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Alaka K Deshpande

PREGNANCY MEDICINE



Forewords
Shashank R Joshi
CN Purandare

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Chapter 2

Fetal Growth and Drugs

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FERTILIZATION

The union of egg (ovum) and sperm is the most important biological process known as fertilization.

A fully mature ovum is the largest cell in the body (130 microns) and the sperm is the smallest cell. Ovum has 23 chromosomes and sperm carries 23 chromosomes.

After union, the ovum becomes a zygote—a diploid cell with 46 chromosomes. Mitotic division of zygote continues till a blastocyst is formed which gets implanted in the endometrium on the 6th day of fertilization with development of chorionic villi. It is conventional to refer to these products of conception as an embryo. The embryonal period commences at the beginning of the third week after fertilization (i.e. about 4 weeks after last menstrual period).

At this stage ectoderm thickens to form neural plate and neural folds by end of 4th week post conception, neural folds fuse to form a neural tube.

The primitive heart beats are noticed on day 21, four-chambered primitive heart is seen. By end of 6 weeks. heart is completely formed. Fingers and toes are present and the arms bend at elbows. The upper lip is complete, the external ears form. By 12 weeks, the centers of ossification appear in bones; skin and nails are developed. The external genitalia are beginning to show definitive signs of the gender.

This, in brief, is embryogenesis.

The gestation period of 40 weeks is also divided into three trimesters each of 13 weeks because important obstetrical milestones can be designated by trimesters.

Thus,	First trimester	Embryogenesis
	Second trimester	Growth and maturation of structures formed during embryonal phase
	Third trimester	Maturation and engaging the head as preparation of labor.

Birth defects: Three percent of all newborns in the US have major structural malformation detectable at birth.

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TERATOGENESIS

The Greek word *teratos* means monster, the appearance due to congenital structural defects. The agents responsible for such defects are called as teratogens and the process as teratogenesis.

Exposure of embryo to certain drugs, chemicals, infections or environmental factors may result into the birth defects.

Therefore, it can be summarized–

1st trimester	Embryogenesis	Embryonal defects
2nd trimester	Degeneration of cytotrophoblast; transplacental entry of organisms	
3rd trimester	Transmission of infections from mother to child	

The first 12–14 weeks is a period of embryogenesis, therefore, the developments of maximum fetal malformations occur during this period while vertical transmission of infections is at its minimum.

The degeneration of cytotrophoblastic layer of the placenta occurs during second trimester potentiating the transplacental entry of the organisms. The best example is syphilis.

Maximum transmissibility of infections from mother to the fetus is seen in third trimester with the least probability of the fetal malformations (Table 2.1).

The challenges to the clinician vary from time to time related to duration of pregnancy which is broadly classified as first, second and the third trimester.

Table 2.1 Shows the routes transmissions

Pathogen	*Intrauterine*	*Perinatal*	*Post-natal*
Treponema pallidum	++	–	–
Neisseria gonorrheae	–	+ + (G)	–
Group B streptococci	+/–	+ + (G,H)	–
Listeria monocytogenes	+ +	+ (G,H)	–
Chlamydia trachomatis	–	+ + (G)	–
Toxoplasma gondii	+ +	–	–
Rubella virus	++	–	+
Cytomegalovirus	+ +	+ + (G,H)	+
Parvovirus	+ +	–	–
Varicella zoster virus (chicken pox)	+	+ (H)	–
HIV	+/–	+ + (H)	+
HBV	+/–	+ + (H)	+
HCV	+/–	+ + (H)	–

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Post-natal Transmission

Birth canal–Neonatal meningitis, sepsis, pneumonia:

- *E. coli.*
- Grp. B streptococci – *Strep. agalactiae.*
- Listeria – Granulomatosis infant septicum
- Genital herpes
- Hep. B
- HIV
- Brestfeeding HIV, HBV

The Food and Drug Administration (FDA) has categorized the risk of teratogenesis of drugs as follows (Tables 2.2 and 2.3):

Table 2.2 FDA safety categories in pregnancy

Pregnancy Category	*Definition*
A	Controlled studies show no risk. Adequate, well-controlled studies in pregnant women have failed to demonstrate risk to the fetus.
B	No evidence of risk in humans. Either animal finding shows risk, but human finding does not; or if no adequate human studies have been done, animal findings are negative.
C	Risk cannot be ruled out. Human studies are lacking, and animal studies are either positive for fetal risk or lacking. **However, potential benefits may justify the potential risks.**
D	Positive evidence of risk. Investigational or post-marketing data show risk to the fetus. Nevertheless, potential benefits may outweigh the potential risks. If needed in a life-threatening situation or a serious disease, the drug may be acceptable if safer drugs cannot be used or are ineffective.
X	Contraindicated in pregnancy. Studies in animals or human, or investigational or post-marketing reports have shown fetal risk which clearly outweighs any possible benefit to the patient.

Table 2.3 Drugs or substances suspected or proven to be human teratogens

ACE inhibitors	Kanamycin
Aminopterin	Lithium
Androgens	Methimazole
A-II antagonists	Methotrexate
Busulfan	Misoprostol
Carbamazepine	Penicillamine
Chlorobiphenyls	Phenytoin
Cocaine	Radioactive iodine
Coumarins	Streptomycin
Cyclophosphamide	Tamoxifen
Danazol	Tetracycline
Diethylstilbestrol (DES)	Thalidomide
Ethanol	Tretinoin
Etretinate	Trimethadione
Isotretinoin	Valproic acid

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PREGNANCY MEDICINE

Highlights of the Book

- Preconception counseling.
- Contribution of updated management of various medical disorders during pregnancy by experts in their field.
- Focus on the clinical approach.
- Problems related to assisted conception.
- Details of cord blood transplantation.
- Most useful to Internists, Obstetricians, Postgraduates of Medicine and Obs-Gyn.
- Simple language and lucid presentation.



Alaka K Deshpande MBBS MD MAMS FIMSA FICP is an Hon Professor of Medicine. She has formerly been a Professor and Head, Department of Medicine; and Director, Centre of Excellence in HIV Care, Grant Medical College and Sir JJ Group of Hospitals, Mumbai, Maharashtra, India.

She has been teaching medicine to the undergraduate and postgraduate students for more than four decades. A great academician with large number of research publications to her credit, an astute clinician with a rich experience of managing thousands of patients in a tertiary care center, her lectures beautifully amalgamate both the knowledge and experience with a very lucid clinical approach. She is revered as one of the finest and the best teachers.

Her popularity is also reflected in her contribution as a faculty in innumerable medical seminars and CMEs. Many professional organizations have felicitated her as the best teacher in various scientific forums.

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Her medical services have been acknowledged and appreciated by the Government of India by conferring on her the highest civilian honor– 'Padmashree' in 2001.

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