MODULE 1 – INTRODUCTION AND CAUSES OF DISEASE

OBJECTIVES:

This module gives you some fundamental definitions of disease and related terminology and the framework in which to classify disease. At completion of the module you should be able to:

1. define pathology.
2. define disease.
3. define sign(s) and symptom(s) and distinguish between them.
4. understand and be able to define some of the commonly used terms to describe various aspects of disease (e.g. etiology, pathogenesis, manifestations, sequelae, prognosis).
5. define morbidity and mortality and distinguish between them.
6. have a general understanding of the leading causes of morbidity and mortality in Canadians.
7. define idiopathic and iatrogenic causes of disease and give an example of each.
8. distinguish between congenital and genetic diseases and be able to give examples of each.
9. define teratogen and examples and their consequences (i.e., infectious agents, drugs & chemicals, maternal disorders, radiation).
10. discuss broadly the causes of disease and the categories under which they can be considered (i.e. genetic versus environmental; or by pathogenesis, e.g. injury, inflammation, infection, immune disorder, neoplastic, vascular, etc.).

There is no assigned reading from the text for this section.

THE DEFINITION AND CAUSES OF DISEASE - KEY TERMS

congenital - present at birth.
chromosomal abnormalities - a change in the normal number of chromosomes (normally 22 pairs plus sex chromosomes (either XX or XY)) or in their normal structure.
disease - very simply, a change in normal body function/structure that leads to abnormal function (e.g. resulting from a direct insult, such as trauma or infection, or an indirect insult, such as a disturbance in metabolism).
etiology - the study of the cause(s) of disease.
genetic - a heritable disorder.
iatrogenic - disease caused as the result of a medical treatment.
idiopathic - of unknown origin; used when we don't know the cause of disease.
morbidity - the impairment of health by illness.
mortality - causing the death of the patient.
pathogenesis - the stages through which a disease progresses; the production and development or mechanism of disease.
pathology - the study of disease and disease processes (their causes, typical characteristics and effects).
prognosis - the most likely course and outcome of disease.
sign - an objective measure found upon physical examination (e.g. body temperature, blood pressure, pulse, weight, edema).
symptom - a subjective complaint from a patient, i.e. not measurable (e.g. fatigue, nausea, pain, dizziness).
teratogen - a chemical (e.g. drug, alcohol), biological (e.g. rubella) or physical agent that causes physical defects in the embryo.

DEFINITION OF DISEASE

PATHOLOGY is the study of disease. Derived from the Greek *pathos* meaning 'disease' or 'suffering', and *logos* or *logia* meaning 'study' pathology is literally the study of suffering and illness. In particular, *pathology is the study of the structural and functional changes in cells, tissues, and organs of the body that cause, or are caused by, disease*.

Review Objective #1
Can you define "pathology"?

DEFINITION OF DISEASE:

All diseases result from some disturbance to cells as a result of physical or environmental insults or as a result of a genetic aberration (inherited or acquired). Most broadly, *disease may be defined as the pattern of response of living organisms to injury. When cells fail to adapt to the injury, or the adaptive mechanism itself becomes harmful, disease results.* Thus, disease is any deviation from, or interruption of, the normal structure or function of a tissue, organ or system.

Review Objective #2
Can you define "disease"?

In practical terms we identify disease by the appearance of **physical signs** - those signs that can be objectively observed by a physician or nurse, e.g. fever, a swollen ankle, an abnormal heart beat or the alteration of some physiological, biochemical or morphological parameter, and **clinical symptoms** - subjective complaints described by the patient, e.g. pain, dizziness, nausea. In most cases though, these changes appear late in the disease process, long after a disease is present and has been acting at the cellular level.

Review Objective #3
What is the difference between 'signs' of disease versus 'symptoms' of disease? Can you give examples of each?

We can understand and describe disease by looking at a number of factors:

- **Etiology:** the study of the cause of a disease (e.g. biological agents, chemical agents or physical forces).
- **Pathogenesis:** the development of a given disease; the mechanism of disease; the sequence of cellular events that take place from time of initial contact with the etiologic agent until the expression of disease.
- **Pathological and morphological manifestations:** the changes in structure and function of tissues, organs and systems. Morphological changes are described as both gross anatomic changes and microscopic changes that are characteristic of disease.
- **Complications and sequelae:** the secondary consequences of a disease.
- **Prognosis:** the anticipated course of the disease and final outcome (i.e. cure, remission, morbidity & mortality).
- **Epidemiology:** Within populations we can look for patterns of disease or study risk factors that predispose to disease. The incidence represents the number of new cases arising in a population over a given time period and the prevalence is the total number of cases of the disease in a given population.

Review Objective #4
Make sure you can define these different terms used to describe disease.

Diseases have an impact on people in two ways.

- **Morbidity**: sickness or illness; the impairment of the well-being or normal functioning of a patient.
- **Mortality**: causing the death of a patient.

*We will go on to look at the leading causes of illness/morbidity and death/mortality in Canadians in the next section. This information has been taken from the **Statistics Canada** web site or the **Health Canada** (Public Health Agency of Canada) web site. These sites contain additional information about morbidity and mortality by gender, by age or by geography. See if you can find:*

- *What is the leading cause of death in Canadian men? in Canadian women?*
- *What is the leading cause of death in your age group?*
- *Which is the 'healthiest' province to live in? the least healthy? (i.e. compare death rates per province).*

Note that rates can be expressed as 'crude rates' or the actual number of people who die of a given disease or as 'age-standardized rates' which takes into account age-related mortality as well as actual numbers of Canadians (i.e. the rate is expressed per 100,000 persons). There are some slight differences when expressing data in each format.

MORBIDITY AND MORTALITY OF CANADIANS

Every episode of hospital care is captured, recorded and coded for the collection of statistics on the health of Canadians and to assist in planning and managing health resources. These statistics are gathered yearly by CIHI (the Canadian Institute for Health Information), Statistics Canada, and Health Canada and provide a snapshot of those diseases that are causing deaths in the population and the major reasons for hospitalization or morbidity.

To give you an idea of which diseases/disorders are of greatest importance (and of interest to pathologists and health care professionals!) I have given you a summary of some of the available statistics from Statistics Canada. If you haven't already had a chance to look at this site have a look at the statistics for **"Leading Causes of Death in Canada**" and **"Leading Causes of hospitalizations in Canada**" which records mortality and morbidity according to age and in YOUR age group determine what are the most frequent causes of morbidity and mortality.

LIFE EXPECTANCY - WOMEN LIVE LONGER

Life expectancy has steadily increased for Canadians since the turn of the last century and females have consistently enjoyed an advantage over male. Life expectancy at birth reached 79.3 years for males and 83.6 years for females in Canada during the 2009/2011 period. Over the last decade, the life expectancy of Canadian males increased on average by 3.6 months every year, while gains for females were lower, at 2.4 months per year. As a result, the gap between the life expectancy at birth between males and females decreased from its peak of 7.4 years reached at the end of the 1970s to 4.3 years in 2009/2011. Improvements in sanitation, medical care and in surgical and drug-related treatments have led to a steady fall in mortality, in recent years from heart and cerebrovascular disease and some forms of cancer.

Mortality rates from all causes have continued to decline during the latter half of the 20th century, most notably for heart and cerebrovascular disease, but also for causes such as death due to injuries or poisoning. Unfortunately this has been offset by a rise in respiratory tract cancers (e.g. lung cancer) and chronic lower respiratory diseases caused overwhelmingly by tobacco smoking.

Up until the 1990s the highest rates of lung cancer deaths were seen in males, but now yearly lung cancer deaths in women exceed the number of deaths due to breast cancer.

The number of deaths rose in Canada in both 2010 and 2011, following a slight decrease between 2008 and 2009. The total number of deaths reached 240,075 in 2010 and 242,074 in 2011, compared with 238,418 in 2009. The number of deaths in 2011 was the highest recorded since the introduction of the Vital Statistics registration system in the 1920s. The increase in the number of deaths can be explained by two factors: *population growth*, as a larger population generates a higher number of deaths; and *population aging*, as the share of the population concentrated in older ages—when mortality is higher—is increasing.

Cancer, the leading cause of death, accounted for 72,476 deaths in 2011 or 30% of all deaths, a proportion that has remained almost unchanged since 2000 (29%). The second leading cause of death was heart disease, accounting for 20% of all deaths followed in third rank by stroke (cerebrovascular diseases) with 6%.

Ranking and number of deaths for the 10 leading causes of death by sex, Canada, 2011

Cause of death	Males			Females			Male-Female ratio[1]
	rank	number	percent	rank	number	percent	
All causes of death	**...**	**121,042**	**100.0**	**...**	**121,032**	**100.0**	**100**
Malignant neoplasms (cancer)	1	37,916	31.3	1	34,560	28.6	110
Diseases of heart (heart disease)	2	24,987	20.6	2	22,640	18.7	110
Accidents (unintentional injuries)	3	6,243	5.2	5	4,473	3.7	140
Chronic lower respiratory diseases	4	5,551	4.6	4	5,633	4.7	99
Cerebrovascular diseases (stroke)	5	5,486	4.5	3	7,797	6.4	70
Diabetes mellitus (diabetes)	6	3,825	3.2	7	3,369	2.8	114
Intentional self-harm (suicide)	7	2,781	2.3	14	947	0.8	294
Influenza and pneumonia	8	2,616	2.2	8	3,151	2.6	83
Alzheimer's disease	9	1,961	1.6	6	4,395	3.6	45
Chronic liver disease and cirrhosis	10	1,830	1.5	11	1,012	0.8	181
All other causes	...	27,846	23.0	...	33,055	27.3	84

... not applicable

Since the end of the 1970s, the leading causes of death in Canada have been cancer and cardiovascular disease (heart disease). Cerebrovascular disease, primarily stroke, is the third leading cause of death with more women than men dying every year from strokes. About 3 times as many women than men die every year from Alzheimer's disease.

An estimated 173,800 new cases of cancer and 76,200 deaths from cancer occurred in Canada in 2010. The most frequently diagnosed cancer continues to be breast cancer for women and prostate cancer for men. Although there continues to be declines in deaths in both women and men due to cancers of the breast, prostate, and colon, the leading cause of cancer death for both sexes continues to be lung cancer. Alarmingly while men's mortality rates for lung cancer have declined, the rate for women has more than doubled and has led to a narrowing in the gap of life expectancy between men and women. Cancer is primarily a disease of older Canadians: 42% of new cancer cases and 60% of cancer deaths will occur among those who are at least 70 years old. We will continue to see an increased number of new cases of cancer due to a growing and aging population.

Crushing Chest Pain

A 60 year-old male presents to the Emergency Department with a 4 hour history of acute, crushing chest pain associated with nausea and profuse sweating (**diaphoresis**).

He has a longstanding (10 years) history of atherosclerotic coronary artery disease with unstable angina and a documented heart attack 3 years previously.

LEADING CAUSES OF HOSPITALIZATION, 2008 (ALL AGES)

These statistics are gathered every year from hospitals through CIHI. The hospitalization data represent the numbers of hospitalizations for treatment of disease or injury - not the numbers of diseases and injuries requiring hospitalization or the numbers of injured or ill people admitted to hospital (that's about 2.7 million hospital visits each year). These numbers do give us an idea of which diseases/disorders cause the greatest degree of illness or morbidity in the population. Diseases of the circulatory system (i.e. heart disease and stroke) account for the largest number of hospitalizations in Canada every year with morbidity due to GI (gastrointestinal) and respiratory diseases as the second and third largest groups requiring hospitalization. You can see that many of the diseases that cause illness/morbidity during our lifetime and send us to the hospital for treatment are not responsible for cause of death, e.g. digestive system or genitourinary diseases or mental disorders.

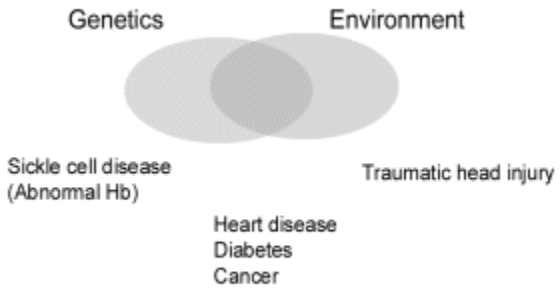
During this course we are going to consider the general mechanisms underlying disease (i.e. cell injury, inflammation, immune responses, neoplasia) and then cover many of the systems responsible for causing morbidity and mortality.

	Cause (Data from PHAC, 2008)	**Total Number**
1	Diseases of the Circulatory System	386,981
2	Diseases of the Digestive System	299,606
3	Respiratory Diseases	240,297
4	Cancer	209,586
5	Unintentional Injuries	194,268
6	Mental disorders	164,240
7	Genitourinary Diseases	162,022
8	Musculoskeletal Diseases	145,297
9	Endocrine Diseases	64,380
10	Diseases of the Nervous System	63,385

Review Objective #6
What are the leading causes of death or mortality in Canadians?
What are the leading causes of illness or morbidity in Canadians?

GENERAL CLASSIFICATION OF THE CAUSES OF DISEASE

Diseases result from a variable interaction between host (i.e. genetic) and environmental factors. Most diseases are *multifactorial* and due to an interplay between both **genetic** and **environmental** components. On one end of the spectrum we can think of diseases that are *predominantly genetic* or can be described as genetic abnormalities, e.g. sickle cell disease caused by a mutation of a single DNA base in the gene coding for hemoglobin, to the other end of the spectrum where we can think of diseases as due to *predominantly environmental* causes, e.g. physical injury or death due to a motor vehicle accident. The vast majority of diseases that cause mortality and illness in Canadians (e.g. cancer and heart disease) lie somewhere in between - a result of BOTH genetic and environmental factors.



Current knowledge of genetic causes of disease, many of which in the past were thought to be **idiopathic** (***of unknown etiology***), is exploding primarily through the use of the techniques of molecular biology and the knowledge of the human genome.

Review Objective #7
Define the term idiopathic.

Genetic alterations can vary from a single mutation in a DNA base pair (e.g. sickle cell disease) to rearrangements of whole chromosomes (e.g., trisomy 21 or Down syndrome). The number of diseases that can be attributed to an inherited genetic defect is relatively small. Far more common are sporadic mutations to DNA that occur throughout life and lead to disease in adult life (e.g., cancer).

Not all inherited diseases occur or are manifest at birth. For example, Huntington's Chorea, a fatal neurological disorder with an autosomal dominant pattern of inheritance, is not evident until adulthood. In addition not all **congenital diseases** (i.e., present at birth) are genetic. For example, the fetus is subject to numerous infections that can result in malformations or impairment of function in specific systems (e.g., rubella or German measles in mom during pregnancy can result in cataracts, microcephaly, heart defects, etc. in her newborn).

Review Objective #8
Terms: congenital versus genetic

Congenital anomalies or abnormalities are *simply structural deficits that are present at birth* - they may or may not have an underlying genetic cause. Some common causes of congenital abnormalities include:

- Malformations - result from an intrinsically abnormal development process. They may involve a single organ or body system or multiple organs and tissues.
  Examples: Congenital heart disease, polydactyly (i.e. extra digits on hands or feet), spina bifida (failure of the bony encasement of the spinal cord to close - the meninges may or may not protrude).

- Disruptions - result from a secondary destruction of an organ or body region that was normal in development, i.e. an extrinsic disturbance in morphogenesis.
  Examples: amniotic bands that may encircle, compress or attach to parts of the developing fetus; limb amputation due to an amniotic band.
- Deformations - also result from a secondary or extrinsic disturbance of the normal development process. May be due to localized or generalized compression of the growing fetus by biomechanical forces leading to a variety of structural abnormalities.
  Example: Mechanical forces (small uterus, large fetus, oligohydramnios - resulting in compression of fetus); positional abnormalities of the feet.

Teratogens

Teratogens *are environmental agents that produce abnormalities during embryonic or fetal development* and hence *congenital malformations*. These include environmental factors such as infections, exposure to drugs, and irradiation.

1. Congenital Infections:

***Examples*: Congenital Rubella (German Measles)**
Maternal rubella occurring in the first trimester will cause fetal malformations. In a child or adult, rubella is a mild disease with fever and a transient skin rash. However, with a primary infection in a pregnant woman, there is hematogenous spread across the placenta to the fetus. The fetus is not capable of producing an immune response to the viral infection. The virus replicates in fetal cells, preventing their proper division resulting in growth retardation, cataracts, deafness and congenital heart disease. The risk is highest if fetal infection occurs during the first 8 weeks.

Other common congenital infections with teratogenic effects include cytomegalovirus, varicella zoster (chicken pox).

2. Drugs and Chemicals:

***Examples*:**
Thalidomide was extensively used in some countries in the late 1950's for symptomatic relief of nausea and vomiting of early pregnancy. In 1960, there was noted an increase in the number of infants born with limb defects. Astute observations by a German physician suggested that this was due to thalidomide. Subsequent studies confirmed this relationship, including reproduction of similar effects in experimental animals. Thalidomide affects the embryo between the third and fifth weeks post-conception by interfering with proper limb growth, producing *phocomelia* ("seal limbs").

Alcohol: Excessive alcohol consumption during pregnancy causes prenatal and post-natal growth retardation, mental retardation, joint anomalies, heart defects and abnormal facies called *Fetal Alcohol Syndrome*. This is the most common cause of mental retardation in the Western world, affecting 1/300 - 1/2000 live births. There is an obvious dose-response effect but no safety line. The harmful effects of maternal alcohol ingestion are not restricted to a sensitive period of early pregnancy but extend throughout gestation.

3. Maternal Disorder:

Diabetes Mellitus: The overall risk for major congenital malformations in diabetic pregnancies is 6%. The risk can be over 20% if diabetes is not appropriately controlled during the first trimester. Mothers with insulin-dependent diabetes have the highest risk. Malformations often involve kidneys, heart and brain. The severity of malformations is related to the degree of control of maternal diabetes during the pregnancy.

4. Ionizing Radiation

Offspring of pregnant women, exposed to the atomic bomb explosions in Hiroshima and Nagasaki, had an increased incidence of microcephaly and mental retardation.

CLASSIFICATION OF DISEASES - GENETIC

Chromosomal Disorders

Chromosomal disorders form a major category of genetic disease accounting for a large proportion of congenital malformations, mental retardation, and early gestational spontaneous abortions. Abnormalities in chromosomes can present as an *abnormal number* (more or less than the normal number of 46 chromosomes) or an *abnormal structure* of chromosomes (deletions, various translocations or exchange of chromosomal material due to breakage and subsequent loss or rearrangement of chromosomes during division).

1. Numerical Abnormalities

The normal complement of chromosomes is 46 (2n). During division, if chromosomes fail to separate this will result in cells with a 2n + 1 (trisomy) or 2n - 1 (monosomy) chromosomal complement. Monosomy in autosomal chromosomes is invariably lethal, but is compatible with life if it occurs in sex chromosomes.

Autosome:

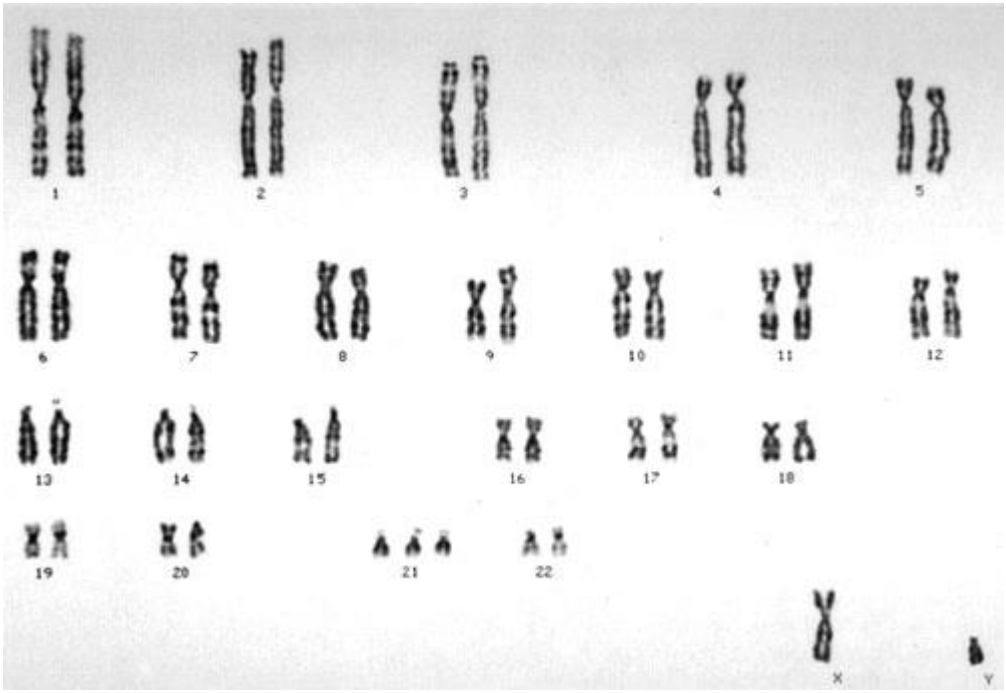
***Example*: Down Syndrome, Trisomy 21**

The chromosomal disorder affects approximately 1/800 live born infants. Malformations include abnormal facies (epicanthic folds, flat facial profile), palmar creases, congenital heart disease, duodenal stenosis or atresia, and mental retardation. There is a significant increased risk with advanced maternal age. With the maternal age 30 years, the incidence is about 1/900 whereas by 45 years the risk is 1/25.

Sex Chromosome:

***Examples*: Turner Syndrome (XO), Klinefelter Syndrome (XXY)**

Abnormal numbers of sex chromosomes produce abnormalities less severe than with abnormal numbers of autosomes. However, these individuals fail to develop normal secondary sexual characteristics, are infertile and have skeletal abnormalities.



Trisomy 21 in the **karyotype** of a male child with Down syndrome.
All other chromosomes are normal.

2. Structural Abnormalities
A number of structural abnormalities have been recognized as a result of chromosomal breakage and the resulting loss or rearrangement of genetic material during division:

- deletions - represent loss of a portion of the chromosome.
- translocations - represent the exchange or transfer of part of one chromosome to another (often these are balanced - fragments are exchanged between the two chromosomes - and the fetus is normal with a normal number of chromosomes and amount of genetic material; problems arise in their offspring).
- inversions - two breaks and reunion of an inverted portion of the chromosome.
- ring chromosome - after a deletion the remaining arms of the chromosme may unite to form a ring.

***Example*s:**
Deletion Syndrome:
Cri-du-chat Syndrome (partial deletion of the short arm of chromosome 5).
Manifestations of this syndrome include cat-like cry in infancy, small head and facial abnormalities.

Microdeletion Syndrome:
Prader-Willi Syndrome (small deletion of chromosome 15)
Affected children have short stature, obesity, small hands and feet, small penis and cryptorchidism, mental retardation.

Balanced Translocations:
The frequency of balanced translocations is about 1/500 in a normal population. If one of the couple carries a balanced translocation, they have an increased risk to have miscarriages and abnormal children with structural chromosome abnormalities.

Single Gene Disorders (Monogenic Disorders)

Mutations involving single genes generally follow one of three patterns of inheritance: autosomal dominant, autosomal recessive, or X-linked. These single gene mutations follow the Mendelian pattern of inheritance.

1. Autosomal Dominant

- Dominant trait always expressed.
- If one parent has the disease a 50% risk to children.
- Both sexes are equally affected.

Examples:

- **Marfan Syndrome**
  This is a disorder of connective tissue associated with widepsread effects in skeleton, eye and cardiovascular system. Manifestations include long limbs, dislocation of lens of eye and abnormal dilatation of aorta. The gene is on chromosome 15.
- **Familial Hypercholesterolemia**
  This is one of the most common genetic diseases and a leading cause of coronary heart disease. The basic defect is mutations in the gene encoding the low-density lipoprotein (LDL) receptor, resulting in an elevated cholesterol level in plasma and deposition of cholesterol in arteries. One of 500 persons carries the abnormal gene and may have coronary heart disease in early middle age. In homozygotes (1/1,000,000), the coronary heart disease is usually fatal in childhood. The gene is located on chromosome 19.

2. Autosomal Recessive

- Both mutated genes need to be present (homozygous) for expression of disease.
- If one altered gene present (heterozygote), parent is a carrier.
- If both parents are normal, but carriers, a 25% risk to children.
- Both sexes are equally affected.

Examples:

- **Cystic Fibrosis**
  This is the most common autosomal recessive disease in Caucasian children with an incidence of 1/1600. Carrier frequency is about 1/20. The respiratory tree mucus is abnormal, causing repeated lung infection with destruction of the lung tissue. The patients also have pancreatic insufficiency resulting in intestinal malabsorption. The gene (cystic fibrosis transmembrane conductance regulator CFTR - regulates chloride ion transport across epithelial cells) is on chromosome 7.
- **Phenylketonuria (PKU)**
  This is an example of metabolic disease resulting from a mutation in phenylalanine hydroxylase, the enzyme that converts phenylalanine to tyrosine. Accumulation of phenylalanine in body fluids damages the developing brain in early childhood and causes severe mental retardation. This disease can be diagnosed by newborn screening and treated by low-phenylalanine diet. Almost all the offspring of female PKU patients not on a low-phenylalanine diet are abnormal with mental retardation, microcephaly, growth retardation, and congenital heart disease. This is due not to their own genetic defect but to the highly *teratogenic effect* of elevated levels of phenylalanine in the mother's circulation.

3. X-Linked Recessive

- Mother carrier.
- 50% chance for sons to be affected.
- 50% chance for daughters to be carriers.
- Note: Very rare X-linked dominant disease (e.g. Vit D-resistant rickets). Disease transmitted to 50% of sons AND daughters.

Example:

- **Hemophilia A**
  Absent normal blood clotting factor with prolonged bleeding time, and bleeding into joints and muscles. This is due to deficiency of coagulation factor VIII which is encoded by a gene on sex chromosome X.

Multifactorial and Polygenic Disorders

These disorders are due to the effect of multiple genes (2 or more) and/or the interaction between the genetic factors and environmental factors.

- appear to run in families.
- do not fit any inheritance pattern of single gene disorders.
  Examples: Cleft palate, congenital heart disease, spina bifida, hypertension, diabetes mellitus.

CLASSIFICATION OF DISEASES - ENVIRONMENTAL

The environment can also predispose to disease not only depending on exposure to pollution, chemicals or occupational hazards, but also depending on lifestyle and personal habits that influence the development of disease (e.g. diet, exercise, weight control, smoking, alcohol consumption). Environmental causes can include a number of physical or chemical agents, infectious organisms, or allergenic substances (substances that induce an immune system response).

Physical Agents

- Mechanical trauma:
  - Cuts, motor-vehicle accidents, gunshots
- Temperature:
  - Burns.
  - Heat stroke: loss of temperature regulating abilities of body can result in death.
  - Frostbite: freezing of intracellular contents, results can range from blistering to gangrene.
- Electrical Burns:
  - natural (lightning) or man-made (high voltage power lines).
- Radiation:
  - cells which divide most frequently are most sensitive.
- Atmospheric Pressure:
  - increased pressure: e.g. can be experienced in diving; results in increased nitrogen being dissolved in blood. Resurfacing to a normal atmospheric pressure too rapidly will result in the formation of bubbles in the vascular system.
  - decreased pressure: e.g. high altitudes will also result in gas bubbles in the blood as well as expansion of gases in body cavities.

Chemical Agents

- Environmental (e.g. organic phosphate pesticides) or industrial exposure (e.g. asbestos).
- Poisons, toxins (biological as well as chemical toxins), pesticides, organic solvents, heavy metals, strong acids or alkalis, components in cigarette smoke.

Infections

A huge variety of infectious organisms exist, from submicroscopic viruses and bacteria to tapeworms several feet long. Although previously thought to be declining in importance as a cause of human disease they have had a recent resurgence, e.g. AIDS, TB, malaria, and SARS. The signs and symptoms of an infectious disease are the product of the inherent virulence or capacity of the organism to cause disease, the host's defence against it, and any therapy that has been given.

Drugs

Both those given for therapeutic purposes (the kind your MD gives you) and the kind you choose for yourself (alcohol, steroids, stimulants). All drugs, even the ones that are life-saving, have side effects.

Iatrogenic disease (***disease caused by medical therapy or any adverse condition occurring as the result of treatment by a physician, surgeon, or other health professional***) is now an extremely important cause of morbidity and mortality. Research into adverse events (AE) or iatrogenic disease has highlighted the need to improve patient safety. AEs are unintended injuries or complications resulting in death, disability or prolonged hospital stay that arise from health care management. The incidence of AEs among patients in Canadian acute care hospitals is estimated at 7.5% (Baker et al, CMAJ 170: 1678-86, 2004). Of the roughly 2.5 million annual hospital admissions in Canada, about 185,000 are associated with an AE and close to 70,000 of these are potentially preventable.

Review Objective #7 Define the term iatrogenic.

Allergens

A variety of exogenous and endogenous substances (mostly proteins) can trigger immune reactions (e.g. weed, tree or grass pollen, peanuts, latex).

Review Objective #10
Discuss the broad classification of disease as genetic or environmentally caused. Be able to give some examples of 'environmental' agents that can cause disease.

ALTERNATIVE CLASSIFICATION OF DISEASES

When we look at mortality rates and at what causes the majority of deaths and morbidity in Canadians (i.e. ischemic heart disease and cancers), the classification of disease as either genetic or environmental uses too broad a brush to paint a detailed portrait of disease and to assist us in understanding disease mechanisms or developing therapeutic interventions. We can turn to a *more detailed classification of disease based on the* ***pathogenesis*** *or disease process* and this will form the basis of our exploration of disease in this course.

Injury
Due a physical or a chemical or biological agent. At the cellular level, injury may be *reversible* and the cell/tissue survives or *irreversible* leading to the death of the cell.

Inflammation
The inflammatory response is common to many diseases, e.g. following cell injury by physical or chemical agents or infection, but some diseases are thought to be primarily inflammatory (e.g. tonsillitis or acute appendicitis). A chronic inflammatory response may also occur in certain allergic-type reactions (e.g. rheumatoid arthritis) and with certain viral or parasitic infections.

Infection
One of the most common forms of disease, usually producing mild to moderate symptoms. Infectious organisms (viruses, bacteria, parasites) can produce more serious illness in those whose immune systems are compromised. The extent of cellular pathology and disease depends on factors of both the attacking organism (virulence) and the host's responses.

Immunological Reactions
The immune response is normally protective, but in some circumstances the reaction may become excessive (e.g. hypersensitivity reactions to allergens - anaphylactic shock) or may act against the body's own cells (e.g. autoimmune disease - thyroiditis, myasthenia gravis) or be absent or depressed (severe combined immunodeficiency disease, immunosuppressive therapy).

Neoplasia
Autonomous proliferation of cells, usually causing tumours or masses. These can be benign (will not spread) or malignant (can spread to distant sites - metastasize). The latter are far more likely to kill the patient.

Metabolic Or Endocrine
Disorders of enzymes, hormones or secretory products (e.g. Type 2 diabetes). Some are genetic (e.g. congenital adrenal hyperplasia).

Nutritional
Deficiencies in proteins or calories due to insufficient supply (e.g. anorexia nervosa, kwashiorkor; marasmus), decreased absorption, transport or utilization (e.g. celiac disease) or specific vitamin or mineral deficiencies (e.g. scurvy). The flipside, excess calories, is also a nutritional disease - obesity - and can increase morbidity due to the increased risk of a number of conditions (e.g., hypertension, diabetes, atherosclerosis, heart attack, some cancers).

Vascular Disease
One of the most common causes of death in developed countries and increasingly world-wide. Narrowing of important blood vessels via the process of atherosclerosis underlies such common causes of morbidity and mortality as heart attacks and strokes.

Psychological Factors

Psychological factors may both cause and effect disease processes. Psychological stress may lead to mental illness or worsen existing somatic disease. Psychological factors are also an important factor in disease caused by addiction (to drugs, alcohol or cigarettes). Psychological factors may even improve existing disease (e.g. the placebo effect).

Review Objective #10
Discuss the classification of diseases according to their pathogenesis.