MINISTRY OF EDUCATION AND SCIENCE OF UKRAINE

State Higher Educational Institution

“UZHHOROD NATIONAL UNIVERSITY”

MEDICAL FACULTY

DEPARTMENT OF OBSTETRICS AND GYNECOLOGY

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Obstetrics lecture notes

Tutorial for practical lessons of obstetrics for students of the 4th -6th course of medical faculty

Uzhhorod - 2023

УДК 618.4-72
К 70

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Obstetrics lecture notes: Tutorial/Korchynska O.O., Lemish N.Y., — TOV «Rik-U», 2023. — 220 p.

According to the resolution of the World Assembly of health care of UN from 1995 the preservation of the reproductive health is established on the global level by the WHO as a priority branch

Knowledge of obstetrics, physiological states and skills to differentiate pathology is necessary in order to preserve health of both -the mother and the child.

This tutorial was made in order to help students of 4^{th} -6^{th} year prepare for practical classes.

ISBN 978-617-8046-98-8

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Approved by the Academic Council of the medical faculty of state higher educational institute "Uzhhorod National University"
protocol № 10 from «15» December 2022 year.

ISBN 978-617-8046-98-8

ABBREVIATIONS

GP – general practitioner

FP – Family planning

PHC – Primary health care

SHC – Secondary health care

THC – Tertiary health care

TPE – treatment-prophylactic establishments

CTG – cardiotocography

MSA – medically-sanitary aid

NST – nonstress test

CST – contraction stress test

SIDS – sudden infant death syndrome

IUGR – intrauterine growth retardation

IVF – in vitro fertilization

CONTENTS

Organization of obstetric care. The subject of obstetrics and gynecology. The main stages of development of obstetrics and gynecology

Obstetrics (from the Latin *obstare* - "to stand by" or from the France *accoucher* – to take delivery) is the health profession or medical specialty that deals with pregnancy, childbirth, and postpartum period (including care of the newborn). It encompasses a variety of health care practices evolved to maintain and restore health by the prevention and treatment of illness in human beings. In addition to being a medical specialty, obstetrics is the study of the reproductive process within the female body, including fertilization, pregnancy and childbirth.

Gynaecology or gynecology is the medical practice dealing with the health of the female reproductive system (vagina, uterus and ovaries) and the breasts. Literally, outside medicine, it means "the science of women". Its counterpart is andrology, which deals with medical issues specific to the male reproductive system. The word "gynaecology" comes from the Greek *gyne* - "woman" and *–logia* - "study."

Almost all modern gynecologists are also obstetricians. In many areas, the specialties of gynecology and obstetrics overlap.

History

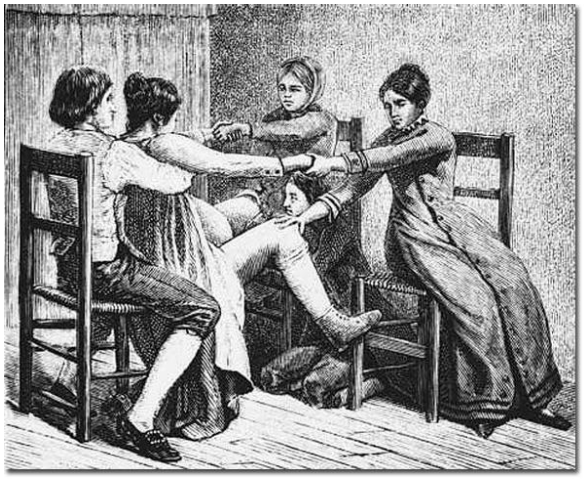
Prior to the 18th century, caring for pregnant women in Europe was confined exclusively to women, and rigorously excluded men. The expectant mother would invite close female friends and family members to her home to keep her company. Skilled midwives managed all aspects of the labour and delivery. The presence of physicians and surgeons was very rare and only occurred once a serious complication had taken place and the midwife had exhausted all measures to manage the complication. Calling a surgeon was very much a last resort and having men deliver women in this era whatsoever was seen as offending female modesty

Leading up to the 18th Century

Obstetrics prior to the 18th and 19th centuries was not recognized on the same level of importance and professionalism as other medical fields, until about two hundred years ago it was not recognized as a medical practice. However, the subject matter and interest in the female reproductive system and sexual practice can be traced back to Ancient Greece and even to Ancient Egypt. Soranus of Ephesus sometimes is called the most important figure in ancient gynecology.

Picture.1. Caring for women in Europe prior to 18th century

Living in the late first century A.D. and early second century he studied anatomy and had opinions and techniques on abortion, contraception – most notably coitus interruptus– and birth complications. After the death of Soranus, techniques and works of gynecology declined but very little of his works were recorded and survived to the late 18th century when gynecology and obstetrics reemerged.



Picture.2 Obstetrics prior to the 18th and 19th centuries

18th century The marked the beginning of many advances in European midwifery. These advances in knowledge were mainly regarding the physiology of pregnancy and labour. By the end of the century, medical professionals began to understand the anatomy of the uterus and the physiological changes that take place during labour. The introduction of forceps in childbirth also took place during the

18th century. All these medical advances in obstetrics were a lever for the introduction of men into an arena previously managed and run by women-midwifery.

The addition of the male-midwife is historically a significant change to the profession of obstetrics. In the 18th century medical men began to train in area of childbirth and believed with their advanced knowledge in anatomy that childbirth could be improved. In France these male-midwives were referred to as "accoucheurs". This title was later on lent to male-midwives all over Europe. The founding of lying-hospitals also contributed to the medicalization and male-dominance of obstetrics. These lying-hospitals were establishments where women would come to have their babies delivered, which had prior been unheard of since the midwife normally came to home of the pregnant woman. This institution provided male-midwives or accoucheurs with an endless number of patients to practice their techniques on and also was a way for these men to demonstrate their knowledge.

Picture.3 18th century European midwifery

Many midwives of the time bitterly opposed the involvement of men in childbirth. Some male practitioners also opposed the involvement of medical men like themselves in midwifery, and even went as far as to say that men-midwives only undertook midwifery solely for perverse erotic satisfaction. The accoucheurs argued that their involvement in midwifery was to improve the process of childbirth.

These men also believed that obstetrics would forge ahead and continue to strengthen.

19th century

Even 18th century physicians expected that obstetrics would continue to grow, the opposite happened. Obstetrics entered a stage of stagnation in the 19th century, which lasted until about the 1880s. The central explanation for the lack of advancement during this time was substantially due to the rejection of obstetrics by the medical community. The 19th century marked an era of medical reform in Europe and increased regulation over the medical profession. Major European institutions such as The College of Physicians and Surgeons considered delivering babies ungentlemanly work and refused to have anything to do with childbirth as a whole. Even when Medical Act 1858 was introduced, which stated that medical students could qualify as doctors, midwifery was entirely ignored. This made it nearly impossible to pursue an education in midwifery and also have the recognition of being a doctor or surgeon. Obstetrics was pushed to the side.

Picture. 4. 1822 drawing by Jacques-Pierre Maygnier

Picture….The historic taboo associated with the examination of female genitalia has long inhibited the science of gynaecology. This 1822 drawing by Jacques-Pierre Maygnier shows a "compromise" procedure, in which the

physician is kneeling before the woman but cannot see her genitalia. Modern gynaecology has shed these inhibitions.

By the late 19th century the foundation of modern day obstetrics and midwifery began develop. Delivery of babies by doctors became popular and readily accepted, but midwives continued to play a role in childbirth. Midwifery also changed during this era due to increased regulation and the eventual need for midwives to become certified. Many European countries by the late 19th century were monitoring the training of midwives and issued certification based on competency. Midwives were no longer uneducated in the formal sense.

As midwifery began to develop so did the profession of obstetrics near the end of the century. Childbirth was no longer unjustifiably despised by the medical community as it once had been at the beginning of the century. But the specialty was still behind in its development stages in comparison to other medical specialities, and remained a generality in this era. Many male physicians would deliver children but very few would have referred to themselves as obstetricians. The end of the 19th century did mark a significant accomplishment in the profession with the advancements in asepsis and anesthesia, which paved the way for the mainstream introduction and later success of the Caesarean Section.

Before the 1880s mortality rates in lying-hospitals would reach unacceptably high levels and became an area of public concern. Much of these maternal deaths were due to Puerperal fever, at the time commonly known as childbed fever. In the 1800s Dr. Ignaz Semmelweis noticed that women giving birth at home had a much lower incidence of childbed fever than those giving birth by physicians in lying-hospitals. His investigation discovered that washing hands with an antiseptic solution before a delivery reduced childbed fever fatalities by 90%. So it was concluded that it was physicians who had been spreading disease from one laboring mother to the next. Despite the publication of this information, doctors still would not wash. It was not until the 20th century when advancements in aseptic technique

and the understanding of disease would play a significant role in the decrease of maternal mortality rates among many populations.

Historical Role of Gender

Women and men inhabited very different roles in natal care up to the 18th century. The role of a physician was exclusively held by men who went to university, an overly male institution, who would theorize anatomy and the process of reproduction based on theological teaching and philosophy. Many beliefs about the female body and menstruation in the 17th and 18th centuries were inaccurate; clearly resulting from the lack of literature about the practice. Many of the theories of what caused menstruation prevailed from Hippocratic philosophy. Midwives of this time were those assisted in the birth and care of both born and unborn children, and as the name suggests this position held mainly by women.

During the birth of a child, men were rarely present. Women from the neighborhood or family would join in on the process of birth and assist in many different ways. The one position where men would help with the birth of a child would be in the sitting position, usually when performed on the side of a bed to support the mother.

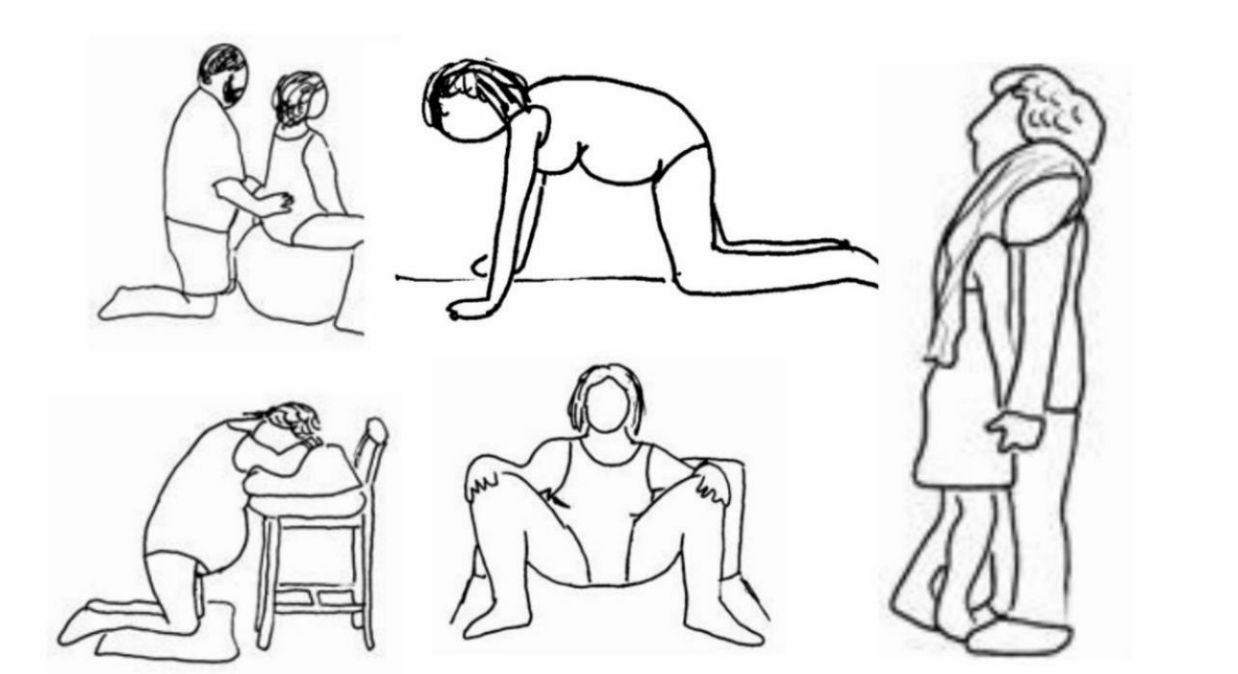
Men were introduced into the field of obstetrics in the nineteenth century and resulted in a change of the focus of this profession. Gynecology directly resulted as a new and separate field of study from obstetrics and focused on the curing of illness and indispositions of female sexual organs. This had some relevance to some conditions as menopause, uterine and cervical problems, and childbirth could leave the mother in need of extensive surgery to repair tissue. But, there was also a large blame of the uterus for completely unrelated conditions. This led to many social consequences of the nineteenth century.

Historical Positions

The process in the past of birthing a child began with very little preparation; improvisation was the rule of thumb. Dilation was determined mostly by touch and

described by obstetricians and midwives very differently. Midwives would refer to the dilation of the cervix by comparing it to body parts, such as the palm of the hand, a finger, or even a fist. Obstetricians, usually men who had experience with using coins would refer to the dilation by relation to the size of currency.

The woman birthing the child would have topical remedies available to calm her nerves, ease pain and encourage her to deliver the baby hastily. The birthing mother was also able to decide her position of delivery as opposed to the standard laying down practice today. There were two main categories of positions, vertical and horizontal. These are expanded upon below.



Picture.5 Historical positions for labour

Crouching

An instinctive position, this ensured full use of gravity to the mother's advantage, and if the child appears suddenly, ensures safety from falling from a height and being injured. This position was most common when a woman was unattended and essentially without help. If necessary, the mother could watch her perineum and disengage the head of the baby herself. Common practice in many cultures apparently thought it essential to lay the newborn upon the ground as a connection to the earth and this position allowed the child to arrive with immediate

contact with the ground. Downsides of this position are it requires great stamina and that the woman be fully nude below the waist.

Kneeling

This position was common in the nineteenth century French provinces and by peasant women. The position called for knee protection and upper limb support, involving possibly a cushion and chair back or by being suspended between two chairs backs if alone.

Downsides to this position were that it caused back aches and cramps. Also, doctors considered it inferior due to the baby being received behind the mother. When a fetus underwent malpresentation (misalignment of the fetus, with the head not exiting the womb first) or when the womb was extremely protruding or comparatively large to the woman, she may have knelt on the ground with hands placed on the ground in front of her. Doctors of the enlightenment period thought this ‘on all fours’ position was too animalistic and indecent, and should be avoided.

Sitting

A sitting position would be used in some cases for women who could not squat for extended periods of time. It was reinvented with the creation and use of the birthing stool. Contrary to the name, this could be either a stool or a chair with a large hole in the seat to use gravity to align and birth the child while supporting the weight of the mother. With the stool variation and the side of the bed position, another person would be used to support the mother’s upper body.

Standing

Accidentally happening or deliberate, this position was rarely used due to the stamina required to do so as well as the tendency for mothers to teach their daughters how to birth otherwise. Daughters who hid their pregnancy could be caught standing and having their water break, instinctively these girls would brace themselves against a wall, table, chair and with the inability to move would deliver the baby

there, allowing it to fall on the ground. This, of course, was extremely dangerous although in the seventeenth and eighteenth centuries, various textbooks show the persistence of the standing position with it persisting until the beginning of the twentieth century in some areas of France.

Horizontal

Compared to the other four vertical positions, this was certainly believed not instinctive and did not provide the labour with the necessary conditions to birth. Today we also know this position is inferior to the vertical positions as it increases the change of fetal distress as malpresentation. It also decreases the space available in the pelvis, as the sacrum is unable to move backwards as it does naturally during labour. This method of childbirth developed after the introduction of the birthing stool and with the change in concentration of births in homes to hospitals. This position was used for women who had some difficulty in bringing the fetus to birth. Women only resorted to lying down especially on the bed because it would mean that the bedclothes would be soiled in the process. It was also avoided because it showed determination and was significant in showing difference from animals that lay down to give birth. This is similar to the resistance to giving birth on all fours.
A sixth position was used in some instances of a poor household, in the countryside and during the winter. It was a combination of the sitting position and laying position usually by a combination of small mattress and a fallen chair used as a backrest. This method was also greatly avoided and only used at the request of the mother because it required that the person helping birth the child—usually an obstetrician and not a midwife at this point—to crouch on the ground, working at nearly ground level.

The Birthing Stool

The birthing stool – sometimes known as a birthing chair – was introduced in the seventeenth and the use of it was encouraged into the eighteenth century by the doctors and administrators who used it to control the child being birthed. The stool

was usually very expensive and came in two types. The more expensive and heavier variety was used by wealthy families as a family heirloom— and typically was adorned with decoration or expensive materials. The second variety was used by village midwives as was lighter and portable so the midwife could carry it from home to home. It became popular in the French territory of (mostly German speaking) Alasace-Lorraine. At the beginning of the 19th century, the birthing stool's use changed, as increased weight restricted its use to medical facilities. It, perhaps indirectly, evolved into the modern delivery table. This contributed to the transition to the modern day hospital setting.

Picture.6 Birthing stoll

This was usually not the method of choice for many mothers, as the stool was very revealing, cold, and later became associated with the pain of childbirth. To decrease the draft on a woman's genitals as she sat on the birthing stool, fabric was draped around the seat. This also provided a bit of privacy and respected the modesty of the mother.

Examination

In Ukraine, women must first see a general practitioner (GP; also known as a family practitioner (FP)) prior to seeing a gynecologist. If their condition requires training, knowledge, surgical procedure, or equipment unavailable to the GP, the patient is then referred to a gynecologist. In Ukraine, however, law and many health insurance plans allow gynecologists to provide primary care in addition to aspects

of their own specialty. With this option available, some women opt to see a gynecological surgeon for non-gynecological problems without another physician's referral.

As in all of medicine, the main tools of diagnosis are clinical history and examination. Gynecological examination is quite intimate, more so than a routine physical exam. It also requires unique instrumentation such as the speculum. The speculum consists of two hinged blades of concave metal or plastic which are used to retract the tissues of the vagina and permit examination of the cervix, the lower part of the uterus located within the upper portion of the vagina. Gynecologists typically do a bimanual examination (one hand on the abdomen and one or two fingers in the vagina) to palpate the cervix, uterus, ovaries and bony pelvis. It is not uncommon to do a recto-vaginal examination for complete evaluation of the pelvis, particularly if any suspicious masses are appreciated. Male gynecologists may have a female chaperone for their examination. An abdominal and/or vaginal ultrasound can be used to confirm any abnormalities appreciated with the bimanual examination or when indicated by the patient's history.

Organization of obstetric care in Ukraine

General principles of obstetric and neonatal care are based on the concept of WHO for rational management of labor (1996), the concept of safe motherhood and on the basis of the state to implement an active demographic politics.

Organization of obstetric care in Ukraine consists of three major stages:

1. The organization of family planning services as the basis of formation reproductive health;
2. The organization of obstetric care based on the principles of safe motherhood;
3. The organization of gynecological care based on the principles of rehabilitation reproductive health as an essential prevention factor of oncological diseases.

The system of **family planning (FP)** in Ukraine belongs to one of the youngest subsystems of healthcare in Ukraine.

Family planning is the planning of when to have children, and the use of birth control and other techniques to implement such plans. Other techniques commonly used include sexuality education, prevention and management of sexually transmitted infections, pre-conception counseling and management, and infertility management.

Family planning is sometimes used as a synonym or euphemism for the use of birth control, however, it often includes a wide variety of methods, and practices that are not birth control. It is most usually applied to a female-male couple who wish to limit the number of children they have and/or to control the timing of pregnancy (also known as spacing children). Family planning may encompass sterilization, as well as abortion.

Family planning services are defined as "educational, comprehensive medical or social activities which enable individuals, including minors, to determine freely the number and spacing of their children and to select the means by which this may be achieved".

The organization of structural units of the family planning system is carried out in accordance with the level to provide consultative medical care. Maternity care includes pregnancy (antenatal) care, labour and birth (intrapartal) care, and care following birth (postnatal). Care can be provided in a number of settings, these being:

- as an outpatient in a hospital or community clinic
- as an in-patient through hospital admission
- in the community
- in the home.

Care in pregnancy and childbirth is provided by a range of health care professionals (both public and private) including general practitioners, obstetricians, midwives as well as maternal and child health nurses provided by local government.

Labour, birth and postnatal services include:

a. all primary maternity care from the time of established labour, from initial assessment of the woman at her home or at a maternity facility, and regular monitoring of the progress of the woman and baby,

b. management of the birth,

c. all primary maternity care until 2 hours after delivery of the placenta, including updating the care plan, attending the birth and delivery of the placenta, suturing of the perineum (if required), initial examination and identification of the baby at birth, initiation of breast feeding (or feeding), care of the placenta, and attending to any legislative requirements regarding birth notification by health professionals.

Primary Health Care (PHC)

The strategy for achieving the goal of "Health for All" emerged in 1978 at an historic conference in Alma-Ata in the former Soviet Union. The conference was sponsored by the United Nation Children's Fund (UNICEF) and WHO. Prior to the Alma-Ata Conference, WHO had identified eight components common to nine successful health programs. The code words "Primary Health Care" (PHC) were selected to describe the following eight components in combination:

- education about common health problems and what can be done to prevent and control them;
- maternal and child health care, including family planning;

- timely identification of pregnant women and the dynamic control of them in cooperation with the obstetrician-gynecologist;
- prevention and control of sexually transmitted diseases;
- organization of preventive examinations of female population;
- basic sanitation;
- timely identification of women with severe pathology for which pregnancy threatens the health or life, for the purpose of directing them to a higher health care level;
- appropriate treatment for common diseases and injuries.

Level I includes - midwifery and first aid stations, district hospitals, outpatient clinics and family doctor ambulatory.

At the primary health care level in rural areas and cities, it is necessary to determine units that are to provide the primary medical care. Primary health care (PHC) refers to "essential health care" that is based on scientifically sound and socially acceptable methods and technology, which make universal health care universally accessible to individuals and families in a community. It is through their full participation and at a cost that the community and the country can afford to maintain at every stage of their development in the spirit of self-reliance and self-determination". In other words, PHC is an approach to health beyond the traditional health care system that focuses on health equity-producing social policy. PHC includes all areas that play a role in health, such as access to health services, environment and lifestyle. Thus, primary health care and public health measures, taken together, may be considered as the cornerstones of universal health systems.

Secondary health care level (SHC)

Secondary Maternity Services are those provided where women and / or their babies experience complications that need additional maternity care involving Obstetricians, Pediatricians, other Specialists and secondary care teams.

At the secondary health care level the network of central district and regional hospitals, central municipal, municipal and district hospitals and independent municipal clinics should be designed in accordance with the needs of the population, territorial accessibility, disease incidence and other criteria. It is reasonable to create a multi-field hospital of intensive treatment that will ensure the provision of specialized medical care as well as entire medical assistance throughout the region.

The secondary Medicare in towns is provided by the city many-types incorporated hospitals and medical sections, in villages there are central district and district hospitals. The secondary specialized treatment-prophylactic aid to the rural population is given in district medical establishments, municipal family planning offices, antenatal clinics (women's consultations), obstetric and gynecological departments, maternity hospitals, services for Child and Adolescent Gynecology, children's clinics.

Secondary and tertiary maternity facilities will have sufficient assessment, antenatal, birth and postnatal rooms for the population serviced by the secondary and tertiary maternity services, and for the level of service provided. Facilities should also have sufficient assessment, antenatal, birth and postnatal rooms for primary births that take place in the secondary and tertiary facilities.

The leading establishments are central district hospitals that also carry out a role of organizationally medical centers in organization and quality of giving the Medicare.

The basic tasks of CDH are:

- direct giving of primary ambulatory-policlinic aid to the population of district centre and attached area;

- giving of the specialized ambulatory-policlinic aid to all the population of the district;

- giving of the specialized stationary aid to all the population of the district;

- providing quick and urgent Medicare to population;

- introduction into the practice of the district's TPE of work modern methods and facilities of prophylaxis, diagnostics and treatment;

- organization of consultative aid;

- organizationally-methodical guidance of the work of all district's TPE, and also control work of their activity;

- development and introduction of measures which are directed to upgrade the quality of medical providing;

- development, organization and realization of measures which can raise qualification of medical personnel; rational usage of medical personnel's and materially-technical resources;

- planning, financing and organization of the materially-technical support of the district's health care establishments;

- qualification raising of medical staff of the district and section TPE.

City hospitals provide about the third part of given Medicare.

Greater part of the city station establishments is united with policlinics, but the independent specialized hospitals also exist.

The main tasks of city hospital are:

- giving of the specialized round-the-clock stationary aid in a sufficient quantity;

- approbation and introduction of modern methods of diagnostics, treatment and prophylaxis;

- complex treatment;

- examination of disabled;

- hygienically education of population.

The facilities will include adequate space, equipment and consumables for:

- LMCs to undertake acute clinical consultations and examinations including antenatal cardiotocographs (CTGs) or other clinical examinations for assessment
- monitoring progress of labour and assisting with facilitating births
- equipment and services for caesarean section and assisted vaginal deliveries
- emergency resuscitation and care of mother
- emergency resuscitation and care of the newborn until transfer of care to neonatal services, if necessary
- newborn hearing screening.

Every stationary department consists of chambers and other premises for medical and economic aim (operating block, bandaging, cabinet for manipulations, intern, cabinets of the Head of the department and of the senior nurse. In order to isolate patients in the infectious hospitals the boxes are prepared.

In the induction center a doctor get acquainted meets with the facts of medical documents, makes an examination, gives necessary urgent aid and sends a patient to the proper department. The induction center provides the order of direction to permanent establishment and conducts:

- registration of patients, that come to permanent establishment and leave it, filling the passport part of the in-patient card;

- establishing of diagnosis;

- substantiation of hospitalizations;

- giving the urgent (aid) aid if it is necessary;

- sanitary treatment;

- taking the material for laboratory researches, express-diagnostics, roentgen- and functional researches; determination of type of the specialized department;
- registration of refusals in hospitalization with determination of reasons;
- giving the additional information for the hospitalized patients.

Except of chamber, the following posts of such nurses are set:

- operating-room;
- bandaging;
- of the dietary feeding;
- medical sister for organization of individual care of seriously sacking;
- procedural cabinet;
- physiotherapy, massage.

Tertiary health care level

WHPO gives to it such determination: it is the aid, that needs highly skilled service, which as a rule can be given only in the centers and hospitals which passed the proper specialization and are specially equipped to that aim.

According to the „Bases of Ukrainian legislation of health care" the tertiary medically-sanitary aid (MSA) is given by a doctor or a group of doctors who have the proper preparation in the field of diseases which are difficult for diagnostics and treatment, in the case of treatment of illnesses which need the special methods of diagnostics and treatment. And also with the purpose of establishment of diagnosis and conducting of treatment of diseases which are rarely met.

At the tertiary health care level a highly specialized health care level should function, which will be ensured by regional hospitals, higher medical education institution departments and institutes for scientific research. Specialist hospitals

(also known as tertiary hospitals) provide statewide services for women with complex or high risk pregnancies.

Two functions of these establishments are considered to be basic:

- organizationally-methodical guidance of the secondary level of MSA;
- giving to the patients highly skilled and strictly specialized Medicare.

Women are best supported when they receive maternity care close to their home and for some women this will mean birthing in a tertiary hospital. Women requiring higher levels of care will be referred to an appropriate service by their general practitioner or hospital and this may require women to travel.

Eligible women and their babies assessed as needing additional care during the antenatal, labour and birth, and postnatal period until six weeks after the birth, will have access to the secondary and / or tertiary services that are clinically indicated for their individual need. Eligible women who do not require secondary or tertiary services may access secondary or tertiary facilities for labour and birth, and the postnatal period. You will ensure that these women receive primary maternity services, as secondary and / or tertiary services are not clinically indicated.

Consultative policlinic is the separate structural subsection of establishment of tertiary MSA. The narrow specialized departments of permanent establishment, auxiliary treatment-prophylactic subsections, clinical, biochemical and bacteriological laboratories, separations of functional diagnostics, path anatomical, physical therapy and radiological departments) are obligatory.

Secondary and Tertiary Maternity Services:

a.) during specified times during normal working hours, a non-acute outpatient service for the assessment, diagnosis and treatment of women and their babies who are referred to the secondary or tertiary maternity service;

b.) a 24 hour / day Outpatient service for the acute assessment, diagnosis and treatment of women and their babies who are referred to the secondary or tertiary maternity service in accordance with the Maternity Referral Guidelines;

c.) a 24 hour/day, Inpatient service for women and their babies whose care is transferred to the secondary or tertiary maternity service;

d.) a follow up service providing consultation with a Specialist, where appropriate until 6 weeks after birth.

The service includes, but is not limited to:

a. the assessment, diagnosis and treatment of women who require a consultation with an Obstetrician or other Specialist and who are referred to the secondary or tertiary service;

b. the assessment, diagnosis and treatment of women whose care is transferred to the secondary or tertiary maternity service;

c. provision of, or facilitation of access to, amniocentesis or chorion villus procedure and tests where there is an increased risk assessment / screening result;

d. authorising, giving advice on, and performing inductions ;

e. anaesthesia services for consultation relating to analgesia in labour which might include administration of epidural analgesia and its ongoing management, care and follow up of the woman;

f. all care in association with complicated deliveries, including operative vaginal deliveries and caesarean sections;

g. midwifery care for woman and her baby when clinical responsibility is with the secondary or tertiary maternity services team, including in cases where the

clinical responsibility for the woman's care has been transferred to the secondary or tertiary team;

h. assessment, diagnosis and treatment of pregnant women and / or newborn babies who require a consultation with the neonatal service;

i. lactation advice from a lactation consultant midwife in line with referral criteria.

The following services are to be provided as an integral part of these services:

- professional services – medical, nursing and allied health
- pathology services, including referrals to private laboratories by hospital medical
- practitioners
- diagnostic imaging services, including referrals to private diagnostic imaging services
- by hospital medical practitioners
- other diagnostic services referred to by hospital medical practitioners, eg,
- cardiography, spirometry, audiology, neurological testing
- operating theatres
- anaesthetic services
- sterile supply services
- pharmacy services
- nuclear medicine
- coronary care
- intensive care
- blood transfusion services
- supply or loan of equipment to support treatment, rehabilitation or aid mobility
- infection control

The department of urgent and planly-consultive aid is other important structural unit of the regional hospital. In its structure there is a 24-hour's dispatcher service of reception and registration of calls from the hospitals of districts and cities of the region. The specialists of regional hospital and other TPE regions employees of higher medical institutes, research institutes are attracted, to the giving of urgent and planly-consultive aid on the agreement with the corresponding establishments and institutions. To engage into this work employees, the special order is given out at the Management of health care.

Physiology of Pregnancy

INTRODUCTION

Pregnancy in the human female is an unusual state in which virtually all maternal systems are dramatically altered to permit the sustenance and growth of the intrauterine conceptus. In very real ways, the maternal organism is life-adapted.

Although pregnancy is unique in many ways, it is particularly so in being limited in time. Pregnancy is a temporary state with a definite point of onset and an equally definite termination. The duration of pregnancy in humans, marked from the first day of the last menstrual period, is classically 280 days. Recent studies, however, using computerized day-counting techniques, show an average duration of 284.2 days.[1] Table 1 shows the mean values and statistical dispersion of gestational duration as well as a number of other gestational milestones.

Table 1. Mean observed intervals to delivery date for last menstrual period (LMP) and obstetric milestones*

Milestone	Mean interval to delivery (days)	Standard deviations (days)
Known LMP	284.2	14.6
Quickening	156.3	18.0
Fetal heart audible	136.2	17.0
Uterus at umbilicus	140.8	14.9

*Data from 418 patients.

(Andersen HF, Johnson TR, Flora JD, Barclay M: Gestational age assessment: II. Prediction from combined clinical observations. Am J Obstet Gynecol 140(7):770, 1981)

The changes brought about in the maternal organism by the state of pregnancy are important, because in many instances they mimic pathophysiologic responses to disease. If the constellation of changes occurring normally in pregnancy are misinterpreted as signs of disease processes, the gravid or puerperal woman may be subjected to diagnostic and therapeutic interventions that are not only unnecessary but may also be dangerous to mother and fetus.

Because so many system-specific changes occur in the course of pregnancy, it is difficult to develop a total physiologic overview. There are, however, a number of well-described adaptive physiologic states that produce changes in human systems similar to those seen in pregnancy. These adaptive states may be used as models or constructs to help integrate the diverse alterations in physiologic systems that occur during the course of normal gestation. Among the physiologic states that produce adaptive changes similar to those seen in pregnancy are the presence of a moderate-sized arteriovenous fistula, acclimation to increased environmental or internal heating, and adjustments to increasing levels of circulating progesterone.

MODELS OF PREGNANCY AS A PHYSIOLOGICALLY ADAPTED STATE

Model I: Pregnancy as an Arteriovenous Fistula

In 1938, Burwell and associates suggested that there are strong similarities between the physiologic alterations seen in normal pregnancy and those seen in patients with large arteriovenous fistulas. Patients on chronic renal dialysis who have peripheral shunts constructed for purposes of dialysis typically have flow rates in their shunts of approximately 600 ml/minute. Because uteroplacental flow rates at term (nearly 600 ml/minute) are essentially the same as those in the artificially produced shunts, it is not surprising that there are similarities between the cardiovascular changes in the shunted patients and cardiovascular alterations in the pregnant woman, particularly as she approaches term.

In both of these circumstances there is evidence of increased peripheral circulation, decreased peripheral resistance, increased heart rate, increased cardiac output, and increased plasma volume. This particular model can be used to explain a number of other changes related not directly to the shunting mechanism but to secondary changes produced by increased peripheral circulation, such as increased renal plasma flow and the physiologic alterations associated with increased renal perfusion.

Model II: Pregnancy as a State of Heat Adaptation

Abrams and associates and others have shown that there is a considerable temperature gradient between the mother and fetus. Aortic temperature measurements made in the pregnant ewe indicate that the fetal core temperature exceeds that of the mother by 0.5°C, which is a significant amount. Thermodynamics and the physics of heat transfer suggest that because of this temperature difference, the flow of heat from the fetus to the mother is relatively constant. As a result, the maternal organism must adjust her thermoregulatory system to permit increased heat loss to the environment. Aside from physical considerations, the need for maternal thermoregulatory adjustments is suggested by the observation that homeothermic mammals function within a very narrow range of internal temperatures. Extremes in either direction produce significant alterations in the function of fundamental systems responsible for the maintenance of life.

Responses of the homeothermic mammal to internal and environmental heating produce similar physiologic alterations. These include increased respiratory rate, increased cardiac output, increased heart rate, expansion of plasma volume, increased peripheral circulation, and a number of other changes similar to those seen in normal human gestation.

Model III: Pregnancy as a Hyperprogestational State

With the onset of normal gestation, all maternal systems are subjected to increasing levels of circulating progesterone. At first the corpus luteum of pregnancy, and later the placenta, produce large amounts of this hormone. At term, serum levels may be as high as 2.5 times those considered normal in the menstruating woman.

Increased basal body temperature and changes in the smooth muscle dynamics of the uterus, the vascular system, the urinary system, the gastrointestinal system, and the respiratory system in pregnancy have often been explained on the basis of increasing levels of serum progesterone. The mechanism proposed to explain many of these changes relates to the effect of progesterone on the electrochemical gradient at the cell membrane of individual smooth muscle fibers.[7] According to this hypothesis, progesterone acts to hyperpolarize the cell membrane, depressing the resting electrical potential at the membrane to a level below that of the normal activation threshold. This effectively puts the muscle at rest, because much greater levels of stimulation are required to produce depolarization and subsequent muscle contraction. Decreased tone and overall decrease in contractile activity is seen in most of the structures that depend on smooth muscle for their action. This includes the uterus, gut, respiratory system, ureters, and peripheral vascular system.

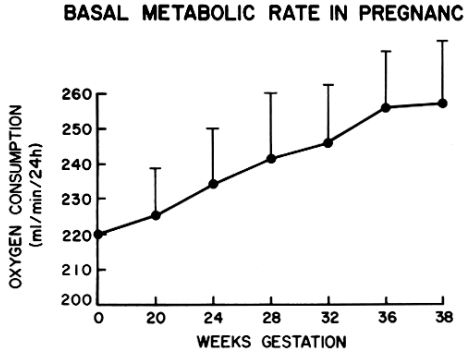
Volume expansion of the intravascular space, decreased peripheral resistance, increased heart rate, and a number of other alterations associated with the pregnant state could theoretically be explained on the basis of progesterone's effect on smooth muscle.

Overall, it seems unlikely that a single model can be invoked to explain the varied changes that take place in the human female during the course of gestation. It is more likely that all of these mechanisms contribute, along with other factors still unidentified, to the myriad changes that constitute the physiologic alterations

associated with the normal human gestation. Each model, nonetheless, helps the clinician to anticipate and integrate the changes in many of the altered systems. The constructs described permit the alterations in individual systems to be fused into a more coherent overview.

METABOLIC CHANGES

Basal metabolic studies carried out in the 1920s and 1930s by Sandiford and Wheeler and Rowe and Boyd demonstrated that pregnancy is characterized by increased metabolic activity as measured by the basal metabolic rate. In these studies, done on a small group of women throughout gestation, they found that the basal metabolic rate increased by approximately 20% as the pregnancy approached term. This trend is pictured in Figure 1. The researchers hypothesized that this increase in metabolic activity primarily represented increased fetal and placental metabolic work, with only a small fraction being attributable to increased maternal metabolic activity. At term, the products of gestation were estimated to be responsible for approximately 13% of the 20% increase in total metabolic activity. More modern studies using oxygen consumption measures and indirect calorimetry estimate the energy output of an average-sized pregnant woman at 36 weeks' gestation to be approximately 98 W (8443 ± 243 kJ/day). This compares with an energy output of approximately 81 W (6971 ± 172 kJ/day) for a similar-sized, nonpregnant, nonlactating woman. Although the more recent studies used different methodologies, they all support the results of the earlier work.



Picture. 7. Metabolic requirements for oxygen during the course of normal pregnancy in 11 normal pregnant women. (Based on data of Emerson K, Saxena GN, Poindexter EL, et al: Caloric cost of normal pregnancy. Obstet Gynecol 40(6):786, 1972).

During the course of normal pregnancy, basal body temperature is elevated. The increased metabolic activity manifested early in the gestation, along with the effects of progesterone, may be responsible for this phenomenon.

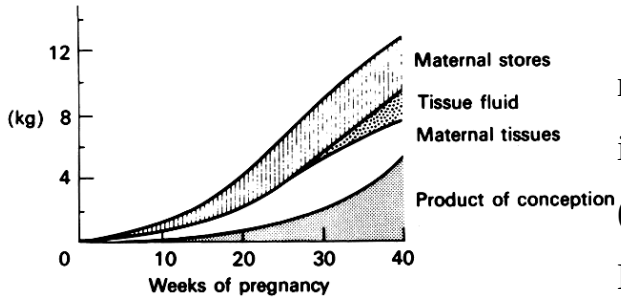
WEIGHT GAIN

Weight gain, one of the hallmarks of pregnancy, has been extensively studied as it relates to the well-being of the fetus and infant. Optimal weight gain in pregnancy has been the subject of considerable discussion, and attitudes regarding what is appropriate have changed with time, even in recent history. Currently, a total weight gain of 10–12 kg is thought to be appropriate. The partitioning of this weight gain and its distribution are illustrated in Table 2 and Figure 2.

Table 2. Average components of weight gain in pregnancy and cumulative gain at the end of each trimester (kg)

Component	**I**	**II**	**III**
Fetus	0	1.0	3.4
Placenta	0	0.3	0.6
Amniotic fluid	0	0.4	1.0
Fetal total		1.7	5.0
Uterus	0.3	0.8	1.0
Breasts	0.1	0.3	0.5
Blood volume	0.3	1.3	1.5
Extracellular fluid	0	0	1.5
Maternal total	0.7	2.4	4.5

(After Pitkin R, Kaminetsky H, Newton M et al: Maternal nutrition. A selective review of clinical topics. Obstet Gynecol 40(6):773, 1972)



Picture 8. Maternal weight gain in normal pregnancy divided in terms of individually identifiable components. (Hytten FE, Leitch I: The Physiology of Normal Pregnancy. Oxford, Blackwell Scientific Publications, 1964)

The total maternal weight gain indicated in Table 2 is that portion that can be explained in terms of measurable elements and is less than the 10–12-kg increase described as optimal. The difference is usually ascribed to fat storage in maternal tissues.

Weight gain in pregnancy is negligible in the first trimester, as can be seen in Table 2 and Figure 2. In the second and third trimesters, weight gain is much more appreciable and, according to the work of Hytten and Leitch, averages approximately 0.41–0.45 kg/week (0.9–1.0 pounds/week) in normal pregnancies in primigravidas.

NUTRITION

Studies carried out in Third World countries indicate that maternal malnutrition may interfere, at least epidemiologically, with appropriate intrauterine nutrition. Women who were marginally nourished before pregnancy deliver a higher proportion of premature and low-birth-weight infants. Feeding programs in Guatemala, Colombia, and other emerging nations have provided information that suggests that the proper nourishment of the pregnant woman may be of considerable benefit to her fetus.

Nutritional authorities in the United States and much of the Western World have established suggested programs for appropriate nutrition in pregnancy. Basically, pregnant women require calories additional to the normal daily requirement. These recommendations, although variable from country to country,

also suggest the addition of protein, iron, and other mineral and vitamin supplements to provide the necessary materials for fetal *and* maternal welfare during the course of gestation. Although common sense indicates that appropriate nutrition is important for maximizing the possibility of healthy offspring, Hytten and Leitch and others have pointed out that it is difficult to focus on nutrition alone as a factor in the growth and development of normal babies. Women who are appropriately nourished during the course of pregnancy are also usually better housed, better educated, and have greater access to the medical antepartum care that seems to be associated with improved pregnancy outcomes. Antepartum nutrition, however, continues to be an area of great interest because the feeding of pregnant women is a simple intervention that may have a significant impact on the outcome of reproduction. The current recommendations proposed by the Food and Nutrition Board of the US National Science Foundation are listed in Table 3.

Table 3. Recommended dietary allowances (Revised in 2005)*

Nutrient	**For nonpregnant woman**	**For pregnant woman**
Protein	45 g/day	+ 30 g/day
Calories	2100	+ 300
Calcium	1000 mg/day	No supplementation
Iron	18 mg/day	+ 9 mg/day
Folic acid	400 μg/day	+ 200 μg/day
Ascorbic acid	75 mg/day	+ 10 mg/day

*Food and Nutrition Board, Institute of Medicine. Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids. Washington, DC, National Academies Press, 2005.

Caloric Requirements

Maternal mass increases by approximately 20% during the course of normal gestation. This increase in mass and the metabolic needs of the fetus require additional calories above the recommended daily allowance. In 1989, the Food and Nutrition Board of the National Academy of Sciences suggested that 300 additional calories be added to the diet of pregnant women to compensate for the additional needs of fetal growth and increased maternal metabolism. In pregnant adolescents, or those still in their active growth phase, additional calories beyond this recommendation are required to sustain needs related to maternal growth. The basal calorie levels for any woman can be determined from tables that take height and body habitus into consideration. A pregnant woman of average size requires approximately 2200 calories/day (Table 3).

Protein Requirements

On the basis of nitrogen balance studies, the Food and Nutrition Board has recommended that an extra 30 g of protein be supplied to pregnant women in addition to the basic requirement based on age and size. In the average-sized woman, this constitutes a total daily protein ration of 44–46 g/day (0.88 g/kg/day) plus the 30 gram supplement (Table 3).

Iron and Mineral Requirements

Iron supplementation is recommended in pregnancy by virtually all nutritional authorities. The requirements of the fetus and placenta and increased maternal red cell production require approximately 500 mg of elemental iron during the course of a normal pregnancy. This exceeds what most women have in terms of physiologic iron stores. The Food and Nutrition Board recommends 27 mg/day of supplemental iron during the course of pregnancy. This amount is usually present in prenatal vitamins. If the maternal diet is likely to have been deficient in iron before

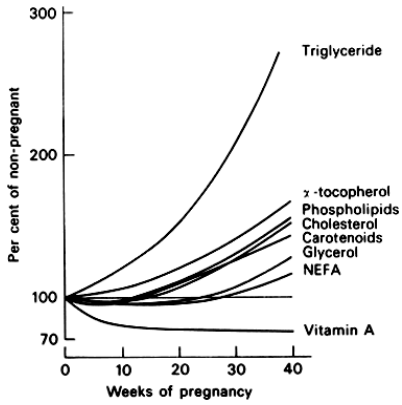
pregnancy, iron stores may be significantly less than normal, and additional iron supplementation should be considered.

Folic acid is a coenzyme essential in purine and pyrimidine metabolism and in the synthesis of DNA. Clinical evidence of folic acid deficiency is usually first evident in tissues that have rapid cell turnover, notably in hematopoiesis. Megaloblastic anemia of pregnancy as a result of inadequate intake of folic acid is not a rare cause of anemia in pregnant women in the United States. Prenatal multivitamins with folic acid often contain 1 mg of folate, which exceeds the recommended supplement.

PLASMA LEVELS OF NUTRIENTS

Changes in nutrients and related materials in the plasma of pregnant women suggest fundamental alterations in the manner in which they handle these materials. Total protein levels fall in pregnancy to levels about 1000 mg/dl less than those observed in the nonpregnant woman. Much of this decrease is in the albumin fraction, which is important in terms of its effect on the colloid osmotic pressure. Lowering of the colloid osmotic pressure allows water to flow from the plasma into cells or from vessels into the extracellular space. Globulins show a relatively small increase in serum concentration during the course of normal pregnancy. Levels of fibrinogen, an important protein in normal blood coagulation, as well as factors VII, VIII, IX, and X, are appreciably increased in the pregnant state. The increased concentration of fibrinogen (approximately 50%), is thought to be responsible for the commonly observed increase in erythrocyte sedimentation rate.

Lipid concentration in the serum is markedly increased in pregnancy (Fig. 3). Triglycerides, phospholipids, cholesterol, and free fatty acids increase markedly in amount. The increase in serum cholesterol seems to occur regardless of the dietary habits of the gravida; vegetarians show the same increase as those who eat meat.

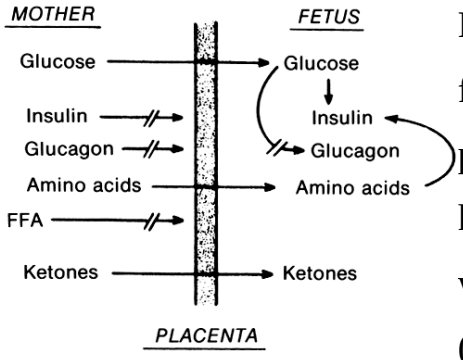


Picture 9. Relative changes in the plasma concentration of various lipids during the course of pregnancy. The normal or nonpregnant level is expressed as 100%. (Hytten F, Chamberlain G: Clinical Physiology in Obstetrics. Boston, Blackwell Scientific Publications, 1980)

CARBOHYDRATE METABOLISM

Carbohydrate metabolism is altered in the course of normal pregnancy, and the pregnant state has been characterized as diabetogenic. Previously undiscovered diabetes may be unmasked during the course of pregnancy, or a woman may develop diabetic levels of blood glucose as a response to pregnancy.

In the fasting state, glucose is transferred to the fetus from the maternal circulation, producing a decrease in maternal serum glucose levels. The major effects of pregnancy on glucose metabolism are related to the fact that the fetus withdraws glucose from the maternal circulation. In a study by Bleicher and colleagues, average plasma glucose values in antepartum women (75.2 mg/dl; standard error of the mean [SEM] = ±2.8 mg/dl) were significantly lower than those in postpartum women (92.5 mg/dl; SEM = ±2.7 mg/dl). This phenomenon is thought to occur because the fetus uses glucose almost exclusively as its metabolic fuel. The rate of delivery of glucose to the fetal circulation is thought to be controlled by the difference in serum concentrations between maternal and fetal serum levels. Glucose also seems to be transferred across the placenta by means of facilitated diffusion. Placental transfer of glucose and other materials related to carbohydrate handling in pregnancy is pictured in Figure 4.



Picture 10. A schematic representation of maternal-fetal nutrient and hormone exchange across the placenta in pregnancy. Glucose, amino acids, and ketones move freely into the fetal circulation, whereas insulin, glucagon, and free fatty acids (FFA) do not. Maternal hyperglycemia and ketosis are thus reflected in the fetal circulation. (Felig P: Body fuel metabolism and diabetes mellitus in pregnancy. Med Clin North Am 61(1):43, 1977)

Glucose utilization studies demonstrate that the fetus uses glucose at a rate of 6 mg/kg/minute at term. This rate is quite high compared with that in the normal adult, which is approximately 2.5 mg/kg/minute.In addition to glucose, amino acids are freely transported across the placenta into the fetal circulation. This transfer produces maternal hypoaminoacidemia, particularly of alanine, an important precursor of glucose in gluconeogenesis. With the fall in serum glucose levels, there is an associated decrease in plasma insulin, producing what Felig has referred to as an accelerated and exaggerated response to starvation. This is one explanation of the elevation in free fatty acids and triglycerides seen in the mother.

In pregnancy, feeding produces hyperglycemia, an increase in serum insulin levels, and hypertriglyceridemia. There is also a diminished response to insulin. The diminished response to insulin, which may be mediated hormonally, produces aberrations in blood sugar testing using both oral and intravenous loading with glucose. Adjusted norms are therefore necessary to diagnose diabetes in pregnancy. Bleicher and others have hypothesized that these changes are related and that the purpose of these changes in the carbohydrate metabolism of the mother is the protection of fetal tissues from fluctuations in glucose by switching the maternal tissues over to free fatty acid and triglyceride metabolism. The placental production of lactogen, a substance known to have lipolytic properties, is thought to explain these phenomena. The anti-insulin effects of placental lactogen seem to provide

additional evidence for this hypothesis. The complexities of carbohydrate metabolism in pregnancy, although partially elucidated, continue to be confusing and require further investigation.

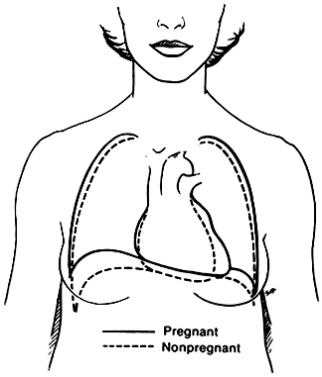
ALTERATIONS IN THE CARDIOVASCULAR SYSTEM

Regardless of the etiologic factors in the many changes that occur in the physiology of the pregnant woman, the system that undergoes some of the most significant alterations is the cardiovascular system. The changes in this system are quite profound and begin to occur almost at the time of conception. Lindhard's observations in 1915 that the cardiac output is increased in pregnancy formed the basis for much of the work subsequently done in delineating the multiple changes that occur in circulatory physiology in the pregnant woman.

Anatomic Alterations

The position of the heart in the chest changes during the course of normal pregnancy. It is rotated slightly, and its apex deviates to the left. Thus, on physical examination of the chest of the pregnant woman, the point of maximum intensity of the cardiac action is often lateral to the midclavicular line and in the fourth rather than the fifth intercostal space.

Because of these changes in position and slightly increased cardiac volume (70–80 ml), the area of relative dullness over the precordium is increased, as is the cardiac shadow on x-ray examination. Lateral x-ray films of the pregnant woman's thorax may, in fact, show findings suggestive of atrial dilation, which is suggestive of stenotic mitral valvular disease. These alterations in morphology are pictured in Figure 5. The changes in heart position, increased output, and increased blood volume are probably responsible for the systolic flow-type murmur that is common in pregnancy.



Picture. 11. Morphologic changes in the heart and lungs. The figure shows the alterations produced by pregnancy. Left axis deviation, changes in the electrocardiogram, and alterations in physical findings are common concomitants of normal pregnancy. (Bonica J: Principles and Practice of Obstetric Analgesia and Anesthesia. Philadelphia, FA Davis, 1967)

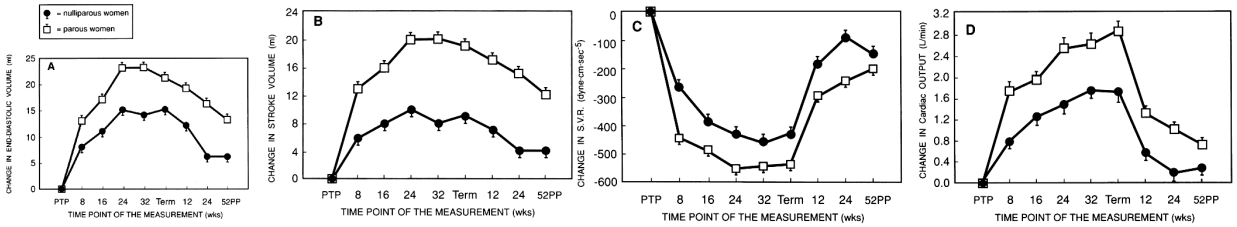
Electrocardiographic Changes

These changes in cardiac position, presumably brought about by some of the functional changes in cardiodynamics, induce certain changes in the electrocardiographic (ECG) findings associated with pregnancy. As would be anticipated, ECG findings are suggestive of left axis deviation of approximately 15 degrees. There may be decreased voltage in the QRS complexes, as well as alterations in T and P waves. In a number of normal pregnant women, there may be flattening or inversion of T waves in lead III, as well as depression of the S-T segment in limb and chest leads. These findings, which are suggestive of myocardial ischemia, have been reported to occur in as many as 14% of normal pregnant women in whom none of the other demonstrable concomitants of true myocardial disease are seen. When this finding occurs in a pregnant woman, it tends to recur in subsequent pregnancies. Cardiac arrhythmias, particularly those of supraventricular origin, are also relatively common in pregnancy but are not generally productive of symptoms significant enough to require therapy.

Alterations in Cardiodynamics

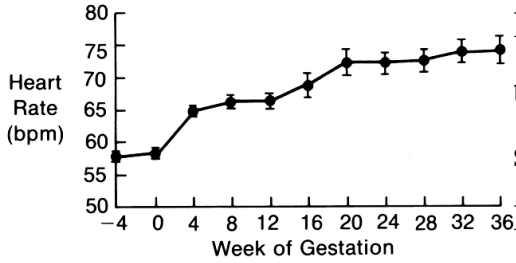
Beginning early in pregnancy, cardiac output increases significantly to maximum levels at around 20–24 weeks (Fig. 6) and maintains that level until after delivery. It is generally accepted that in the course of pregnancy the cardiac output increases to levels 30–35% in excess of that in the nonpregnant woman. Recent work by Clapp and Capeless has demonstrated that this increase in cardiac output may be

enhanced in subsequent pregnancies. Stroke volume and end-diastolic volume are altered in a similar manner. Systemic vascular resistance is also significantly altered.



Picture 12. Changes in cardiovascular dynamics during the course of primiparous and subsequent pregnancies (after Clapp AF III, Capeleas E: Am J Cardiol 80:1469–1473, 1997)

The factors responsible for the change in cardiac output are not completely understood but are thought to be related to one or several of the mechanisms noted in the introductory remarks in this chapter or, more likely, to some combination of all these factors. Almost all of the theories used to explain the observed changes implicate either neurohumoral factors, such as estrogen and progesterone, or the placental circulation acting as an arteriovenous fistula. Maternal heart rate is increased in pregnancy, consistent with a functional arteriovenous fistula; the increase averages approximately 15 beats/minute. Figure 7 demonstrates the increase in heart rate as pregnancy progresses.



Picture 13. Changes in maternal heart rate during the course of gestation. A progressive increase is shown as pregnancy approaches term. (Clapp J: Maternal heart rate in pregnancy. Am J Obstet Gynecol 152(3):251–252, 1985)

Clinical symptoms and findings may be related to these alterations in normal cardiovascular dynamics. The pregnant woman has less measurable cardiac output, as well as decreased uterine perfusion, when in the supine position. The supine hypotensive syndrome, which is characterized by hypotension, tachycardia, diaphoresis, and discomfort, may become magnified by the effects of a conduction

anesthetic that increases venous pooling and further reduces venous return to the heart. By positioning the patient to produce leftward deviation of the uterus, such postural changes in vital signs may be avoided and the need for vasopressors obviated. The case reports of O'Connor and Sevarino, as well as DePace and colleagues, suggest that an appreciation of this posture-related effect may be important in the successful cardiopulmonary resuscitation of pregnant women who have sustained a cardiac arrest.

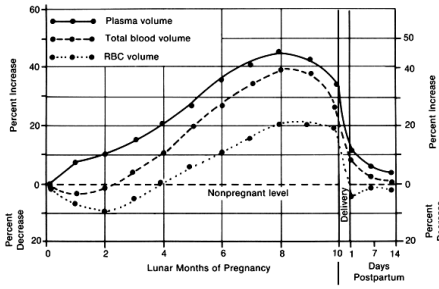
Rapid changes in body position may produce syncope or lightheadedness because of decreased peripheral resistance in the lower extremities. These effects may be further intensified when warm environmental conditions contribute to peripheral vasodilatation. Theories relating to the effects of changes in cardiovascular dynamics on the metabolic heat production of the fetus and other products of conception are notably absent from most discussions of these phenomena, although significant fetal heat production is demonstrable in mammalian gestations.

Intravascular Volume Changes

Large expansion of the intravascular volume, particularly plasma volume, is one of the hallmarks of normal pregnancy. Plasma volume increases to a significant extent early in pregnancy. Maternal blood volume expansion of 40% is not unusual in singleton pregnancy and may be even greater in multiple gestations. This expansion in blood volume is due to an increase in plasma volume of 45–55% and an increase in red cell mass of 20–30%.

The rapid increase in plasma volume, depicted in Figure 8, outstrips the manufacture of new red cells and may produce a virtual anemia in early pregnancy. The increase in plasma volume without a concomitantly rapid production of red cell mass is manifested in an apparent drop in the hemoglobin concentration, hematocrit, and red blood cell count. This plasma expansion requires that the definition of

anemia in pregnancy be altered so that a pregnant woman is not considered anemic in most centers until the hemoglobin falls below 10 g/dl. The red cell mass increases in the course of pregnancy by 20–30%, or approximately 250–500 ml of packed red cells.

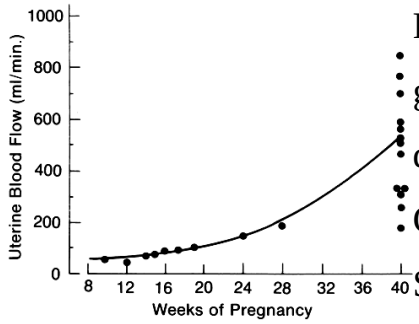


Picture 14. Expansion of plasma volume, total blood volume, and red cell volume in the course of normal gestation. The rapid expansion of plasma volume exceeds the rate of red cell production early in gestation, producing a decrease in hemoglobin and hematocrit concentration. (Bonica J: Principles and Practice of Obstetric Analgesia and Anesthesia. Philadelphia, FA Davis, 1967)

The reasons for this plasma volume expansion are probably numerous, and all suggested major causative factors, including the effects of hormonal level changes, the decrease in peripheral resistance produced by the placental and uterine shunting mechanisms, and heat-adaptive mechanisms, are likely involved to some extent. The role of increased cardiac output in the genesis of these changes is also somewhat speculative in that it is presently uncertain how plasma volume expansion is temporally related to increased cardiac output. To explain this phenomenon, Longo has proposed a set of mechanisms that integrate the effects of various pregnancy hormones, including estrogen and progesterone, as well as the known effects of pregnancy on the renin-angiotensin system and human placental lactogen, coupled with the changes presumably brought about by the increased uterine and placental circulation flow rates as pregnancy approaches term.

The changes in blood volume and plasma volume are associated with changes in the distribution of cardiac output. As the uterine contents increase in size and requirements for oxygen and nutrient materials grow, there is an increase in the volume of uterine artery blood flow. The studies of Romney and colleagues indicate that the increase in uterine perfusion is associated with the increasing size of the

products of conception. The flow rates in the uterine and placental circulation approximate roughly 10 ml/minute per 100 g of fetal tissue. The association between the mass of the conceptus and uterine blood flow in terms of gestational age is displayed in Figure 9.



Picture. 15. Uterine blood flow at various stages of gestation. The flow increases significantly with the duration of pregnancy. (Hytten F, Chamberlain G: Clinical Physiology in Obstetrics. Boston, Blackwell Scientific Publications, 1980)

Alterations in Formed Elements of the Blood

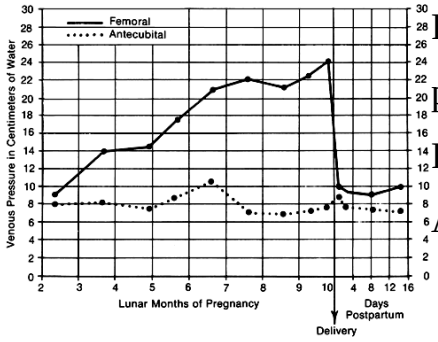
Normal pregnancy is characterized by leukocytosis. This increase in white cell count is mostly due to increased numbers of polymorphonuclear leukocytes, which increase in number from the time of fertilization until the time of labor. A study by Griffin and Beck indicates, as does older literature, that leukocyte counts increase significantly from their previously elevated level in pregnancy at around 35 weeks of gestation and continue to rise until the time of parturition. At the time of delivery in this study, the leukocyte counts were in excess of $14{,}000 \times 10^3$ cells/ml (standard deviation = $\pm 1.62 \times 10^3$ cells/ml). Perhaps because of the rapid production of new cells, a small number of myelocytes or metamyelocytes are normally present in the pregnant woman's peripheral circulation.

Lymphocyte and monocyte numbers are not altered significantly during the course of pregnancy, but eosinophil levels are reported to decrease sharply during labor and delivery. Basophil levels may be reduced in pregnancy.

Platelets are an important element in the coagulation process; their levels decrease slightly during the course of pregnancy. This decrease may be a function of the increase in plasma volume and is not reported to be associated with any significant change in platelet function.

Alterations in Venous Pressure

The state of pregnancy, either through the effects of progesterone on the veins of the periphery or via the shunting mechanisms of placental circulation, increases the venous capacitance. This is more marked in the lower extremities, where dependent edema is seen in as many as 30% of pregnant women at some time during the gestational period. Venous pressure above the level of the umbilicus is generally normal, whereas that below the level of the umbilicus is elevated. These changes are portrayed in Figure 10.



Picture 16. Venous pressure changes associated with pregnancy in femoral and antecubital veins. (Bonica J: Principles and Practice of Obstetric Analgesia and Anesthesia. Philadelphia, FA Davis, 1967)

The clinical effects of this elevation in venous pressure are thought to be responsible for the pedal and pretibial edema seen in many pregnancies, particularly approaching parturition. The increased severity of varicosities of the lower extremities and of the vulva and vagina, as well as hemorrhoids, may be at least partially explained by this effect. Obstruction of the venous return to the right heart as a result of uterine compression of the vena cava producing supine hypotensive syndrome has been mentioned as a cause of hypotension following the administration of conduction anesthesia; spinal, epidural, and caudal anesthesia produce sympathetic blockade, which increases the venous capacitance to even greater levels than that already produced by the effects of progesterone on the smooth muscle of the vessels.

The increased venous pressure below the level of the umbilicus also suggests the use of alternative paths for venous return to the heart, including the azygos and hemiazygos systems and the paravertebral and epidural veins. Such pathways,

particularly the paravertebral and epidural pathways, may be responsible for the decrease in volume of the subarachnoid space. Because of this change, smaller amounts of anesthetic drugs are required for the induction of spinal anesthesia. This is an important point, because excessively high levels of spinal anesthesia may be obtained with what would be a usual dosage in a nonpregnant woman.

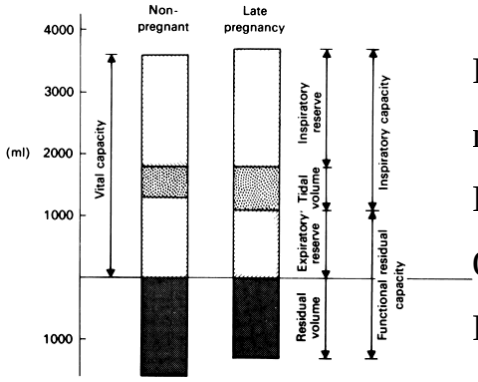
Cardiac examination in pregnancy:

- Many women have a third heart sound after mid-pregnancy.
- Diastolic murmurs should be considered potentially pathological.
- Systolic flow murmurs are common.
- ECG - left axis deviation is common, sagging ST segments and inversion or flattening of the T wave in lead III may also occur.

Respiratory Changes

Along with the changes in the cardiovascular system, numerous changes occur in the pulmonary physiology that reflect changes in lung perfusion and the mechanisms of lung action. As would be expected from the increase in fetal requirements for oxygen as its mass increases, the changes in pulmonary physiology reflect the process of fetal growth. The changes that occur as a result of that growth include changes in the profile of the maternal chest and, obviously, in the level and movement of the diaphragms, which are mechanically interfered with by the presence of the gravid uterus and the displacement of the peritoneal contents. The circumference of the chest in pregnancy increases as the subcostal marginal angle is increased from approximately 70 degrees to more than 100 degrees near term, and the transverse diameter of the chest increases by nearly 2 cm. Although the respiratory rate in pregnancy is not appreciably increased, the pregnant woman experiences a relative hyperventilation during the course of pregnancy. The tidal volume, normally 450 ml/minute, is increased to 650 ml/minute, producing a

greater gaseous exchange despite the same frequency of inspiration and expiration. These alterations in functional parameters are depicted in Figure 11.



Picture. 17. Changes in pulmonary volume measures associated with normal gestation. (Hytten F, Chamberlain G: Clinical Physiology in Obstetrics. Boston, Blackwell Scientific Publications, 1980)

The etiologic factors in the changes in the functional elements of respiration are obscure because the changes seen may be mediated by any number of stimuli present in pregnancy. Increased demand for oxygen for the growing fetus, the need for increasing heat transfer to the external environment, and the effects of progesterone may all play some role in the genesis of the ventilatory changes that take place in the course of normal gestation. The progesterone-related argument is especially cogent because it has recently been demonstrated in animal models that progesterone administered chronically induces hyperventilation in a dosage-related fashion. Factors related to hyperventilation, such as increased arterial pH and decreased PCO_2, are also altered in the progesterone-treated animals in a manner similar to that seen in the pregnant human woman.

Renal Changes

Increased cardiac output results in an increased volume of blood flow to the kidneys. Because of this increase in blood flow, the kidneys are perfused with larger amounts of blood, and therefore with larger amounts of solute and water volume, than usual; thus the kidneys do more filtering of the blood. This extra kidney filtering action reduces the values of some common laboratory blood tests; blood urea nitrogen levels are decreased markedly, as are creatinine levels.

Morphologic changes occur in the kidneys and collecting systems. Marked hydronephrosis and hydroureter often are present in normal pregnant women. In

Fried's series of studies of 109 normal pregnant women, the incidence of hydronephrosis and hydroureter by ultrasonic measurements was 93.6%. In this study, the right side was more profoundly affected than the left. These new data support earlier work using radiographic techniques. These changes are thought to be due to the effects of progesterone or the mechanical obstruction of the ureters and renal pelves by the gravid uterus or markedly distended ovarian veins. The right-sided ureteral and renal dilatation may be produced by pressure on the right ureter at the level of the pelvic rim. On the left side, the ureter is protected and padded by the presence of the sigmoid colon. The increased volume of the collecting system and ureters is thought to predispose to upper urinary tract infection by increasing the urinary dead space and possibly the amount of reflux from the bladder to the ureters.

As the pregnancy progresses, the glomerular filtration rate increases, and it does so more significantly than can be explained by increased cardiac output alone. Atherton and Green have suggested that the mechanisms producing this disparate increase may be related to increased prolactin or dopamine secretion in the pregnant woman. In most studies using rats, progesterone has not had this effect. With cardiac output increasing by 30–35% and renal plasma flow increasing by more than 50%, the tubular reabsorptive capacity for several substances is exceeded. This produces conditions such as glycosuria and aminoaciduria. Although values vary, about 12–15% of gravid women have glycosuria at some time during their pregnancy, often shortly after the woman eats foods high in simple sugars. Lactose and other sugars may also appear in the urine in the course of the pregnancy.

SALT AND WATER

Despite the increase in sodium and water presented to the glomerulus in pregnancy, more reabsorption of both occurs than in the nongravid situation. This implies an increase in total body water of approximately 6–8 L, as well as an increase in sodium content of nearly 950 mEq/L. Among the hormones that are increased in the serum during the course of pregnancy, several have been noted to produce

sodium loss. Among these are progesterone (a partial inhibitor of aldosterone), prostaglandins, and dopamine. Atherton and Green have suggested that several other circulating hormones may act as antinatriuretics. Among these, cortisol, deoxycortisone, estrogen, human placental lactogen, and prolactin may all have some role in opposing the salt-losing properties of progesterone. In addition, the decrease in serum protein concentration, the decrease in arterial pressure, and the effects of postural changes in blood flow in pregnancy may act together in determining the final amount of sodium reabsorption in the pregnant state. The changes in renal physiology in pregnancy, although manifold and presumably related to other changes in maternal physiology, remain somewhat obscure in terms of the underlying mechanisms in pregnancy and where these mechanisms act in the glomerulus and tubule.

THE GASTROINTESTINAL SYSTEM

Among the other profound changes that occur in the course of normal gestation are many alterations in the physiology of the gastrointestinal system. The most marked of these are probably related to the global effects of progesterone on the smooth muscle, which makes up the largest portion of the gut. Kumar, and more recently Gill and colleagues, have described the effects of progesterone on extrauterine smooth muscle. Progesterone has the effect of producing a dose-dependent and reversible inhibition of the electrical and mechanical events associated with the contraction of smooth muscle fibers. Lawson and colleagues demonstrated prolongation of gastrointestinal transit time in the second and third trimesters but showed no statistical differences from the nonpregnant state in the first trimester or postpartum.

Depression of muscular tone and action may explain the numerous alterations commonly seen in the pregnant woman; these alterations may have clinical implications. The increased occurrence of regurgitation and often troublesome pyrosis of pregnancy may be explained by decreased tone at the cardioesophageal

junction, as well as by increased intraabdominal pressure. In animal models, Fisher and associates demonstrated decreased activity of the circular smooth muscle in the lower esophagus in response to both estrogen and progesterone. Decreased muscle action also explains the increased emptying time of the stomach and duodenum, as well as the delay in gallbladder emptying. Constipation may be related to this phenomenon as well, in that decreased colonic motility may provide the opportunity for increased water removal from the stool. This mechanism may aggravate hemorrhoids produced by the increased venous pressure below the level of the gravid uterus.

The major clinical implications of these processes in the gastrointestinal system are most relevant to the problems produced in the administration of general anesthesia. However they are mediated, the effects of pregnancy on the motility of the entire gastrointestinal system make virtually every pregnant woman who requires a general anesthetic during labor a high-risk patient for aspiration pneumonia. Aspiration of gastric contents during or after the administration of general anesthesia continues to be an important cause of maternal mortality. When general anesthesia is indicated, often under emergent conditions, endotracheal intubation should be performed

SKIN CHANGES

Pregnancy produces many changes in the skin that, although physiologic, may cause some concern in the pregnant woman. Among these changes is hyperpigmentation, which often occurs in the areolae, the perineal skin, the anal region, the inner thighs, and the linea nigra, which appears on the abdominal wall. Melasma or chloasma is a blotchy, sharply marginated hyperpigmentation that occurs on the face of dark-haired and dark-complexioned women. It is most often centrally distributed on the face.

Vascular “spiders” occur in about 67% of white patients and 11% of black patients by the time pregnancy has reached the third trimester. These lesions occur on the neck, throat, face, and arms. Most of these fade after the seventh postpartum week. Circulating estrogens in high levels are thought to be responsible for the appearance of these lesions.

Palmar erythema, which is also common in liver disease, hyperthyroidism, and collagen vascular diseases, appears commonly in pregnancy. Approximately 67% of white women and 33% of black women experience palmar erythema during the course of gestation. Striae are common among white women in late pregnancy but are less common in black and Asian women. There seems to be a familial tendency in the occurrence of these lesions. When they occur, they first appear during the sixth and seventh months of gestation on the abdominal skin; they then occur on the breasts, upper arms, lower back, buttocks, and thighs. The cause of these lesions is unclear, but they have been related to a combination of stretching of the skin and increased levels of corticosteroids and estrogen in pregnancy.

Endocrine system (non-reproductive)

Pituitary

- FSH/LH fall to low levels.
- ACTH and melanocyte-stimulating hormone increase.
- Prolactin increases.

Thyroid and parathyroid

- Thyroxine-binding globulin (TBG) concentrations rise due to increased oestrogen levels.
- T4 and T3 increase over the first half of pregnancy but there is a normal to slightly decreased amount of free hormone due to increased TBG-binding.

- TSH production is stimulated, although in healthy individuals this is not usually significant. A large rise in TSH is likely to indicate iodine deficiency or subclinical hypothyroidism.
- Serum calcium levels decrease in pregnancy, which stimulates an increase in parathyroid hormone (PTH).
- Colecalciferol (vitamin D3) is converted to its active metabolite, 1,25-dihydroxycolecalciferol, by placental 1α-hydroxylase.

Adrenal and pancreas

- Cortisol levels increase in pregnancy, which favours lipogenesis and fat storage.
- Insulin response also increases so blood sugar should remain normal or low.
- Peripheral insulin resistance may also develop over the course of pregnancy and gestational diabetes is thought to reflect a pronounced insulin resistance of this sort.

Interpreting blood test results in pregnancy

	Trend in normal pregnancy (compared to non-pregnant state)	**Pregnancy normal values (ALWAYS USE LOCAL REFERENCE RANGES)**	**Abnormalities and possible interpretations**
Haemoglobin	Decreased	10.5-13.5 g/dL	Consider dilutional anaemia of pregnancy.
White cell count	Increased	8-18 $x10^9$/L	Always consider in the light of the patient's clinical status.

Interpreting blood test results in pregnancy

Platelets	Unchanged/slightly increased	200-600 $x10^9$/L	Always consider in the light of the patient's clinical status.
Sodium	Slightly decreased	132-140 mmol/L	Always consider in the light of the patient's clinical status.
Potassium	Slightly decreased	3.2-4.6 mmol/L	Always consider in the light of the patient's clinical status.
Urea	Decreased	1.0-3.8 mmol/L	Increased in dehydration, hyperemesis, late stages of pre-eclampsia and renal impairment.
Creatinine	Decreased	40 - 80 μmol/L	Increased in renal impairment and the late stages of pre-eclampsia.
Fasting glucose	Unchanged	3.0-5.0 mmol/L	Increased in gestational diabetes.
Total calcium	Decreased	2.0-2.4 mmol/l	Increased in primary hyperparathyroidism.
Magnesium	Unchanged	0.6-0.8 mmol/L	Decreased if there is vomiting or hyperemesis gravidarum.

Interpreting blood test results in pregnancy

Albumin	Decreased	24-31 g/L	Decreased further if there is malnutrition, recurrent vomiting or hyperemesis gravidarum.
Bilirubin	Decreased	3-14 μmol/L	Increased in obstetric cholestasis, HELLP, the late stages of pre-eclampsia, acute fatty liver, viral hepatitis. See the separate article on Jaundice in Pregnancy.
ALT	Unchanged/slightly decreased	1-30 U/L	As for bilirubin.
AST	Unchanged/slightly decreased	1-21 U/L	As for bilirubin.
ALP	Increased	125-250 U/L	Increased further in metabolic bone disorders or rare pregnancy-associated conditions - eg, chronic histiocytic intervillositis.

Interpreting blood test results in pregnancy

TSH	Slight decrease in the first trimester, normal in the second trimester, slightly raised in the last trimester	0.1-4.0 IU/L	Less than 0.05 in Graves' disease or hyperemesis gravidarum.
fT4	Unchanged	10-25 pmol/L	Increased in Graves' disease or hyperemesis gravidarum.
fT3	Unchanged	3.5-6 pmol/L	Increased in Graves' disease or hyperemesis gravidarum.

SUMMARY

The pregnant state is characterized by a myriad of alterations in the normal physiology of the gravid woman. An understanding of some of the major mechanisms that produce these changes is helpful in the analysis of symptoms and problems that arise during the course of a normal gestation. When associated disease is present, understanding of these alterations becomes more important in that they must be distinguished from pathophysiologic changes wrought by the disease process. The interaction between disease and gestational physiology may make the appropriate diagnosis and management of the pregnant woman difficult. When a pregnant woman requires medical or surgical therapy, the consultative services of an obstetrician or clinician trained in the complexities of maternal physiology is absolutely critical to the proper management of clinical problems.

Physiology of labor and postpartum period.

Childbirth

Definition

Childbirth includes both labor (the process of birth) and delivery (the birth itself); it refers to the entire process as an infant makes its way from the womb down the birth canal to the outside world.

Description

Childbirth usually begins spontaneously, about 280 days after conception, but it may be started by artificial means if the pregnancy continues past 42 weeks gestation. The average length of labor is about 14 hours for a first pregnancy and about eight hours in subsequent pregnancies. However, many women experience a much longer or shorter labor.

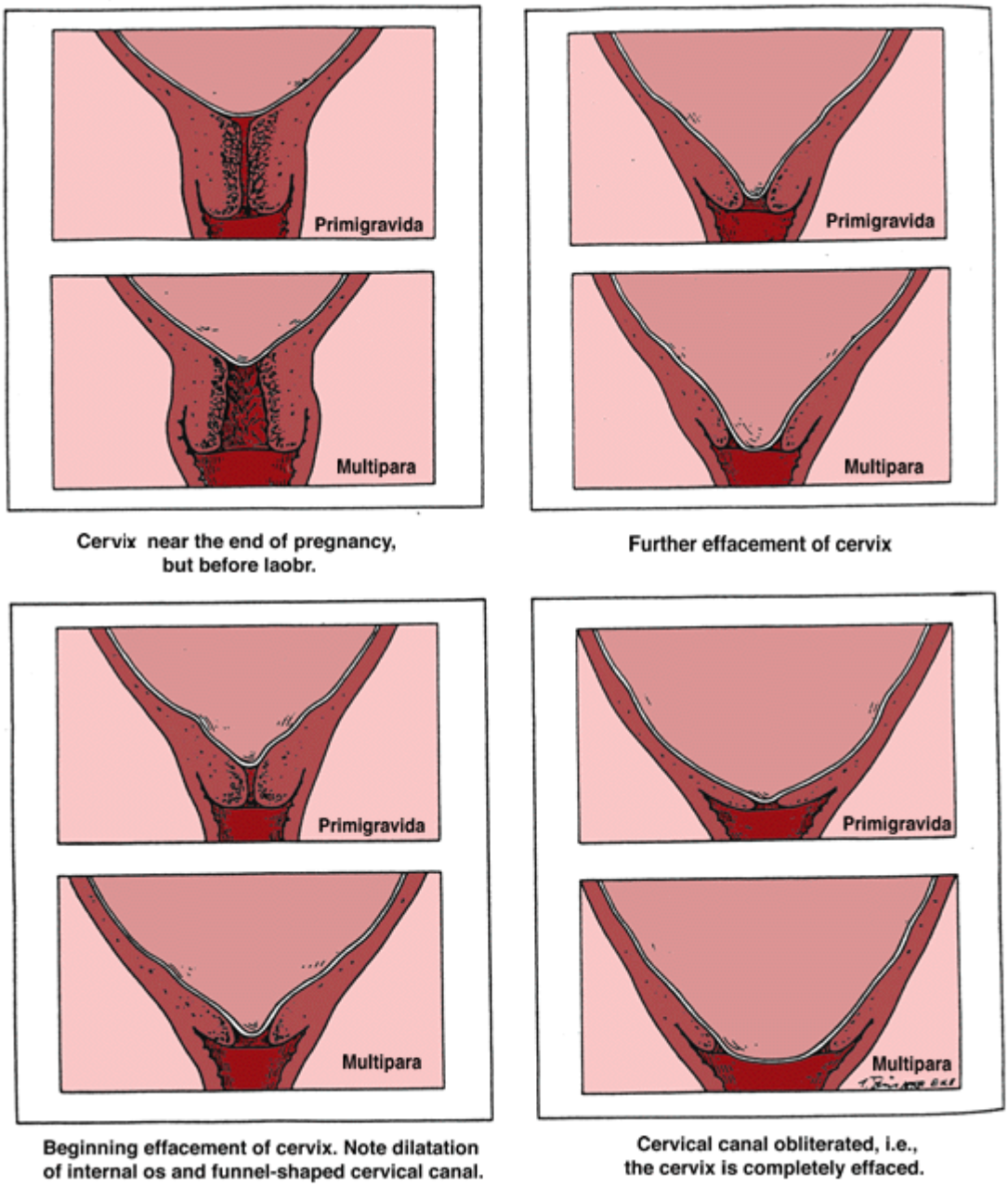
Labor can be described in terms of a series of phases.

First stage of labor

During the first phase of labor, the cervix dilates (opens) from 0-10 cm. This phase has an early, or latent, phase and an active phase. During the latent phase, progress is usually very slow. It may take quite a while and many contractions before the cervix dilates the first few centimeters. Contractions increase in strength as labor progresses. Most women are relatively comfortable during the latent phase and walking around is encouraged, since it naturally stimulates the process.

As labor begins, the muscular wall of the uterus begins to contract as the cervix relaxes and expands. As a portion of the amniotic sac surrounding the baby is pushed into the opening, it bursts under the pressure, releasing amniotic fluid. This is called "breaking the bag of waters."

Stage 1: Dilation of the cervix.



Picture.18. Dilation of cervix

During a contraction, the infant experiences intense pressure that pushes it against the cervix, eventually forcing the cervix to stretch open. At the same time, the contractions cause the cervix to thin. During this first stage, a woman's contractions occur more and more often and last longer and longer. The doctor or nurse will do a periodic pelvic exam to determine how the mother is progressing. If the contractions aren't forceful enough to open the cervix, a drug may be given to make the uterus contract.

As pain and discomfort increase, women may be tempted to request pain medication. If possible, though, administration of pain medication or anesthetics should be delayed until the active phase of labor begins — at which point the medication will not act to slow down or stop the labor.

The active stage of labor is faster and more efficient than the latent phase. In this phase, contractions are longer and more regular, usually occurring about every two minutes. These stronger contractions are also more painful. Women who use the breathing exercises learned in childbirth classes find that these can help cope with the pain experienced during this phase. Many women also receive some pain medication at this point—either a short-term medication, such as Nubain or Numorphan, or an epidural anesthesia.

As the cervix dilates to 8-9 cm, the phase called the transition begins. This refers to the transition from the first phase (during which the cervix dilates from 0-10 cm) and the second phase (during which the baby is pushed out through the birth canal). As the baby's head begins to descend, women begin to feel the urge to "push" or bear down. Active pushing by the mother should not begin until the second phase, since pushing too early can cause the cervix to swell or to tear and bleed. The attending healthcare practitioner should counsel the mother on when to begin to push.

Second stage of labor

As the mother enters the second stage of labor, her baby's head appears at the top of the cervix. Uterine contractions get stronger. The infant passes down the vagina, helped along by contractions of the abdominal muscles and the mother's pushing. Active pushing by the mother is very important during this phase of labor. If an epidural anesthetic is being used, many practitioners recommend decreasing the amount administered during this phase of labor so that the mother has better control over her abdominal muscles

When the top of the baby's head appears at the opening of the vagina, the birth is nearing completion. First the head passes under the pubic bone. It fills the lower

vagina and stretches the perineum (the tissues between the vagina and the rectum). This position is called "crowning," since only the crown of the head is visible. When the entire head is out, the shoulders follow. The attending practitioner suctions the baby's mouth and nose to ease the baby's first breath. The rest of the baby usually slips out easily, and the umbilical cord is cut.

Episiotomy

As the baby's head appears, the perineum may stretch so tight that the baby's progress is slowed down. If there is risk of tearing the mother's skin, the doctor may choose to make a small incision into the perineum to enlarge the vaginal opening. This is called an episiotomy. If the woman has not had an epidural or pudendal block, she will get a local anesthetic to numb the area. Once the episiotomy is made, the baby is born with a few pushes.

Third stage

In the final stage of labor, the placenta is pushed out of the vagina by the continuing uterine contractions. The placenta is pancake shaped and about 10 inches in diameter. It has been attached to the wall of the uterus and has served to convey nourishment from the mother to the fetus throughout the pregnancy. Continuing uterine contractions cause it to separate from the uterus at this point. It is important that all of the placenta be removed from the uterus. If it is not, the uterine bleeding that is normal after delivery may be much heavier.

Breech presentation

Approximately 4% of babies are in what is called the "breech" position when labor begins. In breech presentation, the baby's head is not the part pressing against the cervix. Instead the baby's bottom or legs are positioned to enter the birth canal instead of the head. An obstetrician may attempt to turn the baby to a head down

position using a technique called version. This is only successful approximately half the time.

The risks of vaginal delivery with breech presentation are much higher than with a head-first presentation. The mother and attending practitioner will need to weigh the risks and make a decision on whether to deliver via a cesarean section or attempt a vaginal birth. The extent of the risk depends to a great extent on the type of breech presentation, of which there are three. Frank breech (the baby's legs are folded up against its body) is the most common and the safest for vaginal delivery. The other types are complete breech (in which the baby's legs are crossed under and in front of the body) and footling breech (in which one leg or both legs are positioned to enter the birth canal). These are not considered safe to attempt vaginal delivery.

Even in complete breech, other factors should be met before considering a vaginal birth. An ultrasound examination should be done to be sure the baby does not have an unusually large head and that the head is tilted forward (flexed) rather than back (hyperextended). Fetal monitoring and close observation of the progress of labor are also important. A slowing of labor or any indication of difficulty in the body passing through the pelvis should be an indication that it is safer to consider a cesarean section.

Forceps delivery

If the labor is not progressing as it should or if the baby appears to be in distress, the doctor may opt for a forceps delivery. A forceps is a spoon-shaped device that resembles a set of salad tongs. It is placed around the baby's head so the doctor can pull the baby gently out of the vagina.

Forceps can be used after the cervix is fully dilated, and they might be required if:

- the umbilical has dropped down in front of the baby into the birth canal
- the baby is too large to pass through the birth canal unaided
- the baby shows signs of stress
- the mother is too exhausted to push

Before placing the forceps around the baby's head, pain medication or anesthesia may be given to the mother. The doctor may use a catheter to empty the mother's bladder, and may clean the perineal area with soapy water. Often an episiotomy is done before a forceps birth, although tears can still occur.

The obstetrician slides half of the forceps at a time into the vagina and around the side of the baby's head to gently grasp the head. When both "tongs" are in place, the doctor pulls on the forceps to help the baby through the birth canal as the uterus contracts. Sometimes the baby can be delivered this way after the very next contraction.

The frequency of forceps delivery varies from one hospital to the next, depending on the experience of staff and the types of anesthesia offered at the hospital. Some obstetricians accept the need for a forceps delivery as a way to avoid cesarean birth. However, other obstetrical services do not use forceps at all.

Complications from forceps deliveries can occur. Sometimes they may cause nerve damage or temporary bruises to the baby's face. When used by an experienced physician, forceps can save the life of a baby in distress.

Vacuum-assisted birth

This method of helping a baby out of the birth canal was developed as a gentler alternative to forceps. Vacuum-assisted birth can only be used after the cervix is fully dilated (expanded), and the head of the fetus has begun to descend through the pelvis. In this procedure, the doctor uses a device called a vacuum extractor, placing a large rubber or plastic cup against the baby's head. A pump creates suction that gently pulls on the cup to ease the baby down the birth canal. The force of the suction may cause a bruise on the baby's head, but it fades away in a day or so.

The vacuum extractor is not as likely as forceps to injure the mother, and it leaves more room for the baby to pass through the pelvis. However, there may be problems in maintaining the suction during the vacuum-assisted birth, so forceps may be a better choice if it is important to remove the baby quickly.

Cesarean sections

A cesarean section, also called a c-section, is a surgical procedure in which incisions are made through a woman's abdomen and uterus to deliver her baby.

Cesarean sections are performed whenever abnormal conditions complicate labor and vaginal delivery, threatening the life or health of the mother or the baby. In 2002, just over 26% of babies were born by c-section, an increase of 7% from the previous year. The procedure may be used in cases where the mother has had a previous c-section and the area of the incision has been weakened. Dystocia, or difficult labor, is the another common reason for performing a c-section.

Difficult labor is commonly caused by one of the three following conditions: abnormalities in the mother's birth canal; abnormalities in the position of the fetus; abnormalities in the labor, including weak or infrequent contractions.

Another major factor is fetal distress, a condition where the fetus is not getting enough oxygen. Fetal brain damage can result from oxygen deprivation. Fetal distress is often related to abnormalities in the position of the fetus, or abnormalities in the birth canal, causing reduced blood flow through the placenta.

Other conditions also can make c-section advisable, such as vaginal herpes, hypertension and diabetes in the mother. Some parents choose to have a c-section because they fear the pain or unpredictability of labor or they want to avoid pelvic damage.

Causes and symptoms

One of the first signs of approaching childbirth may be a "bloody show," the appearance of a small amount of blood-tinged mucus released from the cervix as it begins to dilate. This is called the "mucus plug."

The most common sign of the onset of labor is contractions. Sometimes women have trouble telling the difference between true and false labor pains.

True labor pains:

- develop a regular pattern, with contractions coming closer together
- last from 15-30 seconds at the onset and get progressively stronger and longer (up to 60 seconds)
- may get stronger with physical activity
- occur high up on the abdomen, radiating throughout the abdomen and lower back

Another sign that labor is beginning is the breaking of the "bag of waters," the amniotic sac which had cushioned the baby during the pregnancy. When it breaks, it releases water in a trickle or a gush. Only about 10% of women actually experience this water flow in the beginning of labor, however. Most of the time, the rupture occurs sometime later in labor. If the amniotic sac doesn't rupture on its own, the doctor will break it during labor.

Some women have diarrhea or nausea as labor begins. Others notice a sudden surge of energy and the urge to clean or arrange things right before labor begins; this is known as "nesting."

Diagnosis

The onset of labor can be determined by measuring how much the cervix has dilated. The degree of dilation is estimated by feeling the opening cervix during a pelvic exam. Dilation is measured in centimeters, from zero to 10. Contractions that cause the cervix to dilate are the sign of true labor.

Fetal monitoring

Fetal monitoring is a process in which the baby's heart rate is monitored for indicators of stress during labor and birth. There are several types of fetal monitoring.

A special stethoscope called a fetoscope may be used. This is a simple and non-invasive method.

The Doppler method uses ultrasound; it involves a handheld listening device that transmits the sounds of the heart rate through a speaker or into an attached ear piece. It can usually pick up the heart sounds 12 weeks after conception. This method offers intermittent monitoring. It allows the mother freedom to move about and is also useful during contractions.

Electronic fetal monitoring uses ultrasound and provides a view of the heartbeat in relationship to the mother's contractions. It can be used either continuously or intermittently. It is often used in high risk pregnancies, and is not often recommended for low risk ones because it renders the mother immobile and requires interpretation.

Internal monitoring does not use ultrasound, is more accurate than electronic monitoring and provides continuous monitoring for the high risk mother. This requires the mother's water to be broken and that she be two to three centimeters dilated. It is used in high-risk situations only.

Telemetry monitoring is the newest type of monitoring. It uses radio waves transmitted from an instrument on the mother's thigh. The mother is able to remain mobile. It provides continuous monitoring and is used in high-risk situations.

Treatment

Most women choose some type of pain relief during childbirth, ranging from relaxation and imagery to drugs. The specific choice may depend on what's available, the woman's preferences, her doctor's recommendations, and how the labor is proceeding. All drugs have some risks and some advantages.

Regional anesthetics

Regional anesthetics include epidurals and spinals. In this technique, medication is injected into the space around the spinal nerves. Depending on the type of medications used, this type of anesthesia can block nerve signals, causing

temporary pain relief, or a loss of sensation from the waist down. An epidural or spinal block can provide complete pain relief during cesarean birth.

An epidural is placed with the woman lying on her side or sitting up in bed with the back rounded to allow more space between the vertebrae. Her back is scrubbed with antiseptic, and a local anesthetic is injected in the skin to numb the site. The needle is inserted between two vertebrae and through the tough tissue in front of the spinal column. A catheter is put in place that allows continuous doses of anesthetic to be given.

This type of anesthesia provides complete pain relief, and can help conserve a woman's energy, since she can relax or even sleep during labor. This type of anesthesia requires an IV and fetal monitor. It may be harder for a woman to bear down when it comes time to push, although the amount of anesthesia can be adjusted as this stage nears.

Spinal anesthesia operates on the same principle as epidural anesthesia, and is used primarily in cases of c-section delivery. It is administered in the same way as an epidural, but the catheter is not left in place. The amount of anesthetic injected is large, since it must be injected at one time. Because of the anesthetic's effect on motor nerves, most women using it cannot push during delivery. This is a disadvantage in labor, but not an issue during a c-section. Spinals provide quick and strong anesthesia and allow for major abdominal surgery with almost no pain.

Narcotics

Short-acting narcotics can ease pain and do not interfere with a woman's ability to push. However, they can cause sedation, dizziness, nausea, and vomiting. Narcotics cross the placenta and may slow down a baby's breathing; they can't be given too close to the time of delivery.

Natural childbirth and preparation for childbirth

There are several methods to prepare for childbirth. The one selected often depends on what is available through the healthcare provider. Overall, family

involvement is receiving increased attention by the healthcare systems, and many hospitals now offer birthing rooms and maternity centers to help the entire family. There are several choices available for childbirth preparation.

Lamaze, or Lamaze-Pavlov, is the most common in the United States today. It was the first popular natural childbirth method, becoming popular in the 1960s. Breathing exercises and concentration on a focal point are practiced to allow mothers to control pain while maintaining consciousness. This allows the flow of oxygen to the baby and to the muscles in the uterus to be maintained. A partner coaches the mother throughout the birthing process.

The Read method, named for Dick Read, is a technique of breathing that was originated in the 1930s to help mothers deal with apprehension and tension associated with childbirth. This natural childbirth method uses different breathing for the different stages of childbirth.

The LeBoyer method stresses a relaxed delivery in a quiet, dim room. It attempts to avoid overstimulation of the baby and to foster mother-child bonding by placing the baby on the mother's abdomen and having the mother massage him or her immediately after the birth. Then the father washes the baby in a warm bath.

The Bradley method is called father-coached childbirth, because it focuses on the father serving as coach throughout the process. It encourages normal activities during the first stages of labor.

CLINICAL COURSE OF LABOR

The last few hours of human pregnancy are characterized by uterine contractions that effect dilatation of the cervix and force the fetus through the birth canal. Much energy is expended during this time; hence the use of the term labor to describe this process. The myometrial contractions of labor are painful, which is why the term labor pains is used to describe this process.

Before these forceful, painful contractions begin, however, the uterus must be prepared for labor. During the first 36 to 38 weeks of gestation, the myometrium is

unresponsive; after this prolonged period of quiescence, a transitional phase is required during which myometrial unresponsiveness is suspended and the cervix is softened and effaced. Indeed, there are multiple functional states of the uterus that must be implemented during pregnancy and the puerperium; these are described later and categorized as the uterine phases of parturition.

Myometrial contractions that do not cause cervical dilatation may be observed at any time during pregnancy. These contractions are characterized by unpredictability in occurrence, lack of intensity, and brevity of duration. Any discomfort that they produce is usually confined to the lower abdomen and groin. Near the end of pregnancy, as the uterus undergoes preparation for labor, contractions of this type are more common, especially in multiparas, and sometimes are referred to as false labor. In some women, however, the forceful uterine contractions that effect cervical dilatation, fetal descent, and delivery of the conceptus begin suddenly, seemingly without warning.

MYOMETRIUM

ANATOMICAL AND PHYSIOLOGICAL CONSIDERATIONS.

There are unique characteristics of myometrial muscle (and other smooth muscles) compared with skeletal muscle. Huszar and Walsh (1989) point out that these differences create a peculiar advantage for the myometrium in the efficiency of uterine contractions and the delivery of the fetus. First, the degree of shortening of smooth muscle cells with contractions may be one order of magnitude greater than that attained in striated muscle cells. Second, forces can be exerted in smooth muscle cells in any direction, whereas the contraction force generated by skeletal muscle is always aligned with the axis of the muscle fibers. Third, smooth muscle is not organized in the same manner as skeletal muscle; in myometrium, the thick and thin filaments are found in long, random bundles throughout the cells. This arrangement facilitates greater shortening and force-generating capacity of smooth

muscle. Fourth, there is the advantage that multidirectional force generation in myometrial smooth muscle permits versatility in expulsive force directionality that can be brought to bear irrespective of the lie or presentation of the fetus.

BIOCHEMISTRY OF SMOOTH MUSCLE CONTRACTIONS.

The interaction of myosin and actin is essential to muscle contraction. Myosin (Mr about 500,000) is comprised of multiple light and heavy chains and is laid down in thick myofilaments. The interaction of myosin and actin, which causes activation of ATPase, ATP hydrolysis, and force generation, is effected by enzymatic phosphorylation of the 20-kd light chain of myosin (Stull and colleagues, 1988, 1998). This phosphorylation reaction is catalyzed by the enzyme myosin light chain kinase, which is activated by Ca2+.

Ca2+ binds to calmodulin, a calcium-binding regulatory protein, which in turn binds to and activates myosin light chain kinase. In this manner, agents that act on myometrial smooth muscle cells to cause an increase in the intracellular cytosolic concentration of calcium ([Ca2+]i) promote contraction. Conditions that cause a decrease in [Ca2+]i favor relaxation. Ordinarily, agents that cause an increase in the intracellular concentration of cyclic adenosine monophosphate (cAMP) or cyclic guanosine monophosphate (cGMP) promote uterine relaxation. It is believed that cAMP and cGMP act to cause a decrease in [Ca2+]i, although the exact mechanism(s) is not defined. The biochemistry and physiology of smooth muscle contractility have been reviewed by Barany and Barany (1990) and by Sanborn and colleagues (1994).

The three stages of labour. Active labour is divided into three separate stages.

The first stage of labour begins when uterine contractions of sufficient frequency, intensity, and duration are attained to bring abour effacement and progressive dilatation of cervix. The first stage of labour ends when the cervix is fully dilated, that is, when cervix is sufficiently dilated (about 10 cm) to allow

passage of the fetal head. The first stage of albour, therefore, is the stage of cervical effacement and dilatation.

The second stage of labour begins when dilatation of the cervix is complete, and ends with delivery of the fetus. The second stage of labour is the stage of expulsion of the fetus.

The third stage of labour begins immediately after delivery of the fetus, and ends with the delivery of the placenta and fetal membranes. The third stage of labour is the stage of separation and expulsion of the placenta.

CLINICAL ONSET OF LABOR.

A rather dependable sign of the impending onset of active labor (provided rectal or vaginal examinations have not been performed in the preceding 48 hours) is the discharge of a small amount of blood-tinged mucus from the vagina. This represents the extrusion of the plug of mucus that had filled the cervical canal during pregnancy, and is referred to as "show" or "bloody show." This is a late sign, because commonly labor is already in progress or likely will ensue during the next several hours to few days. Normally, only a few drops of blood escape with the mucus plug; more substantial bleeding is suggestive of an abnormal cause.

UTERINE CONTRACTIONS CHARACTERISTIC OF LABOR.

Unique among physiological muscular contractions, those of uterine smooth muscle of labor are painful. The cause of the pain is not known definitely, but several possibilities have been suggested:

1. Hypoxia of the contracted myometrium (as in angina pectoris).

2. Compression of nerve ganglia in the cervix and lower uterus by the interlocking muscle bundles.

3. Stretching of the cervix during dilatation.

4. Stretching of the peritoneum overlying the fundus.

Compression of nerve ganglia in the cervix and lower uterine segment by the contracting myometrium is an especially attractive hypothesis. Paracervical infiltration with a local anesthetic usually produces appreciable relief of pain during subsequent uterine contractions

Uterine contractions are involuntary and, for the most part, independent of extrauterine control. Neural blockage from epidural analgesia does not diminish the frequency and intensity of uterine contractions. Moreover, the myometrial contractions in paraplegic women are normal, though painless, as in women after bilateral lumbar sympathectomy.

Mechanical stretching of the cervix enhances uterine activity in several species, including humans. This phenomenon has been referred to as the Ferguson reflex (1941). The exact mechanism by which mechanical dilatation of the cervix causes increased myometrial contractility is not clear. Release of oxytocin was suggested as the cause, but this is not proven. Manipulation of the cervix and "stripping" the fetal membranes is associated with an increase in the levels of prostaglandin F2a metabolite (PGFM) in blood .

The interval between contractions diminishes gradually from about 10 minutes at the onset of the first stage of labor to as little as 1 minute or less in the second stage. Periods of relaxation between contractions, however, are essential to the welfare of the fetus. Unremitting contraction of the uterus compromises uteroplacental blood flow, and ultimately, fetal-placental flow, sufficiently to cause fetal hypoxemia. In the active phase of labor, the duration of each contraction ranges from 30 to 90 seconds, averaging about 1 minute. There is appreciable variability in the intensity of uterine contractions during apparently normal labor, as emphasized by Schulman and Romney (1970). They recorded the amnionic fluid pressures

generated by uterine contractions during spontaneous labor; the average was about 40 mm Hg, but varied from 20 to 60 mm Hg.

DIFFERENTIATION OF UTERINE ACTIVITY.

During active labor, the uterus is transformed into two distinct parts. The actively contracting upper segment becomes thicker as labor advances. The lower portion, comprising the lower segment of the uterus and the cervix, is relatively passive compared with the upper segment, and it develops into a much more thinly walled passage for the fetus. The lower uterine segment is analogous to a greatly expanded and thinned-out isthmus of the uterus of nonpregnant women, the formation of which is not solely a phenomenon of labor. The lower segment develops gradually as pregnancy progresses and then thins remarkably during labor. By abdominal palpation, even before rupture of the membranes, the two segments can be differentiated during a contraction. The upper uterine segment is quite firm or hard, whereas the consistency of the lower uterine segment is much less firm. The former is the actively contracting part of the uterus; the latter is the distended, normally much more passive, portion.

If the entire wall of uterine musculature, including the lower uterine segment and cervix, were to contract simultaneously and with equal intensity, the net expulsive force would be decreased markedly. Herein lies the importance of the division of the uterus into an actively contracting upper segment and a more passive lower segment that differ not only anatomically but also physiologically. The upper segment contracts, retracts, and expels the fetus; in response to the force of the contractions of the upper segment, the softened lower uterine segment and cervix dilate and thereby form a greatly expanded, thinned-out muscular and fibromuscular tube through which the fetus can be extruded.

The myometrium of the upper uterine segment does not relax to its original length after contractions; rather, it becomes relatively fixed at a shorter length. The

tension, however, remains the same as before the contraction. The upper portion of the uterus, or active segment, contracts down on its diminishing contents, but myometrial tension remains constant. The net effect is to take up slack, maintaining the advantage gained in the expulsion of the fetus, and keeping the uterine musculature in firm contact with the intrauterine contents. As the consequence of retraction, each successive contraction commences where its predecessor left off, so that the upper part of the uterine cavity becomes slightly smaller with each successive contraction. Because of the successive shortening of the muscular fibers with contractions, the upper active uterine segment becomes progressively thickened throughout the first and second stages of labor and tremendously thickened immediately after delivery of the fetus. The phenomenon of retraction of the upper uterine segment is contingent upon a decrease in the volume of its contents. For the contents to be diminished, particularly early in labor when the entire uterus is virtually a closed sac with only a minute opening at the cervical os, the musculature of the lower segment must stretch. This permits increasingly more of the intrauterine contents to occupy the lower segment, and the upper segment retracts only to the extent that the lower segment distends and the cervix dilates.

The relaxation of the lower uterine segment is not a complete relaxation, but rather the opposite of retraction. The fibers of the lower segment become stretched with each contraction of the upper segment, after which these are not returned to the previous length but rather remain relatively fixed at the longer length; the tension, however, remains essentially the same as before. The musculature still manifests tone, still resists stretch, and still contracts somewhat on stimulation. The successive lengthening of the muscular fibers in the lower uterine segment, as labor progresses, is accompanied by thinning, normally to only a few millimeters in the thinnest part. As a result of the thinning of the lower uterine segment and the concomitant thickening of the upper, the boundary between the two is marked by a ridge on the inner uterine surface, the physiological retraction ring. When the thinning of the lower uterine segment is extreme, as in obstructed labor, the ring is very prominent,

forming a pathological retraction ring. This is an abnormal condition also known as Bandl ring. The existence of a gradient of diminishing physiological activity from fundus to cervix was established from measurements of differences in behavior of the upper and lower parts of the uterus during normal labor.

CHANGE IN UTERINE SHAPE.

Each contraction produces an elongation of the uterine ovoid with a concomitant decrease in horizontal diameter. By virtue of this change in shape, there are important effects on the process of labor. First, the decrease in horizontal diameter produces a straightening of the fetal vertebral column, pressing its upper pole firmly against the fundus of the uterus, whereas the lower pole is thrust farther downward and into the pelvis. The lengthening of the fetal ovoid thus produced has been estimated as between 5 and 10 cm. The pressure exerted in this fashion is known as the fetal axis pressure. Second, with lengthening of the uterus, the longitudinal fibers are drawn taut and because the lower segment and cervix are the only parts of the uterus that are flexible, these are pulled upward over the lower pole of the fetus. This effect on the musculature of the lower segment and on the cervix is an important factor in cervical dilatation.

ANCILLARY FORCES IN LABOR.

After the cervix is dilated fully, the most important force in the expulsion of the fetus is that produced by increased maternal intra-abdominal pressure. This is created by contraction of the abdominal muscles simultaneously with forced respiratory efforts with the glottis closed. This is referred to as "pushing." The nature of the force produced is similar to that involved in defecation, but the intensity usually is much greater. The importance of intra-abdominal pressure in fetal expulsion is most clearly attested to by the labors of women who are paraplegic. Such women suffer no pain, although the uterus may contract vigorously. Cervical dilatation, in large measure the result of uterine contractions acting on a softened

cervix, proceeds normally, but expulsion of the infant is accomplished more readily when the woman is instructed to bear down and can do so during a uterine contraction.

Although increased intra-abdominal pressure is required for the spontaneous completion of labor, it is futile until the cervix is fully dilated. Specifically, it is a necessary auxiliary to uterine contractions in the second stage of labor, but pushing accomplishes little in the first stage, except to produce fatigue. Intra-abdominal pressure also may be important in the third stage of labor, especially if the parturient is unattended. After the placenta has separated, its spontaneous expulsion is aided by the mother increasing intra-abdominal pressure.

CERVIX

Before the onset of labor, during the phase of uterine awakening and preparedness, the cervix is softened, which facilitates dilatation of the cervix once forceful myometrial contractions of labor begin.

CHANGES INDUCED IN THE CERVIX WITH LABOR.

The effective force of the first stage of labor is the uterine contraction, which in turn exerts hydrostatic pressure through the fetal membranes against the cervix and lower uterine segment. In the absence of intact membranes, the fetal presenting part is forced directly against the cervix and lower uterine segment. As the result of the action of these forces, two fundamental changes—effacement and dilatation—take place in the already softened cervix. For the head of the average fetus at term to pass through the cervix, the cervical canal must dilate to a diameter of about 10 cm; at this time, the cervix is said to be completely (or fully) dilated. There may be no fetal descent during cervical effacement, but most commonly the presenting fetal part descends somewhat as the cervix dilates. During the second stage of labor, descent of the fetal presenting part typically occurs rather slowly but steadily in

nulliparas. In multi-paras, however, particularly those of high parity, descent may be very rapid.

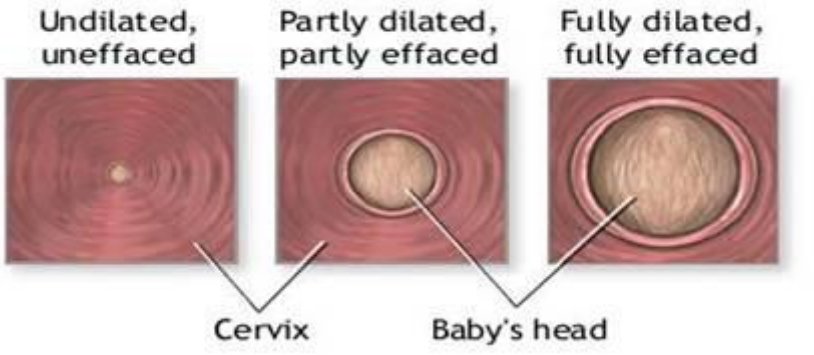
CERVICAL EFFACEMENT.

The "obliteration" or "taking up" of the cervix is the shortening of the cervical canal from a length of about 2 cm to a mere circular orifice with almost paper-thin edges. This process is referred to as effacement and takes place from above downward. The muscular fibers at about the level of the internal cervical os are pulled upward, or "taken up," into the lower uterine segment, as the condition of the external os remains temporarily unchanged. The edges of the internal os are drawn upward several centimeters to become a part (both anatomically and functionally) of the lower uterine segment. Effacement may be compared with a funneling process in which the whole length of a narrow cylinder is converted into a very obtuse, flaring funnel with a small circular orifice for an outlet. As the result of increased myometrial activity during uterine preparedness for labor, appreciable effacement of the softened cervix sometimes is accomplished before active labor begins. Effacement causes expulsion of the mucus plug as the cervical canal is shortened.

CERVICAL DILATATION.

Compared with the body of the uterus, the lower uterine segment and the cervix are regions of lesser resistance. Therefore, during a contraction, these structures are subjected to distention, in the course of which a centrifugal pull is exerted on the cervix. As the uterine contractions cause pressure on the membranes, the hydrostatic action of the amnionic sac in turn dilates the cervical canal like a wedge. In the absence of intact membranes, the pressure of the presenting part against the cervix and lower uterine segment is similarly effective. Early rupture of the membranes does not retard cervical dilatation so long as the presenting part of the fetus is positioned to exert pressure against the cervix and lower uterine segment.

The process of cervical effacement and dilatation causes the formation of the forebag of the amnionic fluid, which is later described in detail.



Picture 18. Cervical effacement and dilatation

LABOR PATTERNS

PATTERN OF CERVICAL DILATATION.

Friedman, in his treatise on labor (1978), stated that "the clinical features of uterine contractions—namely, frequency, intensity, and duration—cannot be relied upon as measures of progression in labor nor as indices of normality. ... Except for cervical dilatation and fetal descent, none of the clinical features of the parturient... appears to be useful in assessing labor progression." The pattern of cervical dilatation that takes place during the course of normal labor takes on the shape of a sigmoid curve. Two phases of cervical dilatation are the latent phase and the active phase. The active phase has been subdivided further as the acceleration phase, the phase of maximum slope, and the deceleration phase (Friedman, 1978). The duration of the latent phase is more variable and subject to sensitive changes by extraneous factors and by sedation (prolongation of latent phase) and myometrial stimulation (shortening of latent phase). The duration of the latent phase has little bearing on the subsequent course of labor, whereas the characteristics of the accelerated phase are usually predictive of the outcome of a particular labor. Friedman considers the maximum slope as a "good measure of the overall efficiency of the machine,"

whereas the nature of the deceleration phase is more reflective of fetopelvic relationships. The completion of cervical dilatation during the active phase of labor is accomplished by cervical retraction about the presenting part of the fetus. After complete cervical dilatation, the second stage of labor commences; thereafter, only progressive descent of the presenting fetal part is available to assess the progress of labor.

PATTERN OF FETAL DESCENT.

In many nulliparas, engagement of the fetal head is accomplished before labor begins, and further descent does not occur until late in labor. In others in which engagement of the fetal head is initially not so complete, further descent occurs during the first stage of labor. In the descent pattern of normal labor, a typical hyperbolic curve is formed when the station of the fetal head is plotted as a function of the duration of labor. Active descent usually takes place after cervical dilatation has progressed for some time. In nulliparas, increased rates of descent are observed ordinarily during the phase of maximum slope of cervical dilatation. At this time, the speed of descent increases to a maximum, and this maximal rate of descent is maintained until the presenting fetal part reaches the perineal floor (Friedman, 1978).

CRITERIA FOR NORMAL LABOR.

Friedman also sought to select criteria that would delimit normal labor and thereby enable identification of significant abnormalities in labor. The limits, admittedly arbitrary, appear to be logical and clinically useful. The group of women studied were nulliparas and multiparas with no fetopelvic disproportion, no fetal malposition or malpresentation, no multiple pregnancy, and none were treated with heavy sedation or conduction analgesia, oxytocin, or operative intervention. All had a normal pelvis, were at term with a vertex presentation, and delivered average-sized infants. From these studies, Friedman developed the concept of three functional divisions of labor—preparatory, dilatational, and pelvic—to describe the

physiological objectives of each division. He found that the preparatory division of labor may be sensitive to sedation and conduction analgesia. Although little cervical dilatation occurs during this time, considerable changes take place in the extracellular matrix (collagen and other connective tissue components) of the cervix. The dilatational division of labor, during which time dilatation is occurring at the most rapid rate, is principally unaffected by sedation or conduction analgesia. The pelvic division of labor begins with the deceleration phase of cervical dilatation. The classical mechanisms of labor, which involve the cardinal movements of the fetus, take place principally during the pelvic division of labor. The onset of the pelvic division is seldom clinically identifiable separate from the dilatational division of labor. Moreover, the rate of cervical dilatation does not always decelerate as full dilatation is approached; in fact, it may accelerate.

RUPTURE OF THE MEMBRANES.

Spontaneous rupture of the membranes most often occurs sometime during the course of active labor. Typically, rupture is evident by a sudden gush of a variable quantity of normally clear or slightly turbid, nearly colorless fluid. Less frequently, the membranes remain intact until delivery of the infant. If by chance the membranes remain intact until completion of delivery, the fetus is born surrounded by them, and the portion covering the head of the newborn infant is sometimes referred to as the caul. Rupture of the membranes before the onset of labor at any stage of gestation is referred to as premature rupture of the membranes.

CHANGES IN THE VAGINA AND PELVIC FLOOR.

The birth canal is supported and is functionally closed by a number of layers of tissues that together form the pelvic floor. Its most important structures are the levator ani muscle and the fascia covering its upper and lower surfaces, which for practical purposes may be considered as the pelvic floor. This group of muscles closes the lower end of the pelvic cavity as a diaphragm and thereby a concave upper

and a convex lower surface is presented. On either side, the levator ani consists of a pubococcygeus and iliococcygeus portion. The posterior and lateral portions of the pelvic floor, which are not filled out by the levator ani, are occupied by the piriformis and coccygeus muscles on either side.

The levator ani varies in thickness from 3 to 5 mm, though its margins encircling the rectum and vagina are somewhat thicker. During pregnancy, the levator ani usually undergoes hypertrophy. By vaginal examination, the internal margin of this muscle can be felt as a thick band that extends backward from the pubis and encircles the vagina about 2 cm above the hymen. On contraction, the levator ani draws both the rectum and vagina forward and upward in the direction of the symphysis pubis and thereby acts to close the vagina. The more superficial muscles of the perineum are too delicate to serve more than an accessory function.

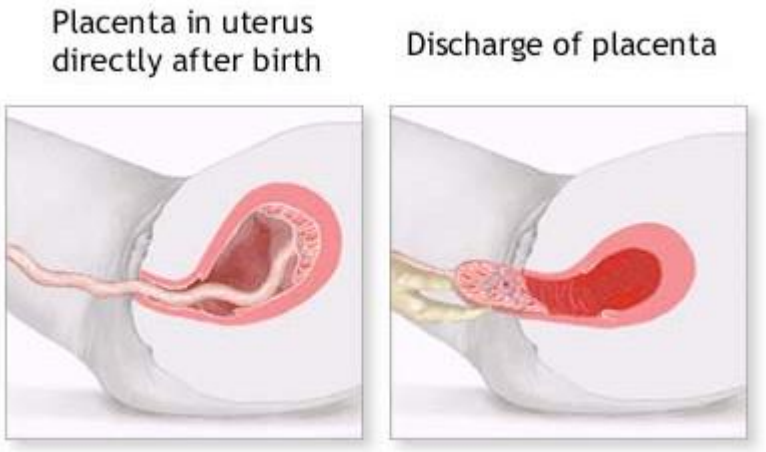
In the first stage of labor, the membranes and presenting part of the fetus serve a role in dilating the upper portion of the vagina. After the membranes have ruptured, however, the changes in the pelvic floor are caused entirely by pressure exerted by the fetal presenting part. The most marked change consists of the stretching of the fibers of the levator ani muscles and the thinning of the central portion of the perineum, which becomes transformed from a wedge-shaped mass of tissue 5 cm in thickness to (in the absence of an episiotomy) a thin, almost transparent membranous structure less than 1 cm in thickness. When the perineum is distended maximally, the anus becomes markedly dilated and presents an opening that varies from 2 to 3 cm in diameter and through which the anterior wall of the rectum bulges. The extraordinary number and size of the blood vessels that supply the vagina and pelvic floor effects a great increase in the amount of blood loss when these tissues are torn.

PLACENTAL SEPARATION.

The third stage of labor begins immediately after delivery of the fetus and involves the separation and expulsion of the placenta. After delivery of the placenta

and fetal membranes, active labor is completed. As the baby is born, the uterus spontaneously contracts down on its diminishing contents. Normally, by the time the infant is completely delivered, the uterine cavity is nearly obliterated and the organ consists of an almost solid mass of muscle, several centimeters thick above the thinner lower segment. The uterine fundus now lies just below the level of the umbilicus. This sudden diminution in uterine size is inevitably accompanied by a decrease in the area of the placental implantation site. For the placenta to accommodate itself to this reduced area, it increases in thickness, but because of limited placental elasticity, it is forced to buckle. The resulting tension causes the weakest layer of the decidua—the spongy layer, or decidua spongiosa—to give way, and cleavage takes place at that site. Therefore, separation of the placenta results primarily from a disproportion created between the unchanged size of the placenta and the reduced size of the underlying implantation site. During cesarean delivery, this phenomenon may be directly observed when the placenta is implanted posteriorly.

Cleavage of the placenta is greatly facilitated by the nature of the loose structure of the spongy decidua, which may be likened to the row of perforations between postage stamps. As separation proceeds, a hematoma forms between the separating placenta and the remaining decidua. Formation of the hematoma is usually the result, rather than the cause, of the separation, because in some cases bleeding is negligible. The hematoma may, however, accelerate the process of cleavage. Because the separation of the placenta is through the spongy layer of the decidua, part of the decidua is cast off with the placenta, whereas the rest remains attached to the myometrium. The amount of decidual tissue retained at the placental site varies.



PIcture.19. Expulsion of placenta

Placental separation ordinarily occurs within a very few minutes after delivery. Brandt (1933) and others, based on results obtained in combined clinical and radiographic studies, supported the idea that because the periphery of the placenta is probably the most adherent portion, separation usually begins elsewhere. Occasionally some degree of separation begins even before the third stage of labor, probably accounting for certain cases of fetal heart rate decelerations that occur just before expulsion of the infant.

SEPARATION OF AMNIOCHORION.

The great decrease in the surface area of the cavity of the uterus simultaneously causes the fetal membranes (amniochorion) and the parietal decidua to be thrown into innumerable folds that increase the thickness of the layer from less than 1 mm to 3 to 4 mm. The lining of the uterus early in the third stage indicates that much of the parietal layer of decidua parietalis is included between the folds of the festooned amnion and chorion laeve. The membranes usually remain in situ until the separation of the placenta is nearly completed. These are then peeled off the uterine wall, partly by the further contraction of the myometrium and partly by traction that is exerted by the separated placenta, which lies in the thin lower uterine segment or in the upper portion of the vagina. The body of the uterus at that time normally forms an almost solid mass of muscle, the anterior and posterior walls of

which, each measuring 4 to 5 cm in thickness, lie in close apposition such that the uterine cavity is almost obliterated.

PLACENTAL EXTRUSION.

After the placenta has separated from its implantation site, the pressure exerted upon it by the uterine walls causes it to slide downward into the lower uterine segment or the upper part of the vagina. In some cases the placenta may be expelled from those locations by an increase in abdominal pressure, but women in the recumbent position frequently cannot expel the placenta spontaneously. An artificial means of completing the third stage is therefore generally required. The usual method employed is alternately to compress and elevate the fundus, while exerting minimal traction on the umbilical cord.

MECHANISMS OF PLACENTAL EXTRUSION.

When the central, or usual, type of placental separation occurs, the retroplacental hematoma is believed to push the placenta toward the uterine cavity, first the central portion and then the rest. The placenta, thus inverted and weighted with the hematoma, then descends. Because the surrounding membranes are still attached to the decidua, the placenta can descend only by dragging the membranes along; the membranes then peel off its periphery. Consequently, the sac formed by the membranes is inverted, with the glistening amnion over the placental surface presenting at the vulva. The retroplacental hematoma either follows the placenta or is found within the inverted sac. In this process, known as the Schultze mechanism of placental expulsion, blood from the placental site pours into the inverted sac, not escaping externally until after extrusion of the placenta. The other method of placental extrusion is known as the Duncan mechanism, in which separation of the placenta occurs first at the periphery, with the result that blood collects between the membranes and the uterine wall and escapes from the vagina. In this circumstance,

the placenta descends to the vagina sideways, and the maternal surface is the first to appear at the vulva.

PHYSIOLOGICAL AND BIOCHEMICAL PROCESSES OF PARTURITION

The physiological processes in human pregnancy that results in the initiation of parturition and the onset of labor are not defined. Until recently, it was generally accepted that successful pregnancy in all mammalian species was dependent upon the action of progesterone to maintain uterine quiescence until near the end of gestation. This assumption was supported by the finding that in the majority of mammalian pregnancies studied, progesterone withdrawal (whether naturally occurring or surgically or pharmacologically induced) precedes the initiation of parturition. In many of these species, a decline, sometimes precipitous, in the levels of progesterone in maternal plasma normally begins after approximately 95 percent of pregnancy. Moreover, the administration of progesterone to these species late in pregnancy delays the onset of parturition.

In primate pregnancy (including humans), however, progesterone withdrawal does not precede the initiation of parturition. The levels of progesterone in the plasma of pregnant women increase throughout pregnancy, declining only after delivery of the placenta, the tissue site of progesterone synthesis in human pregnancy.

PARTURITION THEORIES

Presently, there appear to be two general theorems. Viewed simplistically, these are the retreat from pregnancy maintenance hypothesis and the uterotonin induction of parturition theory. Several combinations of selected tenets of these two postulates are incorporated into the theorems of most investigators. Some researchers also speculate that the mature human fetus, in some undefined fashion,

is the source of the initial signal for the commencement of the parturitional process. This has little direct experimental support in human parturition.

Other investigators suggest that one or another uterotonin, produced in increased amounts or in response to an increase in the population of its myometrial receptors, is the proximate cause of the initiation of human parturition. Indeed, an obligatory role for one or more uterotonins is included in most parturition theories, either as a primary or a secondary phenomenon in the final events of childbirth.

UTERINE PHASES OF PARTURITION

Parturition, the bringing forth of young, encompasses all physiological processes involved in birthing: the prelude to, the preparation for, the process of, and the parturient's recovery from childbirth. From the disparate nature of these physiological processes, it is evident that multiple transformations in uterine function must be accommodated in a timely manner during successful pregnancy and parturition. Parturition can be arbitrarily divided into four uterine phases which correspond to the major physiological transitions of the myometrium and cervix during pregnancy (Casey and MacDonald 1993a, 1993c; MacDonald and Casey, 1996).

UTERINE PHASE OF PARTURITION.

Beginning even before implantation, a remarkably effective period of myometrial quiescence is imposed on the uterus. This phase of parturition is characterized by myometrial smooth muscle tranquility with maintenance of cervical structural integrity. This is the phase in which the inherent propensity of the myometrium to contract is harnessed. During this phase, which persists for about the first 95 percent of normal pregnancy, myometrial smooth muscle is rendered unresponsive to natural stimuli and relative contractile paralysis is imposed against a host of mechanical and chemical challenges that otherwise would promote emptying of the uterine contents. The myometrial contractile unresponsiveness of

phase 0 is so extraordinary that near the end of pregnancy the myometrium must be awakened from this prolonged parturitional diapause in preparation for labor.

During phase 0 of parturition, as the myometrium is maintained in a quiescent state, the cervix must remain firm and unyielding. The maintenance of cervical anatomical and structural integrity is essential to the success of phase 0 of parturition. Premature cervical dilatation, structural incompetence, or both, portend an unfavorable pregnancy outcome that ends most often in preterm delivery. Shortening of the cervix, when identified between 24 and 28 weeks of pregnancy, is indicative of increased risk of preterm delivery (Iams and colleagues, 199

UTERINE PHASE 1 OF PARTURITION.

To prepare the uterus for labor, the uterine tranquility of phase 0 of parturition must be suspended; this is the time of uterine awakening. The morphological and functional changes in myometrium and cervix that prepare the uterus for labor may be the natural outcome of the suspension of uterine phase 0; but whatever the mechanism, the capacity of myometrial cells to regulate the concentration of cytoplasmic Ca2+ is restored; myometrial cell responsitivity is reinstituted, uterotonin sensitivity develops, and intercellular communicability is established. As these functional capacities of myometrial smooth muscle to contract are implemented and the cervix is ripened, phase 1 of parturition merges into phase 2, active labor. Challis and Lye (1994) refer to the change in uterine functionality before labor as "activation."

UTERINE MODIFICATION DURING PHASE 1 OF PARTUITION

Specific modifications in uterine function evolve with the suspension of uterine phase 0:

1. A stiking increase in myometrial oxytocin receptors

2. An increase in gap junctions (number and surface area) between myometrial cells
3. Uterine irritability
4. Responsiveness to uterotonics
5. Transition from a contractile state characterized predominantly by occasional painless contractions to one in which more frequent contractions develop
6. Formation of the lower uterine segment
7. Cervical softening

With the development of a well-formed lower uterine segment, the fetal head oftentimes descends to or even through the maternal inlet of the pelvis, a distinctive event referred to as lightening. The abdomen of the pregnant woman commonly undergoes a change in shape, an event sometimes described by the mother as "the baby dropped." No doubt there are many other modifications of the uterus late in pregnancy during phase 1, some of which may be integral components of uterine preparedness for labor.

Late in pregnancy, at sometime during phase 1 of parturition, there is a striking—50-fold or more—increase in the number of oxytocin receptors in myometrium (Fuchs and associates, 1982). This coincides with the increase in uterine contractile responsiveness to oxytocin (Soloff and co-workers, 1979). Also, prolonged human gestation is associated with a delay in this increase in receptors (Fuchs and collaborators, 1984).

Also during phase 1, the number and size of gap junctions between myometrial cells increase before the onset of labor, continue to increase during labor, and then decrease quickly after delivery. This is true of spontaneous parturition, both at term and preterm (Garfield and Hayashi, 1981).

CERVICAL CHANGES OF PHASE 1 OF PARTURITION.

The body of the uterus (the fundus) and the cervix, although parts of the same organ, must respond in quite different ways during pregnancy and parturition. On the one hand, it is essential that during most of pregnancy, the myometrium be dilatable but remain quiescent. On the other hand, the cervix must remain unyielding and reasonably rigid. Coincident with the initiation of parturition, however, the cervix must soften, yield, and become more readily dilatable. The fundus must be transformed from the relatively relaxed, unresponsive organ characteristic of most of pregnancy to one that will produce effective contractions that drive the fetus through the yielding (dilatable) cervix and on through the birth canal. Failure of a coordinated interaction between the functions of fundus and cervix portends an unfavorable pregnancy outcome. But despite the apparent reversal of roles between cervix and fundus from before to during labor, it is likely that the processes in both portions of the uterus are regulated by common agents.

COMPOSITION OF THE CERVIX.

There are three principal structural components of the cervix: collagen, smooth muscle, and the connective tissue or ground substance. Constituents of the cervix important in cervical modifications at parturition are those in the extracellular matrix and ground substance, the glycosaminoglycans, dermatan sulfate and hyaluronic acid. The smooth muscle content of cervix is much less than that of the fundus, and varies anatomically from 25 to only 6 percent.

CERVICAL SOFTENING.

The cervical modifications of phase 1 of parturition principally involve changes that occur in collagen, connective tissue, and its ground substance. Cervical softening is associated with two complementary changes:

1. Collagen breakdown and rearrangement of the collagen fibers.

2. Alterations in the relative amounts of the various glycosaminoglycans.

Hyaluronic acid is associated with the capacity of a tissue to retain water. Near term, there is a striking increase in the relative amount of hyaluronic acid in cervix, with a concomitant decrease in dermatan sulfate. The role for smooth muscle in the cervical softening process is not clear, but may be more important than previously believed. Rath and colleagues (1998) and Winkler and Rath (1999) have addressed this possibility in some detail.

UTERINE PHASE 2 OF PARTURITION.

Phase 2 is synonymous with active labor, that is, the uterine contractions that bring about progressive cervical dilatation and delivery of the conceptus. Phase 2 of parturition is customarily divided into the three stages of labor described earlier in the chapter. The onset of labor is the transition from uterine phase 1 to phase 2 of parturition.

UTERINE PHASE 3 OF PARTURITION.

Phase 3 encompasses the events of the puerperium—maternal recovery from childbirth, maternal contributions to infant survival, and the restoration of fertility in the parturient. Immediately after delivery of the conceptus, and for about an hour or so thereafter, the myometrium must be held in a state of rigid and persistent contraction/retraction, which effects compression of the large uterine vessels and thrombosis of their lumens. In this coordinated fashion, fatal postpartum hemorrhage is prevented.

During the early puerperium, a maternal-type behavior pattern develops and maternal-infant bonding begins. The onset of lactogenesis and milk let-down in maternal mammary glands also is, in an evolutionary sense, crucial to the bringing forth of young. Finally, involution of the uterus, which restores this organ to the

nonpregnant state, and the reinstitution of ovulation must be accomplished in preparation for the next pregnancy. Four to six weeks usually are required for complete uterine involution; but the duration of phase 3 of parturition is dependent on the duration of breast feeding. Infertility usually persists so long as breast feeding is continued because of lactation (prolactin)-induced anovulation and amenorrhea.

Labor is a physiologic process that permits a series of extensive physiologic changes in the mother to allow for the delivery of her fetus through the birth canal.

It is defined as progressive cervical effacement, dilatation, or both, resulting from regular uterine contractions that occur at least every 5 minutes and last 30-60 seconds.

Labor forces:

1. Uterine contractions – is a regular contractions of uterine musculature. Typically, contractions occur every 5 to 10 minutes and last for 20-25 sec in the onset of labor. As labor proceeds, the contractions become more frequent, more intense, and last longer. In the end of labor the contractions occur every 2-3 minutes and last for 50 to 60 seconds. The are characterized by strength, duration, and frequency which are important in generating a normal labor pattern
2. Bearing – down efforts (or pushing) – is the periodic contractions of diaphragm, pelvic floor muscles and prelum abdominale which are added to the force of uterine contractions. Its voluntary expulsive force.

There are **three stages of labor**, each of which is considered separately.

The *first stage (cervical)* is from the onset of true labor to complete dilatation of the cervix.

The *second stage(pelvic*) starts from complete dilatation of the cervix to the delivery of the baby.

The *third stage (placental)* starts from the birth of the baby to delivery of the placenta. It is divided into two phases: placental separation and its expulsion.

During the first stage of the labor cervical effacement and dilatation occur.

Labor begins with cervical effacement **! Cervical effacement is the thinning of the cervix.**

Although cervical softening and early effacement may occur before labour, during the first stage of labour the entire cervical length is retracted into lower uterine segment as a result of myometrial contractile forces and pressure exerted by either the presenting part of fetal membranes.

The length of the first stage may vary in relation to parity; primiparous patients generally experience a longer first stage than do multiparous patients. The minimal dilatation during the first stage is for primiparous 1-1.2 cm/hour and multiparous women: 1.2-1.5 cm/hour. If the progress is slower than this, evaluation for uterine dysfunction, fetal malposition, or cephalopelvic disproportion should be undertaken.

During the first stage, the progress of labour may be measured in terms of cervical effacement, cervical dilatation and descent of the fetal head. Uterine contractions should be monitored ecery 30 minuutes by palpation for their frequency, duration, and intensity. For high-risk pregnancies, uterine contractions should be monitored continuously along with the fetal heart rate.

Vaginal examination should be done sparingly to decrease the risk of an intrauterine infection. Cervical effacement and dilatation, the station and position of the presenting part, the presence of molding or caput in vertex presentation should be recorded. Additional examinations may be performed if the patient reports the urge to push (to determine if the full dilatation has occurred) or if a significant fetal heart rate deceleration occurs (to examine for a prolapsed umbilical cord).

The fetal heart rate should be evaluated by either auscultation with a stethoscope, by external monitoring with Doppler equipment. In patients with no significant obstetric risk factors, the fetal heart rate should be auscultated at least every 30 minutes in the first stage of labor and after each uterine contraction in the second stage of the labor.

At the beginning of the second stage, the mother usually has a desire to bear down with each contraction. This abdominal pressure, together with uterine contractile force, combines to expel the fetus. In cephalic presentation, the shape of the fetal head may be altered during labor, making the assessment of descent more difficult. *Molding* is the alteration of the relationship of the fetal cranial bones to each other as the result of the compressive forces exerted by the bony maternal pelvis.

The second stage generally takes from 30 minutes to 2 hours in primigravid women and from 10-50 minutes in multigravida women. The median duration is 50 minutes in a primipara and slightly under 20 minutes in a multipara.

Clinical management of the second stage of labor. When delivery is imminent, the patient is usually placed in the lithotomy position.

With each contraction, the mother should be encouraged to hold her breath and bear down with expulsive efforts. As the perineum becomes flattened by the crowning head, an episiotomy may be performed, to prevent perineal lacerations.

As the fetal head crowns (i.e., distends the vaginal opening),

PERINEAL PROTECTIVE MANEUVERS are performed to avoid injury and laceration of perineum:

The first one is prevention of preterm head extension (during pushing efforts the fetal head is flexed)

Second is the delivery of the fetal head out of the pushing by extension of vulval muscles

Photo1. First perineam protective measure

Third one is decreasing of perineal tension by borrowing of the tissues from the upper part of vulva ring to the lower

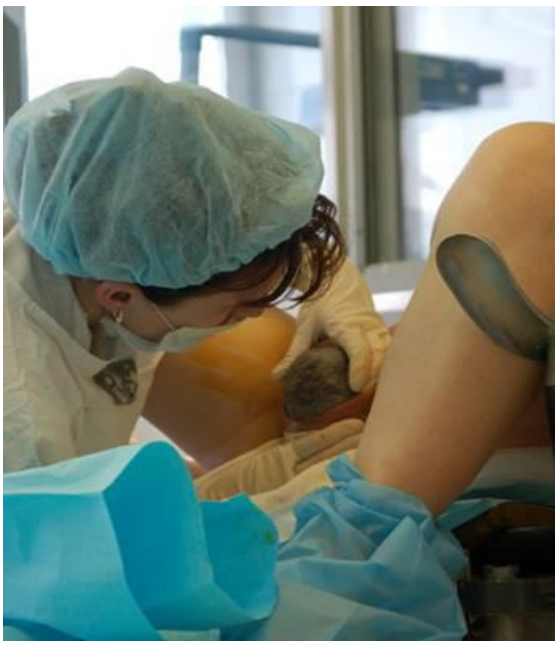


Photo 2. Third perineam protective measure

Fourth is regulations of voluntary maternal effort (pushing) – woman in labour breaths deeply when the fetus is delivered to the level if parietal tubes. At this moment pushing efforts are contraindicated.

Fifth is the delivery of shoulders – first downward, later upward direction of traction are indicated

Photo 3. Fifth perineam protective measure

The delivery of the placenta occurs during the third stage of labor. Separation of the placenta generally occurs within 2 to 10 minutes of the end of the second stage of labor. Squeezing of the fundus to hasten placental separation is not recommended because it may increase the likelihood of passage of fetal cells into the maternal circulation.

SIGNS OF PLACENTAL SEPARATION ARE FOLLOWS:

Alfeld's sign – the umbilical cord lengthens outside the vagina, the clamp, applied on an umbilical cord on the level of pudendal cleft, after placental separation comes down on 10-12 cm

Shreder's sign – the uterine fundus rises up, the uterus becomes firm and globular

Krede-Lasarevich's sign – a doctor presses with his palm above the patient's pubis. Before placental separation umbilical cord comes inside a vagina (sign is negative) after sepatation -comes down (sign is positive).

Only when these signs have appeared the attempt to remove of separated placenta should perform. The placenta should be examined to ensure its complete removal and to detect placental abnormalities. If the patient is at risk of postpartum

hemorrhage (e.g., because of anemia, prolonged oxytocic augmentation of labor, multiple gestation or hydroamnions), manual removal of the placenta, manual exploration of the uterus, or both may be necessary. After the placental delivery, the cervix and vagina should be thoroughly inspected for lacerations and surgical repair performed if necessary.

LABOR WITH OCCIPUT PRESENTATIONS

The fetus is in the occiput or vertex presentation in approximately 95 percent of all labors. Presentation is most commonly ascertained by abdominal palpation and confirmed by vaginal examination sometime before or at the onset of labor. In the majority of cases, the vertex enters the pelvis with the sagittal suture in the transverse pelvic diameter (Caldwell and associates, 1934). The fetus enters the pelvis in the left occiput transverse (LOT) position in 40 percent of labors, compared with 20 percent in the right occiput transverse (ROT) position (Caldwell and associates, 1934). In occiput anterior positions (LOA1 or ROA), the head either enters the pelvis with the occiput rotated 45 degrees anteriorly from the transverse position, or subsequently does so. The mechanism of labor usually is very similar to that in occiput transverse positions.

In about 20 percent of labors, the fetus enters the pelvis in an occiput posterior (OP) position. The right occiput posterior (ROP2) is slightly more common than the left (LOP) (Caldwell and associates, 1934). It appears likely from evidence obtained by radiographic studies that posterior positions are more often associated with a narrow forepelvis. They are also more commonly seen in association with anterior placentation (Gardberg and Tuppurainen, 1994a).

OCCIPUT ANTERIOR PRESENTATION

Because of the irregular shape of the pelvic canal and the relatively large dimensions of the mature fetal head, it is evident that not all diameters of the head can necessarily pass through all diameters of the pelvis. It follows that a process of

adaptation or accommodation of suitable portions of the head to the various segments of the pelvis is required for vaginal delivery. These positional changes in the presenting part constitute the mechanisms of labor.

ENGAGEMENT.

The mechanism by which the biparietal diameter, the greatest transverse diameter of the fetal head in occiput presentations, passes through the pelvic inlet is designated engagement. This phenomenon may take place during the last few weeks of pregnancy, or it may not occur until after the commencement of labor. In many multiparous and some nulliparous women, the fetal head is freely movable above the pelvic inlet at the on-set of labor. In this circumstance, the head is some-times referred to as "floating." A normal-sized head usually does not engage with its sagittal suture directed anteroposteriorly. Instead, the fetal head usually enters the pelvic inlet either in the transverse diameter or in one of the oblique diameters (Caldwell and colleagues, 1934).

Occiput presentations occur in about 95% of all labors. Because of the irregular shape of the pelvic canal and the relatively large dimensions of the mature fetal heard, it is evident that not all diameters of the heard can necessarily pass through all diameters of the pelvis. It follows that a process of adaptation or accommodation of suitable portions of the head to the various segments of the pelvis is required for completion of childbirth.

There are 2 kinds of the occiput presentations – anterior and posterior

The cardinal movements of labour in anterior occiput presentation are:

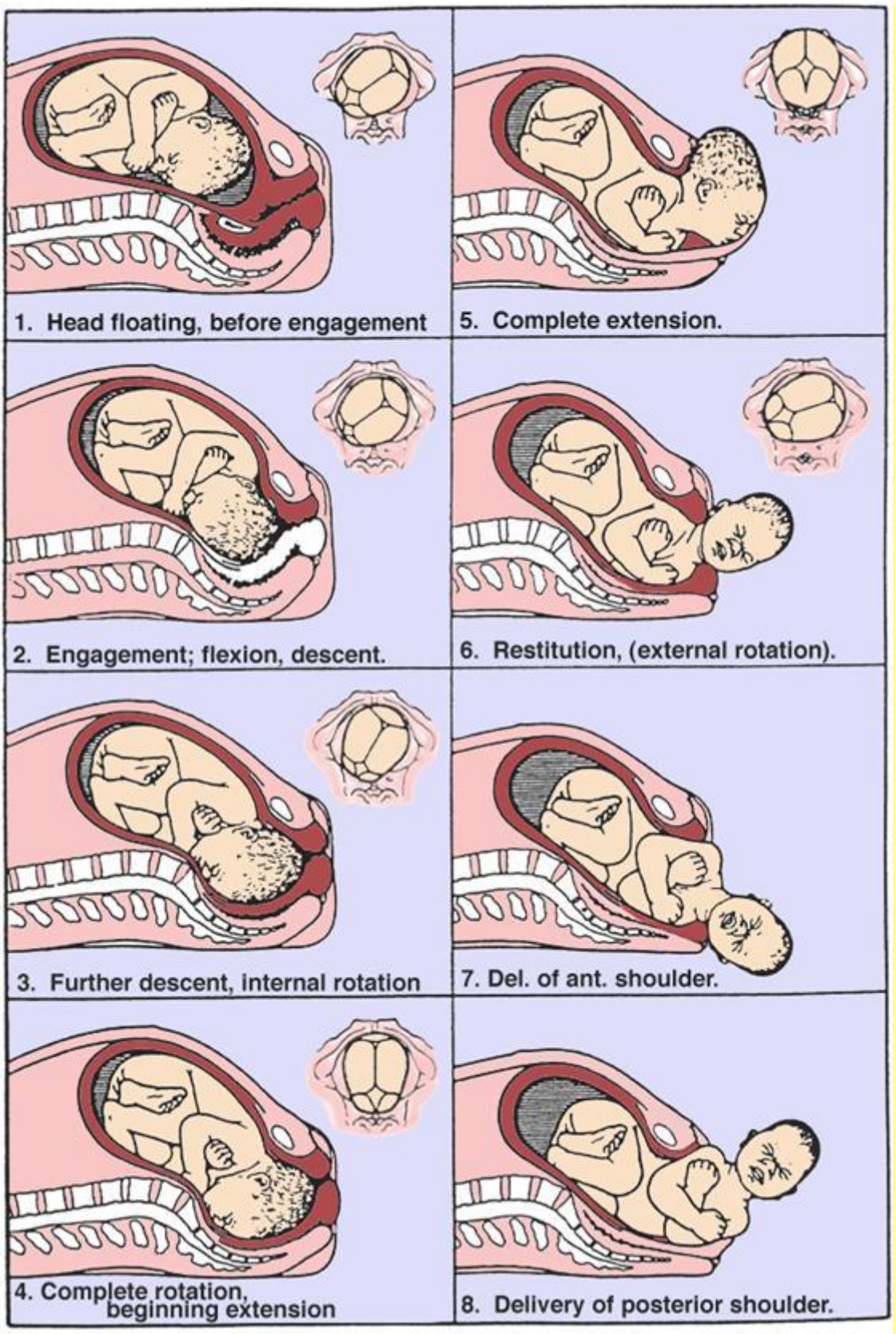
- Flexion

- Internal rotation
- Extension
- Internal rotation of the fetal head and external rotation of the fetal body

The various movements are often described as through they occurred separately and independently. In reality, the mechanism of labor consists of a combination of movements that are going on the same time. For example, as part of process of engagement, there is both flexion and descent of the head. It is manifestly impossible for the movements to be completed unless the presenting part descends simultaneously. The uterine contractions effect important modifications in the attitude, or habitus of the fetus especially after the head has descended into the pelvis. These changes consists principally in a straightening of the fetus, with loss of its dorsal convexity and closer application of the extremities and small parts of the body. As a result, the fetal ovoid is transformed into cylinder with normally the smallest possible cross section passing through the birth canal.

Synclitism and asynclitism. ***Synclitism*** is a position when the sagittal suture is in the transverse pelvic diameter. The sagittal suture lie exactly midway between the symphysis and promontory.

If the sagittal suture approaches the sacral promontory, more of the anterior parietal bone presents itself to the examining fingers and the condition is called ***anterior asynclitism*.** If the sagittal suture lies close to the symphysis more of the posterior parietal bone presents and the condition is called ***posterior asynclitism*.**



Picture 20. Biomechanism of labor in occipito-anterior presentation

The cardinal movements of labour in anterior occiput presentation are:

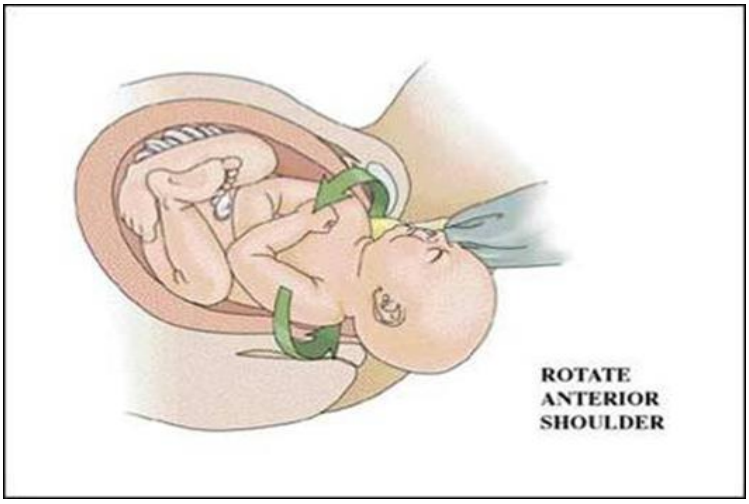
1. Flexion. As soon as descending head meets resistance, whether from the cervix, the walls of the pelvis, of the pelvic floor, flexion of the head are normally results. In this movement, the chin is brought into more intimate contact with the fetal thorax, and the shorter suboocipitobregmatic diameter is substituted for the longer occipito-frontal diameter. The leader point is the area of the small fontanel.
2. Internal rotation. This movement is a manner that the occiput gradually moves from its original position anteriorly towards the symphysis pubis os. The rotation begins when the fetal head descends from the plane of greatest pelvic dimensions to the least pelvic dimensions (midpelvis). The rotation is complete when the head reaches the pelvic floor, the saggital suture is in the anteriorposterior diameter of the pelvic outlet and the small fontanel is under the symphysis.
3. Extension. After internal rotation the sharply flexed head reaches the pelvic floor, two forces come into play. The first, exerted by the uterus, acts more posteriorly, and the second, supplied by the resistant pelvic floor, acts more anteriorly. The resultant force is the direction of the vulvar opening, thereby causing extension, Extension begins when the fixing point (fossa suboccipitalis) is under the inferior margin of the symphysis pubis. With the increasing distension of the perineum and vaginal opening, an increasingly large portion of the occiput gradually appears. The head is born by further extension as the occiput, bregma, forehead, nose, mouse.
4. Internal rotation of the fetal head and external rotation of the fetal bode. During the head extension the fetal body is in the pelvic cavity. The biacromial diameter turns from the oblique to the anteriorposterior diameter of the pelvic outlet. Thus one shoulder is anterior behind the symphysis and the other is posterior. This movement is brought about apparently by the same pelvic factors that effect internal rotation of the

head. The anterioe shoulder comes under the symphysis pubis, the fetal body flexed and posterior shoulder is born first. Then the anterior shoulder is born. Fetal head rotates as a result of the body rotation. In the I position fetal face turns towards the right, in the II position towards the elft. After delivery of the shoulders, the rest of the body of the child is quickly extruded.

The cardinal movements of labor in ***posterior occiput presentation*** are:

1. ***Flexion***. The fetal head flexed and presents the suboccipito-frontal (10 cm) diameter in oblique size of the pelvic inlet. The leader point is a middle part of sagittal suture.

2. ***Internal rotation***. The fetal head passes through the pelvic cavity and in narrow plane it begins rotate. In the outlet plane of pelvis (pelvic floor) the sagittal suture became in the direct (anterioposterior) diameter of the pelvic outlet and the small fontanel is under the sacrum os.



Picture.21. Internal rotation of the heads in case of occipito-posterior

3. **Additional flexion**. After internal rotation the head reaches the pelvic floor. Fetal head fixes with the area of the border of the hair part of head (the first fixing point) under symphysis pubis and flexes. This process leads to delivery of the vertex.

4. **Extension**. Extension begins when the second fixing point (fossa suboccipitalis) become under the tip of the sacrum. The head is born by further extension.

5. **Internal rotation of the fetal head and external rotation of the fetal body**. Shoulder enter to the inlet of small pelvis in oblique size and in pelvic cavity perform the internal rotation to 45 °, in the pelvic floor they stand in the direct (anterioposterior) size. The anterior shoulder comes under the margin of symphysis pubis, the fetal body flexed. The posterior shoulder is born first and then the anterior shoulder is born. The head rotation realize as in anterior occiput presentation.

CHANGES IN SHAPE OF THE FETAL HEAD

CAPUT SUCCEDANEUM

In vertex presentations, the fetal head undergoes important characteristic changes in shape as the result of the pressures to which it is subjected during labor. In prolonged labors before complete cervical dilatation, the portion of the fetal scalp immediately over the cervical os becomes edematous, forming a swelling known as the caput succedaneum. It usually attains a thickness of only a few millimeters, but in prolonged labors it may be sufficiently extensive to prevent the differentiation of the various sutures and fontanels. More commonly the caput is formed when the head is in the lower portion of the birth canal and frequently only after the resistance of a rigid vaginal outlet is encountered. Because it occurs over the most dependent area of the head, in LOT3 position it is found over the upper and posterior portion of the right parietal bone, and in ROT positions over the corresponding area of the

left parietal bone. It follows that after labor the original position may often be ascertained by noting the location of the caput succedaneum.

MOLDING

Molding describes the change in fetal head shape from external compressive forces. Some molding occurs before labor, possibly related to Braxton Hicks contractions. Although taught in previous editions, most studies indicate that there is seldom overlapping of the parietal bones. Instead, a "locking" mechanism at the coronal and lambdoidal connections prevents such overlapping (Carlan and colleagues, 1991). Molding is associated with a shortened suboccipitobregmatic diameter and a lengthening of the mentovertical diameter. These changes are of greatest importance in contracted pelves or asynclitic presentations. In these circumstances, the degree to which the head is capable of molding may make the difference between spontaneous vaginal delivery versus an operative delivery. Some older literature cited severe head molding as a cause for possible cerebral trauma. Because of the multitude of associated factors, for example, prolonged labor with fetal sepsis and acidosis, it is impossible to quantify the effects of molding with any alleged fetal or neonatal neurological sequelae.

CONDUCT OF NORMAL LABOR AND DELIVERY

The ideal conduct of labor and delivery requires two potentially opposing accommodations on the part of obstetrical providers: first, that birthing be recognized as a normal physiological process that most women experience without complications, and second, that intrapartum complications can arise very quickly and unexpectedly. Thus, providers must simultaneously make the woman and her supporters feel comfortable, yet ensure safety for the mother and infant should complications suddenly develop. The American Academy of Pediatrics and the American College of Obstetricians and Gynecologists (1997) have collaborated in the development of Guidelines for Perinatal Care. These provide detailed

information on the appropriate content of intrapartum care to include both personnel and facility requirements..

ADMISSION PROCEDURES

Pregnant women should be urged to report early in labor rather than to procrastinate until delivery is imminent for fear that they might be experiencing false labor. Early admittance to the labor and delivery unit is important; especially so if during antepartum care the woman, her fetus, or both have been identified as being at risk.

IDENTIFICATION OF LABOR. One of the most critical diagnoses in obstetrics is the accurate diagnosis of labor. If labor is falsely diagnosed, inappropriate interventions to augment labor may be made. Conversely, if labor is not diagnosed, the fetus-infant may be damaged by unexpected complications occurring in sites remote from medical personnel and adequate medical facilities. Although the differential diagnosis between false and true labor is difficult at times, it usually can be made on the basis of the contractions.

Contractions of true labour:

1. Contractions occur at regular intervals
2. Intervals gradually shorten
3. Intensity gradually increases
4. Discomfort is in the back and abdomen
5. Cervix dilates
6. Discomfort is not stopped by sedation

Contractions of False labour:

1. Contractions occur at irregular intervals
2. Intervals remain long
3. Intensity remains unchainged

4. Discomfort is chiefly in lower abdomen
5. Cervix does not dilate
6. Discomfort is usually relieved by sedation

In those instances when a diagnosis of labor cannot be established with certainty, it is often wise to observe the woman over a longer period of time. The general condition of mother and fetus should be ascertained accurately by history and physical examination, including blood pressure, temperature, and pulse. The frequency, duration, and intensity of the uterine contractions should be documented, and the time established when they first become uncomfortable. The degree of discomfort that the mother displays is noted. The heart rate, presentation, and size of the fetus should be determined and documented on admission. The fetal heart rate should be checked, especially at the end of a contraction and immediately thereafter, to identify pathological slowing of the heart rate. Inquiries are made about the status of the fetal membranes and whether there has been any vaginal bleeding. The questions of whether fluid has leaked from the vagina and, if so, how much and when the leakage first commenced are also addressed.

FEDERAL REQUIREMENTS FOR INTER-HOSPITAL TRANSFER OF LABORING WOMEN. All Medicare-participating hospitals with emergency services must provide an appropriate medical screening examination for any pregnant women experiencing contractions who comes to the emergency department for evaluation. The definition of an emergency condition makes specific reference to a pregnant woman who is having contractions. Labor is defined as "...the process of childbirth beginning with the latent phase of labor continuing through delivery of the placenta. A woman experiencing contractions is in true labor unless a physician certifies that after a reasonable time of observation the woman is in false labor." A woman in true labor is considered "unstable" for inter-hospital transfer purposes until the child and placenta are delivered. An unstable woman may, however, be transferred at the direction of the patient or when a physician signs a written certification that benefits of treatment at another facility outweigh the risks of

transfer. Physicians and hospitals violating these federal requirements are subject to civil penalties of up to $50,000, as well as termination from the Medicare program.

ELECTRONIC ADMISSION TESTING. Some investigators recommend that a nonstress test (NST) or contraction stress test (CST) be performed on all patients admitted to the labor and delivery unit, the so-called "fetal admission test" (Ingemarsson and associates, 1986). Such fetal surveillance is in reality an assessment of fetal heart rate accelerations or lack of the same with fetal movement (NST1); or an assessment of fetal heart rate before, during, and following a uterine contraction if the patient is in labor (CST2) (Freeman and colleagues, 1991). Fetal heart rate variability and variable decelerations also are used in these evaluations. It has been suggested that such tests of fetal well-being, alone or in combination with fetal acoustic stimulation, will identify unsuspected cases of fetal jeopardy (Ingemarsson and associates, 1988; Sarno and co-workers, 1990). Certainly, if the woman is to be discharged from the labor unit undelivered, this practice is reasonable to ensure, as nearly as possible, that fetal compromise is not identified at this time. At Parkland Hospital, external electronic monitoring is performed for at least one hour before discharging women with false labor.

Vaginal examination. Most often, unless there has been bleeding in excess of bloody show, a vaginal examination under aseptic conditions is performed. Careful attention to the following items is essential in order to obtain the greatest amount of information and to minimize bacterial contamination from multiple examinations.

1. Amniotic fluid. If there is a question of membrane rupture, a sterile speculum is carefully inserted, and fluid is sought in the posterior vaginal fornix. Any fluid is observed for vernix or meconium; if the source of the fluid remains in doubt, it is collected on a swab for further study, as described later.
2. Cervix. Softeness, degree of effacement (length), extent of dilatation, and location of the cervix with respect to the presenting part and vagina are

ascertained, as will be described. The presence of membranes with or without amniotic fluid below the presenting part often can be felt by careful palpation. The fetal membranes often can be visualized if they are intact and the cervix is dilated somewhat.

3. Presenting part. The nature of the presenting part should be positively determined and, ideally, its position as well
4. Station. The degree of descent of the presenting part into the birth canal is identified, as will be described. If the fetal head is high in the pelvis (above the level of the ischial spines), the effect of firm fundal pressure on descent of the fetal head is tested
5. Pelvic architecture. The diagonal conjugate, ischial spines, pelvic sidewalls and sacrum are reevacuated for adequacy

CERVICAL EFFACEMENT.

The degree of cervical effacement is usually expressed in terms of the length of the cervical canal compared to that of an uneffaced cervix. When the length of the cervix is reduced by one half, it is 50 percent effaced; when the cervix becomes as thin as the adjacent lower uterine segment, it is completely, or 100 percent, effaced.

CERVICAL DILATATION.

This is ascertained by estimating the average diameter of the cervical opening. The examining finger is swept from the margin of the cervix on one side to the opposite side, and the diameter traversed is expressed in centimeters. The cervix is said to be dilated fully when the diameter measures 10 cm, because the presenting part of a term-size infant usually can pass through a cervix this widely dilated.

POSITION OF THE CERVIX.

The relationship of the cervical os to the fetal head is categorized as posterior, midposition, or anterior. A posterior position is suggestive of preterm labor.

STATION.

The level of the presenting fetal part in the birth canal is described in relationship to the ischial spines, which are halfway between the pelvic inlet and the pelvic outlet. When the lowermost portion of the presenting fetal part is at the level of the ischial spines, it is designated as being at zero (0) station. In the past, the long axis of the birth canal above the ischial spines was arbitrarily divided into thirds. In 1988, the American College of Obstetricians and Gynecologists began using a classification of station that divides the pelvis above and below the spines into fifths. These divisions represent centimeters above and below the spines. Thus, as the presenting fetal part descends from the inlet toward the ischial spines, the designation is -5, -4, -3, -2, -1, then 0 station. Below the ischial spines, the presenting fetal part passes +1, +2, +3, +4, and +5 stations to delivery. Station +5 cm corresponds to the fetal head being visible at the introitus. An approximate correlation of the two methods of describg station is: +2=+1/3 and +4= +2/3 (American Academy of Pediatrics and the American College of Obstetricians and Gynecologists, 1997).

If the leading part of the fetal head is at 0 station or below, most often engagement of the head has occurred; that is, the biparietal plane of the fetal head has passed through the pelvic inlet. If the head is unusually molded, or if there is an extensive caput formation, or both, engagement might not have taken place even though the head appears to be at 0 station.

DETECTION OF RUPTURED MEMBRANES.

The pregnant woman should be instructed during the antepartum period to be aware of leakage of fluid from the vagina and to report such an occurrence promptly. Rupture of the membranes is significant for three reasons. First, if the presenting part is not fixed in the pelvis, the possibility of prolapse of the umbilical cord and cord compression is greatly increased. Second, labor is likely to occur soon if the pregnancy is at or near term. Third, if delivery is delayed for 24 hours or more after membrane rupture, there is increasing likelihood of serious intrauterine infection.

A conclusive diagnosis of rupture of the membranes is made when amnionic fluid is seen pooling in the posterior fornix or clear fluid is passing from the cervical canal (American College of Obstetricians and Gynecologists, 2000). Although several diagnostic tests for the detection of ruptured membranes have been recommended, none is completely reliable. If the diagnosis remains uncertain, another method involves testing the pH of the vaginal fluid; the pH of vaginal secretions normally ranges between 4.5 and 5.5, whereas that of amnionic fluid is usually 7.0 to 7.5. The use of the indicator nitrazine for the diagnosis of ruptured membranes, first suggested by Baptisti (1938), is a simple and fairly reliable method. Test papers are impregnated with the dye, and the color of the reaction is interpreted by comparison with a standard color chart. The pH of the vaginal secretion is estimated by inserting a sterile cotton-tipped applicator deeply into the vagina, and then touching it to a strip of the nitrazine paper and comparing the color of the paper with the chart supplied with the paper. A pH above 6.5 is consistent with ruptured membranes. False-positive tests occur with blood, semen, or bacterial vaginosis and false-negative tests with minimal fluid (American College of Obstetricians and Gynecologists, 2000).

Other tests have been used as markers for rupture of the membranes. Arborization or ferning of vaginal fluid suggests amnionic rather than cervical fluid. Detection of alpha-fetoprotein in the vaginal vault has been used to identify

amnionic fluid (Yamada and colleagues, 1998). Unequivocal identification comes from injection of various dyes, including Evans blue, methylene blue, indigo carmine, or fluorescein, into the amnionic sac via abdominal amniocentesis.

VITAL SIGNS AND REVIEW OF PREGNANCY RECORD.

The maternal blood pressure, temperature, pulse, and respiratory rate are checked for any abnormality, and these are recorded. The pregnancy record is promptly reviewed to identify complications. Any problems identified during the antepartum period, as well as any that were anticipated, should be displayed prominently in the pregnancy record.

PREPARATION OF VULVA AND PERINEUM.

The woman is positioned to allow inspection and cleansing of the vulva and perineum. Scrubbing is directed from above, downward, and away from the introitus. Attention should be paid to careful cleansing of the vulvar folds. As the scrub sponge passes over the anal region, it is discarded. If hair on the lower half of the vulva or perineum is felt to interfere at the time of delivery, it can be clipped with scissors or a mini-shave prep can be performed. Routine shaving of the perineum is not performed at Parkland Hospital.

VAGINAL EXAMINATIONS.

Ideally, after the vulvar and perineal regions have been properly prepared, and the examiner has donned sterile gloves, the thumb and forefinger of one hand are used to separate the labia widely to expose the vaginal opening and prevent the examining fingers from coming in contact with the inner surfaces of the labia. The index and second fingers of the other hand are then introduced into the vagina. A precise routine of evaluation, as described earlier should be followed. It is important to avoid the anal region and not to withdraw the fingers from the vagina until the

examination is completed. The number of vaginal examinations during labor does correlate with infectious morbidity, especially in cases of early membrane rupture.

ENEMA.

Early in labor, a cleansing enema often is given to minimize subsequent contamination by feces, which otherwise may be a problem during the second stage of labor and delivery. A ready-to-use enema solution of sodium phosphate in a disposable container (Fleet enema) has proven satisfactory. Enemas are not routinely used at Parkland Hospital.

LABORATORY.

When the woman is admitted in labor, most often the hematocrit, or hemoglobin concentration, should be rechecked. The hematocrit can be measured easily and quickly. Blood may be collected in a plain tube from which a heparinized capillary tube is filled immediately. By employing a small microhematocrit centrifuge in the labor-delivery unit, the value can be obtained in 3 minutes. A labeled tube of blood is allowed to clot and is kept on hand for blood type and screen, if needed, and another is used for routine serology. In some units, a voided urine specimen, as free as possible of debris, is examined for protein and glucose. We obtain a urine specimen for protein analysis only in hypertensive women. Patients who have had no prenatal care should be considered to be at risk for syphilis, hepatitis B, and human immunodeficiency virus (American Academy of Pediatrics and the American College of Obstetricians and Gynecologists, 1997). In unregistered patients, these laboratory studies as well as a blood type, Rh, and antibody screen for atypical antibodies should be performed. Some states, for example Texas, now require routine testing for syphilis, hepatitis B, and human immunodeficiency virus in all women admitted to labor and delivery units.

MANAGEMENT OF FIRST STAGE OF LABOR

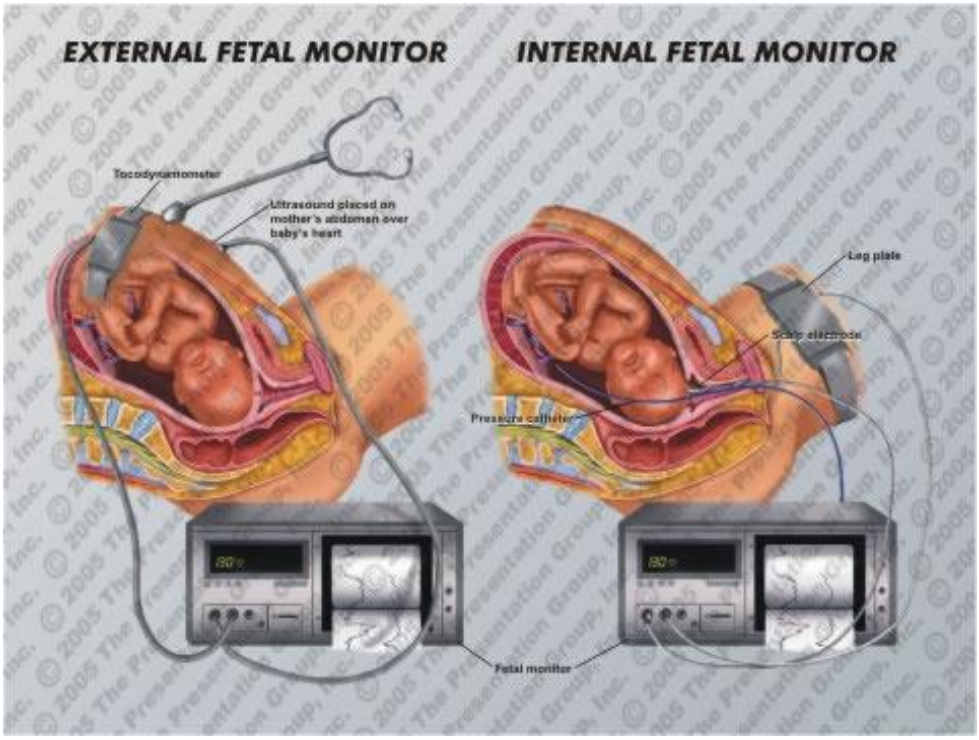
As soon as possible after admittance, the remainder of the general physical examination is completed. The physician can best reach a conclusion about the normalcy of the pregnancy when all examinations, including record and laboratory review, are completed. A rational plan for monitoring labor then can be established based on the needs of the fetus and the mother. If no abnormality is identified or suspected, the mother should be reassured. Although the average duration of the first stage of labor in nulliparous women is about 7 hours and in parous women about 4 hours, there are marked individual variations. Any precise statement as to the duration of labor, therefore, is unwise.

MONITORING FETAL WELL-BEING DURING LABOR

It is mandatory for optimal pregnancy outcome that a well-defined program be established that provides careful surveillance of the well-being of both mother and fetus during labor. All observations must be appropriately recorded. The frequency, intensity, and duration of uterine contractions, and the response of the fetal heart rate to the contractions, are of considerable concern. These features can be promptly evaluated in logical sequence.

FETAL HEART RATE

The fetal heart rate may be identified with a suitable stethoscope or any of a variety of Doppler ultrasonic devices. Changes in the fetal heart rate that most likely are ominous almost always are detectable immediately after a uterine contraction. Therefore, it is imperative that the fetal heart be monitored by auscultation immediately after a contraction. To avoid confusing maternal and fetal heart rates, the maternal pulse should be counted as the fetal heart rate is counted. Otherwise, maternal tachycardia may be misinterpreted as a normal fetal heart rate.



Picture 22. Internal and external fetal monitor

Fetal jeopardy, compromise, or distress—that is, loss of fetal well-being—is suspected if the fetal heart rate immediately after a contraction is repeatedly below 110 bpm. Fetal jeopardy very likely exists if the rate is heard to be less than 100 per minute, even though there is recovery to a rate in the 110 to 160 bpm range before the next contraction. When decelerations of this magnitude are found after a contraction, further labor, if allowed, is best monitored electronically.

The American Academy of Pediatrics and American College of Obstetricians and Gynecologists (1997) recommend that during the first stage of labor, in the absence of any abnormalities, the fetal heart should be checked immediately after a contraction at least every 30 minutes and then every 15 minutes during the second stage. If continuous electronic monitoring is used, the tracing is evaluated at least every 30 minutes during the first stage and at least every 15 minutes during second-stage labor. For women with pregnancies at risk, auscultation is performed at least every 15 minutes during the first stage of labor and every 5 minutes during the second stage. Continuous electronic monitoring may be used with evaluation of the

tracing every 15 minutes during the first stage of labor, and every 5 minutes during the second stage.

UTERINE CONTRACTIONS.

With the palm of the hand lightly on the uterus, the examiner determines the time of onset of the contraction. The intensity of the contraction is gauged from the degree of firmness the uterus achieves. At the acme of effective contractions, the finger or thumb cannot readily indent the uterus. Next, the time that the contraction disappears is noted. This sequence is repeated in order to evaluate the frequency, duration, and intensity of uterine contractions. It is best to quantify the contractions as regards the degree of firmness or resistance to indentation.

MATERNAL MONITORING AND MANAGEMENT DURING LABOR

MATERNAL VITAL SIGNS. Maternal temperature, pulse, and blood pressure are evaluated at least every 4 hours (Table 13-3). If fetal membranes have been ruptured for many hours before the onset of labor, or if there is a borderline temperature elevation, the temperature is checked hourly. Moreover, with prolonged membrane rupture—defined as greater than 18 hours—antimicrobial administration for prevention of group B streptococcal infections is recommended (American College of Obstetricians and Gynecologists, 1996).

SUBSEQUENT VAGINAL EXAMINATIONS. During the first stage of labor, the need for subsequent vaginal examinations to identify the status of the cervix and the station and position of the presenting part will vary considerably. When the membranes rupture, an examination should be repeated expeditiously if the fetal head was not definitely engaged at the previous vaginal examination. The fetal heart rate should be checked immediately and during the next uterine contraction in order to detect an occult umbilical cord compression. At Parkland Hospital, periodic pelvic examinations are often performed at 2- to 3-hour intervals to evaluate the progress of labor.

ORAL INTAKE. Food should be withheld during active labor and delivery. Gastric emptying time is remarkably prolonged once labor is established and analgesics are administered. As a consequence, ingested food and most medications remain in the stomach and are not absorbed; instead, they may be vomited and aspirated. There is a trend toward giving liquids in moderation to laboring women. Guyton and Gibbs (1994) cite studies in which 150 mL of fluids were given orally 2 hours before elective surgery. The incidence of aspiration was not affected. It is unclear whether these studies can be applied to women in labor, who are at risk for urgent cesarean delivery at all times.

INTRAVENOUS FLUIDS. Although it has become customary in many hospitals to establish an intravenous infusion system routinely early in labor, there is seldom any real need for such in the normally pregnant woman at least until analgesia is administered. An intravenous infusion system is advantageous during the immediate puerperium in order to administer oxytocin prophylactically, and at times therapeutically when uterine atony persists. Moreover, with longer labors, the administration of glucose, sodium, and water to the otherwise fasting woman at the rate of 60 to 120 mL/hr is efficacious to prevent dehydration and acidosis

MATERNAL POSITION DURING LABOR. The normal laboring woman need not be confined to bed early in labor. A comfortable chair may be beneficial psychologically and perhaps physiologically. In bed, the laboring woman should be allowed to assume the position she finds most comfortable, which will be lateral recumbency most of the time. She must not be restricted to lying supine. Bloom and colleagues (1998) conducted a randomized trial of walking during labor in over 1000 women with low-risk pregnancies. They found that walking neither enhanced nor impaired active labor and that it was not harmful.

ANALGESIA. Most often, analgesia is initiated on the basis of maternal discomfort. The kinds of analgesia, amounts, and frequency of administration should

be based on the need to allay pain on the one hand and the likelihood of delivering a depressed infant on the other.

The timing, method of administration, and size of initial and subsequent doses of systemically acting analgesic agents are based to a considerable degree on the anticipated interval of time until delivery. A repeat vaginal examination is often appropriate before administering more analgesia. With the onset of symptoms characteristic of the second stage of labor, that is, an urge to bear down or "push," the status of the cervix and the presenting part should be reevaluated.

AMNIOTOMY. If the membranes are intact, there is a great temptation even during normal labor to perform amniotomy. The presumed benefits are more rapid labor, earlier detection of instances of meconium staining of amnionic fluid, and the opportunity to apply an electrode to the fetus and insert a pressure catheter into the uterine cavity. The advantages and disadvantages of amniotomy are discussed in Chapter 18. If amniotomy is performed, an aseptic technique should be used. Importantly, the fetal head must be well applied to the cervix and not be dislodged from the pelvis during the procedure; such an action invites prolapse of the umbilical cord.

URINARY BLADDER FUNCTION. Bladder distention should be avoided, because it can lead to obstructed labor and to subsequent bladder hypotonia and infection. During each abdominal examination, the suprapubic region should be visualized and palpated in order to detect a filling bladder. If the bladder is readily seen or palpated above the symphysis, the woman should be encouraged to void. At times she can ambulate with assistance to a toilet and successfully void, even though she could not void on a bedpan. If the bladder is distended and she cannot void, intermittent catheterization is indicated.

MANAGEMENT OF SECOND-STAGE LABOR

With full dilatation of the cervix, which signifies the onset of the second stage of labor, the woman typically begins to bear down, and with descent of the presenting part she develops the urge to defecate. Uterine contractions and the accompanying expulsive forces may last 11/2 minutes and recur at times after a myometrial resting phase of no more than a minute.

DURATION

The median duration of the second stage is 50 minutes in nulliparas and 20 minutes in multiparas, but it can be highly variable. In a woman of higher parity with a relaxed vagina and perineum, two or three expulsive efforts after the cervix is fully dilated may suffice to complete the delivery of the infant. Conversely, in a woman with a contracted pelvis or a large fetus, or with impaired expulsive efforts from conduction analgesia or intense sedation, the second stage may become abnormally long.

FETAL HEART RATE.

For the low-risk fetus, the heart rate should be auscultated during the second stage of labor at least every 15 minutes, whereas in those at high risk, 5-minute intervals are recommended (American Academy of Pediatrics and the American College of Obstetricians and Gynecologists, 1997). Slowing of the fetal heart rate induced by head compression is common during a contraction and the accompanying maternal expulsive efforts. If recovery of the fetal heart rate is prompt after the contraction and expulsive efforts cease, labor is allowed to continue. Not all instances of fetal heart rate slowing during second-stage labor are the consequence of head compression. The vigorous force generated within the uterus by its contraction and by maternal expulsive efforts may reduce placental perfusion appreciably. Descent of the fetus through the birth canal and the consequent reduction in uterine volume may trigger some degree of premature separation of the

placenta, with further compromise of fetal well-being. Descent is more likely to tighten a loop or loops of umbilical cord around the fetus, especially the neck, sufficiently to obstruct umbilical blood flow. Prolonged, uninterrupted maternal expulsive efforts can be dangerous to the fetus in these circumstances. Maternal tachycardia, which is common during the second stage, must not be mistaken for a normal fetal heart rate.

MATERNAL EXPULSIVE EFFORTS.

In most cases, bearing down is reflex and spontaneous during second-stage labor, but occasionally the woman does not employ her expulsive forces to good advantage and coaching is desirable. Her legs should be half-flexed so that she can push with them against the mattress. Instructions should be to take a deep breath as soon as the next uterine contraction begins, and with her breath held, to exert downward pressure exactly as though she were straining at stool. She should not be encouraged to "push" beyond the time of completion of each uterine contraction. Instead, she and her fetus should be allowed to rest and recover from the combined effects of the uterine contraction, breath holding, and considerable physical effort. Gardosi and associates (1989) have recommended a squatting or semi-squatting position using a specialized pillow. They claim that this shortens second-stage labor by increasing expulsive forces and by increasing the diameter of the pelvic outlet. Eason and colleagues (2000) performed an extensive review of positions and their effect on the incidence of perineal trauma. They found that the supported upright position had no advantages over the recumbent one.

Usually, bearing down efforts result in increasing bulging of the perineum—that is, further descent of the fetal head. The woman should be informed of such progress, for encouragement is very important. During this period of active bearing down, the fetal heart rate auscultated immediately after the contraction is likely to be slow, but should recover to normal range before the next expulsive effort.

As the head descends through the pelvis, feces is frequently expelled by the woman. As the head descends still farther, the perineum begins to bulge and the overlying skin becomes tense and glistening. Now the scalp of the fetus may be visible through the vulvar opening. At this time, or before in instances where little perineal resistance to expulsion is anticipated, the woman and her fetus are prepared for delivery.

PREPARATION FOR DELIVERY.

Delivery can be accomplished with the mother in a variety of positions. The most widely used and often the most satisfactory one is the dorsal lithotomy position in order to increase the diameter of the pelvic outlet. In many birthing rooms this is accomplished with the woman lying flat on the bed. For better exposure, leg holders or stirrups are used. In placing the legs in leg holders, care should be taken not to separate the legs too widely or place one leg higher than the other, as this will exert pulling forces on the perineum that might easily result in the extension of a spontaneous tear or an episiotomy into a fourth-degree tear. The popliteal region should rest comfortably in the proximal portion and the heel in the distal portion of the leg-holder. The leg should not be forced to conform to the preexisting setting. The legs are not strapped into the stirrups, thereby allowing quick flexion of the thighs back onto the abdomen should shoulder dystocia be encountered. Cramps in the legs may develop during the second stage in part because of pressure by the fetal head on nerves in the pelvis. Such cramps may be relieved by changing the position of the leg or by brief massage, but leg cramps should never be ignored.

Preparation for delivery entails vulvar and perineal cleansing. If desired, sterile drapes may be placed in such a way that only the immediate area about the vulva is exposed. In the past, the major reason for care in scrubbing, gowning, and gloving was to protect the laboring woman from the introduction of infectious agents. Although these considerations remain valid, concern today also must be

extended to the health-care providers, because of the threat of exposure to human immunodeficiency virus.

SPONTANEOUS DELIVERY

DELIVERY OF THE HEAD

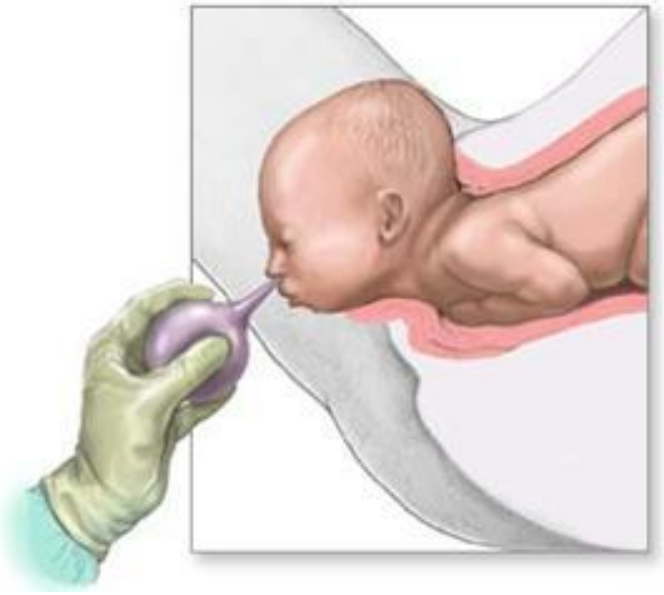
With each contraction, the perineum bulges increasingly and the vulvovaginal opening becomes more dilated by the fetal head), gradually forming an ovoid and finally an almost circular opening. With the cessation of each contraction, the opening becomes smaller as the head recedes. As the head becomes increasingly visible, the vaginal outlet and vulva are stretched further until they ultimately encircle the largest diameter of the fetal head. This encirclement of the largest head diameter by the vulvar ring is known as crowning.

Unless an episiotomy has been made, as described later in the chapter, the perineum by now is extremely thin and, especially in the case of the nulliparous woman, may undergo spontaneous laceration. At the same time, the anus becomes greatly stretched and protuberant, and the anterior wall of the rectum may be easily seen through it. Over many years there has been considerable controversy concerning whether an episiotomy should be cut. We advocate individualization and do not routinely cut an episiotomy. It is now clear that an episiotomy will increase the risk of a tear into the external anal sphincter and/or the rectum. Conversely, anterior tears involving the urethra and labia are much more common in women in whom an episiotomy is not cut.

Immediately after delivery of the infant, there is usually a gush of amniotic fluid, often tingeled with blood but not grossly bloody.

CLEARING THE NASOPHARYNX. To minimize the likelihood of aspiration of amnionic fluid, debris, and blood that might occur once the thorax is

delivered and the infant can inspire, the face is quickly wiped and the nares and mouth are aspirated.



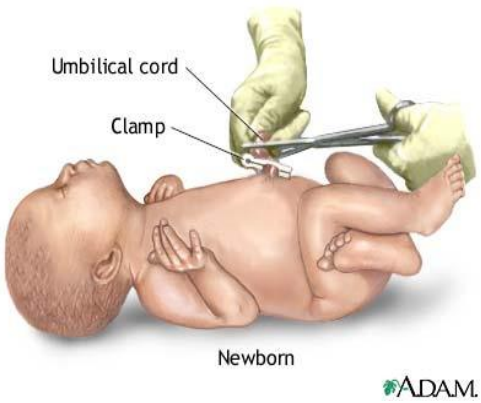
PIcture.23. Clearing the nasopharynx

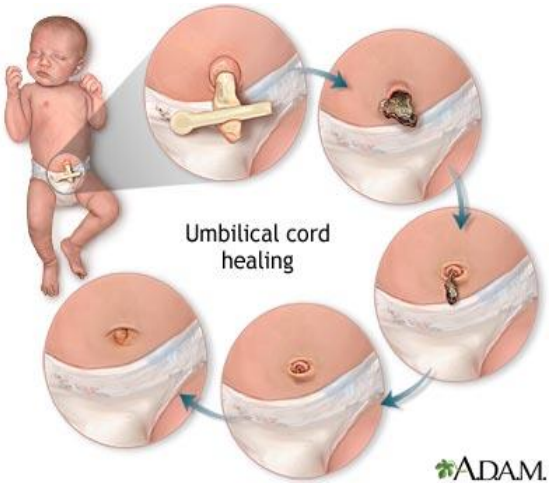
NUCHAL CORD. Following delivery of the anterior shoulder, the finger should be passed to the neck of the fetus to ascertain whether it is encircled by one or more coils of the umbilical cord. Nuchal cords occur in about 25 percent of cases and ordinarily do no harm. If a coil of umbilical cord is felt, it should be drawn down between the fingers and, if loose enough, slipped over the infant's head. If it is applied too tightly to the neck to be slipped over the head, it should be cut between two clamps and the infant promptly delivered.

Picture.24. Cord clamp

CLAMPING THE CORD

The umbilical cord is cut between two clamps placed 4 or 5 cm from the fetal abdomen, and later an umbilical cord clamp is applied 2 or 3 cm from the fetal abdomen. A plastic clamp (Hollister, Double Grip Umbilical Clamp) that is safe, efficient, easy to sterilize, and fairly inexpensive.





PIcture.25 Cord Clamping

Picture.26. Cord healing

TIMING OF CORD CLAMPING.

If, after delivery, the infant is placed at or below the level of the vaginal introitus for 3 minutes and the fetoplacental circulation is not immediately occluded by clamping the cord, an average of 80 mL of blood may be shifted from the placenta to the infant (Yao and Lind, 1974). One benefit to be derived from placental transfusion is that the hemoglobin in 80 mL of placental blood that shifts to the fetus eventually provides about 50 mg of iron, which reduces the frequency of iron-deficiency anemia later in infancy. In the presence of accelerated destruction of erythrocytes, as occurs with maternal alloimmunization, the bilirubin formed from the added erythrocytes contributes further to the danger of hyperbilirubinemia Although the theoretical risk of circulatory overloading from gross hypervolemia is

formidable, especially in preterm and growth-retarded infants, addition of placental blood to the otherwise normal infant's circulation ordinarily does not cause difficulty.

Our policy is to clamp the cord after first thoroughly clearing the airway, all of which usually takes about 30 seconds. The infant is not elevated above the introitus at vaginal delivery or much above the maternal abdominal wall at the time of cesarean delivery.

MANAGEMENT OF THE THIRD STAGE

Immediately after delivery of the infant, the height of the uterine fundus and its consistency are ascertained. As long as the uterus remains firm and there is no unusual bleeding, watchful waiting until the placenta is separated is the usual practice. No massage is practiced; the hand is simply rested on the fundus frequently, to make certain that the organ does not become atonic and filled with blood behind a separated placenta.

SIGNS OF PLACENTAL SEPARATION

Because attempts to express the placenta prior to its separation are futile and possibly dangerous, it is most important that the following signs of placental separation be recognized:

1. The uterus becomes globular and, as a rule, firmer. This sign is the earliest to appear.

2. There is often a sudden gush of blood.

3. The uterus rises in the abdomen because the placenta, having separated, passes down into the lower uterine segment and vagina, where its bulk pushes the uterus upward.

4. The umbilical cord protrudes farther out of the vagina, indicating that the placenta has descended.

These signs sometimes appear within about 1 minute after delivery of the infant and usually within 5 minutes. When the placenta has separated, it should be ascertained that the uterus is firmly contracted. The mother may be asked to bear down, and the intra-abdominal pressure so produced may be adequate to expel the placenta. If these efforts fail, or if spontaneous expulsion is not possible because of anesthesia, and after ensuring that the uterus is contracted firmly, pressure is exerted with the hand on the fundus to propel the detached placenta into the vagina. This approach has been termed physiological management, as later to be contrasted with "active management" of the third stage (Thilaganathan and colleagues, 1993).

DELIVERY OF THE PLACENTA

Placental expression should never be forced before placental separation lest the uterus be turned inside out. Traction on the umbilical cord must not be used to pull the placenta out of the uterus. Inversion of the uterus is one of the grave complications associated with delivery. As pressure is applied to the body of the uterus, the umbilical cord is kept slightly taut. The uterus is lifted cephalad with the abdominal hand. This maneuver is repeated until the placenta reaches the introitus (Prendiville and associates, 1988b). As the placenta passes through the introitus, pressure on the uterus is stopped. The placenta is then gently lifted away from the introitus. Care is taken to prevent the membranes from being torn off and left behind. If the membranes start to tear, they are grasped with a clamp and removed by gentle traction. The maternal surface of the placenta should be examined carefully to ensure that no placental fragments are left in the uterus.

Occasionally, the placenta will not separate promptly. This is especially common in cases of preterm delivery (Dombrowski and colleagues, 1995).. It is unclear as to the length of time that should elapse in the absence of bleeding before

the placenta is manually removed. Manual removal of the placenta is rightfully practiced much sooner and more often than in the past. In fact, some obstetricians practice routine manual removal of any placenta that has not separated spontaneously by the time they have completed delivery of the infant and care of the cord in women with conduction analgesia. Proof of the benefits of this practice, however, has not been established, and most obstetricians await spontaneous placental separation unless bleeding is excessive.

Picture.27. Manual removal of placenta

ACTIVE MANAGEMENT OF THE THIRD STAGE

Thilaganathan and associates (1993) compared a regimen of active management with syntometrine (5 units of oxytocin with 0.5 mg of ergometrine) and controlled cord traction with one of physiological management wherein the cord was not clamped and the placenta was delivered by maternal efforts. Among 103 low-risk term deliveries, active management resulted in a reduction in the length of the

third stage of labor, but no reduction in blood loss compared with physiological management. Mitchell and Elbourne (1993) found that syntometrine administered intramuscularly concurrent with delivery of the anterior shoulder was more effective than oxytocin (5 units intramuscularly) alone in the prevention of postpartum hemorrhage. Duration of the third stage of labor and need for manual removal of the placenta were similar. Side effects of nausea, vomiting, and blood pressure elevations with ergometrine prevented any recommendation for its routine usage.

THE PUERPERIUM

Puerperium is strictly defined as the period of confinement during and just after birth. By popular use, however, the meaning usually includes the 6 subsequent weeks during which normal pregnancy involution occurs (Hughes, 1972). Of course maternal adaptations to pregnancy do not necessarily all subside completely by 6 weeks postpartum.

CLINICAL AND PHYSIOLOGICAL ASPECTS OF THE PUERPERIUM

UTERINE CHANGES

The pueperium consists of the period following delivery of the baby and placenta to approximately 6 weeks postpartum. During the puerperium, the reproductive organs and maternal physiology return toward the pregnancy state although menses may not return for much longer.

Involution of the uterus. Immediate after delivery, the fundus of the uterus is easily palpable on the level of the umbilicus. The immediate reduction in uterine size is the result of delivery of the fetus, placenta and amniotic fluid as well as the loss of hormonal stimulation. Further uterine involution is caused by autolysis of intracellular myometrial protein, resulting in a decrease in cell size but not cell number. Through these changes, the uterus returns.

As the myometrial fibers contract, the blood clots from uterus are expelled and the thrombi in the large vessels of the placental bed undergo organization. Within the first 3 days, the remaining decidua differentiates into a superficial layer, which becomes necrotic and sloughs, and a basal layer adjacent to the myometrium, which contained the fundi of the endometrial glands and is the source of the new endometrium.

Immediately after the delivery of the placenta, the uterus is palpated bimanually to ascertain that it is firm.

This discharge is fairly heavy at first and rapidly decreases in amount over the first 2 to 3 days postpartum, although it may last for several weeks.

Lochia changes:

1-3 day after labor – bloody

4-6 day after labor – bloody-serous

7-9 day after labor- serous-bloody

10 day after labor- serous

For the first few days after delivery, the uterine discharge appears red (lochia rubra) owing the presents of erythrocytes. After 3 to 4 days, the lochia becomes paler (lochia serosa), and by the tenth day, it assumes a white or yellow- white color (lochia alba). By the end of the third week postpartum, the endometrium is reestablished in most patients.

Cervix. Just after the labor the cervix admits the hand. Within several hours of delivery the cervix has reformed, and on 4-5 day it usually admits only one finger (i.e., it is approximately 1cm in diameter), on 9-10 day cervix closed. The round shape of the nulliparous cervix is usually permanently replaced by a transverse, fish-mouth shaped external os, the result of laceration during delivery. Vulvar and

vaginal tissues return to normal over the first several days, although the vaginal mucosa reflects a hypoestrogenic state if the woman breast-feeds because ovarian function is suppressed during breast-feeding.

Abdominal wall. Return of the elastic fibers of the stretched rectus muscles to normal configuration occurs slowly and is aided by exercise.

At time of delivery, the drop of estrogen and other placental hormones is a major factor in removing the inhibition of the action of prolactin. also, suckling by the infant stimulates release of oxytocin from the neurohypophysis. On approximately the second day after delivery, colostrum is secreted. After about 3 to 6 days, the colostrum is replaced by mature milk.

CHANGES IN THE CERVIX AND LOWER UTERINE SEGMENT.

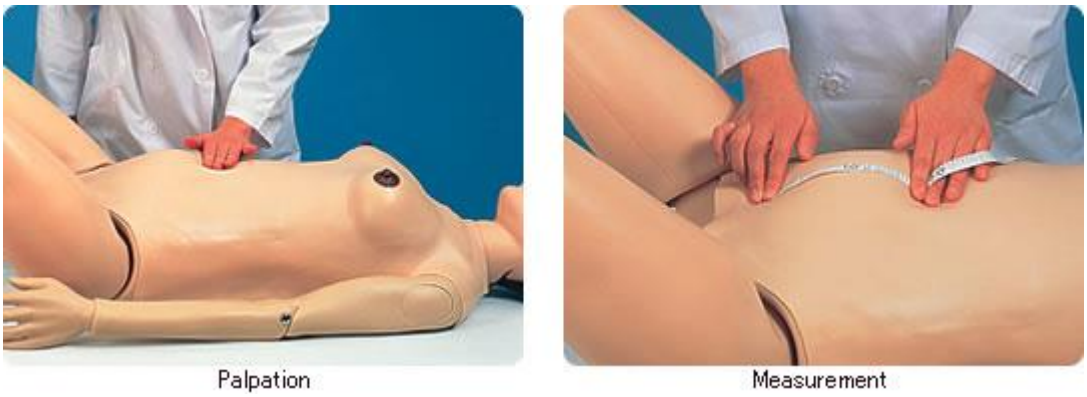
The outer cervical margin, which corresponds to the external os, is usually lacerated, especially laterally. The cervical opening contracts slowly, and for a few days immediately after labor it readily admits two fingers. By the end of the first week, it has narrowed. As the opening narrows, the cervix thickens, and a canal reforms. At the completion of involution, however, the external os does not resume its pregravid appearance completely. It remains somewhat wider, and typically, bilateral depressions at the site of lacerations remain as permanent changes that characterize the parous cervix. It should also be kept in mind that the cervical epithelium undergoes considerable remodeling as a result of childbirth. For example, Ahdoot and colleagues (1998) found that approximately 50 percent of women with high-grade squamous intraepithelial cells showed regression as a result of vaginal delivery.

The markedly thinned-out lower uterine segment contracts and retracts but not as forcefully as the body of the uterus. Over the course of a few weeks, the lower segment is converted from a clearly evident structure, large enough to contain most

of the fetal head, into a barely discernible uterine isthmus located between the uterine corpus above and the internal cervical os below.

INVOLUTION OF THE UTERINE CORPUS.

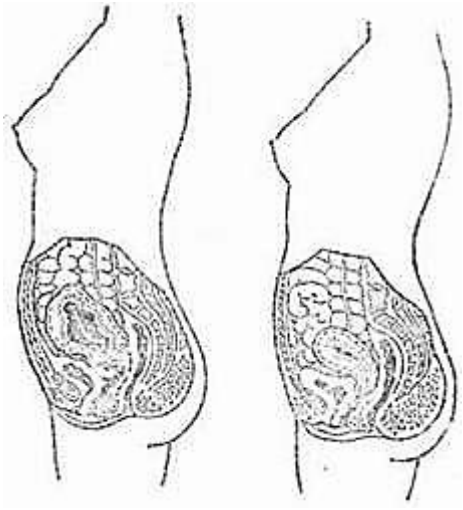
Immediately after placental expulsion, the fundus of the contracted uterus is slightly below the umbilicus. The uterine body then consists mostly of myometrium covered by serosa and lined by basal decidua. The anterior and posterior walls, in close apposition, each measure 4 to 5 cm in thickness. Because its vessels are compressed by the contracted myometrium, the puerperal uterus on section appears ischemic when compared with the reddish-purple hyperemic pregnant organ. After the first 2 days, the uterus begins to shrink, so that within 2 weeks it has descended into the cavity of the true pelvis. It regains its previous nonpregnant size within about 4 weeks. The immediately postpartum uterus weighs approximately 1000 g. As the consequence of involution, 1 week later it weighs about 500 g, decreasing at the end of the second week to about 300 g, and soon thereafter to 100 g or less. The total number of muscle cells does not decrease appreciably; instead, the individual cells decrease markedly in size. The involution of the connective tissue framework occurs equally rapidly.



Picture.28-29. Palpation and measurement of uterine fundus

Because separation of the placenta and membranes involves the spongy layer, the decidua basalis remains in the uterus. The decidua that remains has striking variations in thickness, an irregular jagged appearance, and is infiltrated with blood, especially at the placental site.

Picture. 30. Separation of placenta



AFTERPAINS. In primiparas the puerperal uterus tends to remain tonically contracted. Particularly in multiparas, the uterus often contracts vigorously at intervals, giving rise to afterpains. Occasionally these pains are severe enough to require an analgesic. Afterpains are noticeable particularly when the infant suckles, likely because of oxytocin release. Usually, they decrease in intensity and become mild by the third postpartum day.

Conventional obstetrical wisdom has for many years taught that lochia lasted for approximately 2 weeks after delivery. Recent studies, however, have indicated that lochia persists for up to 4 weeks and may stop and resume up to 56 days after delivery (Oppenheimer and colleagues, 1986; Visness and co-workers, 1997). Maternal age, parity, infant weight, and breast feeding do not influence the duration of lochia.

In some centers, it is routine to prescribe an oxytocic agent to hasten uterine involution by promoting uterine contractility. This also presumably diminishes bleeding complications. Newton and Bradford (1961), however, concluded that after the period immediately following delivery, routine administration of intramuscular oxytocin to normal women was of no value in decreasing blood loss or hastening uterine involution.

ENDOMETRIAL REGENERATION.

Within 2 or 3 days after delivery, the remaining decidua becomes differentiated into two layers. The superficial layer becomes necrotic, and it is sloughed in the lochia. The basal layer adjacent to the myometrium remains intact and is the source of new endometrium. The endometrium arises from proliferation of the endometrial glandular remnants and the stroma of the interglandular connective tissue.

Endometrial regeneration is rapid, except at the placental site. Within a week or so, the free surface becomes covered by epithelium, and the entire endometrium is restored during the third week. Sharman (1953) identified fully restored endometrium in all biopsy specimens obtained from the 16th postpartum day onward. So-called endometritis identified histologically during the puerperium is only part of the normal reparative process. Similarly, in almost half of postpartum women, fallopian tubes, between 5 and 15 days, demonstrate microscopical inflammatory changes characteristic of acute salpingitis. This, however, is not infection, but only part of the involutional process (Andrews, 1951).

SUBINVOLUTION. This term describes an arrest or re-tardation of involution, the process by which the puerperal uterus is normally restored to its original proportions. It is accompanied by prolongation of lochial discharge and irregular or excessive uterine bleeding and sometimes by profuse hemorrhage. On bimanual examination, the uterus is larger and softer than normal for the particular period of the puerperium. Among the recognized causes of subinvolution are retention of placental fragments and pelvic infection. Because most cases of subinvolution result from local causes, they are usually amenable to early diagnosis and treatment. Ergonovine (Ergotrate) or methylergonovine (Methergine), 0.2 mg every 3 to 4 hours for 24 to 48 hours, is recommended by some clinicians, but its efficacy is questionable. On the other hand, metritis responds to oral antimicrobial therapy. Wager and colleagues (1980) reported that almost a third of cases of later

postpartum uterine infection are caused by Chlamydia trachomatis; thus tetracycline therapy may be appropriate.

Andrew and colleagues (1989) described 25 cases of hemorrhage between 7 and 40 days postpartum associated with noninvoluted uteroplacental arteries. These abnormal arteries were characterized by no detectable endothelial lining and the vessels were filled with thrombi. Periauricular trophoblasts were also present in the walls of these vessels and the authors postulated that subinvolution, at least with regard to the placental vessels, may represent an aberrant interaction between uterine cells and trophoblast.

PLACENTAL SITE INVOLUTION. According to Williams (1931), complete extrusion of the placental site takes up to 6 weeks. This process is of great clinical importance, for when it is defective, late-onset puerperal hemorrhage may ensue. Immediately after delivery, the placental site is about the size of the palm of the hand, but it rapidly decreases thereafter. By the end of the second week, it is 3 to 4 cm in diameter. Within hours of delivery, the placental site normally consists of many thrombosed vessels that ultimately undergo the typical organization of a thrombus.

Williams (1931) explained involution of the placental site as follows:

Involution is not effected by absorption in situ, but rather by a process of exfoliation which is in great part brought about by the undermining of the implantation site by growth of endometrial tissue. This is affected partly by extension and downgrowth of endometrium from the margins of the placental site and partly by the development of endometrial tissue from the glands and stroma left in the depths of the decidua basalis after placental separation. Such exfoliation should be regarded as very conservative, and as a wise provision; otherwise great difficulty might be experienced in sloughing obliterated arteries and organized

thrombi which, if they remained in situ, would soon convert a considerable part of the uterine mucosa and subjacent myometrium into a mass of scar tissue.

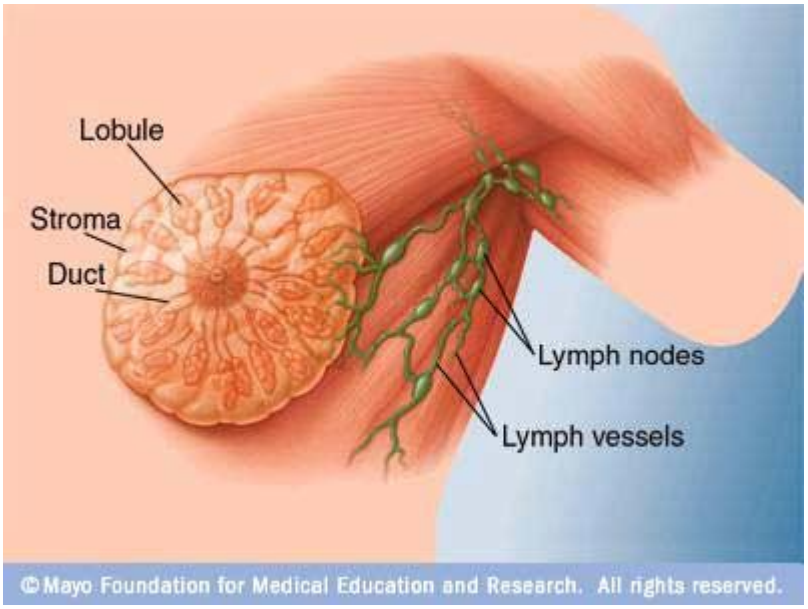
Anderson and Davis (1968) concluded that placental site exfoliation is brought about as the consequence of sloughing of infarcted and necrotic superficial tissues followed by a reparative process.

MAMMARY GLANDS

BREAST ANATOMY

Anlagen of mammary glands are contained in ectodermal ridges that form on the ventral surface of the embryo and extend laterally from forelimb to hindlimb. The multiple pairs of buds normally disappear from the embryo except for one pair in the pectoral region that eventually develops into the two mammary glands . At times, however, the buds elsewhere may not completely disappear, but instead they may participate to an amazing degree in the pattern of growth that characterizes the two normal mammary glands.

Picture.31. Lactation settlement - 1



At midpregnancy, each of the two fetal mammary buds destined to form the breasts begins to grow and divide. This results in the formation of 15 to 25 secondary buds that provide the basis for the duct system in the mature breast. Each secondary bud elongates into a cord, bifurcates, and differentiates into two concentric layers of cuboidal cells and a central lumen. The inner layer of cells eventually gives rise to the secretory epithelium, which synthesizes the milk. The outer cell layer becomes myoepithelium, which provides the mechanism for milk ejection .

Picture.32.

Lactation settlement - 2

Thelarche is the onset of rapid breast growth that begins about the time of puberty when estrogen production rises. The previously infantile mammary glands respond to estrogen with growth and development of mammary ducts and fat deposition. With ovulation, progesterone stimulates development of the alveoli for future lactation.

Anatomically, each mature mammary gland is composed of 15 to 25 lobes that arose from the secondary buds described previously. The lobes are arranged radially and are separated from one another by varying amounts of fat. Each lobe consists of several lobules, which in turn are made up of large numbers of alveoli Every alveolus is provided with a small duct that joins others to form a single larger duct for each lobe. These lactiferous ducts open separately upon the nipple, where

they may be distinguished as minute but distinct orifices. The alveolar secretory epithelium synthesizes the various milk constituents.

BREAST FEEDING

LACTATION. Colostrum is the deep lemon-yellow colored liquid secreted initially by the breasts. It usually can be expressed from the nipples by the second postpartum day.

COLOSTRUM.

Compared with mature milk, colostrum contains more minerals and protein, much of which is globulin, but less sugar and fat. Colostrum nevertheless contains large fat globules in so-called colostrum corpuscles. These are thought by some investigators to be epithelial cells that have undergone fatty degeneration and by others to be mononuclear phagocytes containing fat. Colostrum secretion persists for about 5 days, with gradual conversion to mature milk during the ensuing 4 weeks. Antibodies are demonstrable in the colostrum, and its content of immunoglobulin A may offer protection for the newborn against enteric pathogens. Other host resistance factors, as well as immunoglobulins, are found in human colostrum and milk. These include complement, macrophages, lymphocytes, lactoferrin, lacto-peroxidase, and lysozymes.

MILK.

Human milk is a suspension of fat and protein in a carbohydrate-mineral solution. A nursing mother easily makes 600 mL of milk per day. Milk is isotonic with plasma, with lactose accounting for half of the osmotic pressure. Major proteins, including a-lactalbumin, ß-lactoglobulin, and casein, are also present. Essential amino acids are derived from blood, and nonessential amino acids are derived in part from blood or synthesized in the mammary gland. Most milk proteins are unique and not found elsewhere. Whey has been shown to contain large amounts

of interleukin-6 (Saito and co-workers, 1991). Peak levels of this cytokine were found in colostrum, and there was a positive correlation between its concentration and the number of mononuclear cells in human milk. Additionally, interleukin-6 was associated closely with local immunoglobulin A production by the breast. Prolactin appears to be actively secreted into breast milk (Yuen, 1988). Epidermal growth factor (EGF) has also been identified in human milk (Koldovsky and associates, 1991; McCleary, 1991). Because this factor is not destroyed by gastric proteolytic enzymes, it may be absorbed orally and promote growth and maturation of intestinal mucosa.

There are major changes in milk composition by 30 to 40 hours postpartum, including a sudden increase of lactose concentration. Lactose synthesis from glucose in alveolar secretory cells is catalyzed by lactose synthase. Some lactose enters the maternal circulation and is excreted by the kidney. This may be misinterpreted as glucosuria unless specific glucose oxidase is used in testing. Fatty acids are synthesized in the alveoli from glucose and are secreted by an apocrine-like process.

All vitamins except vitamin K are found in human milk, but in variable amounts, and maternal dietary supplementation increases the secretion of most of these (American Academy of Pediatrics, 1981). Vitamin K administration to the infant soon after delivery is required to prevent hemorrhagic disease of the newborn.

Human milk contains a low iron concentration and maternal iron stores do not seem to influence the amount of iron in breast milk. Therefore, the use of supplemental iron-fortified infant formulas, or a weaning formula also fortified with iron, is recommended (American Academy of Pediatrics, 1997). Such formulas apparently have eliminated iron-deficiency anemia during childhood (Yip and associates, 1987). These formulas are well tolerated by most infants and there is no evidence that they impair absorption of zinc or copper (Nelson and associates, 1988; Yip and colleagues, 1985).

Mennella and Beauchamp (1991) documented what experienced nursing mothers have long known: breast-fed infants are aware of what their mothers eat and drink. They studied the effects of maternal ethanol ingestion equivalence to one can of beer. This caused the infants to suck more frequently during the first minute of feeding, but ultimately they consumed significantly less milk.

The mammary gland, like the thyroid gland, concentrates iodine and several other minerals, including gallium, technetium, indium, and possibly sodium. Radioactive isotopes of these minerals should not be given to nursing women because they rapidly appear in breast milk. The American Academy of Pediatrics (1997) recommends consultation with a nuclear medicine physician before performing a diagnostic study, so that a radionuclide with the shortest excretion time in breast milk can be used. They further recommend that the mother pump her breasts before the study and store enough milk in a freezer for feeding the infant. After the study, she should pump her breasts to maintain milk production, but discard all milk produced during the time that radioactivity is present. This ranges from 15 hours up to 2 weeks, depending upon the isotope used.

The concentrations vary depending upon maternal diet and when studied in the puerperium (Brasil and co-workers, 1991; Giovannini and colleagues, 1991; Ogunleye and associates, 1991). Gestational weight gain has little, if any, impact on the subsequent milk quantity or quality (Institute of Medicine, 1990).

ENDOCRINOLOGY OF LACTATION.

The precise humoral and neural mechanisms involved in lactation are complex. Progesterone, estrogen, and placental lactogen, as well as prolactin, cortisol, and insulin, appear to act in concert to stimulate the growth and development of the milk-secreting apparatus of the mammary gland (Porter, 1974). With delivery, there is an abrupt and profound decrease in the levels of progesterone and estrogen, which removes the inhibitory influence of progesterone on the

production of a-lactalbumin by the rough endoplasmic reticulum . The increased a-lactalbumin serves to stimulate lactose synthase and ultimately increased milk lactose. Progesterone withdrawal also allows prolactin to act unopposed in its stimulation of a-lactalbumin production.

The intensity and duration of subsequent lactation are controlled, in large part, by the repetitive stimulus of nursing. Prolactin is essential for lactation; women with extensive pituitary necrosis, as in Sheehan syndrome, do not lactate. Although plasma prolactin falls after delivery to lower levels than during pregnancy, each act of suckling triggers a rise in levels (McNeilly and associates, 1983). Presumably a stimulus from the breast curtails the release of prolactin-inhibiting factor from the hypothalamus; this, in turn, transiently induces increased prolactin secretion.

The neurohypophysis, in pulsatile fashion, secretes oxytocin. This stimulates milk expression from a lactating breast by causing contraction of myoepithelial cells in the alveoli and small milk ducts. Milk ejection, or "letting down," is a reflex initiated especially by suckling, which stimulates the neurohypophysis to liberate oxytocin (McNeilly and associates, 1983). It may be provoked even by the cry of the infant or inhibited by fright or stress.

In women who continue lactating but who resume ovulation, there are acute alterations in breast milk composition 5 to 6 days before and 6 to 7 days following ovulation (Hartmann and Prosser, 1984). These changes are abrupt and characterized by increased concentrations of sodium and chloride, along with decreased potassium, lactose, and glucose concentrations. In women who become pregnant but who continue to breast feed, milk composition undergoes progressive alterations suggesting gradual loss of metabolic and secretory breast activity

Nipple care is also important during breast-feeding. The nipples should be washed with water and exposed to the air for 15 to 20 minutes after each feeding. A

water-based cream such as lanolin or vitamin A and D ointment may be applied if the nipples are tender.

Mastitis is an uncommon complication of breast-feeding and usually develops 2 to 4 weeks after beginning breast-feeding. The first symptoms are usually slight fever and chills. These are followed by redness of a segment of the breast, which becomes indurated and painful. The etiologic agent is usually Staphylococcus aureus, which originates from the infant's oral pharynx. Milk should be obtained from the breast for the culture and sensitivity, and mother should be started on a regimen of antibiotics immediately. Because the majority of staphylococcal organisms are penicillinase-producing, a penicillinase-resistant antibiotic, such as dicloxacillin, should be used. Breast-feeding should be discontinued, and an appropriate antibiotic should be continued for 7 to 10 days. If a breast abscess ensues, it should be surgically drained. A breast pump can be used to maintain lactation until the infection has cleared, but the milk should be discarded. The infant, along with other family members, should be evaluated for staphylococcal infections that may be source of reinfection if breast-feeding is resumed.

Placental insufficiency. Fetal hypoxia (acute, chronic). Retardation, malnutrition of the fetus.

Placental insufficiency or Utero-placental insufficiency is insufficient blood flow to the placenta during pregnancy. The term is also sometimes used to designate late decelerations of fetal heart rate as measured by electronic monitoring, even if there is no other evidence of reduced blood flow to the placenta, normal uterine blood flow rate being 600mL/min.

Causes

Placental insufficiency can be induced experimentally by bilateral uterine artery ligation of the pregnant rat.

The following characteristics of placentas have been said to be associated with placental insufficiency, however all of them occur in normal healthy placentas and full term healthy births, so none of them can be used to accurately diagnose placental insufficiency:

- Abnormally thin placenta (less than 1 cm)
- Circumvallate placenta (1% of normal placentas)
- Amnion cell metaplasia, (amnion nodosum) (present in 65% of normal placentas)
- Increased syncytial knots
- Calcifications
- Infarcts due to focal or diffuse thickening of blood vessels
- Villi capillaries occupying about 50% of the villi volume or when <40% of capillaries are on the villous periphery

Placental insufficiency should not be confused with complete placental abruption, in which the placenta separates off the uterine wall, which immediately results in no blood flow to the placenta, which leads to immediate fetal demise. In the case of a

marginal, incomplete placental abruption of less than 50%, usually weeks of hospitalization precedes delivery and outcomes are not necessarily affected by the partial abruption

Pathophysiology

Maternal effects

Several aspects of maternal adaptation to pregnancy are affected by dysfunction of placenta. Maternal arteries fail to transform into low-resistance vessels (expected by 22–24 weeks of gestation). This increases vascular resistance in fetoplacental vascular bed eventually leading to reduction in metabolically active mass of placenta like a vicious cycle.

Fetal effects

Placental insufficiency can affect the fetus, causing fetal distress. Placental insufficiency may cause oligohydramnios, preeclampsia, miscarriage or stillbirth. Placental insufficiency is most frequent cause of asymmetric IUGR.

Fetal metabolic changes

Metabolic changes occurring in uteroplacental insufficiency:

Substrate	**Change**
Glucose	Decreases in proportion to degree of fetal hypoxemia
Amino acids	• Decrease in branched chain amino acids (valine, leucine, isoleucine), serine and lysine. • Increase in hydroxyproline • Glycine: Valine ratio increases in amniotic fluid • Increase in ammonia in amniotic fluid (positive correlation with ponderal index)
Fatty acids	• Decrease in long-chain polyunsaturated fatty acids • Decrease in overall fatty acid transport via umbilical cord

Oxygen and Carbon dyoxide	• Degree of hypoxemia is proportional to villous damage • Hypercapnia, acidemia, hyoiglycemia and hyperlacticemia and in proportion to hypoxemia

Fetal hormonal changes

Decrease in overall thyroid function is correlated with fetal hypoxemia. Serum glucagon, adrenaline, noradrenaline levels increase, eventually causing peripheral glycogenolysis and mobilization of fetal hepatic glycogen stores.

Fetal hematologic changes

Fetal hypoxemia triggers erythropoietin release. This stimulates RBC production from medullary and extramedullary sites and eventually results in polycythemia. Oxygen carrying capacity of blood is thus increased. Prolonged tissue hypoxemia may cause early release of erythrocytes from maturation sites and thus count of nucleated RBCs in blood increases. These factors, increase in blood viscosity, decrease in cell membrane fluidity and platelet aggregation are important precurosrs in accelerating placental vascular occlusion.

Fetal immunological changes

There is decrease in immunoglobulin, absolute B-cell counts and total WBC count. T-helper and cytotoxic T-cells are suppressed in proportion of degree of acidemia. These conditions lead to higher infection susceptibility of infant after delivery.

Fetal cardiovascular changes

There is decrease in magnitude of umbilical venous volume flow. In response to this, proportion of umbilical venous blood diverted to fetal heart increases. This eventually leads to elevation of pulmonary vascular resistance and increased right ventricular afterload. This redistribution of blood flow is early response to placental

insufficiency. Blood flow is selectively redirected to myocardium, adrenal glands and, particularly, brain. The last phenomenon is called "brain-sparing effect".

In late stage, the redistribution becomes ineffective, there is decrease in cardiac output, ineffective preload handling and elevation of central venous pressure. This deterioration in cardiovascular state may ultimately lead to tricuspid insufficiency and fetal demise. Peripheral circulatory disturbances also accompany these central circulatory changes.

Fetal behavioral changes

Chronic hypoxemia leads to delay in all aspects of CNS maturation. With worsening fetal hypoxemia, there is decline in fetal activity. With further hypoxemia, fetal breathing ceases. Gross body movements and tone decrease further. Fetal heart rate decreases due to spontaneous deceleration due to direct depression of cardiac contractility. This leads to intrauterine fetal death.

Risk of later metabolic disease

According to the theory of thrifty phenotype, placental insufficiency triggers epigenetic responses in the fetus that are otherwise activated in times of chronic food shortage. If the offspring actually develops in an environment rich in food it may be more prone to metabolic disorders, such as obesity and type II diabetes.

Placental insufficiency (or uteroplacental vascular insufficiency) is a complication of pregnancy when the placenta is unable to deliver an adequate supply of nutrients and oxygen to the fetus, and, thus, cannot fully support the developing baby. Placental insufficiency occurs when the placenta either does not develop properly or because it has been damaged. It is commonly defined as a reduction in the maternal blood supply (reduced uterine artery blood flow). However, we define placental insufficiency to include reduction in maternal blood supply AND/OR the failure of the maternal blood supply to increase or adapt appropriately by mid-

pregnancy. Placental insufficiency can result pregnancy complications, including fetal growth restriction, pre-eclampsia and others, all of which are described below. The management of placental insufficiency is dependent upon additional tests and the unique characteristics of each patient. Factors considered during management of complicated pregnancies are maternal medical and obstetrical history, weight, ethnicity, and blood pressure. Findings of placental insufficiency on placental function testing

The following diagram outlines the list of abnormal findings which signal utero-placental vascular insufficiency (UPVI), as assessed by the following placental function tests: umbilical artery Doppler (baby's blood flow to the placenta), maternal biochemistry, placental morphology, and uterine artery Doppler (mother's blood flow to the placenta).

Management of placental insufficiency

Once placental insufficiency has been diagnosed, the next steps depend on when in pregnancy the diagnosis is made.

Management before the developing baby is viable (<24 weeks):

By offering women a program of serial testing at 12, 16 and 20 weeks, the diagnosis of placental insufficiency is typically made before any ill effects on the mother (pre-eclampsia) or the developing baby (growth restriction) are evident. Rarely, one or both may be seen before 20 weeks, and, if so, the outcome is often poor, unfortunately. Although most women and their developing babies with multiple test abnormalities before 24 weeks are healthy at that point, showing early signs of pre-eclampsia and growth restriction increases the risk of preterm delivery (<32 weeks), with a chance of it happening being 30%.

The management approach of these patients is as follows:

- *Provide co-care with the referring obstetrician/family doctor/midwife, or assume full care, if requested*: since the risk of preterm delivery is high, maintaining an ongoing relationship with the regional high-risk pregnancy unit is essential; this permits a smooth transfer of care as needed;
- *Educate the woman about pre-eclampsia so she can self-monitor at home*: this prevents late diagnosis when severe uncontrolled hypertension may result in earlier delivery (than if the blood pressure was found early and treated carefully) and can sometimes cause injury to the mother or her developing baby;
- *Provide a plan of fetal monitoring using ultrasound* so that IUGR is recognized and monitored carefully;
- Integrate this plan with regular visits (standard antenatal care).

Management after the developing baby is viable (>24 weeks):

If placental insufficiency is diagnosed in later stages of pregnancy, the disease can either remain *sub-clinical* (not be expressed as IUGR and/or pre-eclampsia), or one or more of several issues develop:

- Excess maternal weight gain, leg swelling, headaches (signs of pre-eclampsia)
- The mother's stomach measures small, the baby is not moving very well (signs of IUGR)
- The baby has not moved for two days and no fetal heart beat can be found in the Clinic using a Doptone (signs of stillbirth)
- Some vaginal bleeding and/or contractions develop (signs of preterm labour with placental separation, or abruption)

The following steps will be taken if any of the above mentioned conditions are noted:

- If a degree of either pre-eclampsia or IUGR develops, then visit frequency is increased from bi-weekly to every week, then to twice a week and ultimately hospital admission for daily monitoring;
- If a concern about the need for delivery arises before 32 weeks, then the mother will be offered a course of steroids (2 intra-muscular [thigh] injections). These steroids diffuse across the placenta to strengthen the developing baby's lungs, helping the fetus prepare in the event that an early delivery is indicated;
- If pre-eclampsia and/or IUGR are more severe and are likely to require delivery before 32 weeks, then a high-risk Obstetrician or Maternal-Fetal Medicine specialist takes over to provide intensive outpatient or inpatient care.

Placental insufficiency, also referred to as uteroplacental vascular insufficiency, is a rare pregnancy complication, affecting only 1 in every 300 pregnancies. However, it’s a serious complication, and if not detected and treated as soon as possible, can lead to life-threatening health complications for both infant and mothers.

Placental Insufficiency Causes

Placental insufficiency is a blood disorder marked by inadequate blood flow to the placenta during pregnancy. In turn, the infant is unable to receive adequate nutrients and oxygen, making it difficult for the baby to grow and thrive while in utero. The earlier placental insufficiency surfaces in pregnancy, the more serious the health risks become.

The most common causes and risk factors associated with placental insufficiency include:

- Preeclampsia
- Diabetes

- Smoking and/or taking illegal drugs
- Taking blood thinner medications
- Maternal blood clotting

Placental Insufficiency Symptoms

Unfortunately, placental insufficiency doesn't have any outward symptoms. However, women who have been pregnant before may notice less fetal movement when compared to previous pregnancies.

Dangers of Placental Insufficiency

In most cases, mothers are not at risk for death if placental insufficiency develops, but preeclampsia, one of the most common risk factors of the condition, may heighten the risk. Preeclampsia alone brings on its own set of dangers to the mother, including extremely high blood pressure, abnormal weight gain, edema, protein in the urine, and severe headaches.

Other maternal dangers if placental insufficiency develops include:

- Heightened risk of premature labor and delivery
- Placental abruption
- Bleeding and premature contractions
- Heightened risk of an emergency cesarean surgery (C-section)
- Maternal infections and blood clotting
- Post-term pregnancy

For infants, the risks of placental insufficiency can be life-threatening, especially if it develops during the first trimester. Some of the risks include:

- Oxygen deprivation during the labor and delivery period
- Hypothermia
- Low blood sugar

- Intrauterine growth restriction (IUGR)
- Excessive red blood cell count

Infants are also at risk for numerous birth defects. According to a study performed by the American College of Obstetrics & Gynecology (ACOG), an early onset of placental insufficiency places infants at 40% higher risk of developing the following birth defects:

- Brain damage
- Lung dysfunction
- Gastrointestinal problems

Diagnosis and Treatment for Placental Insufficiency

Prenatal care by a qualified physician is imperative for the diagnosis and treatment of placental insufficiency. During a routine ultrasound, placental insufficiency can be detected due to the smaller uterus and the placement of the placenta. Additionally, checking the mother's alpha-fetoprotein levels can help detect the condition as well as a monitoring and measuring the baby's heart rate.

Since preeclampsia, as mentioned earlier, is one of the leading risk factors of placental insufficiency, getting the mother's high blood pressure under control can help the infant thrive and grow. If the mother has diabetes, the blood sugar must be monitored and kept under control.

Since preterm labor is a risk factor, some physicians may opt to give the mother steroid shots in order to strengthen the baby's lungs.

It's important for physicians to detect and monitor women suffering from placental insufficiency. If left untreated, the aforementioned dangers are heightened.

Placental Insufficiency Prognosis

Although there is no cure for placental insufficiency, it can be managed with the correct medical assistance and intervention. Again, early diagnosis and treatment is vital for not only the management of placental insufficiency, but also for the health of both mother and baby.

Placental Insufficiency

Placental insufficiency, also known as placental dysfunction or uteroplacental vascular insufficiency, is an uncommon but serious complication of pregnancy. It occurs when the placenta does not develop properly, or is damaged.

The placenta is an organ that grows in the womb during pregnancy. When the placenta malfunctions, it is unable to supply adequate oxygen and nutrients to the baby from the mother's bloodstream. Without this vital support, the baby cannot grow and thrive.

Placental insufficiency is a blood flow disorder. It is marked by a reduction in the mother's blood supply, and/or the failure of the blood supply to increase adequately by mid-pregnancy.

Placental insufficiency can lead to low birth weight, premature birth, and birth defects. It also carries increased risks of complications for the mother.

It is important to diagnose this problem early and get proper prenatal care.

Vital Functions of the Placenta

The placenta is a highly complex biological organ. It forms and grows where the fertilized egg attaches to the wall of the uterus.

The umbilical cord grows from the placenta to the baby's navel. The umbilical cord allows blood to flow from mother to baby, and back again. The mother's blood and the baby's blood are filtered through the placenta, but never actually mix.

The placenta's primary jobs are to:

- move oxygen into the baby's bloodstream
- carry carbon monoxide away
- pass nutrients to the baby
- transfer waste for disposal by the mother's body

The placenta has an important role in hormone production as well. It also protects the fetus from harmful bacteria and infections.

A healthy placenta continues to grow throughout the pregnancy. It weighs about 1.5 lbs. at the time of birth.

Causes of Placental Insufficiency

Placental insufficiency is linked to blood flow problems, and maternal blood and vascular disorders can trigger it. Certain medications and unhealthy habits can also cause it.

The most common conditions linked to placental insufficiency are:

- diabetes
- chronic high blood pressure
- blood clotting disorders
- anemia
- certain medications (particularly blood thinners)
- smoking
- drug abuse (especially cocaine, heroin, and methamphetamine)

Placental insufficiency may also occur if the placenta doesn't attach properly to the uterine wall, or if the placenta breaks away from it (placental abruption).

Placental Insufficiency Risks

Mother

Placental insufficiency is not usually considered life threatening to the mother. However, if she has high blood pressure or diabetes, the risks increase.

During pregnancy, the mother is more likely to experience:

- pre-eclampsia (elevated blood pressure and protein in the urine)
- placental abruption (placenta pulls away from the uterine wall)
- preterm labor and delivery

The symptoms of pre-eclampsia are excess weight gain, leg and hand swelling (edema), headaches and high blood pressure.

If the baby is not growing properly, the mother's abdomen will be small, and the baby's movements will not be felt much.

Vaginal bleeding or pre-term labor contractions may occur with placental abruption.

Baby

The earlier in the pregnancy that placental insufficiency occurs, the more severe the problems can be for the baby. The baby's risks include:

- greater chance of death during delivery
- greater risk of oxygen deprivation at birth (can cause cerebral palsy and other complications)
- greater chance of learning disabilities

- intrauterine growth restriction (IUGR) (low weight in the womb; specifically, the baby weighs 90 percent less than he or she should)
- hypothermia (low body temperature)
- hypoglycemia (low blood sugar)
- hypocalcemia (too little calcium in the blood)
- polycythemia (excess red blood cells)
- premature labor
- cesarean delivery

According to a 2007 study by the American College of Obstetrics & Gynecology, birth defects occurred in nearly 40 percent of infants affected by early-onset placental insufficiency.

Sadly, the most common birth defects seen in this study were:

- lung disease
- brain hemorrhage
- gastrointestinal disease

According to the study, approximately 20 percent of the babies did not survive (Baschat et al.).

Symptoms of Placental Insufficiency

There are no maternal symptoms associated with placental insufficiency. However, certain clues can lead to early diagnosis. The mother may notice that the size of her uterus is smaller than in previous pregnancies. Additionally, the fetus may be moving less than expected.

Diagnosis and Management of Placental Insufficiency

Getting proper prenatal care beginning at 12 weeks can lead to an early diagnosis. This can improve outcomes for the mother and the baby.

Tests that can detect placental insufficiency include:

- pregnancy ultrasound to measure the size of the placenta
- ultrasound to monitor the size of the fetus
- alpha-fetoprotein levels in the mother's blood (a protein made in the baby's liver)
- fetal non-stress test (involves the wearing of two belts on the mother's abdomen and sometimes a gentle buzzer to wake the baby) to measure the baby's heart rate and contractions

Treating maternal high blood pressure or diabetes can help improve the baby's growth.

The plan of maternity care may recommend:

- education on pre-eclampsia, as well as self-monitoring for the disease
- more frequent doctor visits
- bed rest to conserve fuel and energy for the baby
- consultation with a high-risk maternal fetal specialist

You may need to keep a daily record of when the baby moves or kicks.

If there is concern about premature birth (32 weeks or earlier), the mother may receive steroid injections. Steroids dissolve through the placenta and strengthen the baby's lungs.

You may need intensive outpatient or inpatient care if pre-eclampsia or IUGR become severe.

Long-Term Outlook

Placental insufficiency cannot be cured, but it can be managed. It is extremely important to receive an early diagnosis and adequate prenatal care. These can

improve the baby’s chances of normal growth and decrease the risks of birth complications.

Placental insufficiency

Alternate Names

- placental dysfunction

Definition

Placental insufficiency is the failure of the placenta to supply nutrients to the unborn child and remove toxic wastes.

What is going on in the body?

When the placenta fails to develop or function properly, the baby cannot grow and develop normally. The earlier in the pregnancy that this occurs, the more severe the problems.

If placental insufficiency occurs for a long time during the pregnancy, it may lead to intrauterine growth restriction (IUGR).

Risks

What are the causes and risks of the condition?

Between 3 to 7% of all pregnancies are complicated by IUGR due to placental insufficiency. A low birth weight may be suspected if the size of the woman's uterus is smaller than what is expected for each week of pregnancy. The woman has a higher risk of having a child with IUGR if the following are present:

- defects of the placental membranes
- defects of the umbilical cord
- abnormal implantation of the placenta in the uterus
- a break in the placental membrane that causes the baby's blood to mix with the mother's blood

- Rh incompatibility, a condition in which the mother's blood is not compatible with the baby's blood
- being pregnant with twins or triplets
- previous low-birth-weight infant
- long-term high blood pressure
- diabetes
- severe kidney disease
- heavy smoking
- insufficient weight gain by the mother during pregnancy, defined as less than 10 pounds
- preeclampsia or eclampsia, conditions which raise the mother's blood pressure
- high altitude
- drug addiction, such as addiction to cocaine
- blood thinners such as warfarin
- immunosuppressive medications
- human immunodeficiency virus (HIV) infection in the mother
- alcohol abuse
- infection with cytomegalovirus, toxoplasmosis, rubella, or syphilis, known collectively as TORCH infections
- poor nutrition of the mother
- unborn child with known birth defects or chromosome abnormalities
- frequent vaginal bleeding due to placenta previa, a condition in which the placenta is attached to the uterus over or near the cervix
- certain blood disorders in the mother, such as sickle cell anemia or thalassemia
- premature placental separation, known as placental abruption

Prevention

What can be done to prevent the condition?

Most cases of placental insufficiency and IUGR cannot be prevented.

However, there are several tests that can be done early in pregnancy to help detect problems. These include:

- pregnancy ultrasound scans to check the condition and size of the placenta
- alpha-fetoprotein (AFP) levels in a sample of the mother's blood
- amniocentesis to check for problems with the baby's chromosomes

Pregnant women can also do the following to help prevent these conditions:

- avoid close contact with persons carrying the rubella virus or cytomegalovirus
- avoid toxoplasmosis, by not coming in contact with uncooked meat and animal excrement, especially from cats
- avoid alcohol, smoking, and illicit drugs
- get treatment for high blood pressure and diabetes

Before becoming pregnant, women should follow a healthy diet that contains folate. This can help to decrease the rate of certain anomalies in the baby.

Diagnosed

How is the condition diagnosed?

Pregnancy ultrasounds can be used to check on the growth of the baby and placenta. It is important that this condition be diagnosed early in the pregnancy. This is to prevent the serious complications that may arise for the baby during labor as well as in later life.

Long Term Effects

What are the long-term effects of the condition?

Long-term effects of placental insufficiency depend on the underlying cause. During the pregnancy a mother may be restricted to bed and have to take several precautions.

The long-term effects for a baby born following placenta insufficiency can be serious. After birth, he or she will tend to remain physically small. There is a higher risk for neurological and intellectual impairments. Major disabilities include severe mental retardation, cerebral palsy, and seizures.

Other Risks

What are the risks to others?

With placental insufficiency, there are many risks to the fetus during the pregnancy, at delivery, and after delivery. These risks include:

- 8-fold higher risk of death during delivery
- 5-fold higher risk of poor oxygenation at birth that may lead to cerebral palsy and other complications
- hypothermia, or low body temperature
- hypoglycemia, or low blood sugar
- 30 to 40% chance of learning disabilities
- premature delivery
- poor tolerance of labor
- increased chance of cesarean birth
- increased chance of having birth defects
- increased chance of meconium aspiration, in which the baby inhales some of the amniotic fluid during labor
- polycythemia, which is an excess of red blood cells
- hypocalcemia, which is too little calcium in the blood

Treatments

What are the treatments for the condition?

To treat this condition, the healthcare provider may recommend that the pregnant woman:

- stop smoking
- stop taking illicit drugs, such as cocaine
- stop drinking alcohol
- eat a healthy diet that includes more than 2500 calories per day
- rest in bed during the day, lying on the left side as much as possible
- take low-dose aspirin to prevent tiny blood clots from forming in the placenta, as well as to dilate, or open, the blood vessels
- pay attention to the movement of the baby, any contractions, or rupture of the membranes ("breaking water") earlier than expected
- deliver in a hospital setting
- have the baby monitored electronically during labor
- use as little anesthesia as possible and no narcotics during labor
- have a cesarean birth or forceps delivery if fetal distress is detected

Side Effects

What are the side effects of the treatments?

The side effects of surgery include bleeding, infection, and allergic reaction to the anesthesia . Medications have various side effects, including stomach upset, rash, and allergic reaction.

After Treatment

What happens after treatment for the condition?

Placental insufficiency is not considered life-threatening to the mother. However, she may be at risk for significant illness or even death if she has an underlying condition such as high blood pressure or diabetes.

Placental insufficiency may cause serious conditions in the newborn, such as pneumonia, cerebral palsy, or other respiratory problems. A newborn who is born prematurely or with serious medical conditions may need an incubator, a special enclosed bed that can control temperature and oxygen levels.

If a child is born with cerebral palsy, there may be disabilities that require therapy, use of appliances such as crutches or canes, and a daily struggle with medical problems. As the child gets older, there may be a need for special education programs for learning disabilities caused by oxygen and nutritional deprivation while in the uterus.

Monitor

How is the condition monitored?

If testing later in pregnancy shows that the baby's lungs are mature, then labor should be induced and the baby delivered. The following tests should be done when the baby is very premature or the lungs haven't matured fully:

- nonstress testing performed weekly or biweekly, to monitor uterine contractions
- biophysical profile done weekly or biweekly
- Doppler umbilical artery waveforms, a special test for baby's health
- pregnancy ultrasound scans every 10 to 14 days
- Intrauterine hypoxia occurs when the fetus is deprived of an adequate supply of oxygen. It may be due to a variety of reasons such as prolapse or occlusion of the umbilical cord, placental infarction and maternal smoking. Intrauterine growth restriction (IUGR) may cause or be the result of hypoxia. Intrauterine hypoxia can cause cellular damage that occurs within the central nervous system (the brain and spinal cord). This results in an increased mortality rate, including an increased risk of sudden infant death syndrome (SIDS). Oxygen deprivation in the fetus and neonate have been implicated as either a primary or as a contributing risk factor in numerous neurological and neuropsychiatric disorders such as epilepsy, ADHD, eating disorders and cerebral palsyCause
- There are various causes for intrauterine hypoxia (IH). The most preventable cause is maternal smoking. Cigarette smoking by expectant mothers has been

shown to have a wide variety of deleterious effects on the developing fetus. Among the negative effects are carbon monoxide induced tissue hypoxia and placental insufficiency which causes a reduction in blood flow from the uterus to the placenta thereby reducing the availability of oxygenated blood to the fetus. Placental insufficiency as a result of smoking has been shown to have a causal effect in the development of pre-eclampsia. While some previous studies have suggested that carbon monoxide from cigarette smoke may have a protective effect against preeclampsia, a recent study conducted by the Genetics of Pre-Eclampsia Consortium (GOPEC) in the United Kingdom found that smokers were five times more likely to develop pre-eclampsia. Nicotine alone has been shown to be a teratogen which affects the autonomic nervous system, leading to increased susceptibility to hypoxia-induced brain damage. Maternal anemia in which smoking has also been implicated is another factor associated with IH/BA. Smoking by expectant mothers causes a decrease in maternal nucleated red blood cells (NRBC), thereby reducing the amount of red blood cells available for oxygen transport.

- The perinatal brain injury occurring as a result of birth asphyxia, manifesting within 48 hours of birth, is a form of hypoxic ischemic encephalopathy. Treatment of infants suffering birth asphyxia by lowering the core body temperature is now known to be an effective therapy to reduce mortality and improve neurological outcome in survivors, and hypothermia therapy for neonatal encephalopathy begun within 6 hours of birth significantly increases the chance of normal survival in affected infants.

Epidemiology

- In the United States, intrauterine hypoxia and birth asphyxia were listed together as the tenth leading cause of neonatal death

Fetal hypoxia (FH) (also known as **intrauterine hypoxia (IH)**) occurs when the fetus is deprived of an adequate supply of oxygen.

Pathology

Fetal hypoxia can occur from a number of reasons:

- Umbilical cord prolapse
- Cord occlusion or cord thrombosis
- Placental infarction
- maternal smoking
- IUGR can also be a consequence

Three categories are proposed for the origins of fetal hypoxia:

1. Pre-placental hypoxia
2. Utero-placental hypoxia
3. Post-placental hypoxia

Radiographic assessment

Doppler ultrasound

The severity of fetal hypoxia can be assessed with several Doppler parameters which include

- Umbilical arterial Doppler assessment
- Umbilical vein Doppler assessment :can become pulsatile
- Fetal MCA Doppler assessment
- Ductus venosus Doppler assessment

Complications – hypoxic ischaemic encephalopathy

Until today the role of oxygen in the development of the fetus remains controversially discussed. It is still believed that lack of oxygen in utero might be responsible for some of the known congenital cardiovascular malformations. Over the last two decades detailed research has given us new insights and a better

understanding of embryogenesis and fetal growth. But most importantly it has repeatedly demonstrated that oxygen only plays a minor role in the early intrauterine development. After organogenesis has taken place hypoxia becomes more important during the second and third trimester of pregnancy when fetal growth occurs. This review will briefly adress causes and mechanisms leading to intrauterine hypoxia and their impact on the fetal cardiovascular system.

1. Introduction

Embryogenesis, fetal growth, and survival of the perinatal period all depend on optimal maternal health and normal placental development. Maternal exposure to a persistently hypoxic environment may lead to critical injury to vital organs. Failure of the normal placental function may have profound acute and chronic effects on the developing fetus and lead to intrauterine growth restriction (IUGR), asphyxia, multiorgan failure, premature delivery, and perinatal demise. In the United States, IUGR and prematurity complicate about 12% of the deliveries and represent the leading cause of perinatal mortality and morbidity to this day, accounting for up to 75% of perinatal deaths. Long-term disabilities such as cerebral palsy, hearing loss, retinopathies, and chronic lung disease are associated with a substantial emotional burden for affected families and health care costs to the society.

2. Normal Pregnancy

The process of placentation is initiated once the blastocyst makes contact with the epithelium of the uterus. An initial trophoblastic shell is penetrated by columns of proliferating extravillous cytotrophoblast that form the anchoring vili and provide specialized invasive cells that transform the decidual and proximal portions of the decidual spiral arteries. During the initial phase of implantation and uterine wall invasion, the main role of extravillous trophoblast is to form plugs that occlude capillaries in the endometrial gland stroma; this prevents maternal hemorrhage form disrupting the conceptus and maternal blood from entering the lacunar spaces of the trophoblastic shell. Embryogenesis thus takes place in a hypoxic environment for

the first 10 weeks of pregnancy because oxygen tension within the placenta is much lower than in the surrounding endometrial glands. The “plugging” mechanism protects the growing embryo and the primitive placental villi against oxidative damage; antioxidant enzymes such as mitochondrial superoxide dismutase are not expressed by the syncytiotrophoblast before 8 to 9 weeks of gestation. In the period of 11–13 weeks, the trophoblastic plugs are breached by maternal blood that now enters the intervillous space. Uteroplacental blood flow increases exponentially from less than 50 mL/min in the nonpregnant state to approximately 350 mL/min by fullterm. The demands of this large rise in uteroplacental blood flow (to 20% of the total maternal cardiac output), require large adaptations in maternal physiology.

The maternal cardiac output increases by 20% to 25% during the first trimester. It reaches its peak at the beginning of the third trimester when it exceeds the prepregnancy output by 30% to 40%. This is primarily achieved by an increase in the circulating blood volume resulting in a rise in stroke volume of about 30%, by an increase in the resting heart rate of 10 to 20 beats/min and by lowering the systemic arterial blood pressure secondary to the effects of gestational hormones, circulating prostaglandins, the excessive release of human placental growth factors, and the low-resistance uteroplacental unit. The increase of total blood volume is related to plasma expansion by 30 to 40 mL/kg body weight rather than an increase in total red blood cells and accounts for the relative anemia of pregnant women. The increased cardiac output together with the low blood viscosity lead to a rightward shift of the hemoglobin-oxygen dissociation curve . The maternal gas exchange adapts in parallel with the hemodynamic changes. The increase in fetal-maternal oxygen demand is achieved by mild hyperventilation and anatomical changes that allow the mother to maintain her natural lung capacity despite the increase of the intra-abdominal volume.

Increased production of endothelial nitric oxide and other vasodilators in conjunction with attenuated adrenergic vascoconstriction is thought to be responsible for maintaining uterine artery flow. By midgestation, the human uterine

artery has doubled its diameter and the increased flow is accommodated by hyperplasia of all cell layers.

2.1. Embryonic Heart Development

The embryonic heart develops early post conception from its origins in the heart field to a completely looped 4-chamber organ by 8 weeks of gestation. During this period the oxygen saturation never exceeds 20%, protecting the embryo from oxidative damage. By the time the extravillous spaces of the trophoblast are starting to be filled with maternal blood, the newly-formed fetal heart is ready to meet the increasing oxygen and nutritional demands of the growing fetus. The fetal oxygen saturation gradually increases during the 2nd trimester to about 60%. To maintain an adequate circulation, the fetal heart adjusts continuously to the rise in circulatory blood volume and pressure load. The right and left ventricles work in parallel, adjusting their outputs via several prenatal shunts that will close in the immediate postnatal period.

3. Intrauterine Hypoxia

Intrauterine hypoxia is associated with a variety of maternal, placental, and fetal conditions which may manifest differently and have different outcomes. Kingdom and Kaufmann suggested to classify hypoxic pregnancy conditions into 3 subtypes: (1) preplacental hypoxia, where both the mother and her fetus will be hypoxic (i.e., high-altitude, cyanotic maternal heart disease; etc.); (2) uteroplacental hypoxia, where the maternal oxygenation is normal but the utero-placental circulation is impaired (i.e., preeclampsia, placentar insufficiency, etc.); (3) postplacental hypoxia, where only the fetus is hypoxic. We will focus on the first 2 subtypes as the post-placental hypoxia is mainly related to fetal diseases rather than to the direct impact of hypoxia onto the fetus.

3.1. Pre-Placental Hypoxia

Main causes of pre-placental hypoxia are a hypoxic environment (high-altitude) and pre-existing maternal cardiovascular disease such as cyanotic heart

disease, heart failure, or pulmonary hypertension. Maternal anemia, infections, and chronic inflammation may further limit the maternal oxygen uptake and oxygen delivery to the fetus, thereby increasing the risk for adverse pregnancy outcomes.

Chronic hypoxia associated with placental insufficiency plays a key role in the etiology of intrauterine growth restriction (IUGR). High-altitude exposure mimics this condition and its adverse effects on birth weight exceed those of most other risk factors for IUGR, such as maternal low weight gain, smoking, primiparity, or pre-eclampsia. A 1000 meter gain in altitude results in a natural average decline of the birth weight of 100 grams. Intrauterine growth of the chronically hypoxemic fetus generally begins to slow down between gestational week 25 to 31, a time when fetal growth normally increases exponentially. Interestingly, high-altitude exposure appears also to be associated with an increased risk of pre-eclampsia that may further contribute to low birth weights in high-altitude populations. Nevertheless, in most cases arterial hypertension during pregnancy at high-altitude is probably related to chronic hypoxia rather than to classic pre-eclampsia. In line with this concept, pregnant women at high-altitude lack the physiological blood pressure fall at the beginning of the second trimester. A possible explanation is that chronic hypoxia diminishes the vasodilatory effect of nitric oxide while the sympathetic nervous system (∝1-/∝2-adrenergic receptor) is activated. In addition, potent vasoconstrictors like endothelin-1 and the hypoxia-inducible factor (HIF) are stimulated early in pregnancy by excessive generation of reactive-oxygen species (ROS) . Altitude may also influence cardiac performance and the circulating blood volume. Cardiac output is lower presumably due to a lower heart rate and smaller stroke volumes related to a decreased blood volume of women living permanently at high-altitude. Finally, uterine arteries are typically smaller in diameter and less well perfused during pregnancy at high-altitude. A direct association between uterine arterial flow and birth weight is supported by studies conducted in women from different origins.

Women with congenital heart disease are at increased risk of developing pregnancy complications. The probability of maternal complications has been classified as low, intermediate, or high, with estimates of 5%, 25%, and 75%, respectively, of experiencing cardiac events such as arrhythmias, pulmonary edema, stroke, or cardiac death during pregnancy. The highest risk is observed in mothers with severe left-sided obstructive lesions (i.e., aortic stenosis, coarctation), pulmonary hypertension, Marfan syndrome with aortic root dilatation, as well as with symptoms of moderate or severe heart failure (NYHA functional class III and IV). Increasing maternal hypotension is the most important factor associated with intrauterine growth restriction (20% to 25%) and prematurity (20% to 25%). Interestingly, unrepaired or palliated cyanotic congenital heart disease does not belong to the high-risk group for an adverse maternal outcome but is associated with an increased risk of fetal loss. The live-birth rate is reportedly only 40% to 45% if the mother has cyanotic heart disease. This rate decreases to 10%–15% if the maternal oxygen saturation drops below 85%. In addition, extreme prematurity affects 35% to 40% of these pregnancies. Fetal or neonatal death, brain hemorrhage secondary to maternal anticoagulation or to extreme prematurity, as well as IUGR are common findings in offspring of pregnant women with congenital or acquired heart disease.

Chronic pulmonary disease may have similar maternal-fetal consequences as chronic exposure to hypoxia. Poorly controlled asthma is associated with pre-eclampsia, uterine hemorrhage, preterm delivery, and low birth weight. Among chronic lung diseases, cystic fibrosis (CF) and tuberculosis are the most common conditions: 5% of the world population is carrying the CF gene and 30% of humans have been infected with mycobacterium tuberculosis. Pregnancy in cystic fibrosis patients seems to have a positive effect on maternal long-term survival, despite the increased maternal risk for infections and insulin resistance and the increased fetal risk of prematurity and IUGR.

Acute respiratory infections during pregnancy are common. 1% of women experience symptoms of bronchitis or pneumonia during the course of pregnancy. Current antibiotic regimens have decreased maternal mortality from bacterial pneumonia dramatically, with the exception of cystic fibrosis. Nowadays viral pneumonias are responsible for the major part of maternal deaths during pregnancy. The major risk for the fetus lies in maternal respiratory failure due to ARDS. Fetal complications include stillbirth, spontaneous preterm labor, and a need for early delivery by Cesarean section to improve the effectiveness of maternal ventilation for respiratory failure.

Maternal hematological disorders may directly affect oxygen transfer. Iron deficiency anemia (IDA) is common in pregnancy and often related to malnutrition or micronutrient diets. IDA is associated with increased risk for IUGR and prematurity. In contrast to IDA, the oxygen carrier capacity is altered in hemoglobinopathies. Sickle cell disease is particularly common in Africans and Afro-Americans. It may be present in combination with hemoglobin C or β-thalassemia (Hb S/C or Hb S/β). The most severe form (homozygous HbS) is called sickle cell anemia but any Hb S combination (Hb S/C or Hb S/β) can potentially cause vaso-occlusive crisis and hemolysis. This problem is caused by the abnormal rigid sickle shape of the red blood cells with decreasing oxygen tension. Patients with sickle cell disease are at higher risk for maternal (i.e., preterm labor, preterm rupture of membranes, and postpartum infections) and fetal complications (i.e., abortion, prematurity, IUGR, low birth weight, and stillbirth). Close fetal monitoring during pregnancy and prophylactic exchange transfusion seem to be often effective in abolishing life-threatening intrauterine hypoxic events.

Thalassemia is an autosomal recessive blood disease which is particularly prevalent in Asians (α-form) and among Mediterranean people (-form). The genetic defect results in a reduced synthesis rate of α - or β -globin chains that make up hemoglobin. Homozygous individuals present with severe anemia (Cooley's anemia) and extramedullary erythropoiesis. Alpha-Thalassemia major (Hb Bart's) is

associated with hydrops fetalis, intrauterine death, and pre-eclampsia. β-Thalassemia is a result of a mutation in the β-globin gene causing deficient or absent β chain production with absence of hemoglobin. The clinical picture of β-thalassemia varies in severity in function of the expression of Hb A. Pregnancy in thalassemia carriers is usually uncomplicated. Successful pregnancies in women with α- and β-thalassemia major have been reported but were associated with a higher incidence of IUGR, low birth weight, and prematurity.

3.2. Utero-Placental Hypoxia

Utero-placental hypoxia is related to abnormal placentation early in gestation and to placental vascular disease later in pregnancy. Abnormal placental implantation is a common finding in pregnancies complicated by IUGR, by gestational hypertension, and by pre-eclampsia. There exists an increased risk for both the mother and the fetus to develop cardiovascular disease later in life.

Pre-Eclampsia

It is a complex multisystem disorder observed in human pregnancy. Maternal clinical manifestations range from mild hypertension and proteinuria to fully established HELLP syndrome (Hemolysis, Elevated Liver enzymes, Low Platelet count) or eclampsia with severe hypertension, proteinuria, and multiorgan involvement (pulmonary edema, CNS symptoms, oliguria, thrombocytopenia, and liver failure).

Causes for its origin are largely unknown but may be the result of a systemic inflammatory response perhaps related to an immature maternal immune response [35]. Key abnormalities of pre-eclampsia include a rise in systemic vascular resistance, endothelial dysfunction, and activation of the coagulation system with enhanced platelet aggregation. Endothelial dysfunction is responsible for the impaired generation and activity of vasodilators such as prostacyclin and NO and could explain surface-mediated platelet activation and fibrin formation in the uteroplacental circulation.

Depending on the severity of the pre-eclampsia, the condition may lead to intrauterine hypoxia and/or oxidative stress in the fetus. Pre-eclampsia is associated with IUGR and prematurity. Fetal morbidity and mortality increase significantly when pre-eclampsia develops prior to 33 gestational weeks. Pre-eclamptic mothers and their offspring are at an increased risk for premature cardiovascular disease later in life.

3.3. Post-Placental Hypoxia

In post-placental hypoxia, only the fetus becomes hypoxic which is either related to diminished uterine artery flow (i.e., mechanical compression, rupture, and thrombotic occlusion), progressive fetal cardiac failure (i.e., complete congenital heart block, complex congenital heart malformations), or due to important genetic anomalies. As mentioned earlier, we will not further explore the post-placental hypoxia as it is mainly related to fetal diseases rather than to the impact of hypoxia onto the fetus.

3.4. Effects of Hypoxia on the Fetus

A main consequence of chronic hypoxia is the failure of the fetus to achieve its genetically determined growth potential. About 10% of all babies grow poorly inutero and are born small for gestational age. IUGR is associated with distress and asphyxia and a 6- to 10-fold increased perinatal mortality. Frequent hypoxia-mediated complications include meconium aspiration, metabolic and hematologic disturbances, cognitive dysfunction, and cerebral palsy. Acute and chronic hypoxia is also associated with a variety of morphological and functional fetal cardiac changes that aim either to compensate for the reduced oxygenation of vital organs or are the result of hypoxia-mediated fetal tissue damage.

3.4.1. Hemodynamic Consequences

At an initial stage, the human fetus may be able to adapt to hypoxia by increasing the blood supply to the brain, myocardium, and upper body and decreasing the perfusion of the kidneys, gastrointestinal tract, and lower extremities.

This redistribution of blood allows preferential delivery of nutrients and oxygen to the most vital organs. Cerebral vasodilatation to spare the brain from hypoxic damage leads to a decrease in left ventricular afterload while systemic arterial vasoconstriction of lower body vessels increases right ventricular afterload. In line with this concept, echocardiographic studies in the hypoxic fetus demonstrate an increased middle cerebral artery blood flow and a shift of the cardiac output in favor of the left ventricle. With further deterioration of the fetal oxygenation, this protective mechanism is overwhelmed by the decline in cardiac output and the emergence of fetal distress. The final stage is characterized by a decline in systolic and diastolic fetal cardiac function, secondary to myocardial ischemia. Moreover, raised atrial contraction results in the transmission of atrial pressure waves into the venous duct and umbilical vein, causing end-diastolic umbilical vein, pulsation. At this stage, reduced or reversed end-diastolic flow velocity may also be found in pulmonary veins and coronary blood flow may become visible with increased systolo-diastolic flow velocities ("heart sparing"). If not delivered, intrauterine death occurs usually within a few days.

In line with these findings in the hypoxic human fetus, in the hypoxic fetal sheep the cardiac output is reduced whereas the hemoglobin level is increased to maintain a near-normal oxygen delivery to the fetal myocardium. Moreover, in this hypoxic animal model, the coronary blood flow of the fetus is increased although there is no change in capillary/muscle fiber ratio, capillary volume density, or capillary diameter, and myocardial contractility is reduced.

While chronic hypoxia has detrimental consequences for the fetal heart, chronic anemia appears to have less detrimental effects because the higher oxygen affinity of fetal hemoglobin allows to compensate for this problem. In maternal anemia-related hypoxia, the fetus is able to increase the cardiac output and to increase the transplacental oxygen transfer by actively interfering with the iron metabolism of the mother.

Surviving babies seem to be particularly susceptible to the development of arterial hypertension and cardiovascular disease later in life. An association between low birth weight and early onset of essential arterial hypertension has first been postulated by Barker in the “fetal origins of adult disease hypothesis”. Barker’s theory states that physiologic adaptations that enable the fetus to survive a period of intrauterine deprivation result in permanent reprogramming of the development of key organs that may have pathological consequences in postnatal life. In older children and adults, a low birth weight has been linked with increased arterial stiffness, systolic blood pressure, premature coronary heart disease, stroke and diabetes, and ischemia/reperfusion injury. Despite the strong epidemiologic evidence that supports the concept of “fetal programming”, we still do not know its underlying mechanisms.

3.4.2. Teratogenicity

Recently it has also been suggested that hypoxia early in gestation may be teratogenic to the human embryo. As such, maternal asthma exacerbation during the first trimester of pregnancy reportedly increased the risk for congenital malformations including the risk of cardiovascular malformations. As described above, maternal blood enters the intervillous space of the human placenta only after 10 to 12 gestational weeks and until this moment the placental metabolism is anaerobic. Yet, the human heart forms early in the period of anaerobic metabolism between day 15 and day 60 postconception. Interestingly, if animal embryos are exposed to chronic hypoxia, cardiac malformations seem not occur more frequently.

3.4.3. Cellular Effects of Hypoxia

In rats, early fetal hypoxia triggers cardiac remodeling associated with enhanced apoptosis and a significant increase in binucleated myocytes. At the age of 4 months, fetal hypoxia was associated with increased heart/body weight ratio presumably due to hypertrophy of myocardium in presence of slowed fetal growth, increased β-/α-myosin heavy chain ratio, increased collagen I and III expression, and

lower matrix metalloproteinase-2 activity. The consequences of these changes are higher end-diastolic pressure related to less compliant left ventricle and a reduced capability to recover from ischemia.

Apoptosis is a controlled active physiologic process that removes unwanted or defective cells by intrinsic programmed cellsuicide. In rat hearts exposed to oxidative stress, it could be shown that many genes that affect cell communication, survival and signaling were downregulated. This downregulation is believed to be partly responsible for the long-term consequences of intrauterine hypoxia and leaves a persistent cardiovascular "imprint" that leads to cardiovascular disease in later life. The transcription of the heat shock gen Hsp70 might be an example of this observed cardiac programming phenomenon. Hsp70 is a protein that protects against myocardial ischemia and stress (hyperthermia) and inhibits apoptosis by preventing the formation of caspase-9. In chronic intrauterine hypoxia conditions, the expression of Hsp70 is down-regulated. This effect persists into adulthood and may explain why some adult hearts are more vulnerable against ischemia/reperfusion injury. The expression of endothelial nitric oxide is also important for the long-term cardioprotection of the cardiomyocytes. eNOS levels are also decreased in rat hearts who were exposed to intrauterine hypoxia. Similar changes were observed in the regulation of the β-adrenoreceptors (βARs) and the coupling G proteins. β2AR and G s α are upregulated in adult rat hearts that were inutero exposed to chronic hypoxia. This upregulation preserves cardiac contractility in hypoxia, but the regulatory mechanism appears to be lost in adulthood presumably due to wrong prenatal programming.

4. Conclusion

Hypoxia does not play a major role in the early development of structural cardiac malformations probably because early embryogenesis already takes place under anaerobic conditions. Only during the second and third trimester, oxygen becomes more important for the normal fetal organogenesis and growth. If at that

stage exposed to hypoxia, the fetus has a number of protective options. Immediate protection against oxidative stress is established by up-regulation of genes. Stimulation of nitric oxide synthesis enhances cell signaling for defense mechanisms, platelet inhibition, and regulation of apoptosis. β2AR and G s α will be up-regulated to maintain a sufficient cardiac output. With persistent hypoxia, premature exit of cell cycle is initiated, together with enhanced apoptosis resulting in fewer, but hypertrophied cardiomyocytes. This process aims for better energy efficiency during hypoxic conditions but also results in less compliant ventricles. Altered regulatory gene expression in response to in-utero hypoxia appears to extend into adulthood and mimics the changes that are found in adults with chronic heart failure. Hypoxia slows fetal growth, and growth restriction is now considered a risk factor of premature arterial hypertension and cardiovascular disease, probably secondary to endothelial dysfunction. Further investigations are needed to explore preventative strategies such as the early use of antioxidants and selective vasodilators to limit the effects of intrauterine hypoxia. Abstract

Fetal cerebrovascular responses to acute hypoxia are fundamentally different from those observed in the adult cerebral circulation. The magnitude of hypoxic vasodilatation in the fetal brain increases with postnatal age although fetal cerebrovascular responses to acute hypoxia can be complicated by age-dependent depressions of blood pressure and ventilation. Acute hypoxia promotes adenosine release, which depresses fetal cerebral oxygen consumption through action of adenosine on neuronal A1 receptors and vasodilatation through activation of A2 receptors on cerebral arteries. The vascular effect of adenosine can account for approximately half the vasodilatation observed in response to hypoxia. Hypoxia-induced release of nitric oxide and opioids can account for much of the adenosine-independent cerebral vasodilatation observed in response to hypoxia in the fetus. Direct effects of hypoxia on cerebral arteries account for the remaining fraction, although the vascular endothelium contributes relatively little to hypoxic vasodilatation in the immature cerebral circulation. In contrast to acute hypoxia, fetal

cerebral blood flow tends to normalize during acclimatization to chronic hypoxia even though cardiac output is depressed. However, uncompensated chronic hypoxia in the fetus can produce significant changes in brain structure and function, alteration of respiratory drive and fluid balance, and increased incidence of intracranial hemorrhage and periventricular leukomalacia. At the level of the fetal cerebral arteries, chronic hypoxia increases protein content and depresses norepinephrine release, contractility, and receptor densities associated with contraction but also attenuates endothelial vasodilator capacity and decreases the ability of ATP-sensitive and calcium-sensitive potassium channels to promote vasorelaxation. Overall, fetal cerebrovascular adaptations to chronic hypoxia appear prioritized to conserve energy while preserving basic contractility. Many gaps remain in our understanding of how the effects of acute and chronic hypoxia are mediated in fetal cerebral arteries, but studies of adult cerebral arteries have produced many powerful pharmacological and molecular tools that are simply awaiting application in studies of fetal cerebral artery responses to hypoxia.

Synopsis

The outcome of perinatal hypoxia-ischemia is highly variable, with only a very broad relationship to the ‘severity’ of oxygen debt as shown by peripheral base deficit and the risk of damage. The present review examines the pathophysiology of asphyxial injury. We dissect the multiple factors that modify the risk of injury, including the depth (‘severity’), duration, and repetition of the insult, the maturity, and condition of the fetus, pre-existing hypoxia, and exposure to pyrexia and infection/inflammation.

Introduction

Acute neonatal encephalopathy remains a significant cause of death and long-term disability. Despite the highly adverse outcomes of moderate to severe encephalopathy around birth the predictive value for cerebral palsy of abnormal fetal

heart rate patterns is consistently weak . Indeed, even measures of total oxygen debt such as base deficit (BD) or lactate show only a broad relationship with later encephalopathy. For example, profound acidosis (BD>18 mmol/L at 30 minutes of life) was associated with moderate to severe encephalopathy in nearly 80% of patients, and no cases occur with mild BDs below approximately 10–12 mmol/L. However, it is striking that Low and colleages found that less than half of babies born with cord blood BDs over 16mmol/L (and pH <7.0) developed significant encephalopathy, and that encephalopathy still occurred, although at low frequency (~10% of cases), in cases with moderate metabolic acidosis of between 12 and 16 mmol/L. These data contrast with the presence of (very) non-reassuring fetal heart rate tracings and severe metabolic acidosis in those infants who do go on to develop neonatal encephalopathy.

Early onset neonatal encephalopathy is important, because it is the key link between exposure to asphyxia and subsequent neurodevelopmental impairment. Newborns with mild encephalopathy are completely normal to follow-up, while all of those with severe (stage III) encephalopathy die or have severe handicap. In contrast, only half of those with moderate (stage II) hypoxic–ischemic encephalopathy develop handicap. However, even those who do not develop cerebral palsy have increased risk of learning and more subtle neurological problems in later childhood. This strongly infers that much of the variation in outcome is related to the immediate insult period.

This chapter focuses on recent developments that help shed light on the factors that determine whether the brain is or is not damaged after apparently similar asphyxial insults. In part, this variation is simply because the fetus is spectacularly good at defending itself against such insults. Thus, it appears that injury occurs only in a very narrow window between intact survival and death. The fetus's ability to defend itself though is modified by multiple factors including the depth, duration, and repetition of the insult, the gestational age, sex and condition of the fetus, and

its environment, and particularly pyrexia and exposure to sensitizing factors such as infection/inflammation.

Most of the studies discussed here were undertaken in chronically instrumented fetal sheep. The sheep is a highly precocial species, whose neural development around 0.8–0.85 of gestation approximates that of the term human. Earlier gestations have also been studied; the 0.7 gestation fetus is broadly equivalent to the late preterm infant at 30 to 34 weeks, before the onset of cortical myelination, while at 0.6 gestation the sheep fetus is similar to the 26 to 28 week gestation human.

What initiates neuronal injury?

It is useful to consider what is required to trigger injury of brain cells, independent of the fetus's defenses. At the most fundamental level, injury requires a period of insufficient delivery of oxygen and substrates such as glucose (and in the fetus other aerobic substrates such as lactate) such that neurons (and glia) cannot maintain homeostasis. If oxygen is reduced but substrate delivery is effectively maintained (i.e. pure or nearly pure hypoxia), the cells adapt in two ways. First, they can to some extent reduce non-obligatory energy consumption, initially switching to lower energy requiring states and then, as an insult becomes more severe, completely suppressing neuronal activity, at a threshold above that which causes neuronal depolarization. This reduced activity is actively mediated by inhibitory neuromodulators such as adenosine. Second, they can use anaerobic metabolism to support their production of high-energy metabolites for a time. The use of anaerobic metabolism is of course very inefficient since anaerobic glycolysis produces lactate and only 2 ATP, whereas aerobic glycolysis produces 38 ATP. Thus glucose reserves are rapidly consumed, and a metabolic acidosis develops due to accumulation of lactic acid, with local and systemic consequences such as impaired vascular tone and cardiac contractility.

In contrast, under conditions of combined reduction of oxygen and substrate the neuron's options are much more limited, as not only is less oxygen available, but there is also much less glucose for anaerobic metabolism. This may occur during either pure ischemia (reduced tissue blood flow) and even more critically during conditions of hypoxia–ischemia, i.e. both reduced oxygen content, and reduced total blood flow. Under these conditions depletion of high energy metabolites will occur much more rapidly and profoundly than during hypoxia alone, while at the same time there may actually be less metabolic acidosis both because there is much less glucose being delivered for metabolism to lactate, and because the insult is evolving more quickly. This is important, since the fetus is commonly exposed to hypoxia–ischemia due to hypoxic cardiac compromise.

These concepts help to explain the consistent observation discussed below that across multiple paradigms in the fetus most cerebral injury after acute insults occurs in association with hypotension and consequent tissue hypoperfusion or ischemia. Technically, asphyxia is defined as the combination of impaired respiratory gas exchange (i.e. hypoxia and hypercapnia) accompanied by the development of metabolic acidosis. To understand much of the apparent variation in outcome it is critical to keep in mind that this definition tells us much about things that can be measured relatively easily (blood gases and systemic acidosis) and essentially nothing about blood pressure or perfusion of the brain.

Cerebral injury: an 'evolving' process

The seminal concept to emerge from both experimental and clinical studies is that brain cell death does not necessarily occur during hypoxia-ischemia (the 'primary' phase of injury), but rather that the injurious event may precipitate a cascade of biochemical processes leading to delayed cell death hours or even days afterwards (the 'secondary' phase). Experimental studies have demonstrated the existence of both a primary phase of energy failure during hypoxia– ischemia, a 'latent' phase during which oxidative metabolism normalizes, followed by

secondary failure of oxidative metabolism in piglets, immature rats, and the fetal sheep. Consistent with these studies, although some newborn infants exposed to profound asphyxia show no initial recovery of oxidative metabolism after birth and typically have very severe brain injury and high mortality, in many other cases infants show initial, transient recovery of cerebral oxidative metabolism followed by a secondary deterioration, with cerebral energy failure from 6 to 15 hours after birth. The severity of secondary energy failure correlates closely with the severity of neurodevelopmental outcome at 1 and 4 years of age. Critically, for hypoxia associated with labor insults, experimental studies show that a single 'sub-threshold' insult that causes either minor or no neural injury can lead to a phase of increased vulnerability to further insults in a similar window of around 6 or more hours.

Mild to moderate hypoxia is not injurious

The fetus can fully adapt to mild to moderate reductions in oxygen tension without injury, from normal values of greater than 20mmHg down to 10 to 12mmHg. The late gestation fetal sheep fetus shows an initial transient, moderate bradycardia followed by tachycardia and an increase in blood pressure, typically accompanied by a minor initial increase in circulating lactate. There is a rapid peripheral vasoconstriction reducing blood flow to peripheral organs such as the gut, lungs, skin and muscle, in favor of the brain, heart and adrenal gland. Thanks to this increased blood flow to the brain that helps to restore oxygen delivery, greater oxygen extraction, and a switch to lower frequency EEG states with approximately a 20% reduction in oxygen consumption, brain oxygen consumption is maintained at normal values. If the hypoxia is sustained, the fetus can fully adapt essentially indefinitely shown by normalization of heart rate and blood pressure and the return of normal sleep state cycling, although redistribution of blood flow is maintained, resulting in reduced somatic growth.

Asphyxia, hypotension and hypoxic-ischemic brain injury

Asphyxia by definition involves both hypoxia and hypercapnia with metabolic acidosis. It is important to appreciate that experimental studies of asphyxia have typically involved a greater depth of hypoxia than is possible using maternal inhalational hypoxia. Brief, total clamping of the uterine artery or umbilical cord leads to a rapid reduction of fetal oxygenation within a few minutes. In contrast, gradual partial occlusion induces a slow fetal metabolic deterioration without the initial fetal cardiovascular responses of bradycardia and hypertension; this is a function of the speed and relative depth of hypoxia that was attained. During profound asphyxia, corresponding with a severe reduction of uterine blood flow to 25% or less and a fetal arterial oxygen content of less than 1 mmol/L, the fetus responds very differently than during mild to moderate hypoxia. Typically, we can distinguish two phases: an initial, rapid chemoreflex-mediated period of compensation, followed by progressive hypoxic-decompensation, ultimately terminated by profound systemic hypotension with cerebral hypoperfusion

Changes in fetal heart rate (FHR, bpm, top panel), mean arterial pressure (MAP, mmHg, second panel), femoral blood flow (FBF, ml/min, third panel) and carotid blood flow (CaBF, ml/min, bottom panel) in 0.6 (∀), 0.7 ()) and 0.85 gestation (*) fetuses **...**

Term and preterm fetuses alike respond to asphyxia in a qualitatively similar manner, albeit the preterm fetuses can survive for much longer without injury. A wide range of studies suggest that it is the period of hypotension during severe asphyxia that is associated with cerebral injury across paradigms, likely because of the close relationship between maintenance of fetal blood pressure during severe asphyxia and changes in brain perfusion (carotid blood flow (CaBF)) In these fetuses, MAP initially rose with intense peripheral vasoconstriction; at this time CaBF was maintained at around baseline values, but with profound suppression of EEG activity. Microsphere studies have shown that although total brain flow did not

change, within the brain blood flow is diverted away from the cerebrum and increased in the brain stem. As umbilical cord occlusion was continued MAP eventually fell. The key mediators include impaired cardiac function secondary to of hypoxia, acidosis, depletion of myocardial glycogen and cardiomyocyte injury and loss of the initial peripheral vasoconstriction. Once MAP fell below baseline, carotid blood flow fell in parallel, consistent with the known relatively narrow low range of autoregulation of cerebrovasculature in the fetus, and there is loss of redistribution of flow within the brain.

In the near-term fetus neural injury has been commonly reported in areas such as the parasagittal cortex, the dorsal horn of the hippocampus, and the cerebellar neocortex after a range of insults including pure ischemia, prolonged single complete umbilical cord occlusion, and prolonged partial asphyxia and repeated brief cord occlusion. These areas are ‘watershed’ zones within the borders between major cerebral arteries, where perfusion pressure is least, and in both adults and children lesions in these areas are typically seen after systemic hypotension.

The distribution of neuronal loss assessed after 3 days recovery from two different paradigms of repeated prenatal asphyxia in near-term fetal sheep. The top panel shows the effect of five minute episodes of umbilical cord occlusion, repeated four times, **...**

There are some data suggesting that limited, or localized white or gray matter injury may occur even when significant hypotension is not seen, particularly when hypoxia is very prolonged. Clearly it remains possible that regional hypoperfusion may have occurred or that perfusion was insufficient for particular, highly metabolically active regions. Nevertheless, the magnitude of damage reported after insults without hypotension is modest and there is a strong correlation between either the depth or duration of hypotension and the amount of neuronal loss within individual studies of acute asphyxia. This is also seen between similar asphyxial paradigms causing severe fetal acidosis which have been manipulated to either cause

fetal hypotension or not. In fetal lambs exposed to prolonged severe partial asphyxia induced by partial occlusion of the uterine artery neuronal loss occurred only in fetuses in whom one or more episodes of acute hypotension occurred. In contrast, in a similar study where an equally ‘severe’ insult was induced gradually and titrated to maintain normal or elevated blood pressure throughout the insult no neuronal loss was seen except in the cerebellum.

The relationship between hypotension and neuronal damage. The severity of fetal systemic hypotension during asphyxia induced by partial common uterine artery occlusion is closely related to the degree of neuronal loss and risk of death in the near-term **...**

Basal ganglia injury: cardiovascular collapse and repeated insults?

Although the watershed-type injuries described above are a commonly recognized clinical MRI pattern, basal ganglia and thalamic damage is widely recognized. It is typically associated with more severe or “sentinel” events at birth, and with more severe neurodevelopmental disability. Although the basal ganglia seem to be relatively mildly affected in the experimental settings mentioned above, the clinical association with more severe acute events at birth raises the possibility that it may be a function of more severe cardiovascular collapse. Blood to the brain during the initial adaptation to asphyxia is not distributed evenly, but rather reduced to the cortex and increased in the basal ganglia/thalamus and brainstem. This suggests that in part the apparent sparing of the basal ganglia and other critical deep nuclei during many insults reflects this greater residual perfusion, and that it must fail during profound hypotension which would expose the deep nuclei to overt ischemia.

Another contributing factor is suggested by the experimental association between relatively repeated but prolonged episodes of asphyxia selective neuronal damage to the striatal nuclei. Further, whereas a single 30 minute period of cerebral

ischemia leads to predominantly parasagittal cortical neuronal loss, with only moderate injury to the dorsolateral striatum, when the insult was divided into three episodes of 10 minutes of ischemia, a greater proportion of striatal injury was seen relative to cortical neuronal loss. Intriguingly, significant striatal involvement was also seen after prolonged partial asphyxia in which distinct episodes of bradycardia and hypotension occurred.

The effects of different intervals between periods of cerebral ischemia insults on the distribution of cerebral damage the near-term fetal sheep. Cerebral ischemia induced by bilateral occlusion of the carotid arteries was applied either for 10 minutes, **...**

The striatum is not in a watershed zone but rather within the territory of the middle cerebral artery. Thus it is likely that the pathogenesis of striatal involvement in the near-term fetus is related to the precise timing of the relatively prolonged episodes of asphyxia and not to more severe local hypoperfusion. The mechanism is unclear, however, the relatively greater striatal predominance with greater spacing between insults suggests that it is in part a consequence of the evolving neural dysfunction and sensitivity triggered by noninjurious single insults, and thus speculatively, with slower recovery of this period of sensitivity to further insults in the basal ganglia than the cortex. Further, we should note that the inhibitory striatal neurons were primarily damaged by repeated ischemia, raising the possibility that this enhanced injury is related in part to abnormal excitatory inputs to these neurons.

Pre-existing metabolic status, and chronic hypoxia

While the original studies of factors influencing the degree and distribution of brain injury, primarily by Myers, focused on metabolic status, the issue remains controversial. There is evidence, for example, that hyperglycemia during hypoxia-ischemia reduces damage in the infant rat whereas it was associated with greater damage in adult rats, but had no effect in the piglet. These differences may reflect

species specific maturational differences in the activity of cerebral glucose transporters. The most common metabolic disturbance to the fetus is intrauterine growth retardation (IUGR) associated with placental dysfunction. Although clinically IUGR is usually associated with a greater risk of brain injury, recent studies have suggested that the risk of encephalopathy has fallen markedly over time. One interpretation of this finding is that the apparently increased sensitivity to injury is mostly due to reduced aerobic reserves, leading to early onset of systemic compromise during labor.

Consistent with this hypothesis, chronically hypoxic fetuses from multiple pregnancies developed much more severe, progressive metabolic acidosis than previously normoxic fetuses during brief (1 minute) umbilical cord occlusions repeated every 5 minutes (pH 7.07 ± 0.14 *vs* 7.34 ± 0.07)) and hypotension (a nadir of 24 ± 2 mmHg *vs* 45.5 ± 3 mmHg after 4 hours of repeated occlusion). The fetuses with pre-existing hypoxia were smaller on average, and had lower blood glucose values and higher PaCO2 values. Similarly, in normally grown fetuses, 5 days of induced chronic hypoxemia was associated with increased striatal damage after acute exposure to repeated umbilical cord occlusion for 5 minutes every 30 minutes for a total of four occlusions. Together, these data support the clinical concept that fetuses with chronic placental insufficiency are vulnerable even to relatively infrequent periods of additional hypoxia in early labor.

Less obvious adverse intrauterine events may also modify fetal responses to hypoxia. There is considerable interest on the effects of stimuli such as maternal undernutrition and steroid exposure, particularly at critical times in pregnancy, not only on the fetal responses to challenges to its environment such as hypoxia, but also on risks for adverse health outcomes in adult life. Intriguingly, mild maternal undernutrition that does not alter fetal growth may still affect development of the fetal hypothalamic-pituitary-adrenal function, with reduced pituitary and adrenal responsiveness to moderate hypoxia. There is some evidence that exposure to glucocorticoids may also detrimentally alter the responses to hypoxia.

Brain maturity

The effect of maturation on sensitivity to injury is of great importance, for two reasons. First, in recent years improvements in obstetric and pediatric management have resulted in significantly increased survival of preterm infants from 24 weeks of gestation, with continuing very high rates of physical disabilities and long-term learning, cognitive and behavioral problems. Second, many infants may sustain neural injuries well before birth, including a significant number of infants with cerebral palsy. The characteristic patterns of cerebral injury in the preterm fetus differ from those seen at term or after birth, with preferential injury of subcortical structures and white matter.

Their high rate of disability intuitively suggests that premature infants are more vulnerable to hypoxic damage than at term. Recent experimental studies now show that in fact the premature fetus is *less* vulnerable to a given duration of asphyxia than at term, and further that tolerance to hypoxia-ischemia falls with postnatal age. For example, the premature sheep fetus at 90 days gestation (term is 147 days), prior to the onset of cortical myelination, can tolerate extended periods of up to 20 minutes of umbilical cord occlusion without neuronal loss. The very prolonged cardiac survival during profound asphyxia corresponds with the peak in cardiac glycogen levels that occurs near mid-gestation in the sheep and other species including man.

Interestingly, while the preterm fetal response to mild to moderate hypoxia appears to be different to that seen at term, the overall pattern of cardiovascular and cerebrovascular response during severe asphyxia was very similar to that seen in more mature fetuses, with sustained bradycardia, accompanied by circulatory centralization, initial hypertension, then a progressive fall in pressure. As also reported in the term fetus, there was no increase in blood flow to the brain during this initial phase, and again this was due to a significant increase in vascular resistance rather than to hypotension. Compared with the term fetus 0.6 and 0.7 gestation fetuses showed significantly slower suppression of EEG activity at the start

of umbilical cord occlusion. Speculatively, this delay is indicative of the relative anerobic tolerance of the preterm brain. As shown in, as in the term fetus, once blood pressure begins to fall blood flow to the brain falls in parallel. The fall in pressure is partly a function of continuing fall in fetal heart and thus of combined ventricular output and partly the loss of redistribution of blood flow with a rise in femoral blood flow (FBF). Similar responses are also seen in the kidney and gut.

In the latter half of maximum survivable interval of asphyxia in the preterm fetus there is progressive failure of combined ventricular output, with a fall in both central and peripheral perfusion, both associated with falling blood pressure. This phase is much less likely to be seen for any significant duration in the term fetus as cardiac glycogen stores are depleted more quickly at term. Thus, at 0.6 gestation the majority of fetuses survived up to 30 minutes of complete umbilical cord occlusion. In contrast, term fetuses are unable to survive such prolonged periods of sustained hypotension, and typically will recover spontaneously from up to a maximum of 10–12 minutes of cord occlusion, whereas after a 15 minute period of complete occlusion the majority of fetuses either died or required active resuscitation with adrenaline after release of occlusion. Thus, as a consequence of this extended survival during severe asphyxia, the premature fetus is exposed to extremely prolonged and profound hypotension and hypoperfusion. At 0.6 gestation, for example, no injury occurs after 20 minutes of complete umbilical cord occlusion even though hypotension is already present, but severe subcortical injury occurs if the occlusion is continued for 30 minutes. It may be speculated that during this final 10 minutes of asphyxia there is a catastrophic failure of redistribution of blood flow within the fetal brain which places previously protected areas of the brain such as the brainstem at risk of injury, consistent with clinical observations.

Temperature and hypoxia-ischemia

Brain temperature during and after hypoxia-ischemia potently modulates outcome. Whereas hypothermia during experimental cerebral ischemia is

consistently associated with potent, dose-related, long-lasting neuroprotection, hyperthermia of even 1 to 2 °C extends and markedly worsens damage, and promotes pan-necrosis. The impact of cerebral cooling or warming the brain by only a few degrees is disproportionate to the known changes in brain metabolism (approximately a 5% change in oxidative metabolism per ºC), suggesting that changes in temperature modulate the secondary factors that mediate or increase ischemic injury. Mechanisms that are likely to be involved in the worsening of ischemic injury by hyperthermia include greater release of oxygen free radicals and excitatory neurotransmitters such as glutamate, enhanced toxicity of glutamate on neurons, increased dysfunction of the blood brain barrier, and accelerated cytoskeletal proteolysis.

These data logically lead to the concept that although mild pyrexia during labor might not necessarily be harmful in most cases, in those fetuses also exposed to an acute hypoxic-ischemic event it would be expected to accelerate and worsen the development of encephalopathy. Case control and case series studies strongly suggest that maternal pyrexia is indeed associated with an approximately four fold increase in risk for unexplained cerebral palsy, or newborn encephalopathy.

Clearly, this association could potentially be mediated by maternal infection or by the fetal inflammatory reaction. However, maternal pyrexia was a major component of the operational definition of chorio-amnionitis in all of these studies, and in several studies pyrexia was either considered sufficient for diagnosis even in isolation, or was the only criterion. Consistent with the hypothesis that pyrexia can have a direct adverse effect, in a case control study of 38 term infants with early onset neonatal seizures, in whom sepsis or meningitis were excluded, and 152 controls, intrapartum fever was associated with a comparable 3.4-fold increase in the risk of unexplained neonatal seizures in a multifactorial analysis.

In newborn rodents recent studies suggest intriguingly that exposure to mild infection or inflammation can sensitize the brain, so that short or milder periods of

hypoxia-ischaemia, which do not normally injure the developing brain, can trigger severe damage. The effect is complex and time dependent. A low dose of LPS given either shortly (four or six hours) or well before (72 hours or more) hypoxia in rat pups was associated with *increased* injury ('sensitization') . In contrast, when given at an intermediate time (24 hours) before hypoxia-ischemia, LPS actually *reduced* injury ('tolerance'). In mice, fetal exposure to endotoxin affected the responses to hypoxia-ischemia even in adulthood, with both reduced and increased injury, in different regions. Thus given that profound asphyxia or septic shock causing acute injury around the time of birth are only seen in a minority of preterm infants, these data raise the intriguing possibility that sensitization by infection/inflammation may compromise the fetus such that even normally non injurious periods of hypoxia can be transformed into a damaging event.

Final conclusions

The experimental studies reviewed above, and clinical experience, strongly suggest that there is, and can be, no close, intrinsic pathophysiological relationship between the severity of metabolic acidosis, and fetal compromise. Peripheral acidosis is primarily a consequence of peripheral vasoconstriction, and reflects peripheral oxygen debt which occurs during redistribution of combined ventricular output. Thus severe acidosis may accompany both successful protection of the brain, and catastrophic failure. Conversely, brief but intense insults such as complete cord occlusion may cause brain injury in association with comparatively modest acidosis. In contrast, we now know that there are very strong relationships both within and between paradigms between the development and severity of fetal blood pressure and impairment of cerebral perfusion, and the development of subsequent cerebral injury. The impact of hypotension is directly related to both its depth and cumulative duration in relationship to the brains' metabolic requirements given its developmental stage.

How this hypoxia-ischemia triggers different patterns of injury is not fully understood, but key factors include profound hypotension and the pattern of the insult. The link between profound hypotension/hypoperfusion during asphyxia and subcortical damage in the preterm fetus likely reflects compromise of the initial intracerebral redistribution of blood flow from the forebrain to the subcortical areas. Of particular interest to clinicians, it is striking that repeated, relatively prolonged episodes of asphyxia or ischemia (5 to 10 minutes) are associated with selective basal ganglia damage, and that the proportion of basal ganglia damage relative to cortical injury increases as the interval between insults is increased. This relationship emphasizes the importance of interaction between even relatively benign, non-injurious individual periods of hypoxia-ischemia in labor that can lead to regionally specific, compounding damage.

Fetal hypoxia can arise due to a number of different causes, from infection of the placenta to occlusion of the umbilical cord. The subsequent decrease in oxygen supply to the developing fetus can lead to serious health complications, permanent disability and stillbirth. Current prenatal tests to detect fetal hypoxia, in order to inform the timing of delivery, are unable to determine the severity of the condition. In a recent study in *BMC Medicine*, Stephen Tong, Clare Whitehead and Susan Walker from Mercy Hospital for Women and the University of Melbourne, Australia, and colleagues, present a new non-invasive maternal blood test to detect and determine the extent of fetal hypoxia. Here, Tong, Whitehead and Walker discuss how their maternal blood test for fetal mRNAs could benefit clinical practice and neonatal outcomes**.**

What is fetal hypoxia and what are its consequences?

Fetal hypoxia is the dangerous situation of low oxygen levels. Tissues such as the brain – tissues with high energy demands – are particularly sensitive and at risk

of permanent damage if oxygen needs aren't met. Thus, severe hypoxia can result in major disability. Ultimately however, unrelenting hypoxia leads to stillbirth.

There are two clinically important situations of fetal hypoxia. Acute hypoxia can arise over hours during labor, and occurs because each uterine contraction slows maternal blood flow to the placenta.

Placental insufficiency can give rise to chronic hypoxia, where the diseased placenta fails to supply adequate oxygen. If unsuspected, a stillbirth can occur. Of three million annual stillbirths occurring globally, hypoxia may be potentially responsible for half.

How is fetal hypoxia currently assessed?

The underlying principle of all our current tests of fetal hypoxia is that they set out to identify specific fetal physiological responses to hypoxia. For instance, the cardiotocograph is used in labor to detect fetal heart rate patterns associated with the presence of significant acute hypoxia.

Faced with chronic hypoxia, fetuses will grow less (thus, fetal growth restriction flags the presence of chronic hypoxia), move less, produce less amniotic fluid and divert blood flow to the brain. With more critical levels of hypoxia, flow of blood during the diastolic phase of the cardiac cycle can decrease, cease, or even flow backwards. Current tests to identify chronic fetal hypoxia are ultrasound based and seek to capture the presence of these physiological adaptions to low oxygenation.

While these tests have helped improve outcomes, they are not perfect. For example, the cardiotocograph is notorious for overcalling the presence of hypoxia, where clinicians deliver by caesarean section, only to find normal fetal oxygenation levels. Not infrequently, the ultrasound tests to identify chronic hypoxia provide conflicting results (e.g. decreased fetal movements, low amniotic fluid levels but

normal fetal blood flow in diastole). Such conflicting findings make it difficult to judge how hypoxic the fetus truly is, and whether immediate delivery is actually required.

What are the clinical implications of having a non-invasive test for fetal hypoxia?

In clinical practice, once the baby is delivered, a sample of blood is taken from the placenta and pH (or lactate levels) is measured. With true fetal hypoxia, the pH will decrease and blood lactate levels will increase. Thus, this readout – which can only be obtained after birth – provides a 'gold standard' to reflect the degree of fetal hypoxia during its last moments *in utero*.

We set out to develop a non-invasive maternal blood test to provide an estimate of fetal blood pH levels *in utero*. If successful, it could improve on current tests, all of which are relatively insensitive at determining the degree of fetal hypoxia (none appear to be able to provide a reliable estimate of fetal blood pH).

The clinical implications of such a test are that clinicians could better time delivery of fetuses, reducing neonatal morbidity and mortality.

What are hypoxia-induced mRNAs and how could they be used in a test for fetal hypoxia?

With significant cellular hypoxia, hundreds of genes are predictably upregulated, which we call 'hypoxic-induced mRNAs'.

Amazingly, it was discovered over the past decade that mRNAs of placental origin leak into the maternal circulation where they can be sampled and quantified. We therefore hypothesized when the fetus is hypoxic, it will upregulate and release hypoxia-induced mRNAs into the maternal blood. Furthermore, we hypothesized the relative abundance of these mRNAs would correlate with the degree of hypoxia.

If correct, then measuring hypoxia-induced mRNAs could form the basis of a non-invasive clinical blood test of fetal hypoxia.

In our study, we examined acute hypoxia by serially sampling blood from women undergoing labor. We also investigated chronic hypoxia, recruiting women with pregnancies complicated by severe preterm fetal growth restriction. We found hypoxia-induced mRNAs abundance in maternal blood taken close to delivery indeed correlated with the hypoxic status of the fetus during its last moments *in utero* (determined by measuring fetal blood pH, or lactate levels from the placenta at birth).

Thus, our data provides proof of principle evidence that measuring hypoxia-induced mRNAs abundance in maternal blood could be used to determine the degree of fetal hypoxia *in utero*.

How were you able to determine that the mRNAs you detected were from the fetus and not the mother?

We did not definitely prove the mRNAs we were measuring in the maternal blood were from the fetus or placenta. However, as discussed in our paper, we feel we have presented strong circumstantial evidence to suggest they were of placental origin.

Ultimately, if hypoxia induced mRNA were validated to accurately reflect fetal hypoxia status *in utero*, it would not be absolutely essential to establish their origin, although we think a fetal/placental source is most likely.

It is technically possible to prove that the hypoxia-induced mRNA are of placental origin using next generation sequencing technologies. mRNA sequence information can be compared with the maternal and fetal genomes. Such studies are on the cards.

In what situations could this test be used?

We believe there may be a variety of clinical situations where this test to determine fetal hypoxia levels could be useful. However, we think the greatest impact could be in monitoring fetuses that are growth restricted at very preterm gestations.

With preterm fetal growth restriction, the risks of stillbirth are high and clinicians face the tricky situation of having to time delivery. The clinician is required to balance the probability of stillbirth, or permanent disability (caused by leaving the baby too long in an environment of severe chronic hypoxia) if the pregnancy is left to continue versus the risk of causing 'iatrogenic' prematurity if the preterm fetus is delivered unnecessarily early (severe prematurity has, itself, serious complications including cerebral palsy).

A test that is able to more precisely estimate fetal blood pH *in utero* could be used to help the clinician make more informed decisions regarding delivery, improving outcomes.

What's next for your research?

Excitingly, we have implemented a large observational multicentre study (seven referral centres in Australia and New Zealand) to verify our findings and develop a test with clinical care in mind. Called the 'FOX study' (Fetal Oxygenation study), we hope to recruit 180 participants with severe preterm growth restriction. We hope to confirm the inverse correlation between hypoxic–induced mRNAs abundance and fetal blood pH determined at delivery, but with greatly expanded numbers.

The vision is that we will develop a tool where clinicians can measure hypoxic-induced mRNAs in the maternal blood, look up a 'reference' chart that this study will generate, and obtain an estimate of the fetal blood pH. Hypothetically, an

estimated pH reading of 7.3 would suggest the fetus could be safely left to gain gestation, whereas, a pH of 7.05 would mandate delivery.

If the FOX study validates our hypothesis, we believe this test has exciting potential to improve fetal outcomes and perhaps decrease the burden of major disabilities and stillbirth.

MULTIPLE PREGNANCY

Multiple pregnancy occurs when two or more ova are fertilised to form **dizygotic** (non-identical) twins *or* a single fertilised egg divides to form **monozygotic** (identical) twins.

In dizygotic multiple pregnancies, each fetus has its own placenta (either separate or fused), amnion and chorion. In monozygotic multiple pregnancies, the situation is more complex depending on the timing of the division of the ovum:

- Embryo splits at 3 days: two chorions, two amnions.
- Embryo splits at 4-7 days: single placenta, one chorion, two amnions.
- Embryo splits at 8-12 days: single placenta, one chorion and one amnion (rare).
- Embryo splits at 13 days: conjoined twins (Siamese twins) - very rare.

In monochorionic twin pregnancies, one twin can receive a reduced blood supply and have a slower growth rate (twin-twin transfusion). Sometimes, one fetus dies and forms a mummified fetus papyraceous or is reabsorbed.

Epidemiology

Normal incidence of twins is 1 in 90 pregnancies (approximately 1/3 are monozygotic) and of triplets 1 in 8,100 pregnancies.

However, use of in vitro fertilization (IVF) and ovulation induction techniques have greatly increased the incidence of multiple pregnancies. Figures from the North of England twin register suggest a twinning rate of 13.6-16.6/1,000 maternities (or 1 in 60-74 pregnancies).

Risk factors

For dizygotic twinning include:

- Previousmultiplepregnancy.
- Familyhistory (maternalside).
- Increasingmaternalage.
- Racial origin (more common in women of West African ancestry, less common in those of Japanese ancestry).
- Assisted conception

Presentation

- Nearly all multiple pregnancies are now diagnosed in the first trimester by ultrasound. However, some twins die and are absorbed in the first half of

pregnancy ('the disappearing twin' syndrome) and early scanning increases awareness of this phenomenon.
- Early symptoms may include hyperemesis and other exaggerated pregnancy-related symptoms. The uterus may be palpated abdominally earlier than 12 weeks of gestation.
- In the second half of pregnancy, may present with large-for-dates uterine size, higher than expected weight gain, >2 fetal poles on palpation and 2 or more fetal heart rates heard on auscultation.

Prenatal diagnosis

The women should be informed about the greater likelihood of Down's syndrome in twin and triplet pregnancies before screening. They should be made aware of the different options for screening and the higher false-positive rate of screening tests in twin and triplet pregnancies. As a result of this they have a greater likelihood of being offered invasive testing and of complications occurring from this testing. Screening should be performed between approximately 11 weeks 0 days and 13 weeks 6 days:

- The fetal positions should be noted.
- The risk per pregnancy in monochorionic pregnancies and for each baby in dichorionic and trichorionic pregnancies should be calculated.
- Women whose risk of Down's syndrome exceeds 1:150 should be offered a referral to a fetal medicine specialist in a tertiary level fetal medicine centre.
- Twin pregnancies should use the 'combined test' and consider second trimester serum screening if the woman books too late for first trimester screening. Explain the potential problems (particularly the increased likelihood of pregnancy loss associated with double invasive testing because the risk cannot be calculated separately for each baby).
- Triplet pregnancies should use nuchal translucency and maternal age. Theyshouldnotusesecondtrimesterserumscreening.

If one fetus is detected as abnormal, selective termination (if desired) must be accurately targeted. Selective termination in monochorionic pregnancies risks co-twin sequelae.

Antenatal care

Referral

Twin pregnancies should be referred to obstetricians for shared care, due to the higher risk they present. There should be a special care baby unit (SCBU) available. A tertiary level fetal medicine centre referral is indicated for:

- Monochorionicmonoamniotictwinpregnancies.

- Monochorionicmonoamniotictripletpregnancies.
- Monochorionicdiamniotictripletpregnancies.
- Dichorionicdiamniotictripletpregnancies.
- Pregnancies complicated by any of the following:
    - Asymmetricalfetalgrowth.
    - Fetalanomaly.
    - Deathofonefetus.
    - Twin-twintransfusionsyndrome.

Scanning

Women with multiple pregnancies should be offered a first trimester ultrasound scan when approximately 11 weeks 0 days to 13 weeks 6 days:

    - This is to estimate gestational age, determine chorionicity and screen for Down's syndrome.
    - Ideally these should all be performed at the same scan.
    - Chorionicity should be determined using the number of placental masses, the lambda or T-sign and membrane thickness.
- Monochorionic twins should be scanned fortnightly to detect twin-twin transfusion from 16 to 24 weeks of gestation.

Multiple pregnancies should be monitored carefully for intrauterine growth restriction (IUGR):

- Differences in fetal weight should be monitored using two or more parameters at each ultrasound scan from 20 weeks.
- Ideally scans should be at intervals of less than 28 days.
- If there is a 25% or greater difference in size between twins or triplets, this is a clinically important indicator of IUGR. A referral to a tertiary level fetal medicine centre should be offered.

First-line management is usually laser surgery of inter-twin vascular placental anastomoses where the syndrome develops before 26 weeks of gestation. Other options include intrauterine blood transfusions, serial amnioreduction or elective delivery.

All twin pregnancies (regardless of chorionicity) are regularly scanned after about 30 weeks to monitor growth and fetal well-being, with early delivery induced in cases of growth cessation and/or poor Doppler blood flow indices.

Maternal health

There is a higher incidence of anaemia in women with twin and triplet pregnancies. FBC should be taken at 20-24 weeks to identify a need for early

supplementation with iron or folic acid. This should be repeated at 28 weeks as in routine antenatal care.

Maternal complications (eg pre-eclampsia) are more common and carers should be vigilant for early signs. Women are advised to take 75 mg of aspirin daily from 12 weeks until the birth of the babies if they have one or more of the following risk factors for hypertension:

- Firstpregnancy.
- Age 40 yearsorolder.
- Pregnancy interval of more than 10 years.
- BMI of 35 kg/m^2 or more at first visit.
- Family history of pre-eclampsia.

Because of the extra load on the heart, previously women were recommended bed rest. However, there is no clear evidence to support this.

Timing of delivery

- Women with uncomplicated monochorionic twin pregnancies should be offered elective birth from 36 weeks 0 days, after a course of antenatal corticosteroids has been advised.
- Women with dichorionic twin pregnancies should be offered elective birth from 37 weeks 0 days.
- Women with triplet pregnancies should be offered elective birth from 35 weeks 0 days, after a course of antenatal corticosteroids has been advised.

If the woman declines elective birth, weekly appointments should be offered with the specialist obstetrician. An ultrasound scan and biophysical profile assessment should be part of each appointment, with fortnightly fetal growth scans.

Intrapartum management

On admission in labour:

- Obtainintravenous (IV) access.
- Monitor fetal heart rates separately.
- Check the position of the lead fetus:
    - In 45% of cases, both fetuses present as cephalic.
    - In 25% of cases, the first twin is cephalic, the second breech.
    - In 10% of cases, breech/breech or first twin breech/second cephalic.

Vaginal delivery of twins

With no complicating factors, the mother can go into spontaneous labour*provided* the first twin has a cephalic presentation.

- Where the first twin presents in a breech position or transversely, Caesarean section is preferred.
- In most cases, vaginal birth proceeds as normal.
- With rupture of membranes, check for prolapse of umbilical cord.
- Immediately after the first baby is born:
    - Determine the position of the second fetus by vaginal examination.
    - If longitudinal, rupture the second amniotic sac (once the presenting part is engaged, usually after a couple of contractions) and proceed to delivery.
    - If transverse, external cephalic or internal podalic version may be attempted to bring into longitudinal position.
    - If successful, as confirmed by vaginal examination, then rupture the second amniotic sac **when** the fetal head is engaged.
    - If unsuccessful, deliver by Caesarean section.
- Contractions can reduce after the birth of the first fetus and, if they do not quickly return (within 15 minutes), set up an IV oxytocin infusion, following which birth of the second fetus should be straightforward. The second twin should deliver within 20-45 minutes of the first twin.
- Where there are difficulties with the delivery of the second twin or if it develops a bradycardia, a vacuum extraction (in cephalic position) or breech extraction can be performed without necessarily resorting to Caesarean delivery.
- Third stage should be actively managed by intramuscular (IM) injection of Syntometrine® or Syntocinon® as the fetal head is being born, in order to avoid postpartum haemorrhage.
- Twin deliveries should be attended by two paediatricians, two obstetricians and an anaesthetist.

Operative delivery of twins

Vaginally delivered second twins have an increased perinatal morbidity and mortality thought to be due to intrapartum anoxia. The question of whether all women with twin pregnancies should have a Caesarean section is contentious.

National Institute for Health and Clinical Excellence (NICE) guidance recognises the increased risk for the second twin in uncomplicated twin pregnancies at term but feels that evidence as to whether section for the second twin improves outcome, remains uncertain and therefore should not be routinely offered, except as part of research. Some studies have concluded that Caesarean delivery is beneficial for the second twin, with an NNT to prevent an adverse outcome of 33. Other studies advocate that, provided labour is actively managed in experienced centres and that complicated twin pregnancies are excluded, it continues to be a safe option.

Complications

Although a naturally occurring phenomenon, multiple pregnancies are considered high-risk because:

- Smaller babies - fetuses tend to be individually smaller than those in a singleton pregnancy because of greater demand for nutrients and slower in utero growth, ie light-for-dates. Monozygotictwinstendtobesmallerthandizygotictwins.
- Increased risk of prematurity - the mean gestation for twins is 37 weeks and for triplets 31 weeks. In particular, there is a higher risk of spontaneous preterm birth if they have had a spontaneous preterm birth in a previous singleton pregnancy. Neither cervical length, nor fetal fibronectin alone, should be routinely used to predict preterm birth. There is insufficient evidence to support the use of vaginal progesterone, bed rest at home or in hospital, cervical cerclage or oral tocolytics to prevent prematurity.
- Higher risk of congenital abnormality associated with multiple pregnancies (x 2-4 rate in singleton pregnancies).
- Higher rates of cerebral palsy found in twins (1-1.5%) and triplets (7-8%).
- Perinatal mortality rate for twins is significantly higher than singletons (x 5) and even higher for triplets (x 6). Rates are higher for monochorionic twins than dichorionic twins (49 versus 11.5/1,000).
- Higher rate of maternal pregnancy-related complications, such as hyperemesis gravidarum, polyhydramnios, pre-eclampsia, anaemia, antepartum haemorrhage.
- Higher rate of complications in labour - malpresentation, vasa praevia, cord prolapse, premature separation of placenta, cord entanglement, postpartum haemorrhage.

Complications of multiple pregnancy do not end with birth. Language and speech delay, more general cognitive delay or motor problems, behavioural problems and difficulty in parent-child interactions all appear to be more common in multiple birth children.

Also, the non-medical financial, social and emotional consequences of caring for twins or higher-order multiples need to be considered.

Prevention

Clearly, the outcomes of multiple pregnancies (particularly higher-order multiples) are poorer than singleton pregnancies. A few have challenged this consensus, based on the argument that, if more than once child is desired via fertility treatment, the risk and costs are diminished where analysis is based on born children rather than pregnancies.

Primary prevention should be aimed for. Limiting the number of embryos transferred in IVF and close counselling/monitoring of those using ovulation-induction therapies. The Human Fertilisation and Embryology Authority has criteria for single embryo transfer. If the woman does not fulfil them, a maximum of two embryos can be transferred per cycle.

Secondary prevention in the form of multifetal pregnancy reduction (MFPR) appears effective but is not acceptable to all, particularly those with a past history of infertility. Evidence is not gold standard, as RCTs are ethically and practically very difficult in these situations.

MFPR is performed early in pregnancy, usually between 9 and 12 weeks with a transabdominal (TA) or transvaginal (TV) ultrasound-guided injection of potassium chloride into the selected fetus(es). Usual practice is to reduce higher-order pregnancies to a twin pregnancy, although some now argue in favour of reduction to a singleton pregnancy, as the likelihood of taking home a baby is higher than remaining with a twin pregnancy.

Risks of a triplet pregnancy compared with a triplet-reduced-to-twin pregnancy:

	Births and losses of twins after MFPR	**Births and losses of triplets (no MFPR)**
Percentage of planned babies born and taken home	93%	79%
Premature birthbefore 32 weeks	10%	20%
Prematurebirth before 28 weeks	3%	8.5%
Miscarriage before 24 weeks	5%	11.5%
One or more fetal deaths during pregnancy	27/1,000	92/1,000

Risksof MFPR:

- Miscarriage of remaining fetuses (approximately the same rate as in normal twin pregnancies).
- Emotionalconsequencestoparents.
- Infection (rare).
- A **multiple birth** occurs when more than one fetus result from a single pregnancy.The preceding pregnancy is called a **multiple pregnancy**. Different names for multiple births are used, depending on the number of offspring. Common multiples are two and three, known as twins and **triplets**, respectively. These and other multiple births occur to varying degrees in most animal species, although the term is most applicable to placental species.

- Multiple birth siblings are either ***monozygotic*** or ***polyzygotic***. The former result from a single fertilized egg or zygote splitting into two or more embryos (identical), each carrying the same genetic material (genes). Siblings created from one egg are commonly called identical. Since identical multiples share the same genetic material, they are always of the same sex. Polyzygotic (or *fraternal*) multiples instead result from multiple ova being ripened and released in the same menstrual cycle by a woman's ovaries, which are then fertilized to grow into multiples no more genetically alike than ordinary full siblings, sharing 50% of their genetic material. Multiples called "dizygotic" represent multiples from two eggs specifically. For example, a set of triplets may be composed of identical twins from one egg and a third non-identical sibling from a second egg.
- The most common form of multiple births for humans is twins. Many placental species give birth to multiples as a matter of course, with the resulting group called a litter.
- In the United States, it has been estimated that by 2011, 36% of twin births and 77% of triplet and higher-order births resulted from conception by assisted reproductive technology.

- Monozygotic – multiple (typically two) fetuses produced by the splitting of a single zygote
- Dizygotic – multiple (typically two) fetuses produced by two zygotes
- Polyzygotic – multiple fetuses produced by two or more zygotes

Terms used for the order of multiple birth:

- Twooffspring - twins
- Threeoffspring - triplets
- Fouroffspring - quadruplets
- Fiveoffspring - quintuplets
- Sixoffspring - sextuplets
- Sevenoffspring - septuplets
- Eightoffspring - octuplets
- Nineoffspring - nonuplets
- Tenoffspring - decaplets
- Elevenoffspring - undecaplets
- Twelveoffspring - duodecaplets
- Thirteenoffspring - tridecaplets
- Fourteenoffspring - quadecaplets
- Fifteenoffspring - quindecaplets
- Sixteenoffspring - sexdecuplets
- Seventeenoffspring - sepdecuplets
- Eighteenoffspring - octdecuplets
- Nineteenoffspring - nondecuplets
- Twentyoffspring - vigintuplets

High orders of multiple births (three or more offspring in one birth) may result in a combination of fraternal (genetically different) and identical (genetically identical) siblings. The latter are also called *super twins*. For example, a set of triplets may consist of two identical siblings and one fraternal sibling. This happens when two eggs are fertilized and one of these subsequently divides into two fetuses. By analogy with monozygotic and dizygotic twins, such a combination is called *dizygotic triplets*. The Kübler triplets (see Elisabeth Kubler -Ross) were of this type.

Identical triplets or quadruplets are very rare and result when the original fertilized egg splits and then one of the resultant cells splits again (for triplets) or, even more rarely, a further split occurs (for quadruplets). The odds of having identical triplets is unclear. News articles and other non-scientific organizations give odds from one in 60,000 to one in 200 million pregnancies.

Human multiple births

Fraternal twin sisters taking a nap. Nonidentical twins, the most common kind of multiple birth among humans, occur in about 1 out of every 80 pregnancies.

Twins are by far the most common multiples born alive. Multiple births of as many as eight babies have been born alive, the first set on record to the Chukwu Family in Texas in 1998; one died and seven survived. In 2009, a second set, the Suleman Octuplets, was born in Bellflower, California. The most recent report that all were still alive was shortly before their fifth birthday.

Photo 4 Fraternal twins

There have been a few sets of nonuplets (nine) in which a few babies were born alive, though none lived longer than a few days. There have been cases of human pregnancies that started out with ten, eleven, twelve or fifteen fetuses, but no instances of live births. The pregnancies of the 10, 11 and 15 fetuses have all resulted from fertility medications and assisted reproductive technology (ART). However there has been one documented case when 12 fetuses were conceived naturally.

Multiple pregnancies in humans are usually born prior to 38 weeks of gestation, the average length of pregnancy. Thirty-six weeks is average for twin births, thirty-two weeks for triplets and thirty weeks for quadruplets.

Quadruplets

Quadruplets are much rarer than twins or triplets. As of 2007, there were approximately 3500 sets recorded worldwide. Quadruplet births are becoming increasingly common due to fertility treatments. There are around 70 sets of all-identical quadruplets worldwide. Many sets of quadruplets contain a mixture of identical and fraternal siblings, such as three identical and one fraternal, two identical and two fraternal, or two pairs of identicals. One famous set of identical quadruplets was the Genian quadruplet, all of whom developed schizophrenia. Quadruplets and quintuplets are sometimes referred to as "quads" and "quins" in Britain or "quints" in the USA.

Causes and frequency

The frequency of *N* multiple births from natural pregnancies has been give as approximately $1:89^{N-1}$ (Hellin's law) and traditionally as about $1:80^{N-1}$ (1:80 means 1 time in 80). hisgives:

- 1:89 (= 1.1%) or 1:80 (= 1.25%) fortwins
- $1:89^2$ (= 1:7921, about 0.013%) or $1:80^2$ (= 1:6400) fortriplets $1:89^3$ (= approx. 0.000142%, less than 1:700,000) or $1:80^3$ for quadruplets

North American dizygotic twinning occurs about once in 83 conceptions, and triplets about once in 8000 conceptions. US figuresfor 2010 were:

- Twins, 132,562, 3.31%
- Triplets, 5,503, 0.14%
- Quadruplets, 313, 0.0078%
- Quintupletsandmore, 37, 0.00092%

The Canadian Dionne sisters seen in this 1947 photograph, were the first quintuplets known to survive infancy.

Photo 5. The Canadian Dionne sisters

Human multiple births can occur either naturally (the woman ovulates multiple eggs or the fertilized egg splits into two) or as the result of infertility treatments such as IVF (several embryos are often transferred to compensate for lower quality) or fertility drugs (which can cause multiple eggs to mature in one ovulatory cycle).

For reasons that are not yet known, the older a woman is, the more likely she is to have a multiple birth naturally. It is theorized that this is due to the higher level of follicle-stimulating hormone that older women sometimes have as their ovaries respond more slowly to FSH stimulation.

The number of multiple births has increased over the last decade. For example, in Canada between 1979 and 1999, the number of multiple birth babies increased 35%. Before the advent of ovulation-stimulating drugs, triplets were quite rare (approximately 1 in 8000 births) and higher-order births much rarer still Much of the increase can probably be attributed to the impact of fertility treatments, such as in-vitro fertilization. Younger patients who undergo treatment with fertility medication containing artificial FSH, followed by intrauterine insemination, are particularly at risk for multiple births of higher order.

The Gosselin sextuplets with their parents and sisters, cover of KoreAm, May 2008

Certain factors appear to increase the likelihood that a woman will naturally conceive multiples. These include:

- mother's age: women over 35 are more likely to have multiples than younger women
- mother's use of fertility drugs: approximately 35% of pregnancies arising through the use of fertility treatments such as IVF involve more than one child

Photo 6. The Gosselin sextuplets

The increasing use of fertility drugs and consequent increased rate of multiple births has made the phenomenon of multiples more frequent and hence more visible. In 2004 the birth of sextuplets, six children, to Pennsylvania couple Kate and Jon Gosselin helped them to launch their television series, originally *Jon & Kate Plus 8*, which became the highest-rated show on the TLCnetwork.

Risks

Premature birth and low birth weight

Babies born from multiple-birth pregnancies are much more likely to result in premature birth than those from single pregnancies. 51% of twins and 91% of triplets are born preterm, compared to 9.4% in singletons. 14% of twins and 41% of triplets are even born *very preterm*, compared to 1.7% in singletons.

The preterm births also result in multiples tending to have a lower birth weight lower birth weight compared to singletons.

Some evidence indicates that only 1.10% of singletons are born with a very low birth weight and 10.12% twins and 31.88% triplets were found to be born with very low birth weight. This study was conducted by looking at the statistics from the U.S. Natality Files.

Among the exceptions are the Kupresak triplets of Missisauge, Ontario, Canada; their combined weight at birth in 2008, of 17 lbs, 2.7 ounces, set a world record.

Cerebral palsy

Cerebral palsy is more common among multiple births than single births, being 2.3 per 1,000 survivors in singletons, 13 in twins, and 45 in triplets in North West England. This is likely a side effect of premature birth and low birth weight.

Incomplete separation

Further information: Twin and Degree separation

Multiples may be monochorionic, sharing the same chorion, with resultant risk of twin-to-twin transfusion syndrome. Monochorionic multiples may even be monoamniotic, sharing the same amniotic sac, resulting in risk of umbilical cord compression and nuchal cord. In very rare cases, there may be conjoined twins, possibly impairing function of internal organs.

Mortality rate (stillbirth)

Multiples are also known to have a higher mortality rate. It is more common for multiple births to be stillborn, while for singletons the risk is not as high. A literary review on multiple pregnancies shows a study done on one set each of septuplets and octuplets, two sets of sextuplets, 8 sets of quintuplets, 17 sets of quadruplets, and 228 sets of triplets. By doing this study, Hammond found that the mean gestational age (how many weeks when birthed) at birth was 33.4 weeks for triplets and 31 weeks for quadruplets. This shows that stillbirth happens usually 3–5 weeks before the woman reaches full term and also that for sextuplets or higher it almost always ends in death of the fetuses. Though multiples are at a greater risk of being stillborn, there is inconclusive evidence whether the actual mortality rate is higher in multiples than in singletons.

Prevention in IVF

Today many multiple pregnancies are the result of in vitro fertilization (IVF). In a study in 1997 of 2,173 embryo transfers performed as part of IVF, 34% were successfully delivered pregnancies. The overall multiple pregnancy rate was 31.3%

(24.7% twins, 5.8% triplets, and .08% quadruplets). Because IVFs are producing more multiples, a number of efforts are being made to reduce the risk of multiple births- specifically triplets or more. Medical practitioners are doing this by limiting the number of embryos per embryo transfer to one or two. That way, the risks for the mother and fetuses are decreased.

The appropriate number of embryos to be transferred depends on the age of the woman, whether it is the first, second or third full IVF cycle attempt and whether there are top-quality embryos available. According to a guideline from The National Institute for Health and Care Excellence (NICE) in 2013, the number of embryos transferred in a cycle should be chosen as in following table:

Age	Attempt	No. Embryostransferred
<37 years	1st	1
	2nd	1 iftop-quality
	3rd	Nomorethan 2
37–39 years	1st & 2nd	1 iftop-quality 2 ifnotop-quality
	3rd	Nomorethan 2
40–42 years		2

Also, it is recommended to use single embryo transfer in all situations if a top-quality blastocyst is available.

Management of multiple pregnancy
Selective reduction

Selective reduction is the termination of one or more, but not all, of the fetuses in a multiple pregnancy. This is often done in pregnancies with multiple gestations to increase the likelihood that one child may live a healthy life. Armour reported a loss rate of 5.4% in a review of 1,000 cases of selective reduction. Fifteen percent of the losses occurred within 4 weeks of the procedures and more than 50% occurred after 8 weeks. This suggests that the reduction was successful at reducing the embryos from multiple gestations to single.

Though selective reduction seems to be effective, mothers of multiples who undergo this procedure are at a higher risk of miscarrying compared to that of an unreduced multiple pregnancy. A study done by looking at 158 pregnant women who underwent selective reduction from higher order multiples to twins showed that the mother had a 10.6% chance of miscarriage. Mothers of twin pregnancies without reduction only had a 9.5% chance of miscarriage. A study by Antsaklis showed a small increase in mortality for reduced twin pregnancies versus unreduced twin pregnancies.

Competition among fertility clinics does not appear to increase rates of multiple births from fertility treatment by promoting more aggressive embryo transfer decisions.

Cesarean section or vaginal delivery

A study in 2013 involving 106 participating centers in 25 countries came to the conclusion that, in a twin pregnancy of a gestational age between 32 weeks 0 days and 38 weeks 6 days, and the first twin is in cephalic presentation, planned Cesarean section does not significantly decrease or increase the risk of fetal or neonatal dealth or serious neonatal disability, as compared with planned vaginal delivery. In this study, 44% of the women planned for vaginal delivery still ended up having Cesarean section for unplanned reasons such as pregnancy complications. In comparison, it has been estimated that 75% of twin pregnancies in the United States were delivered by Cesarean section in 2008. Also in comparison, the rate of Cesarean section for all pregnancies in the general population varies between 40% and 14%.

Cesarean delivery is needed when first twin is in non cephalic presentation or when it is a monoamniotic twin pregnancy.

Neonatal intensive care

Multiple-birth infants are usually admitted to neonatal intensive care immediately after being born. The records for all the triplet pregnancies managed and delivered from 1992-1996 were looked over to see what the neonatal statistics were. Kaufman found from reviewing these files that during a five-year period, 55 triplet pregnancies, which is 165 babies, were delivered. Of the 165 babies 149 were admitted to neonatal intensive care after the delivery.

Insurance Coverage

A study by the U.S. Agency for Healthcare Research and Quality found that, in 2011, pregnant women covered by private insurance in the United States were older and more likely to have multiple gestation than women covered by Medicaid.

Cultural aspects

Certain cultures consider multiple births a portent of either good or evil.

Mayan culture saw twins as a blessing, and was fascinated by the idea of two bodies looking alike. The Mayans used to believe that twins were one soul that had fragmented.

In Ancient Rome, the legend of the twin brothers who founded the city (Romus and Remus) made the birth of twin boys a blessing, while twin girls were seen as an

unlucky burden, since both would have to be provided with an expensive dowry at about the same time.

In Greek mythology, fraternal twins Castor and Polydeuces, and Heracles and Iphicles, are sons of two different fathers. One of the twins (Polydeuces, Heracles) is the illegitimate son of the god Zeus; his brother is the son of their mother's mortal husband. A similar pair of twin sisters are Helen (of Troy) and Clytemnestra (who are also sisters of Castor and Polydeuces). The theme occurs in other mythologies as well, and is called superfecundation.

In certain medieval European chivalric romances, such as Marie de France’s Le-Fresne, a woman cites a multiple birth (often to a lower-class woman) as proof of adultery on her part; while this may reflect a widespread belief, it is invariably treated as malicious slander, to be justly punished by the accuser having a multiple birth of her own, and the events of the romance are triggered by her attempt to hide one or more of the children. A similar effect occurs in the Knight of the Swan romance, in the Beatrix variants of the Swan-Children; her taunt is punished by giving birth to seven children at once, and her wicked mother-in-law returns her taunt before exposing the children

The term "multiple births" refers to the delivery of twins and higher-order multiples (ie, triplets, quadruplets, etc). Multiple births occur when multiple fetuses are carried during a pregnancy with the subsequent delivery of multiple neonates. Pregnancies complicated by multiple births are associated with a higher rate of neonatal morbidity and mortality, paralleling the increased risk of preterm delivery, low birth weight, and other associated high-risk morbidities. Maternal morbidity and mortality are also increased in pregnancies complicated by multiple gestations and multiple births. Frequency

The incidence of monozygotic twins is constant worldwide, approximately four per 1000 births. The incidence of multiple zygotic pregnancies varies in relation to maternal age, the use of assisted reproductive technology (ART), and ethnicity.

The incidence of multiple births increased significantly in the late 20th century in the United States and worldwide. A combination of factors contributed to this, the two most prominent of these being the use of ART and advanced maternal age at the time of conception.

United States

As previously stated, the incidence of monozygotic twins is constant worldwide (approximately 4 per 1000 births). Approximately two thirds of twins are dizygotic. Birthrates of dizygotic twins vary by race (10-40 per 1000 births in blacks, 7-10 per 1000 births in whites, and approximately 3 per 1000 births in Asians) and maternal age (ie, the frequency has risen with increasing maternal age ≤40 years). Dizygotic-

twin birthrates are also influenced by other factors, such as parity and mode of fertilization (ie, most artificially conceived twins are dizygotic; however, 6-10% are monozygotic).

Naturally occurring triplet births occur in approximately 1 per 7000-10,000 births; naturally occurring quadruplet births occur in approximately 1 per 600,000 births.

In the United States, a plateau in the prevalence of multiple births has been observed since 2004. Statistics from 2004–2010 showed that the prevalence of twin deliveries in the United States remained stable at approximately 32 per 1000 live births, compared with a decreasing prevalence of higher-order multiple deliveries.

International

Birthrates of dizygotic twins vary by race. The highest birthrate of dizygotic twins occurs in African nations, and the lowest occurs in Asia. The Yorubas of southwestern Nigeria have a birthrate of 45 twins per 1000 live births, with approximately 90% being dizygotic.

Mortality/Morbidity

Maternal morbidity

Multiple-gestation pregnancies are associated with a significantly higher maternal complication rate than are singleton gestations. Multiple-gestation pregnancies carry an increased risk of hypertensive disorders of pregnancy; gestational diabetes mellitus; hyperemesis; preterm labor; premature rupture of membranes; anemia; placental abruption; postpartum hemorrhage; cardiac complications, such as myocardial infarction and left ventricular heart failure; operative deliveries, both vaginal and cesarean; required hysterectomy; and prolonged hospital stay.

Fetal/neonatal morbidity

The increase in fetal and neonatal morbidity and mortality associated with multiple- gestation/birth pregnancies correlates with an increased risk of preterm delivery, low birth weight, and intrauterine growth retardation. Ie, the neonatal mortality rate in multiple-fetus pregnancies is similar to singleton rates, increasing with decreasing gestational age.

The average gestational age for twin deliveries is 35.3 weeks; for triplet deliveries, 32.2 weeks; and for quadruplet deliveries, 29.9 weeks. Although the percentage of preterm multiple-birth deliveries in the United States declined between 2006 and 2010 (as did the incidence of preterm births in general), the rate still remained significantly high; in 2011, approximately 60% of multiples delivered at less than 37 weeks' gestation.

Birth weight is closely associated with gestational age, so the increased incidence of preterm delivery influences the rate of reduced birth weights in multiple-birth neonates. These neonates also have an increased incidence of intrauterine growth retardation. Divergence from singleton growth curves occurs at approximately 32-33 weeks in twin gestations, at 29-30 weeks in triplet gestations, and at 27-28 weeks in quadruplet gestations.

Comparing specific morbidities and mortality in multiple-gestation pregnancies is difficult due to the complexity of contributing factors. For example, some evidence suggests a link between ART and perinatal morbidity unrelated to the risks associated with multiple births. As previously reviewed, chorionic-amniotic placentation also affects multiple-gestation outcomes.

Neonatal outcomes at specific gestational ages and birth weights are similar in multiple-birth neonates to those in singleton pregnancies. Neonates from multiple-gestation pregnancies may have a higher risk of acute respiratory morbidity, such as respiratory distress syndrome, but do not have a higher incidence of chronic lung disease. Other major morbidities, including intraventricular hemorrhage, preventricular leukomalacia, retinopathy of prematurity, necrotizing enterocolitis, patent ductus arteriosus, and nosocomial infection, as well as length of hospital stay, demonstrate no statistical difference between singletons and multiples.

The risk of cerebral palsy in multiple-fetus pregnancies parallels decreasing gestational age. A second association during the late preterm period (34-37 weeks' gestation) may correlate with the increasing maternal morbidities of multiple-fetus pregnancies during this time frame (ie, fetal growth restriction, hypertensive disorders, placental insufficiency).

In a prospective cohort study of monochorionic twins followed from the first trimester to a mean age of 24 months, Ortibus et al found that twin-to-twin transfusion syndrome (a specific morbidity in multiple-gestation pregnancies) and assisted conception increased the risk of both death and neurodevelopmental impairment, whereas early onset discordant growth increased only the risk of death. Of the 136 pregnancies studied, 90% resulted in both twins surviving, 4% resulted in one survivor, and 6% resulted in no survivors. Overall mortality was 8%, and neurodevelopmental impairment occurred in 10% of infants.

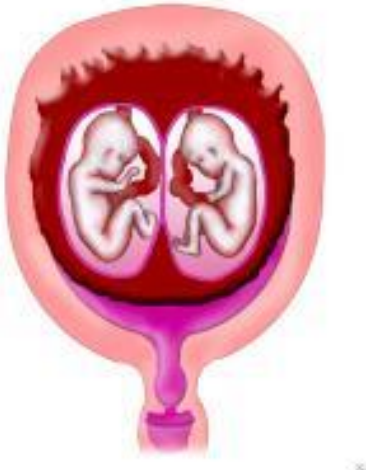
Placental physiology has a significant impact on fetal and neonatal outcome. Monochorionic twins have increased neonatal morbidities such as prematurity, intrauterine growth retardation, congenital anomalies, twin-to-twin transfusion syndrome, and increased perinatal mortality. Twin-to-twin transfusion syndrome has been reported in 8-10% of monochorionic pregnancies. Triplet gestations with monochorionic placentation may also experience an increased complication rate.

Determination of placental chorionicity can be evaluated by obstetric ultrasonography during the first and early second trimester. Evaluation of the placenta(s) after birth may also be helpful in the perinatal evaluation process.

Monozygotic pregnancies involve the fertilization of a single ovum by a single sperm. Monozygotic twins develop when a single fertilized ovum splits after conception. An early splitting of the ovum (ie, within 2 days of fertilization) produces separate chorions and amnions. These dichorionic twins have different placentas, which can be separate or fused. Approximately 30% of monozygotic twins have dichorionic/diamniotic placentas.

Later splitting (ie, 3-8 days after fertilization) results in monochorionic/diamniotic placentation

Approximately 70% of monozygotic twins are monochorionic/diamniotic. If splitting occurs later (ie, 9-12 days after fertilization), monochorionic/ monoamniotic placentation occurs (see the image below).



Picture. 31. Monochorionic/diamniotic placentation.

Monochorionic/monoamniotic twins are rare; only 1% of monozygotic twins have this form of placentation. Monochorionic/monoamniotic twins have a common placenta, with the possibility of significant vascular communication between the 2 fetal circulations. These twins can develop twin-to-twin transfusion syndrome. If twinning occurs more than 12 days after fertilization, then the monozygotic fertilized ovum only partially splits, resulting in conjoined twins.

Dizygotic, trizygotic, and other higher-order pregnancies involve the fertilization of multiple ova. Dizygotic twins, for example, develop when two ova are fertilized. Dizygotic twins have separate amnions, chorions, and placentas (see the image below).

Picture. 32. Monochorionic/monoamniotic placentation.

The placentas in dizygotic twins may fuse if the implantation sites are proximate. The fused placentas can be easily separated after birth.

Triplet pregnancies result from various fertilization, splitting, and development scenarios that involve ova and sperm. For example, triplets can be monozygotic, dizygotic, or trizygotic. Trizygotic triplets occur when three sperm fertilize three ova. Dizygotic triplets develop from one set of monozygotic cotriplets and a third cotriplet derived

Picture. 33. Dichorionic/diamniotic placentation.

from a different zygote. Finally, two consecutive zygotic splittings with a vanished fetus can also result in monozygotic triplets. Zygosity in quadruplets and higher order multiples also varies.

Although the evaluation of the placenta(s) following birth is important in all multifetal pregnancies, the examination may not always help to determine zygosity.

- Women with multifetal pregnancies may have a uterine size that is inconsistently large for dates and may experience accelerated weight gain.
- Upon auscultation, more than one fetal heart rate may be heard.
- Risk factors for multifetal pregnancy can be divided into natural and induced.
- Risk factors for natural multifetal pregnancy include advanced maternal age, family history of dizygotic twins, and race.
- Induced multifetal pregnancies occur following infertility treatment via the use of ovulation-inducing agent or multiple gamete/zygote transfer.

The evaluation of a multifetal pregnancy involves routine prenatal and postnatal care, as well as specific assessment directed by the type of multiple pregnancy and neonatal complications. Guidelines for the evaluation of multifetal pregnancies have been established by American College of Obstetricians and Gynecologists.

- Obstetrical: Routine prenatal laboratory studies are indicated.
- Neonatal: A CBC count is obtained to evaluate for anemia and polycythemia.
- Neonatal arterial blood gas and cord blood gas: These are measured to evaluate for respiratory distress, hypoxia, acidosis, and perinatal depression.
- Metabolic panel: Fluid status and electrolyte levels should be evaluated and metabolic status should be determined, including through screening for hypoglycemia and hypocalcemia.
- Bilirubin level: This is obtained to screen for increased risk of hyperbilirubinemia associated with prematurity and polycythemia
- Obstetrical: Prenatal ultrasonography is used to confirm multifetal pregnancy and to monitor intrauterine fetal growth.
- Fetal echocardiography: This is used to screen for congenital heart disease in neonates.
- Fetal MRI: This is used to screen for fetal anomalies.
- Neonatal: Chest radiography is used to evaluate respiratory distress.
- Ultrasonography: This is used to screen for intraventricular hemorrhage, periventricular leukomalacia, and abdominal abnormalities.

- Echocardiography: This is used to screen for congenital heart disease.

Multiple pregnancy means carrying more than one baby, normally twins.

Multiple pregnancies are getting more common because they are linked to infertility treatments, which are becoming more available. The most common multiple is twins.

Twins can be monozygotic (one fertilised egg splits in two) or dizygotic (two eggs are fertilised). Monozygotic twins will normally be the same sex. Infertility treatments are linked to dizygotic twins.

Most women who are pregnant with twins deliver healthy babies but carrying more than one baby increases the health risks for the mother and baby.

Multiple pregnancy is normally spotted in routine pregnancy scans and most women know by 20 weeks that they are carrying more than one baby.

Premature birth

Carrying more than one baby means you are more likely to have a premature delivery.

The average gestation for multiples is:

- Twins: 37 weeks
- Triplets: 34 weeks
- Quadruplets: 32 weeks

If the baby is not born by then, most twin pregnancies are induced by 38 weeks because the health risks increase after that.

What are the risks and complications of multiple pregnancy

Most women with twins stay healthy through the pregnancy and deliver healthy babies. However, you will be at higher risk of some of the potential complications that can cause premature birth or lead to induction, including:

- preeclampsia
- antepartum haemorrhage (severe vaginal bleeding)
- polyhydramnios (too much amniotic fluid)
- placental abruption
- IUGR
- Gestational diabetes
- needing delivery with forceps, ventouse or caesarean section
- a problem called twin to twin transfusion syndrome if the babies share the same placenta.

Most mums who are expecting twins give birth to healthy babies. So try not to worry if you've been told that carrying twins means a high-risk pregnancy.

Misscariage

Risk of having a miscarriage is higher than with a single pregnancy. But it's impossible to say exactly how much higher this risk is, as most early misscarriages aren't identified.

Most miscarriages, for single and multiple pregnancies, happen in the first 12 weeks. Sometimes one baby is lost, but if this happens during your first trimester, it won't usually affect the development of your remaining baby. The fetus that has died is often completely reabsorbed (vanishing twin syndrome), and you may have few or no symptoms.

Vanishing twin syndrome happens in between 21 per cent and 30 per cent of multiple pregnancies. It's more common than we think, because many of these early twin pregnancies are never discovered.

High blood pressure (gestational hypertension) is two to three times more likely than if you were expecting a single baby.

Preeclampsia is three times more common if you're expecting twins or more than if you were expecting one baby. This is because having more than one baby places more strain on the placenta. One survey found that 13 per cent of mums expecting twins or triplets experienced the condition.

Low dose (75mg) of aspirin each day from 12 weeks in order to reduce risk of high blood pressure and pre-eclampsia in case of:

- primigravida
- age 40 or over
- family history of pre-eclampsia
- BMI 35 or over
- 10 years since last pregnancy

Diabetes during pregnancy (gestational diabetes) is two to three times more common if you are expecting more than one baby.

Urine will be checked for sugar at antenatal appointments. In case of diabetes suspicion glucose tolerance test is recommended.

Anaemia may develop due to increased blood flow causing iron levels to drop. doctor may recommend iron supplement. Having mild anaemia isn't harmful to babies.

Because anaemia is more common in mums expecting more than one baby, an extra blood test should be made between 20-24 weeks.

Obstetric cholestasis is a rare condition that affects the liver. It's thought to be caused by the pregnancy hormones oestrogen and progesterone. It is more common in twin and triplet pregnancies, which are associated with higher levels of hormones. The condition causes extreme itching without a rash. Some itching is common in

pregnancy, but if your symptoms are severe, contact your doctor or midwife straight away.

Fetal complications:

1. **Fetal growth restriction**
2. **Twin – to -twin transfusion syndrome (**when one twin shares the other's blood supply, is a rare but potentially serious complication. It happens in up to 15 per cent of identical twins who share a placenta. One baby (the recipient) gets too much blood and the other (the donor) gets too little.

   The donor twin may become smaller and anaemic due to not having enough blood supply. The recipient twin's higher blood volume may strain his heart and lead to heart failure. If your twins share a placenta, your pregnancy will be closely monitored with frequent ultrasound scans for signs of TTTS)
3. **Premature delivery.** More than half of all twins are born before 37 weeks, and 10 per cent are born before 32 weeks. Those most at risk are very premature babies who are born before 30 weeks.

4. **Stillbirth .** The rate of babies who are stillborn is higher for multiple births. The stillbirth rate is 12 per 1,000 twin births and 31 per 1,000 triplet births. This compares with about five in 1,000 singleton pregnancies. Loss in the first month of life is also more likely.

   The risk of stillbirth in twins increases slightly after 38 weeks.

Preeclampsia, also known as toxemia, occurs 2 to 5 times more often in multiple pregnancies. Fifteen percent to 20% of women with twin pregnancies will experience preeclampsia, and an even higher percentage is preeclamptic in triplet or high-order pregnancies. Preeclampsia is diagnosed when the mother’s blood pressure becomes elevated and protein is detected in the urine. The condition may progress and threaten the health of the mother and baby. When severe, the mother may have seizures, and stroke or other life-threatening complications are possible.

Diabetes

Women with multiple pregnancies are more likely to develop gestational Diabetes during pregnancy. Babies of diabetic mothers are more likely to experience **respiratory distress** and other newborn complications.

However, gestational diabetes is common even in singleton pregnancies, and treatment is well established and effective.

Fetal and Newborn Complications

Although uncommon in twin deliveries, about 20% of triplet pregnancies will result in the delivery of at least one child with a major long-term handicap. Preterm delivery places an infant at increased risk for severe complications or early death. A baby's lungs, brain, circulatory system, intestinal system, and eyes may be not fully developed.

Of the premature babies who die, 50% succumb to respiratory distress syndrome, caused by immature lungs. Brain damage is responsible for almost 10% of premature newborn deaths. Prematurity also may result in visual impairment or blindness. Birth defects and stillbirths account for about 30% of the deaths in twins and multiple pregnancies. Neonatal intensive care unit admission is required for one-fourth of twin and three-fourths of triplet deliveries.

Despite these numbers, it is important to note that the vast majority of multiple-birth infants do survive. Fetal death occurs in about 1.6% of twins and 2.7% of triplets. Furthermore, compared to singleton pregnancies of the same birth weight, there is no significant increase in the incidence of chronic lung disease or brain, eye, or gastrointestinal problems in multiple-birth infants.

Low birth weight of less than 5.5 pounds (lb.) [2,500 grams] occurs in over half of twins. The average birth weight is approximately 4 lb. (1,660 grams) for triplets and 3 lb. (1,300 grams) for quadruplets. As a result of prematurity, the risk for cerebral palsy is 4 times more likely to occur in twins. The rates are even greater for triplets and high-order multiple births.

The overall survival rate is 85% for newborns over 2 lb., 3 oz. (1,000 grams) but less than 40% for those under 2 lb., 3 oz. Birth weight also corresponds closely to the severity of disability throughout the childhood years. Disability occurs in almost 25% of children with a birth weight less than 2 lb. As noted above, the average birth weight even for quadruplets is well above this number.

PREVENTION OF MULTIPLE PREGNANCY

Prevention during infertility treatment is the best approach to avoiding a multiple pregnancy. In ART cycles, limiting the number of embryos transferred is an effective approach. Consult the ASRM Practice Committee Report titled

Guidelines on Number of Embryos Transferred for recommendations regarding the optimal number of embryos to transfer based on patient age, embryo quality, and other criteria.

In the United States, physicians and patients jointly decide how many embryos to transfer. However, in England, no more than two embryos may be transferred in most cases. In Canada, a maximum of three embryos are recommended for transfer.

The ultimate goal of ART is to achieve a high pregnancy rate while transferring a single embryo. While physicians can transfer two embryos and still maintain acceptable pregnancy rates, the transfer of one embryo is associated with good pregnancy rates in certain patient groups, thereby resolving the problem of multiple pregnancies caused by multiple embryo transfer. Approximately 10% of embryo transfers in the United States are now performed using elective single embryo transfer.

Multiple pregnancies are a known complication of ovulation stimulation drugs. Most physicians monitor patients with ultrasound examinations and blood tests. A woman with a large number of ovarian follicles or high hormone levels has an increased risk of a multiple pregnancy, and the cycle may be canceled to avoid the risk. No proven way of reducing multiple pregnancies with superovulation has been identified, although preventing fertilization with development of more than three follicles is helpful in reducing high-order multiples.

Multifetal Pregnancy Reduction

When a triplet or high-order multiple pregnancy occurs, multifetal pregnancy reduction may be considered to improve the chance for survival of the fetuses. While multifetal pregnancy reduction carries some risk of a complete miscarriage, it also reduces the chances of extreme premature birth. For more information, see the ASRM Patient Fact Sheet Challenges of Parenting Multiples.

CARRYING A MULTIPLE PREGNANCY

In order to achieve the best outcome with a multiple pregnancy, the expectant mother must work as part of the health care team. A nearly total change in lifestyle can be expected, especially after about 20 weeks into the pregnancy.

Metabolic and Nutritional Considerations

There is an increased need for maternal nutrition in multiple pregnancies. An expectant mother needs to gain more weight in a multiple pregnancy, especially if she begins the pregnancy underweight. With multiples, weight gain of approximately 37-54 lb. is recommended for normal-weight women. The pattern of weight gain is important too. Healthy birth weights are most likely achieved when the mother gains nearly one pound per week in the first 20 weeks. The increase in fetal growth with appropriate nutrition and weight gain may greatly improve pregnancy outcome at a minimum of cost.

Activity Precautions

Many physicians who manage multiple pregnancies believe that a reduction in activities and increased rest prolongs these pregnancies and improves outcomes. However, routine hospitalization for bed rest in multiple pregnancy has not been shown to prevent preterm birth. Women with high-order multiple pregnancies usually are advised to avoid strenuous activity and employment at some time between 20 and 24 weeks. Bed rest improves uterine blood flow and may be helpful for fetal growth problems.

Intercourse generally is discouraged when bed rest is recommended.

Monitoring a Multiple Pregnancy

Since preterm birth and growth disturbances are the major contributors to newborn death and disability in multiples, frequent obstetric visits and close monitoring of the pregnancy are needed.

Prenatal diagnosis using a variety of new techniques can be done near the end of the first trimester to screen for Down syndrome and other genetic abnormalities. Amniocentesis may be performed between 16 and 20 weeks.

Amniocentesis may be complicated and difficult to perform in twins and triplets and may not be possible in high-order multiple pregnancies.

However, reasonable data exist for the use of serum screening in the setting of multiple pregnancies and can be a helpful tool to assess risk of these and other conditions.

Many physicians perform cervical examinations every week or two beginning early in pregnancy to determine if the cervixis thinning or opening prematurely. If an exam or ultrasound shows that the cervix is thinning or beginning to dilate prematurely, a cerclage, or sutureplaced in the cervix, may prevent or delay premature dilatation. However, preventativecerclage has not been shown to prevent preterm birth in twins or triplets.

Tocolytic agents

are medications that may slow or stop premature labor. These medications are given in hospital "emergency" settings in an attempt to stop premature labor. It is important to attempt to delay delivery to minimize the risks of premature delivery. Ultrasound examinations in the second trimester can identify some birth defects. Assessment of fetal growth by ultrasound every 3 to 4 weeks during the second half of pregnancy is commonly performed.

Every multiple pregnancy should be considered at high risk, and obstetricians experienced with the management of multiple gestations should provide care. A neonatal intensive care unit nursery should be available to provide immediate and comprehensive support to premature newborns.

Method of Delivery

Vaginal delivery of twins may be safe in some circumstances. Many twins can be delivered vaginally if the lowest infant is in the head-first position.

Most triplets will be delivered by cesarean section. Appropriate anesthesia and neonatal support are essential, whether delivery is performed vaginally or requires

cesarean section. Delivery of multiples requires planning by the entire medical team and availability of full intensive-care support following birth.

Psychosocial Effects of Multiples on a Family

Although the majority of women with a multiple pregnancy do very well, their families may experience significant stress. If prolonged hospitalization is needed, arrangements must be made for work, home, and family care.

Even when medical problems are overcome and the infants survive without disability, the effect of multiple births on family life is substantial. The impact of a multiple birth clearly affects the parents, but also the babies, other siblings, and the extended family. Financial stresses are common, due to the additional costs of feeding, clothing, housing, and caring for multiple children. Postpartum depression also is more common after delivery of multiple pregnancies in both the mother and the father and may be long-term.

Psychological counseling and support groups may provide a lifeline for the parents of multiples, who may feel isolated or depressed. Most physicians can provide appropriate referrals to a mental health professional or a support group. For more information, see the ASRM Patient Fact Sheet titled

Challenges of Parenting Multiples.

CONCLUSION

The objective of infertility treatment is the birth of a healthy child. In a small percentage of patients, treatment results in multiple pregnancy that may place the mother and the babies at increased risk for an unhealthy outcome. Since multiple pregnancies and their complications are an inevitable risk of fertility therapies, education about these risks is crucial prior to treatment. Ultimately, prevention is the key to reducing the risk of multiplepregnancy.

Recommended literature

1. Obstetrics: підручник англійською мовою (edit by I.B. Ventskivska). - K.: Medicine, 2008.-334 p.

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6. DC Duttas textbook on gynecology, six edition/ New Dehli-London-Philadelphia, 2013 p.

Навчальний посібник

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АКУШЕРСТВО. КОНСПЕКТ ЛЕКЦІЙ

2023 р.

Затверджено вченою радою медичного факультету
ДВНЗ «Ужгородський національний університет»
протокол № 10 від «15» грудня 2022 року.

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Олександр Задорожний, Наталія Леміш

Коректура:

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Комп'ютерний набір тексту
та упорядкування фотоматеріалу: *Наталія Леміш*

Віддруковано з наданого оригінал-макету:
ТОВ «РІК-У» 88000, м. Ужгород, вул. Гагаріна, 36.
Свідоцтво Серія ДК 5040 від 21 січня 2016 р.

Підписано до друку 16.01.2023 р. Шрифт «Times New Roman».
Папір офсетний, щільність 80г/м^2. Друк цифровий. Ум. друк. арк. 12,8.
Формат 60х84/16. Замовлення № 60К. Тираж 300 прим.

Оксана Корчинська, Наталія Леміш
К 70 Акушерство конспект лекцій. Навчальний посібник/Автори: Оксана Корчинська, Наталія Леміш. Ужгород: ТОВ «РІК-У», 2023.- 220с. (англійською мовою)

ISBN 978-617-8046-98-8

Відповідно до резолюції Всесвітньої асамблеї охорони здоров'я ООН від 1995р. збереження репродуктивного здоров'я визначено на глобальному рівні ВООЗ як пріоритетну галузь.

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Цей навчальний посібник створено з метою допомогти студентам 4-6 курсів підготуватися до практичних занять.

УДК 618.4-72