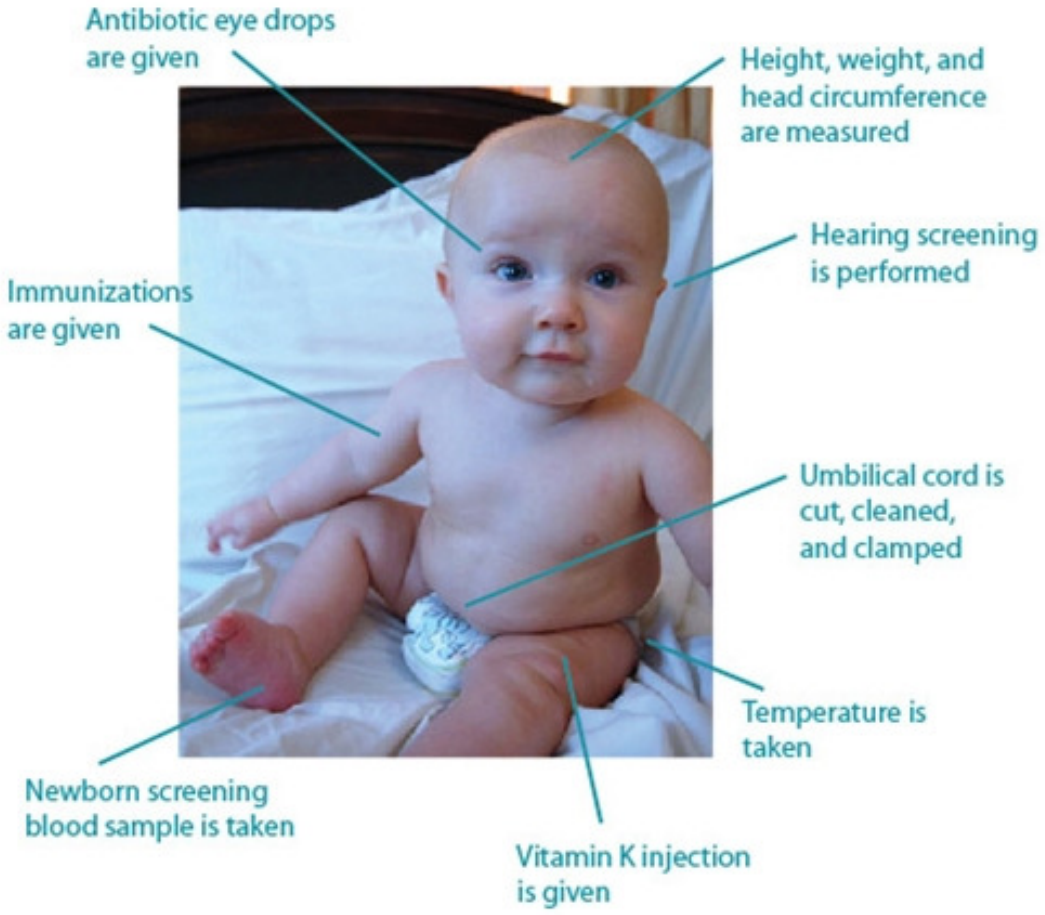

Figure 12. Head to toe examination of the infant (26)

https://youtu.be/hW3n9seV4SY - Head to toe examination of the infant

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