BGD Tutorial - Applied Embryology and Teratology

From Embryology

from Embryology (11 Mar 2014)	**[show] Translate this page**

Introduction

This Medicine Phase 2 tutorial introduces the topics of Applied Embryology and Teratology. This one and a half hour presentation uses your existing knowledge of normal human development in an applied clinical manner in relation to our existing knowledge of teratogens. In addition, you should begin considering the variables that will not change and those that will in future medical practice. Due to time limitations, only a brief coverage can be given of any one topic.

Self-Directed Learning boxes on this page will not be discussed within the tutorial. You should also return here and later work through the linked online resources for more detailed descriptions and an understanding of these issues. This current page appears in the lefthand menu under Medicine as **BGD 2 Tutorial**.

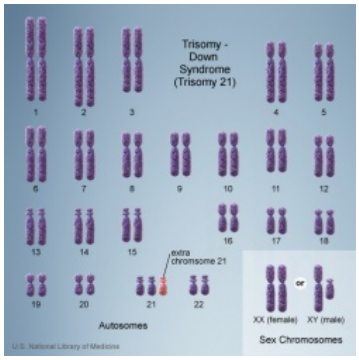
Page is currently being updated for 2014 (This notice removed when complete).

2013 Print Version PDF (10 pages, 670kb)

Similar content was covered in the previous online tutorials in 2012 (http://php?title=BGD_Tutorial_-_Applied_Embryology_and_Teratology&oldid=117268) | 2012 PDF | 2011 PDF and 2010.

[hide] Whats in the News?

News - DNA sequencing versus standard prenatal aneuploidy screening



"In high-risk pregnant women, noninvasive prenatal testing with the use of massively parallel sequencing of maternal plasma cell-free DNA (cfDNA testing) accurately detects fetal autosomal aneuploidy. Its performance in low-risk women is unclear. ...In a general obstetrical population, prenatal testing with the use of cfDNA had significantly lower false positive rates and higher positive predictive values for detection of trisomies 21 and 18 than standard screening. (Funded by Illumina; ClinicalTrials.gov number, NCT01663350.)."

(More? Trisomy 21 | Trisomy 18 | Prenatal Diagnosis)

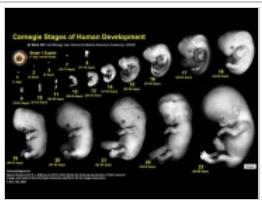
Reference: Diana W Bianchi, R Lamar Parker, Jeffrey Wentworth, Rajeevi Madankumar, Craig Saffer, Anita F Das, Joseph A Craig, Darya I Chudova, Patricia L Devers, Keith W Jones, Kelly Oliver, Richard P Rava, Amy J Sehnert, CARE Study Group **DNA sequencing versus standard prenatal aneuploidy screening.** N. Engl. J. Med.: 2014, 370(9);799-808 PMID:24571752 | N Engl J Med. (http://www.nejm.org/doi/full/10.1056/NEJMoa1311037)

Older News Articles

Objectives

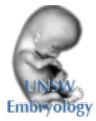
Applied Embryology: birth statistics, unintended pregnancies, ART, abnormalities statistics, timeline of development, trophoblastic disease, embryonic development, placenta, fetal development, maternal diet, multiple pregnancies.

Teratology: definitions, critical periods, medications, chromosomal abnormalities, environmental factors and infections.



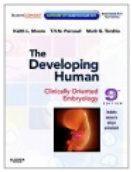
Human Embryonic Development (week 1 to 8)

Textbooks



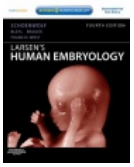
Hill, M.A. (2014). *UNSW Embryology* (14th ed.) Retrieved March 11, 2014, from http://php.med.unsw.edu.au/embryology

Diagnosis Links: Prenatal Diagnosis | Pregnancy Test | Amniocentesis | Chorionic villus sampling | Ultrasound | Alpha-Fetoprotein | Pregnancy-associated plasma protein-A | Fetal Blood Sampling | Magnetic Resonance Imaging | Computed Tomography | Preimplantation Genetic Screening | Comparative Genomic Hybridization | Genome Sequencing | Neonatal Diagnosis | Category:Prenatal Diagnosis | Fetal Surgery | Classification of Diseases | Category:Neonatal Diagnosis
Neonatal Diagnosis: APGAR test | Guthrie test | Hearing test | Electrocardiogram (ECG/EKG) | X-ray | Tandem mass spectrometry | Classification of Diseases
Abnormality Links: Introduction | Genetic | Environmental | Unknown | Teratogens | Cardiovascular | Coelomic Cavity | Endocrine | Gastrointestinal Tract | Genital | Head | Integumentary | Musculoskeletal | Limb | Neural | Neural Crest | Renal | Respiratory | Placenta | Sensory | Twinning | Developmental Origins of Health and Disease | ICD-10



Citation: The Developing Human: clinically oriented embryology 9th ed. Keith L. Moore, T.V.N. Persaud, Mark G. Torchia. Philadelphia, PA: Saunders, 2011. (chapter links only work with a UNSW connection)

- Chapter 20 – Human Birth Defects (http://er.library.unsw.edu.au/er/cgi-bin/eraccess.cgi?url=http://www.mdconsult.com/books/page.do?eid=4-u1.0-B978-1-4377-2002-0..00020-5&isbn=978-1-4377-2002-0&uniqId=330028653-2#4-u1.0-B978-1-4377-2002-0..00020-5)
- Appendix : Discussion of Clinically Oriented Problems (http://er.library.unsw.edu.au/er/cgi-bin/eraccess.cgi?url=http://www.mdconsult.com/books/page.do?eid=4-u1.0-B978-1-4377-2002-0..00030-8&isbn=978-1-4377-2002-0&uniqId=330028653-2#4-u1.0-B978-1-4377-2002-0..00030-8)



Citation: Larsen's human embryology 4th ed. Schoenwolf, Gary C; Larsen, William J, (William James). Philadelphia, PA : Elsevier/Churchill Livingstone, c2009. (chapter links only work with a UNSW connection)

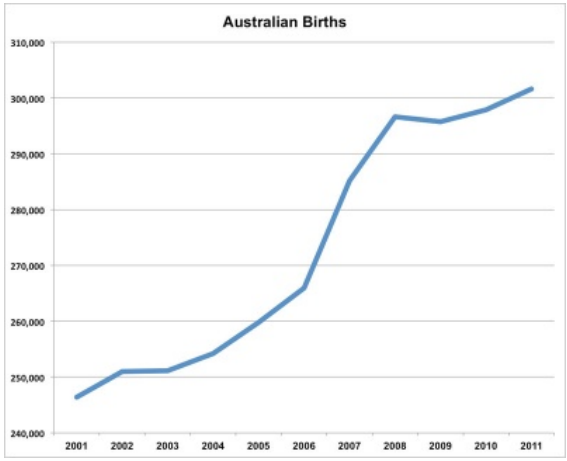
- Chapter 6 - Fetal Development and the Fetus as Patient (http://er.library.unsw.edu.au/er/cgi-bin/eraccess.cgi?url=http://www.mdconsult.com/books/linkTo?type=bookPage&isbn=978-0-443-06811-9&eid=4-u1.0-B978-0-443-06811-9..10006-5)

Applied Embryology

--Mark Hill (talk) 17:55, 16 February 2014 (EST) Notes are currently being updated for 2011 edition.

This recent data summarised below from Australia's mothers and babies 2011[1], 2009[2], 2008[3] and 2007[4]. This data should help you as a clinician and researcher to understand the current trends in reproductive medicine within Australia. Also see recent general population data in Australian Statistics.

- **2011** - 301,810 live births and 2,220 fetal deaths
- **2009** - 296,791 live births and 2,341 fetal deaths
- **2008** - 294,737 live births and 2,188 fetal deaths
- **2007** - 292,027 live births and 2,177 fetal deaths



Australia's mothers and babies (2011) cover

[show] Mothers

[show] Babies

[show] 2013 National core maternity indicators

Unintended Pregnancy

Approximately one-half of pregnancies in the United States (2001) were unintended (Finer 2006, Perspectives on Sexual and Reproductive Health).

An earlier 1995 USA National Survey of Family Growth (NSFG) found:

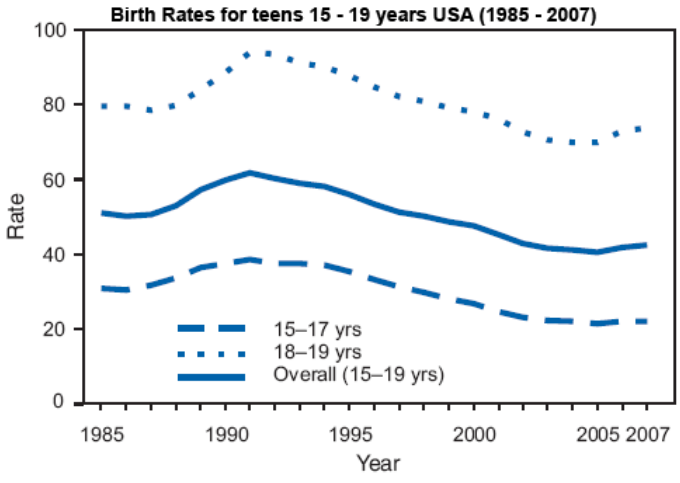
- 49% of pregnancies in the USA (excluding miscarriages)
- 31% of pregnancies resulting in a live birth are unintended

Unintended pregnancy is either mistimed (woman wanted to be pregnant later) or unwanted (did not want to ever be pregnant).

[show] Teen Pregnancy

Self-Directed Learning 2

Links: CDC Unintended Pregnancy Prevention (http://www.cdc.gov/reproductivehealth/UnintendedPregnancy/index.htm) | Pregnancy Risk Assessment Monitoring System USA (http://www.cdc.gov/prams/) | The Measurement and Meaning of Unintended Pregnancy (http://www.guttmacher.org/pubs/journals/3509403.html)



Teen pregnancy (USA)

Assisted Reproduction Technology

Assisted Reproduction Technology (ART) is also sometimes also used to identify In vitro fertilization (IVF) but now includes many new techniques.

Assisted reproductive technology in Australia and New Zealand 2010[8] 26 Oct 2012 (http://www.aihw.gov.au/publication-detail/?id=10737423259)

2010 ART treatment cycles

- 61,774 assisted reproductive technology (ART) treatment cycles performed in Australia and New Zealand.
- 23.9% resulted in a clinical pregnancy
- 18.1% in a live delivery (the birth of at least one liveborn baby).
- 12,056 liveborn babies following ART treatments in 2010.

Assisted reproductive technology in Australia and New Zealand 2010

Trends in ART procedures

- In the last 5 years there has been a shift from day 2-3 embryo (cleavage stage) transfers to day 5-6 embryo (blastocyst) transfers.
- The proportion of blastocyst transfers has increased from 27.1% in 2006 to 52.1% in 2010.
- Increase in the transfer of vitrified (ultra-rapid frozen) embryos. Compared with 2009, the proportion has more than doubled from 18.3% to 38.2%.
- reduction in the rate of multiple birth deliveries, with a decrease from 12% in 2006 to 7.9% in 2010.
- shifting to single embryo transfer, the proportion of which increased from 56.9% in 2006 to almost 70% in 2009 and 2010.
- decrease in the multiple delivery rate was achieved while clinical pregnancy rates remained stable at about 23% per cycle.

[show] 2009 Data

Links: Assisted Reproductive Technology | In Vitro Fertilization

Self-Directed Learning 3

Early Development Issues

Abnormal Implantation

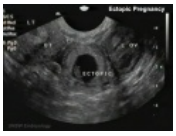
Ectopic Implantation (Pregnancy)

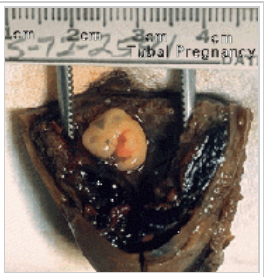
Abnormal implantation sites or Ectopic Pregnancy occurs if implantation is in uterine tube or outside the uterus.

- sites - external surface of uterus, ovary, bowel, gastrointestinal tract, mesentry, peritoneal wall
- If not spontaneous then, embryo has to be removed surgically

Tubal pregnancy - 94% of ectopic pregnancies

- if uterine epithelium is damaged (scarring, pelvic inflammatory disease)
- if zona pellucida is lost too early, allows premature tubal implantation
- embryo may develop through early stages, can erode through the uterine horn and reattach within the peritoneal cavity


Ectopic Pregnancy
Page | Play



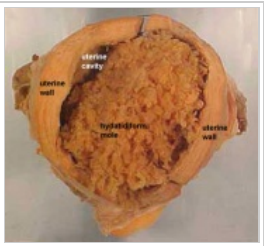
Ectopic tubal pregnancy

This is also the most common cause of pregnancy-related deaths in the first trimester. A United Kingdom enquiry into maternal deaths[10], identified ectopic pregnancy as the fourth most common cause of maternal death (73% of early pregnancy deaths).

Hydatidiform Mole

Another type of abnormality is when only the conceptus trophoblast layers proliferates and not the embryoblast, no embryo develops, this is called a "hydatidiform mole", which is due to the continuing presence of the trophoblastic layer, this abnormal conceptus can also implant in the uterus. The trophoblast cells will secrete human chorionic gonadotropin (hCG), as in a normal pregnancy, and may appear maternally and by pregnancy test to be "normal". Prenatal diagnosis by ultrasound analysis demonstrates the absence of a embryo.

There are several forms of hydatidiform mole: partial mole, complete mole and persistent gestational trophoblastic tumor. Many of these tumours arise from a haploid sperm fertilizing an egg without a female pronucleus (the alternative form, an embryo without sperm contribution, is called parthenogenesis). The tumour has a "grape-like" placental appearance without enclosed embryo formation. Following a first molar pregnancy, there is approximately a 1% risk of a second molar pregnancy.



Hydatidiform Mole

This topic is also covered in Placenta - Abnormalities

Twinning

- **Twin deliveries and place of birth in NSW 2001-2005**[11] "Both infant and maternal morbidity increase from 39 weeks gestation. Delivery of twins before 36 weeks at smaller hospitals (< 500 deliveries per annum) should be avoided. A twin pregnancy where there is a greater or equal to 20% difference in estimated fetal weights should be considered for referral to a tertiary obstetric unit."

Dizygotic Twinning

Dizygotic twins (fraternal, non-identical) arise from separate fertilization events involving two separate oocyte (egg, ova) and spermatozoa (sperm). Dizygotic twinning can be increased by Assisted Reproductive Technologies (ART) that use double embryo transfer techniques.

Monoygotic Twinning

Monoygotic twins (identical) produced from a single fertilization event (one fertilised egg and a single spermatazoa, form a single zygote), these twins therefore share the same genetic makeup. Occurs in approximately 3-5 per 1000 pregnancies, more commonly with aged mothers. The later the twinning event, the less common are initially separate placental membranes and finally resulting in conjoined twins.

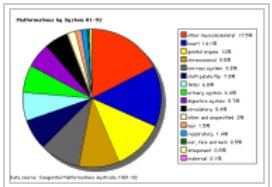
Week		Week 1							Week 2						
Day	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Cell Number	1	1	2	16	32	128				bilaminar					
Event	Ovulation	fertilization	First cell division	Morula	Early blastocyst	Late blastocyst Hatching	Implantation starts			X inactivation					
															
Monoygotic		Diamniotic			Diamniotic			Monoamniotic							
Twin Type		Dichorionic			Monochorionic			Monochorionic			Conjoined				

Table based upon recent Twinning Review.[12]

Links: Twinning

Self-Directed Learning 4

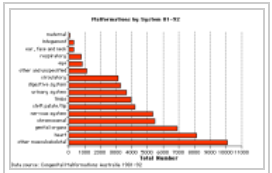
Abnormal Development


Australian abnormalities by System

Embryological development is a robust biological system able to cope with many stresses without long-term consequences. When development does go wrong there are generally 3 major types groups: **Genetic** (inherited), **Environmental** (maternal) derived and **Unknown** (not determined or known) abnormalities. Also often not considered, is that pregnancy itself can also expose abnormalities in the mother (congenital heart disease, diabetes, reproductive disorders) that until the pregnancy had gone undetected.

Genetic abnormalities in medicine are still mainly about determining a family history and good prenatal/neonatal diagnosis. Realise that there exists in all of us genetic variations and some variations which eventually expand be expressed as a genetic disorder (CAG expansions).

[show] Abnormality Links


Australian abnormalities by System

Prenatal diagnosis are the clinical tools used to determine both normal and abnormal development. There are a growing number of new diagnostic techniques that are being applied to human embryonic development.

[show] Prenatal Diagnosis Links

While genetic abnormalities will have well-defined impacts upon development, environmentally derived effects can be harder to define and often variable depending on many different factors (timing, exposure level, and the combination effects with other factors). This combination effect can also be seen between genetic and environmental interacting to give an even broader spectrum of both major and minor abnormalities.

[show] Environmental Links

International Classification of Diseases

The International Classification of Diseases (ICD) World Health Organization's classification used worldwide as the standard diagnostic tool for epidemiology, health management and clinical purposes. This includes the analysis of the general health situation of population groups. It is used to monitor the incidence and prevalence of diseases and other health problems. Within this classification "congenital malformations, deformations and chromosomal abnormalities" are (Q00-Q99) but excludes "inborn errors of metabolism" (E70-E90).

ICD Links: XVII Congenital Malformations | XVI Perinatal Period | Chapter XV Pregnancy Childbirth | Abnormal Development | Reports

Australian Birth Anomalies System

"*The national collation and reporting of birth anomalies data has been suspended in recent years due to concerns about data quality and comparability.*"

- Variability among states and territories in scope of birth anomalies data collections: sources of birth anomalies notifications and definitions and classifications used; method of data collection and available resources.
- Variability among the states and territories in the timing and method of the provision of birth anomalies data to the AIHW National Perinatal Statistics Unit (NPSU) for national collation and reporting.
- New **Australian Birth Anomalies System** should be data for birth anomalies detected up to 1 year of age
  - including data on terminations of pregnancies with birth anomalies and regardless of gestational age (i.e. including less than 20 weeks gestation)
- System will initially be based on data from the states able to detect birth anomalies at least up to 1 year of age (NSW, VIC, WA and SA), further extending the period of detection in the future.
- Congenital anomalies are coded using the British Paediatric Association Classification of Diseases (ICD-9-BPA), based on the International Classification of Diseases, 9th Revision (ICD-9).

The Australian Congenital Anomalies Monitoring System (ACAMS) supersedes the National Congenital Malformations and Birth Defects Data Collection (NCM&BD).

Links: Australian Congenital Anomalies Monitoring System (http://www.npsu.unsw.edu.au/PRERUWeb.nsf/page/CADC) | Congenital Anomalies in Australia 2002-2003 (http://www.preru.unsw.edu.au/PRERUWeb.nsf/page/ba3)

NSW Data

Congenital Conditions Register

Scheduled congenital conditions (section 2) detected during pregnancy or in infants up to one year of age in NSW are required to be reported under the NSW Public Health Act 1991.

Scheduled congenital conditions include:

1. All structural malformations. Examples include spina bifida, microcephaly, transposition of the great vessels, ventricular septal defects, pulmonary agenesis, polycystic lungs, duodenal atresia, exomphalos, hypospadias, cleft lip/palate, microphthalmia, limb reductions, polydactyly, birthmarks greater than 4 cms diameter, cystic hygroma and multisystem syndromes including at least one structural malformation.
2. Chromosomal abnormalities. Examples include Down syndrome and unbalanced translocations.
3. Four medical conditions: cystic fibrosis, phenylketonuria, congenital hypothyroidism and thalassaemia major.

Congenital conditions that are not notifiable include:

1. Minor anomalies occurring in isolation (Examples of minor anomalies include skin tags, deviated nasal septum, tongue tie, benign heart murmurs, clicky non-dislocating hips, sacral dimples, positional talipes, abnormal palmar creases, dysmorphic features).
2. Birth injuries.
3. Congenital infections which do not result in a structural malformation.
4. Tumours and cysts.
5. Conditions arising from prematurity or asphyxiation.

Links: NSW Health - Congenital Conditions Register - Reporting Requirements 2012 (http://www0.health.nsw.gov.au/policies/pd/2012/PD2012_055.html) | PDF (http://www0.health.nsw.gov.au/policies/pd/2012/pdf/PD2012_055.pdf)

Mothers and Babies Report 2010

- preterm birth (less than 37 weeks gestation) was 7.4%.
- rate of low birth weight (less than 2,500 grams) was 6.1%
  - in Aboriginal or Torres Strait Islander babies was 11.2%.
- About 2% of infants are born with congenital conditions each year in NSW.
- In 2004–2010, anomalies of the **cardiovascular** system were most commonly reported, followed by anomalies of the **musculoskeletal** system and the **genito-urinary** system.
- Congenital conditions were more common among premature infants compared to full term infants, and among male infants compared to female infants.
- rate of congenital conditions increases with increasing maternal age, especially after age 35.
  - However, as most babies are born to mothers aged less than 35 years, the majority of babies with congenital conditions were born to younger mothers.
- perinatal deaths 755, 134 (17.7%) of these deaths were unexplained stillbirths.
- neonatal death was extreme prematurity (41.3%), followed by congenital abnormalities (21.5%).

Data<refCentre for Epidemiology and Evidence. New South Wales Mothers and Babies 2010. Sydney: NSW Ministry of Health, 2012.</ref>

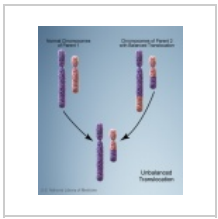
Links: New South Wales Mothers and Babies Report 2010 (http://www.health.nsw.gov.au/publications/Pages/mothers-and-babies-2010.aspx)

[show] Victoria - 10 most reported birth anomalies

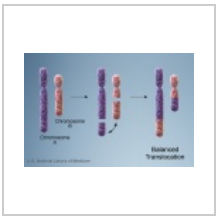
[show] USA Statistics

[show] European Statistics

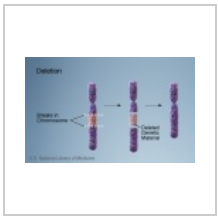
Genetic



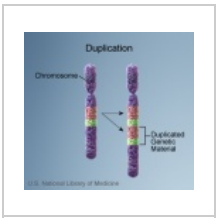
Chromosome - unbalanced translocation



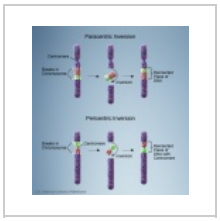
Chromosome - balanced translocation



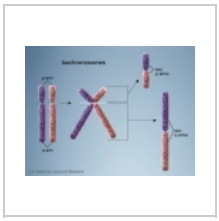
Chromosome - deletion



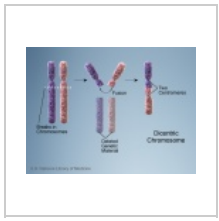
Chromosome - duplication



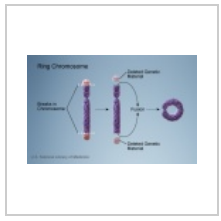
Chromosome - inversion



Chromosome - isochromosomes



Chromosome dicentric



Chromosome - ring chromosome

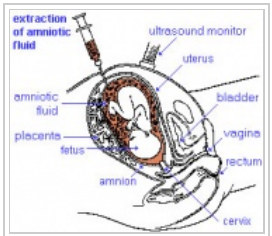
Links: Abnormal Development - Genetic

Self-Directed Learning 5

Teratology

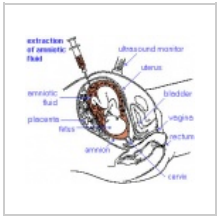
Prenatal Screening

How and why do things go wrong in development?

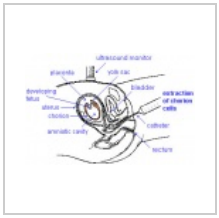


Amniocentesis

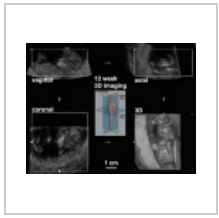
These notes cover abnormalities that can occur during development often described as congenital defects or birth defects. There are many different ways that developmental abnormalities can occur the 3 major types are **Genetic** (inherited), **Environmental** (maternal) and **Unknown** (not determined) derived abnormalities. The environmental factors that cause or lead to any of these abnormalities are described as Teratogens.



Amniocentesis



Chorionic villus sampling



Ultrasound

Diagnosis Links: Prenatal Diagnosis | Pregnancy Test | Amniocentesis | Chorionic villus sampling | Ultrasound | Alpha-Fetoprotein | Pregnancy-associated plasma protein-A | Fetal Blood Sampling | Magnetic Resonance Imaging | Computed Tomography | Preimplantation Genetic Screening | Comparative Genomic Hybridization | Genome Sequencing | Neonatal Diagnosis | Category:Prenatal Diagnosis | Fetal Surgery | Classification of Diseases | Category:Neonatal Diagnosis

[show] Ultrasound

Now consider the terms used to describe the different environmental effects that can occur during pregnancy that may influence outcomes.

- **Teratogen** (Greek, *teraton* = monster) any agent that causes a structural abnormality (congenital abnormalities) following fetal exposure during pregnancy. The overall effect depends on dosage and time of exposure.
- **Absolute risk** the rate of occurrence of an abnormal phenotype among individuals exposed to the agent. (e.g. fetal alcohol syndrome)
- **Relative risk** the ratio of the rate of the condition among the exposed and the nonexposed. (e.g. smokers risk of having a low birth weight baby compared to non-smokers) A high relative risk may indicate a low absolute risk if the condition is rare.
- **Mutagen** a chemical or agent that can cause permanent damage to the deoxyribonucleic acid (DNA) in a cell. DNA damage in the human egg or sperm may lead to reduced fertility, spontaneous abortion (miscarriage), birth defects and heritable diseases.
- **Fetotoxicant** is a chemical that adversely affects the developing fetus, resulting in low birth weight, symptoms of poisoning at birth or stillbirth (fetus dies before it is born).
- **Synergism** when the combined effect of exposure to more than one chemical at one time, or to a chemical in combination with other hazards (heat, radiation, infection) results in effects of such exposure to be greater than the sum of the individual effects of each hazard by itself.
- **Toxicogenomics** the interaction between the genome, chemicals in the environment, and disease. Cells exposed to a stress, drug or toxicant respond by altering the pattern of expression of genes within their chromosomes. Based on new genetic and microarray technologies.

Teratogens

- **Infections**, collectively grouped under the acronym TORCH for Toxoplasmosis, Other organisms (parvovirus, HIV, Epstein-Barr, herpes 6 and 8, varicella, syphilis, enterovirus) , Rubella, Cytomegalovirus and Hepatitis. See also the related topics on **maternal hyperthermia** and bacterial infections. (More? Postnatal Immunisation)
- **Maternal diet** the best characterised is the role of low folic acid and Neural Tube Defects (NTDs) see also abnormal neural development and Neural Tube Defects (NTDs). More recently the focus has been on dietary iodine levels and the role they also play on neural development.
- **Maternal drugs** effects either prescription drugs (therapeutic chemicals/agents, thalidomide limb development), non-prescription drugs (smoking), and illegal drugs (Cannabis/Marijuana, Methamphetamine/Amphetamine, Cocaine, Heroin, Lysergic Acid Diethylamide)

- **Environment** (smoking, chemicals, heavy metals, radiation) and maternal endocrine function (maternal diabetes, thyroid development) and maternal stress.
- **Teratogen synergism**, different environmental effects can act individually or in combination on the same developing system. For example, neural development can be impacted upon by alcohol (fetal alcohol syndrome), viral infection (rubella) and/or inadequate dietry folate intake (neural tube defects). These effects may also not be seen as a direct effect on a system or systems but result in a reduced birth weight and the potential postnatal developmental effects. Consider also this in relation to the increasing support to the **fetal origins hypothesis**.

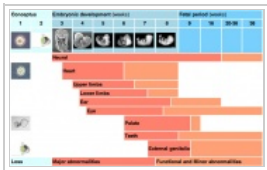
Links:

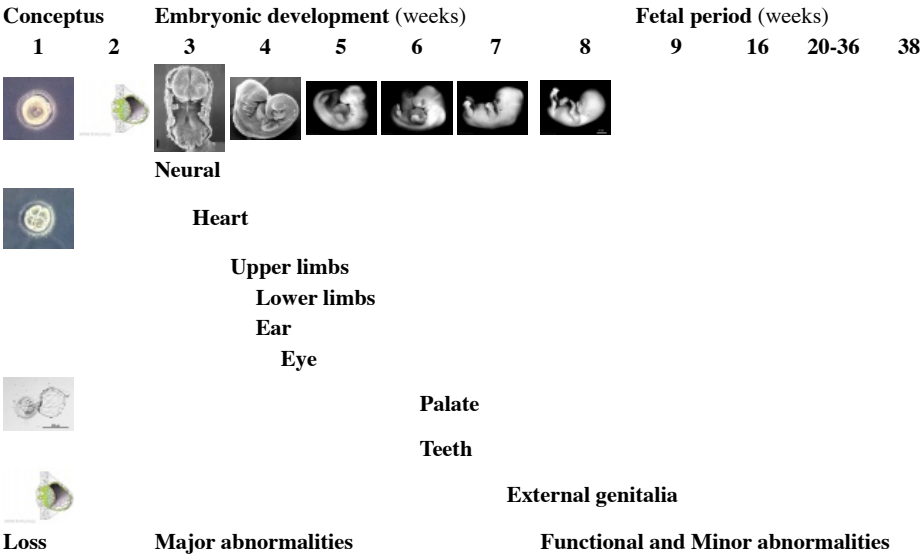
Abnormality Links: Introduction | Genetic | Environmental | Unknown | Teratogens | Cardiovascular | Coelomic Cavity | Endocrine | Gastrointestinal Tract | Genital | Head | Integumentary | Musculoskeletal | Limb | Neural | Neural Crest | Renal | Respiratory | Placenta | Sensory | Twinning | Developmental Origins of Health and Disease | ICD-10
Environmental Links: Introduction | Low Folic Acid | Iodine Deficiency | Nutrition | Drugs | Australian Drug Categories | USA Drug Categories | Thalidomide | Herbal Drugs | Illegal Drugs | Smoking | Fetal Alcohol Syndrome | TORCH Infections | Viral Infection | Bacterial Infection | Zoonotic Infection | Toxoplasmosis | Malaria | Iodine Deficiency | Maternal Diabetes | Maternal Hyperthermia | Maternal Inflammation | Biological Toxins | Chemicals | Heavy Metals | Radiation | Prenatal Diagnosis | Neonatal Diagnosis | International Classification of Diseases | Fetal Origins Hypothesis

Genetic Links: Introduction | Genetic risk maternal age | Trisomy 21 | Trisomy 18 | Trisomy X | Fragile X | Williams | Philadelphia chromosome | Prenatal Diagnosis | Neonatal Diagnosis | International Classification of Diseases | Molecular Development - Genetics

Critical Periods of Development

- Finally, when studying this topic remember the concept of critical periods of development that will affect the overall impact of the above listed factors. This can be extended to the potential differences between prenatal and postnatal effects, for example with infections and outcomes.


Human critical periods of development



Self-Directed Learning 6

Links: Embryonic Development | Timeline human development | Movie - Human Development annotated cartoon | Human - critical periods

Australian Drug Categories

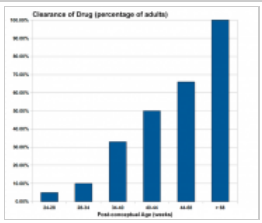
Legal drugs are classified, usually by each country's appropriate regulatory body, on the safety of drugs during pregnancy. In Australia, the Therapeutic Goods Authority has classes (A, B1, B2, B3, C, D and X) to define their safety. In the USA, drugs are classified by the Food and Drug Administration (FDA) into classes (A, B, C, D, and X) to define their safety. (More? Australian Drug Categories)

- **Pregnancy Category A** - Have been taken by a large number of pregnant women and women of childbearing age without an increase in the frequency of malformations or other direct or indirect harmful effects on the fetus having been observed.
- **Pregnancy Category B1** - Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed. Studies in animals have not shown evidence of an increased occurrence of fetal damage.
- **Pregnancy Category B2** - Have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed. Studies in animals are inadequate or may be lacking, but available data show no evidence of an increased occurrence of fetal damage.
- **Pregnancy Category B3** - Have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed. Studies in animals have shown evidence of an increased occurrence of fetal damage, the significance of which is considered uncertain in humans.
- **Pregnancy Category C** - Have caused or may be suspected of causing, harmful effects on the human fetus or neonate without causing malformations. These effects may be reversible.
- **Pregnancy Category D** - Have caused, are suspected to have caused or may be expected to cause, an increased incidence of human fetal malformations or irreversible damage. These drugs may also have adverse pharmacological effects.
- **Pregnancy Category X** - Have such a high risk of causing permanent damage to the fetus that they should NOT be used in pregnancy or when there is a possibility of pregnancy.

Infant Drug Clearance

The drug clearance data below are only approximate calculated rates for the fetus and infant from NZ Drug Safety in Lactation (http://www.medsafe.govt.nz/Profs/PUarticles/lactation.htm#Infants)

Post-conceptual Age (weeks)	**Clearance of Drug** (percentage of adults)
24-28	5%
28-34	10%
34-40	33%
40-44	50%
44-68	66%
> 68	100%



Drug clearance rates

Links: Abnormal Development - Drugs | Australian Fetal Risk Categories | USA FDA Fetal Risk Categories | Therapeutic Goods Authority (http://www.tga.gov.au/) | Australian Drug Evaluation Committee (ADEC) (http://www.tga.gov.au/docs/html/adec/adec.htm) | TGA - Medicines Pregnancy Database (http://www.tga.gov.au/hp/medicines-pregnancy.htm) | Appendix A: Therapeutic goods exempted from pregnancy classification (http://www.tga.gov.au/docs/html/mip/exempt.htm) | NSW Poisons Information Centre (http://www.chw.edu.au/poisons)

Self-Directed Learning 7

References

1. ↑ Li Z, Zeki R, Hilder L & Sullivan EA 2013. **Australia's mothers and babies 2011**. Perinatal statistics series no. 28. Cat. no. PER 59. Canberra: AIHW.
2. ↑ Li Z, McNally L, Hilder L & Sullivan EA 2011. **Australia's mothers and babies 2009** AIHW Perinatal statistics series no. 25 (http://www.aihw.gov.au/publication-detail/?id=10737420870) Cat. no. PER 52. Sydney: AIHW National Perinatal Epidemiology and Statistics Unit.
3. ↑ Laws P & Sullivan EA 2010 **Australia's mothers and babies 2008** AIHW Perinatal statistics series no. 24 (http://www.aihw.gov.au/publications/index.cfm/title/11813) Cat. no. PER 48. Sydney: AIHW National Perinatal Statistics Unit.
4. ↑ Laws P & Sullivan EA 2009. **Australia's mothers and babies 2007** AIHW Perinatal statistics series no. 23 (http://www.aihw.gov.au/publications/index.cfm/title/10972) Cat. no. PER 48. Sydney: AIHW National Perinatal Statistics Unit.
5. ↑ Daniel F MacKay, Gordon C S Smith, Richard Dobbie, Jill P Pell **Gestational age at delivery and special educational need: retrospective cohort study of 407,503 schoolchildren.** PLoS Med.: 2010, 7(6);e1000289 PMID:20543995 | PLoS Medicine (http://www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.1000289)
6. ↑ AIHW National Perinatal Epidemiology and Statistics Unit and AIHW 2013. National core maternity indicators. Cat. no. PER 58. (http://www.aihw.gov.au/publication-detail/?id=60129542685) Canberra: AIHW.
7. ↑ Nathalie Fleming, Natalia Ng, Christine Osborne, Shawna Biederman, Abdool Shafaaz Yasseen, Jessica Dy, Ruth Rennicks White, Mark Walker **Adolescent pregnancy outcomes in the province of ontario: a cohort study.** J Obstet Gynaecol Can: 2013, 35(3);234-45 PMID:23470111
8. ↑ AIHW, Macaldowie A, Wang YA, Chambers GM & Sullivan EA 2012. Assisted reproductive technology in Australia and New Zealand 2010. Assisted reproduction technology series. Cat. no. PER 55. Canberra: AIHW. Online Summary (http://www.aihw.gov.au/publication-detail/?id=10737423259) | PDF (http://www.aihw.gov.au/WorkArea/DownloadAsset.aspx?id=10737423255)
9. ↑ Wang YA, Macaldowie A, Hayward I, Chambers GM, & Sullivan EA 2011. **Assisted reproductive technology in Australia and New Zealand 2009.** Assisted reproduction technology series no. 15. Cat. no. PER 51. Canberra: AIHW. Online Summary (http://www.aihw.gov.au/publication-detail/?id=10737420465) | PDF (http://www.aihw.gov.au/WorkArea/DownloadAsset.aspx?id=10737420484&libID=10737420483)
10. ↑ **Confidential Enquiry into Maternal Deaths (CEMD) Why Mothers Die 2000–2002** PDF (http://www.rcpe.ac.uk/journal/issue/journal_35_4/why%20mothers%20die.pdf) PDF2 (http://www.cmqcc.org/resources/27/download)
11. ↑ Charles S Algert, Jonathan M Morris, Jennifer R Bowen, Warwick Giles, Christine L Roberts **Twin deliveries and place of birth in NSW 2001-2005.** Aust N Z J Obstet Gynaecol: 2009, 49(5);461-6 PMID:19780726
12. ↑ Judith G Hall **Twinning.** Lancet: 2003, 362(9385);735-43 PMID:12957099

Links

The following are links to relevant notes pages that cover the key embryology concepts in this tutorial. These pages and their links will provide further detailed information.

Applied Embryology

Timeline human development | Fetal Development | Birth | Apgar test | Neonatal Development | Week 2 Abnormalities - Trophoblastic Disease | Placenta Development | Neural Abnormalities | Abnormal Development - Folic Acid and Neural Tube Defects | Week 3 | Cardiovascular Abnormalities | Twinning | Blastocyst | Molecular Development

Teratology Links

Human Abnormal Development | Genetic Abnormalities | Environmental Factors | Drugs | Trisomy 21 (Down Syndrome) | Fetal Alcohol Syndrome | Viral Infection | Rubella Virus | Hyperthermia

Self-Directed Learning

Self-Directed Learning 1 - Australian Statistics

Once you have thought about the Australian statistics, now look at the latest report summary Australia's mothers and babies 2010 and Australian Statistics.

- What are the current trends in Australia?
- What factors may be contributing to these changes?
- Are there any long-term trends in birth statistics?

- What does this mean for future health care provision?

Self-Directed Learning 2 - Pregnancy

- What indications would prompt a woman to take a pregnancy test?
- What test are available and where is test information provided?
- How much do these tests cost?
- When does a doctor become involved and what issues should be discussed?

Self-Directed Learning 3 - Assisted Reproductive Technologies

- Why is this more than "in vitro fertilization"?
- How many different Assisted Reproductive Technologies are available in Australia?
- How has the change from DET to SET impacted on reproductive outcomes?
- What other clinical issues should be considered when discussing ART?
- What preimplantation genetic tests are currently available?

Self-Directed Learning 4 - The First Few Weeks

- After fertilization, when does initial implantation occur?
- Which hormone maintains the initial pregnacy, where is it from and how does it act?
- How would an ectopic pregnancy differ at this stage?
- What additional maternal issues should be considered for multiple pregnancies?

Self-Directed Learning 5 - Abnormal Development

- What are the 3 major forms of abnormal development?
- What are the main chromosomal abnormalities and how do they occur?
- How are congenital abnormalities reported and classified within Australia?

Self-Directed Learning 6 - Prenatal Diagnosis

- What maternal lifestyle issues should be considered for a pregnancy?
- What diagnostic techniques are currently available and in development?
- What can ultrasound normally identify?

Self-Directed Learning 7 - Medications in Pregnancy

- How does drug classification differ between countries?
- Do european and asian countries apply the same drug classification system(s)?
- How are teratogens identified?
- Why does fetal drug clearance differ from maternal clearance?

External Links

External Links Notice *- The dynamic nature of the internet may mean that some of these listed links may no longer function. If the link no longer works search the web with the link text or name.*

- **Department of Health and Ageing** The National Maternity Services Plan 2010 (http://www.health.gov.au/internet/main/publishing.nsf/Content/maternityservicesplan) | National Maternity Services Plan: 2010 -2011 Annual Report (http://www.health.gov.au/internet/main/publishing.nsf/Content/349C976EEDDB5EB0CA257862001B3657/$File/NMSP%202011%20Annual%20Report.pdf)

- **Australia** AIHW National Perinatal Statistics Unit (http://www.preru.unsw.edu.au/PRERUWeb.nsf/page/AIHW+National+Perinatal+Epidemiology+and+Statistics+Unit) | Victorian Birth Defects Register (VBDR) (http://www.health.vic.gov.au/perinatal/vbdr/index.htm) | Victorian Birth Defects Register brochure (http://www.health.vic.gov.au/perinatal/downloads/vbdr_brochure.pdf)

- **National Perinatal Statistics Unit** Congenital Anomalies Neural tube defects in Australia - An epidemiological report (http://www.preru.unsw.edu.au/PRERUWeb.nsf/page/NeuralTubeDefects) | Congenital Anomalies in Australia 2002-2003 (http://www.preru.unsw.edu.au/PRERUWeb.nsf/page/ba3) | Congenital Anomalies in Australia 1998-2001 (http://www.preru.unsw.edu.au/PRERUWeb.nsf/page/ba2) | Congenital Malformations Australia 1981-1997 (http://www.preru.unsw.edu.au/PRERUWeb.nsf/page/ca4) | Congenital Malformations Australia 1995 and 1996

(http://www.preru.unsw.edu.au/PRERUWeb.nsf/page/ca3) | Congenital Malformations Australia 1993 and 1994 (http://www.preru.unsw.edu.au/PRERUWeb.nsf/page/ca2) | Congenital Malformations Australia 1981-1992 (http://www.preru.unsw.edu.au/PRERUWeb.nsf/page/ca1)

- **Neonatal Networks**
  - **Australian & New Zealand Neonatal Network** (ANZNN) Neonatal Intensive Care Units (http://www.preru.unsw.edu.au/PRERUWeb.nsf/page/ParticipatingUnit)
  - **Canada** Canadian Neonatal Network (http://www.canadianneonatalnetwork.org/portal)
  - **European Neonatal Network** EuroNeoNet (http://www.euroneostat.org/paginas/publicas/euroneo/euroNeoNet/index.html)
  - **USA and Other International** Vermont Oxford Network (http://www.vtoxford.org/)

- **Therapeutic Goods Authority** TGA (http://www.tga.gov.au/) | Australian Drug Evaluation Committee (ADEC) (http://www.tga.gov.au/docs/html/adec/adec.htm) | Prescribing Medicines in Pregnancy (http://www.tga.gov.au/docs/html/medpreg.htm) | Appendix A: Therapeutic goods exempted from pregnancy classification (http://www.tga.gov.au/docs/html/mip/exempt.htm)

- **NSW Poisons Information Centre** Poisons Information Centre (http://www.chw.edu.au/poisons)

- **USA** Food and Drug Administration Evaluating the Risks of Drug Exposure in Human Pregnancies (http://www.fda.gov/cber/gdlns/rvrpreg.htm) | Centers for Disease Control and Prevention (CDC, USA) Pregnancy Risk Assessment Monitoring System (PRAMS) (http://www.cdc.gov/prams/) collects state-specific, population-based data on maternal attitudes and experiences before, during, and shortly after pregnancy.
- **Other** Motherisk (Canada) Drugs, chemicals, radiation and herbal products in pregnancy (http://www.motherisk.org/women/drugs.jsp) | International Society for the Study of Trophoblastic Diseases Trophoblastic Diseases (http://www.isstd.org/intro/index.html)

Glossary Links

A | B | C | D | E | F | G | H | I | J | K | L | M | N | O | P | Q | R | S | T | U | V | W | X | Y | Z | Numbers | Symbols

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