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Essential Notes on Pathophysiology for Advanced Practice Nurses

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Preface

This text is a compilation of lecture notes from pathophysiology courses I have taught over the last ten years. The goal of the text is to equip future advanced practice nurses with knowledge of pathophysiology for common diseases and disorders they may encounter in the primary care setting. The creation of this text was possible because of the Open Educational Resources Awards Program at East Tennessee State University.

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Genes and Genetic Diseases

RNA and DNA

Genetics is the study of inheritance of biologic heredity. A **gene** is the basic unit of heredity, which means that a gene carries enough information, to transfer or to pass one or more traits; the traits will be passed based on genetic composition. Don't confuse genes with **chromosomes**, a unit of heredity or codons- codons alone, don't have enough information to transfer traits, and chromosomes contain multiple genes. Usually, in order to pass one trait, only a single gene is required.

Genomics is the field of genetics, that studies the structure of the genome. A **genome** is the DNA that represents all the genes for a given type of **species.** A genome will be representing the complete genetic information - all types of genes for the type of species. This pertains to not only human physiology and human pathophysiology, but also to animals and plants, or even microbial world. Heredity information is controlled by genomes, genetics and genes that carry the information in living structures.

When discussing heredity, a focus is on DNA and genes. Genes are the sections or sequences of **DNA** that have the instructions to make a single protein. One strand of DNA may contain a multitude of genes. The building blocks that make up genes are called **bases**. There are four bases that make up DNA:

Adenine

Thymine --------- Uracil in RNA

Guanine

Cytosine.

RNA consists of similar bases; however, thymine is replaced by **uracil** in RNA. The amino acids are strung together and attach to one another to make a protein. **Protein** is a polypeptide chain, a polymer molecule that consists of peptides or amino acids. The DNA resides in the nucleus and contains codes for future protein. DNA has a double-stranded structure, but one of the strands has no function at all, but to compliment the other strand. The main strand, the meaningful strand, carries the genetic information while the meaningless strand just acts as a complement.

The main strand is complemented with meaningless strand to give a *structure* to DNA. However, when DNA replicates, the result is two identical molecules of DNA. During the replication the DNA “unzips.” The original meaningful strand attaches to another new meaningless strand, and meaningless strand attaches to a new meaningful strand.

Transcription is the initial step to get the genetic information out of the nucleus and move it to the cytoplasm for the creation and construction of the proteins. **Transcription** occurs

inside of the nucleus. This process can only occur in *eukaryotic* cells because eukaryotic cells are the only cells that have a *nucleus*, and the nucleus contains DNA. *Prokaryotic* cells do not contain a nucleus.

Human cells are all eukaryotic, in this situation messenger RNA will create a copy of complementary strand of DNA will move to the cytoplasm. The main players in this concept are the stop codons. The stop codon marks the point where the transcription will end. However, before the messenger RNA moves into cytoplasm, some other changes have to occur.

Initially the transcribed RNA is immature. Immature in this context applies to the fact that the RNA contains a combination of two different nucleotide sequences: *exons and introns*. Only exons carry the information necessary for protein synthesis. Introns and exons are nucleotide sequences within a gene. The immature RNA will be modified and eventually the introns will be removed. This process is called **splicing**. After removal of the introns, the RNA is reassembled and sent out from the nucleus to cytoplasm.

In the cytoplasm the RNA seeks the ribosome, you may view the ribosome as the assembling production line where protein synthesis occurs. In the ribosome the messenger RNA will attach to ribosomal RNA and will start running through the ribosome. Simultaneously, the amino acids are carried into the ribosome by the transfer RNA. The transfer RNA continues to carry the amino acids and the whole process creates a chain of proteins or a polypeptide chain. Everything in this process works like an assembly line. There are 20 amino acids and 20 different types of transfer RNAs; they all work to assemble proteins.

After the protein is assembled, it must be folded and transported to an appropriate place in the cells. The folding process occurs with the help of particles called molecular chaperones. The chaperones oversee the protein and control the proteins behavior; the chaperones act as need to make sure the protein does not unfold. However, it is possible that eventually the protein may unfold. In this case, the protein may contribute and attach to another protein. This process of attaching and unfolding of proteins is known as **denaturation**. This process can lead to many diseases; an example of this may be Alzheimer's disease. Heat, chemical exposure may lead to the denaturation of the proteins. You may see the denaturation of the proteins in your everyday life: when cooking a raw egg the proteins in the translucent egg white denaturate resulting in a solid white color of the cooked egg white.

In review, when the cell divides, it needs the duplication of DNA. Ribosomal RNA moves along the messenger RNA and then moves the transfer RNAs into position. However, even though this process involves teamwork of three different RNAs, the only RNA that goes into the nucleus is the messenger RNA. The other two work only in the cytoplasm.

Mitosis and Meiosis

Mitosis is a regular cell division. Mitosis is needed for the for the replenishment of some wear and tear, such as creating new blood cells or skin cells.

Meiosis leads to the creation or production of gametes, or sex cells, or otherwise called sperm or ovum. In meiosis, the chromosomes duplicate, and one pair will go to each daughter cell on the first division, however, one chromosome of each pair, will go to the daughter cell, on the second division.

This is important in relevance to genetic disorders and the phenomenon of **crossing-over**. When chromosome pairs are lining up during meiosis, and then they will exchange ends. This will result in gametes or sex cells. The gametes will have different combination of genes where the tips are exchanged. This results in richer, broader, genetic variety. Another phenomenon is **linkage**, when two genes are standing close together that the chromosome become linked; they will be very inseparable and have difficulty separating in the crossing-over stage. This results in the genes being inherited together.

Inheritance and Mendel's Law

A **Punnet Square** describes the genetic inheritance process, by using probability of inheriting each trait. The capital 'D' represents a dominant allele and a small 'd' represents a recessive allele.

	D	d
D	DD	Dd
d	Dd	dd

If two dominant traits interact together to create a new cell, it will result in dominant traits. If a dominant trait interacts with a recessive trait to create a new cell, it will result in a dominant trait. If two recessive traits interact to create a new cell, it will result in recessive trait. It is much harder to develop recessive traits. Two recessive traits must be supplied from each parent in order to inherit a recessive trait; it is much easier to inherit dominant traits. Each square represented in a Punnet Square with four squares represents a 25% of inheritance. In cases of phenomenon's, such as inbreeding, the supply of recessive material or genes increases. This raises concern about these types of relations because recessive genes can sometimes be related to diseases. This is way off-springs of partners close in familial relations may have health problems or cognitive or physical deficits. **Alleles** are the copies of a genes. If the copies of genes are alike it is **homozygous**; if the copies are different, they are considered **heterozygous**. If the allele is heterozygous, the recessive trait is not shown, however, the individual is still a carrier of the recessive trait. If only one copy of the gene is present, it is considered **hemizygous**. Only dominant genes will be expressed.

Genotype versus Phenotype

Genotype is the genetic material and **phenotype** is the appearance of actual physical characteristics. For example, blue eyes this is a recessive trait and brown eyes are a dominant trait. A person with brown eyes may have genotype of two genes supplied, one from the mother and father both dominant, or he or she may have a genotype of one set of blue eyes, recessive gene, from one parent and brown eyes, dominant gene, from the other. The person will have brown eyes, but may be a carrier of a recessive gene for blue eyes.

Gene Expression refers to the process of genes being turned on or turned off, induction and repression. During **induction** there must be a trigger or external factor present to start a gene or turn a gene on. **Repression** refers to a factor that turns the gene off. If a gene is turned off, the code for the protein is not. Gene expression simply refers to the gene being expressed when trait is visible. However, if the gene is turned off, the protein is not. If a recessive gene is expressed, it is called **intermediate penetrance**.

If a person exhibits a trait, and the trait is secondary to many genes it is **polygenic**. If trait is expressed secondary to genes and the environment can also influence it, it is a **multifactorial expression**. Multifactorial refers to several factors having an influence on something. Very early events can be secondary to a single factor. When one gene masks the effect of another one, it is referred to as **epistasis**; one of the genes will never be expressed. When genes depend on each other, they work collaboratively and complementary. Two genes may work together to create a new phenotype; this is referred to as **collaborative**. The difference between complementary and collaborative is that in a **complementary** type the genes depend on another; they cannot work separately.

Mutations

A **mutation** is always a change; however, it may not be a positive change. A mutation may occur at any time, and the changes in the organism may not be apparent in behavior, appearance or in function. Mutations can be transmitted to offspring, only in gametes. When gametes are mutated, there is a generation of transmissions, and the children or offspring will present with the mutations already that occurred in the parent in somatic cells. The harm of a mutation can have effect on the parent, however **somatic cell mutation** will not be transmitted to the offspring. In order to produce a healthy new generation, mutations in gametes should be prevented.

Point mutations is a type of mutation that is caused by a single nucleotide base pair change, in the DNA's. When a single nucleotide base pair changes in DNA, there may be no consequence because of the repetition in the DNA. Point mutations may not have any consequences; rates of spontaneous mutation may vary and vary per gene; and is dependent on the factors that can also influence the genes at a given point of time. A mutation can be described as anything that alters the genetic materials, chromosome aberrations, or base pair substitution. This definition applies to all types of mutations. Substitution of the base pair may result in the change of amino acid sequence. This substitution causes the protein to not be produced the way it was designed. This can result in drastic consequences if a change in the

protein occurs. If a silent substitution occurs, it may not result in an amino acid change because of the redundancy of the genetic code. When the amino acid sequence is changed by a base pair substitution, drastic consequences can occur because a change in the base pair causes a change in the amino acid sequence which results in a change in the protein synthesis.

Mutagens are the agents that are known to cause or increase the frequency of mutations, agents, or influencing factors. These terms can be used interchangeably, but a mutagen is something that will cause the DNA to mutate. Radiation is a very well-known and studied 20th century cause of mutation. Chemicals can also cause mutations. Some chemicals can be extremely harmful, while others can cause mild or insignificant mutations. Chemicals such as pesticides, herbicides and fertilizers have a very low rate of related mutations. Sodium nitrate is also a relatively harmless chemical that is widely used in fertilizer.

A **silent mutation** is a DNA sequence change that does not change the amino acid sequence of the gene. **Missense mutation** is a type of mutation that results in a single amino acid change in the translated gene product. A protein is a polypeptide chain of amino acids which are peptides. If only one of the amino acids is changed, then a missense mutation has occurred, and the consequences can be drastic. The change in the amino acid may result in a significant change in the protein due to a missense mutation or a consequence of a missense mutation. A **nonsense mutation** is a type of mutation in which the messenger RNA stop codon and the produced protein will have a premature termination of the sequence or production of the long protein. The nonsense mutation will affect the messenger RNA stop codon and result in a protein that is too short or too long. This results in a different protein being created. **Frameshift mutation** occurs when the DNA is altered, and an addition or deletion of base pair takes place. The shift causes the entire frame to become transposed and changed. If one base is inserted into a DNA molecule, every base beyond that one inserted is now changed, and as a result every codon and base is incorrect. The consequences of the addition or deletion will be apparent because everything has been shifted in the strand. A frame shift mutation can result in an entire change in the protein appearance and protein amino acid sequence.

Consequences of mutations

A mutation can result in either a gain of function or loss of function. An overproduction of protein can cause and over expression, under expression, or inappropriate expression on a gene. DNA is read and protein is produced secondary to DNA composition. Gain of function disorders can be a consequence of mutations. Although there is a gain in function, this still may not be a positive change and can still be taking on the organism. Loss of function can also occur and is associated with recessive disorders.

Chromosomal abnormalities can be quite widespread; the most common chromosomal abnormality presentation is early miscarriage. Most of the early miscarriages, occur secondary to chromosomal abnormalities; sometimes they are not detected as a pregnancy because it is so early in the gestation period. **Euploid cells** ('eu' prefix in Greek means normal or true) have a stable, correct number of chromosomes; these are also known as diploid cells. Haploid cells have the half number of chromosomes. **Gametes**, sex cells (sperm and eggs), are considered both haploid and euploid; they have 23 unpaired chromosomes. Diploid cells have paired

chromosome- human cells have 46 total chromosomes and 23 chromosome pairs. When a euploid cell has more than double number of chromosomes, it is a **polyploid cell**. **Triploid cells** occur when a zygote contains three copies of each chromosome, 69 chromosomes total. A t**etraploid cell** contains four copies of each chromosome, 92 chromosomes total. Triploid and Tetraploid fetuses don't survive.

A lack of the normal number of chromosomes is referred to as **aneuploid cells**- a lack of normal cells in contrast to euploid. Euploid cells contain multiple of normal 23 chromosomes. Euploid cells can be tetraploid, which is abnormal and has no chances to survive, but still it's euploid. Aneuploid refers to a lack of number of chromosomes that is a multiple of 23- the number of chromosomes cannot be divided by 23. **Monosomy cells** only have one copy of the chromosome; there is a missing member of the pair of the chromosome. Monosomy is quite commonly fatal. If there is a chromosome missing from the pair and an extra copy of the chromosome is present, the infant may survive and lead a relatively normal life. One well known example is **trisomy 21** (Down Syndrome). Individuals with Down Syndrome may develop mentally and physically and progress in their development. It is better to have extra copies of a chromosome than to have a missing chromosome. If there is extra genetic material, chances of survival increase with genetic abnormality. If there is missing genetic material, chances of survival decrease.

When chromosomes separate normally during cell division, they go through **disjunction**. Chromosome abnormalities are due to nondisjunction. **Nondisjunction** is a non-division or non-separation; it usually results in aneuploid cells or and aneuploid chromosome number. A member of a chromosomal pair disappeared or separated to a different place. This missing pair may cause trisomy or monosomy. If the homologous chromosomes are failing to separate normally during the division in either meiosis or mitosis, it can lead to nondisjunction and resulting in aneuploid cells.

Alterations in Chromosome Structures

Translocation can be described as an exchange of genetic material between chromosomes. The genetic material from one chromosome is transferred to another. There are many types of translocations. **Robertsonian translocation** is when the long arms of two chromosomes fuse at the centromere and form single chromosome. Robertsonian translocation can happen in chromosomes 13, 14, 15, 2, and 22 because the short arms of these chromosomes are very small and they don't have any essential genetic material. When the translocation happens in Robertsonian, the short arms are lost completely during the next cell division. This can result in a loss of no important genetic material and only 45 chromosomes in each cell. When this occurs, the individual will present as normal with no disorders because there is no essential genetic material lost. However, monosomies and trisomies are common in this occurrence. The fusion of the arms of chromosome 21 and 14 when a baby is born from a parent who has this, the child can receive an extra copy of the long arm of chromosome 21 resulting in Down Syndrome.

A **ring chromosome** occurs when the telomers of each chromosomal arm have been deleted, and the broken arm joins together and form a ring. A ring chromosome can actually trigger series of breakage and fusion bridge events which will cause continuous DNA breakage. It is a chain reaction and recombination of chromosomal material. The ring itself is not a big danger, but because of the chain reactions, it can cause ring syndrome to display very diverse symptoms resulting from DNA breakage and recombination. The deletions of the chromosomal material will occur, and duplications and the diverse presentation will exist. However, all individuals with congenital ring chromosome will show signs of failure to thrive.

Failure to thrive is a consequence of cells not proliferating normally and suggests that mitotic instability of the ring is the cause. Again, the ring itself is not the danger, but the consequences may cause diverse presentation of symptoms. When chromosomal breakage occurs, physiological mechanisms try to repair the break, however, the break would heal differently than the original chromosome. The effects of a ring chromosome can be very mild or drastic. Ionizing radiation, chemicals, and viruses can may all have an effect on the chromosomes in autosomal structures rather than in sex cells. When these factors have an effect on the cell, they cause breakage and the healing process results in distortion of the chromosome and DNA. The healing process continues to alter the structure of the chromosome. Duplication is a relatively rare occurrence in alteration in chromosomal structures. When a repeated gene or gene sequence occurs as a result of duplication, the consequences are more severe compared to deletion. The reason for this is because more genetic material better than less, so when deleting something of occurs the result is a viable infant. It is more difficult to add something like trisomy 21 to a viable fetus. Examples of duplications include **Cri-du-chat syndrome.** This syndrome is a result of a short arm on chromosome five and results in intellectual disabilities and several physical abnormalities such as microcephaly. If duplication occurs in the short arm of chromosome 5, there will be no physical presentation, but the infant will present with intellectual disabilities.

Fragile sites are sites that the breaks or gaps within chromosome. Fragile sights can be seen by a microscope when the cells are cultured or developed. There is no evidence that this may be related to some disorder. **Fragile chromosome X syndrome,** or **fragile X syndrome** does present with severe intellectual disabilities. It is fairly prevalent in the population: one in 4,000 males will develop it, and one in 8,000 females. The distinct ratio between male and female is due to females having two x chromosomes and males only having one. Females who inherit the chromosome mutation associated with fragile x syndrome, will not express the disease, but males will express the symptoms. The female may or may not express the symptoms of the disease but can pass it down to her children. Most of the fragile sites will not be present with any relation to the disease, fragile X chromosome is the exception. When the mutation of the fragile X chromosome occurs, it occurs on the long side of the X chromosome. The mutation is related to intellectual disabilities. It is one of the most common genetic disorder, second compared to Down Syndrome, and has a higher occurrence in males due to one x chromosome.

Mendel and Mendelian Laws

Gregor Mendel was an Austrian monk, who started a garden pea experiment. Mendel had no formal knowledge or education about genetics health or medicine. During his experiment, he noticed that different varieties of peas, and how when the different peas were crossed, they were present differently. His observations were not the first examples of hybridization. The notion of hybridization had been around for generations. However, Mendel is noted as the father of discovery because he was the first to notice some kind of law or regularity in crossbreeding his plants. Before Mendel, the breeding of the plants and animals was considered a rather random process, but after Mendel's discovery the notion of a rule or **Mendelian Laws** appeared.

Locus refers to the location occupied by a gene on the chromosome, and an allele is the alternative version of a gene at the locus. Each individual has two alleles for each gene. A **homozygous gene** has two identical alleles. A **heterozygous gene** will possess two different alleles of the given gene. The **allele** is the same gene, which is responsible for the same trait, but it is the alternative version. For example, eye color is controlled by the same gene, but by a different allele. **Polymorphism** occurs when the locus has two or more alleles that will occur with a certain frequency. Loci on a pair of a chromosome are homozygous if the alleles are identical. If the loci on a pair of chromosomes have different alleles, it is heterozygous.

Genotype vs Phenotype

A **genotype** is the genetic makeup of the organism. The **phenotype** is what the individual will demonstrate or show; it is the visible physical trait or traits that can be detected through other measures. The phenotype determines the appearance of the organism. An example of a genotype is blood type. I person with type A blood can have AA or AO; A is the phenotype, but AA or AO is the genotype. When two alleles are found together, and one of them will be dominant.

The **dominant allele** will be the one that' will be the presentation of the feature or is observable. The allele that is not expressed is the **recessive**. The dominant allele is always represented by a capital letter and the recessive is always lower-case letter. Alleles can appear together and be called dominant- this is referred to as **codominant alleles**. When the individual has a recessive gene that is not expressed, he or she is a carrier of that allele. When a recessive disease is presented, and patient demonstrates the recessive disease, both genes in the pair are recessive. For example, in the case of sickle-cell anemia, a capital 'S' would represent no sickle-cell trait and the lower case 's' does. Only the patient that has both lowercase 's' will demonstrate the disease. If the patient has two capital 'S', the patient is neither a carrier nor presents with the disease. This patient can not pass the disease to his or her offspring.

Penetrance is a term that refers to the percentage of people with a specific genotype who may express an expected phenotype. For example, retinoblastoma has incomplete penetrance. This means that 10% of affected children with the gene will have not have the disease.

Expressivity is the variation of a phenotype associated with the genotype. Expressivity is the rate of presentation of a disease, disorder, or trait. This can be caused by modifier genes and can vary in degree of how it affects the individual. Modifier genes at other loci can modify the expression of the disease-causing genes. Environmental factors can influence the expression of the disease-causing gene and result in mutations at the locus. Hemophilia A is an example of when a mutation alters just one amino acid at the factor eight gene, and it will result in milder hemophilia A. If a stop codon is introduced, it will terminate the translation prematurely resulting in a severe form of hemophilia. **Von Recklinghausen disease** is an autosomal dominant disorder that affects the long arm of chromosome 17. The expressivity can vary significantly and may have a dramatic appearance of the disease. Single gene disorders are autosomal dominant disorders and autosomal recessive disorders. Abnormal allele is dominant, and the normal allele is recessive. Only one allele is needed to express the disease an autosomal dominant disorder. Autosomal dominant disorders may present equally in males and females because it's not sex related. Approximately half of the children affected heterozygous individuals will show the condition; homozygous affected individuals are rare. Homozygous refers to two copies of the allele that carry and are responsible for the disease. The probability of generational skipping is fairly low. However, generational skipping can happen with recessive traits.

In homozygous affected individuals, both parents have the trait. The probability of the offspring having the disease is 75%. More commonly, one parent will have the disease and one will not. The probability of the offspring having the disease is only 50% one parent will donate the affected gene and the other will donate an unaffected. If the affected parent is heterozygous and presents with disease, the affected parents still have one gene that's normal. If one recessive gene can pair with a normal gene, the disease may be eradicated. Traits can do these as well. Autosomal recessive disorders are not linked to sex and will be expressed equally in males and females. Most often, offspring have parents who are carriers, but don't have the disease, and are unaware of the disease.

For the condition to be expressed, the individual will be **homozygous** - two disease genes will be present. Generational skipping can occur. Probability of an autosomal recessive disorder can be increased significantly if two related individuals' mate and have offspring. This can dramatically will increase the recurrence of recessive disorders. If both related individuals have the recessive gene, the probability of having an offspring with an autosomal recessive disorder increases significantly. Therefore consanguinity may present such a risk for development of autosomal recessive disorders. Like autosomal dominant diseases, autosomal recessive diseases are fairly rare because two recessive genes must connect to create the recessive disorder expression.

Aneuploidies

Autosomal Aneuploidy is when the cell doesn't contain a multiple of 23 chromosomes and results in aneuploid cells. Aneuploidy can occur in any chromosome. However, only the 13th,18th, and 21st chromosome can be presented in live births, otherwise the chromosomes aneuploidy will result in a still birth. For example, trisomy 16, is quite common, unfortunately the baby is not viable, and the birth isn't live.

The most common example of Aneuploidy is **Down syndrome**; the frequency is one out of 800 life births. **Down syndrome** was first described by Langdon Down who described the disease in 1866.Since then, extensive research has been conducted on Down syndrome. One of the most significant findings is that the incidence of Down syndrome vastly increases with maternal age. After the maternal age of 45 years old, the risk can be as high as 5% probability of having baby with Down syndrome. Because women are born with all maternal egg cells, the eggs are held in a dormant state. During the dormant state, the eggs may acquire damage from external factors. Damage also occurs from cellular proteins that govern meiosis. Nondisjunction may occur resulting in trisomy 21 or Down syndrome.

Speculation that **paternal age** plays a role in development of Down syndrome, however, there is no steady evidence that will point on paternal age. The famous Columbia University conducted research in 2003. Data was collected on births of infants from 1983 to 1997. Approximately 3,400 cases were examined. A similar study was conducted at New York State University and paternal age was linked to influence the baby having Down syndrome. When babies born with Down syndrome, there is a chance of intellectual disabilities- the degree may vary significantly. Individuals with Down syndrome may present with significantly high IQ, and there were cases described in literature that persons diagnosed with Down syndrome were able to enter and complete the college and be successful in professional employment. However, majority of individuals with Down syndrome may present with relatively low IQ. Physical features will include, low nasal bridge, epicanthal folds will be present, protruding tongue, and poor muscle tone. Patients with Down syndrome may present with increased risk of heart disease and congenital heart disease. It's important to screen a baby for congenital heart disease. Individuals may also have GI disorders and a higher risk of developing leukemia. Because of the development of the health sciences, the management of Down syndrome and consequences is much more elaborate. Today, the quality of life is much higher compared to decades ago. Trisomy 13 and 18 or other trisomies that can be present in live births, but unfortunately the patients with trisomy 13 and 18, will present with much more significant and severe complications, than the person with trisomy 21. In these cases, the probability of having more profound deficits is much higher. Intellectual disabilities can be present, as well as the physical disorders may be present. The chromosomal trisomies will not survive to term. Trisomy 16 is the most common one in spontaneous abortions- it never results in live births. Partial trisomies may also occur when an extra portion of chromosome is present in each cell. The consequences of a partial trisomy is not as severe as a complete trisomy.

Individuals who are partial trisomy are considered **chromosomal mosaics**; this means the individual organism has ***several cell lines***. Each cell line has a different karyotype, and mosaics are formed by early mitotic nondisjunction. This can occur in one embryo cell, but not in other embryos cells. Partial trisomy is not as severe because a portion of a chromosome is present in the cell. If a portion of the chromosome is left, it is not a complete trisomy. A missing chromosome is worse than having a portion of a chromosome missing. Sex chromosome aneuploidy is similar to autosomic chromosomal aneuploidy. However, the

consequences are less severe. For example, when there is an abnormality related to Y chromosome the consequences may be relatively insignificant. This is due to the small amount of genetic material carried by the Y chromosome, and the approximate location on the gene. When X chromosome aneuploidy occurs, more serious consequences may occur. For instance, when there is no X chromosome, and only Y chromosome the chances of survival are non-existent. The zygote won't survive if there is no X chromosome. Instead of two X chromosomes, some females may have three x chromosomes or even four X chromosomes. This is called **metafemale.** No physical abnormalities occur, but a female with three X chromosomes may have sterility, menstrual irregularity, abnormal menstrual cycle, and may have intellectual disabilities. When the number of X chromosome increases, the chances of developing disorders especially intellectual disabilities increases, and with five chromosomes the chances are even higher. The presentation of the disorders will increase, and the consequences will be more severe with each additional X chromosome.

Turner syndrome is a disorder when only one X chromosome present. With only one X chromosome, survival is still possible, *but without X chromosome the survival is impossible*. When an individual only has 45 chromosomes in Turner syndrome, and only one X chromosome there is no corresponding X chromosome or Y chromosome. The gender of the individual will be female, but she will be presenting with absence of ovaries and sterility. Short height and webbing of the neck is also a characteristic, and individuals may have some edema. They can also have coarctation of the aorta. Newborns will have edema in lower extremities and gonadal streaks. Gonadal streaks are similar to undeveloped ovaries; they are not fertile, but can still can be susceptible to neoplasm. This should be monitored and treated of if there is a suspicion for cancer. Turner syndrome will have relatively high mortality rate presented as spontaneous abortion, but survival rate is relatively high, and the individual will present with all the symptoms described. The X chromosome will be inherited from mother; the paternal X chromosome will not be present. The father, in this case, does not donate anything. Turner syndrome is possible with only one X chromosome**.**

Klinefelter's syndrome is another sex chromosome aneuploidy and results in the individual having at least two X chromosomes and one Y chromosome. The individual will have a male appearance and karyotype can be described as 47 XXY karyotype. The individual will have all the consequences of having excess in X chromosomes. Some individuals will have symptoms of sterility, they will have still testicles, but they won't be developed. The individual may have gynecomastia, long limbs, and sparse body hair. Some individuals may have 3 X chromosomes, or even 4 X chromosomes, but the more X chromosomes, the increase in abnormality rate.

In addition to, when losing or gaining a chromosome, sometimes, parts of chromosome can be lost, or interchanged, or duplicated. When the sex cells are formed the arrangement may be altered, because of the small amount of genetic material involved. Consequences may not be as serious as changes that involve an entire chromosome or may not even be present at

all. If abnormalities of the chromosome are present, they can produce a serious disease in some cases, and may influence the children. If it is some type of sex transfer trait, it may show up in the next generation.

Deletion is when a chromosome loses part of the DNA. When a gamete with deletion is present, the probability of uniting with another gamete with deletion is very low. In most cases, the gamete with deletion unites with a normal gamete. **Inversion** is another type of alteration in chromosomal structure. It occurs when there is a rearrangement of a segment of the chromosome; the segment flips around and is reversed end to end. The deletion can result in Cri du chat syndrome. Translocation can be described as an exchange of genetic material between chromosomes. Robertsonian translocation occurs when the long arms of two chromosomes fuse at the centromere to form a single chromosome.

Robertsonian translocation can occur on chromosomes 13, 14, 15, 21 and 22 because short arms of these chromosomes are very small and do not have any essential genetic material. When the translocation happens in Robertsonian translocation, the short arms are lost completely during the next cell divisions. In this type of translocation, there is no loss of important genetic material. The individual will have 45 chromosomes in each cell and present at typical developing with no disorders. In other cases, the individual can have monosomies and trisomies. It is common in Robertsonian translocation for the fusion of the arms of chromosome 21 and 14 to occur and result in an extra copy of the long arm of chromosome 21. Chromosome 21 is the chromosome related to Down syndrome, and this can result in the disorder.

Ring chromosome occur when the telomers of each chromosomal arm have been deleted, and the broken arm joins together to form a ring. This can trigger a series of breakage, fusions, and bridge events that will cause continuous DNA breakage. It occurs like a chain reaction of recombination of chromosomal material. The ring itself is not the danger, however, the chain reactions have severe consequences. Individuals with ring syndrome may display very diverse symptoms as a result from DNA breakage and recombination. Deletions of the chromosomal material will occur as well as duplications and the diverse presentation. Individuals will show failure to thrive. Failure to thrive is a consequence of cells not proliferating normally and is suggested to be due to mitotic instability of the ring that prevents the forming of somatic cells. Chromosomal breakage occurs and physiological mechanisms trying to repair the break. Unfortunately, the break heals differently than the original chromosome, and this may result in diverse presentation of different abnormalities. The abnormalities can be very mild or drastic. Ionizing radiation, chemicals, and viruses may affect chromosome in autosomal structures.

Duplication is a relatively rare occurrence that alters the chromosomal structure. When a repeated gene sequence occurs, the consequences are less severe than deletion. Duplication can occur in the short arm of chromosome 5 and result in **Cri du chat syndrome**. This syndrome results in several physical abnormalities such as microcephaly and intellectual disabilities.

Fragile sites are sites that the breaks or gaps within a chromosome. They can be seen by a microscope when the cells are cultured or developed. There is no evidence that this may be related to some disorder in most of the fragile sites. However, **Fragile chromosome X syndrome** or **fragile x syndrome** can occur. It presents with intellectual disabilities and is prevalent in the population. The ratio is 1:4,000 males a 1:8,000 females. The distinct ratio between male and females is due to females having two X chromosomes and males only having one. If a female inherits the mutation, they may not express the disease, but a male because of only having one chromosome. Therefore, the prevalence is so much higher in males. So, that's why the prevalence is two times more in males. A female may have mutation and not present with the disease, but she can still pass the mutation along to her offspring. Fragile sites will not be presenting any relation to the disease except for fragile X chromosome. When fragile X chromosome occurs, it occurs on the long side of X chromosome and will be related to intellectual disabilities. Fragile X syndrome is one of the most common genetic disorder second to Down syndrome.

Inflammation and Infection

Immune response and inflammation are a part of defense mechanism created to protect the body against the foreign invaders. There are three types of protective barriers. **Physical and surface barriers**, such as intact skin, is the first line of defense. The skin by itself is a physical barrier and at the same time skin surface is acidic. This makes it an antimicrobial barrier against infection. However, this does not always happen, and sometimes it's possible to have skin infections, but if everything functions well skin can be an efficient barrier against infection. Thousands of microorganisms are on the skin's surface. Some sources cite that more than 100 trillion microorganisms are carried by one individual. This is a normal bacterial flora on the skin. It prevents opportunistic infections by other bacteria. So, on the other Skin has sebaceous glands that secretes sweat. This creates an acidic environment and antibacterial enzymes.

Mucus membranes can serve as another physical barrier and serves to trap and destroy invaders. Besides physical barriers, the human body also uses inflammation and immune response. Inflammation is a nonspecific response. When a physical barrier is broken by a scratch, stab knife wound, or a simple splinter the bacteria or other microorganisms penetrate the tissues causing a trigger in **inflammatory response**. This process begins with a vascular response. The **vascular response** happens within seconds of the physical barrier being broken. It is an unspecific process that follows the same pattern regardless of what caused the break. An immune system response is a specific response; it is even referred to as "a third line of defense." Every cell has proteins that we are called **antigens** on the surface that can identify the cell. When a response occurs, the body's immune system identifies the invader by the antigen and the lymphocytes produce antibodies. The antibodies link to the antigen and either kill the cell or disable it. The immune system has the ability to remember the invader and produce antibodies to fight against it.

Inflammation is a nonspecific response in which the process does not distinguish they type of invader that is attacking the body. The invader is usually a reaction to distortion in tissue integrity, destruction in tissue integrity, trauma, injury, or a burn. Inflammation will not occur if there is no blood supply. The blood supply creates the vascular and cellular component of the inflammation. Inflammation cannot occur in necrotic tissue, however if there is a decubitus ulcer, an inflammation response may occur around borders of the ulcer. If there is inflammation in a tissue, an injury occurred when the individual was alive. If an injury has occurred after the person is already deceased, there will be no evidence of inflammation because blood supply is needed for the inflammatory response. Inflammation benefits as a second line of defense. However, it may be harmful to the individual and destructive to the tissues and severe inflammation can even be deadly. Type 1 and anaphylactic shock reactions are an example. Inflammation by itself is a blind mechanism and its nonspecificty can make it harmful. When inflammation occurs, there are several signs and symptoms including redness, heat, edema and pain. For redness, heat, edema and pain, Latin equivalents can be used: heat is *calor*, edema is *tumor*, pain *dolor*, and redness is *rubor*. These are the signs of inflammation, that visible and reported. Some types of inflammation are acute and chronic.

Acute refers to the inflammation lasting less than ten days; it is a relative term, so if inflammation lasts elven days it is still acute but two weeks is usually the cut off point. If inflammation last more than two weeks, it is considered to be **chronic**. When a inflammation occurs, basophils or mast cells are involved. When the injury is detected, the inflammatory response is triggered, and mast cells may release histamine. Histamine will cause dilation vasodilation in local capillaries. Dilation will increase the blood flow to the area and cause rubor or erythema and heat in the area. When this happens, dilation also works to bring neutrophils into the area. Neutrophils lines the endothelium of the vessels and wait for an opportunity to move inside of the tissue. When this happens, the neutrophil influx is a short-term process. It cannot be caught in lab work unless interval blood drawls are done. Interval blood draws should be done every few hours because neutrophils will move into the tissues within a 24-hour period. When the capillaries dilate, because of the histamine and other substances, vascular permeability will increase. Permeability is when the capillaries leak and cells in the endothelium are stretched. The blood then begins to produce exudate. The fluid from the blood leaks into the tissue and causes edema. Edema is a sign of inflammation. As the edema increase, the pressure build-up causes pain. Swelling can prevent functioning of the organs. An individual will lose mobility if the swelling happens in an extremity due to pain- like a sprain or strain.

Vascular permeability helps the neutrophils to run into the tissues. Diapedesis is the process by which the neutrophils squeeze between the epithelial cells; it is a very effective process that happens very rapidly in which millions of neutrophils will invade and area within a few hours. Neutrophils are the first cell that attack the inflammatory process. These cells are attracted to the injured area by **chemotaxis force** or the process of chemotaxis. The **chemoreceptors** are located on the neutrophils. The detect the source of the release of

chemically active substances, and make the neutrophils move toward the site of the injury. When neutrophils arrive to the site of the injury, phagocytosis begins.

Phagocytosis is the "eating" process of the cells. This process starts with the destroying the foreign materials, and the cells start dying because neutrophil cells do not live long. As the cells are dying, they produce the **purulent exudate** or pus. Another type of exudate is **fibrinous exudate**. This occurs in a larger injury with more severe inflammation. The fibrinous exudate is composed of fluids and a large amount of fibrinogen. When comparing two serous exudates, the leakage of the fibrinogen will signify more severe inflammation. The presence of fibrinogen is observed, in streptococcal laryngopharyngitis, pneumonia, other infections with bacterial origin. In these cases, the lesion will have a mesh like structure. The superficial wound may be covered with dried fibrinogen exudate or a scab; it is a collection of dead neutrophils. Approximately three to four days after the inflammatory process begins, monocytes will appear. Monocytes leave the bloodstream and move into the tissue, become phagocytic cells, and then turn into macrophage cells. Monocytes remain the same, but the name changes because it moves from the blood into the tissue. Neutrophils, may be dead, is still present at the location and the injury and may create an abscess.

An **abscess** is a collection of pus; it typically needs to be drained and may cause significant pain and/or trigger further inflammation and infection. **Empyema** is the accumulation of pus in body cavity. **Ulcers** can happen secondary to inflammation. An ulcer is the absence of the tissue. It is a result of the injury and the inflammatory response that follows the injury. An ulcer is the result of necrotic tissue sloughing off and leaving a crater or excavated area. Examples of ulcers include stomach ulcers or duodenum, gastric or duodenal ulcers or peptic ulcer disease. **Cellulitis** is a diffuse and widespread acute inflammation that can be seen in tissue on the surface, like skin, and subcutaneous tissue. Cellulitis is caused often by of streptococcus or Staphylococcus bacteria, or failure of immune system. When opportunistic infection takes over and the immune system fails to protect the surface pathogen, cellulitis can be very dangerous and spread. If an antibiotic treatment is introduced or intravenously in severe cases it is usually treated effectively.

Infection is an invasion of the organism or microorganism that can cause cell and tissue injury. Injury or damage is a part of the infection process. If colonization occurs with no injury, then the term 'infection' cannot be used. When discussing microorganisms that have the potential to cause pathology or pathogenesis, normal flora will become pathogenic under certain conditions. An example includes the e.coli infection, which can be considered an opportunistic infection under certain conditions, but in other cases, it may be just considered a normal flora of the gut. The resistance of the pathogen to the barriers, physical barriers to immune barriers, and the number of pathogens invading, and area are factors to be considered. In order for the normal flora to become pathogenic, the barrier must first be broken and create a port of entry. The pathogens must be somewhat resistant to the defenses of the host. The number of pathogens along with the types of comorbidities that are present in the host will

facilitate the invasion of the pathogens. Infectious diseases are the leading cause of death worldwide, in the United States next to cancer and heart disease. Infectious diseases are not as rampant in the United States because of the country's ability to identify, track, and control the spread of diseases. The **Center for Disease Control and Prevention (CDC)** can provide the services and is providing the services in the United States.

There are many pathogens that may cause infection. Bacterial infections may occur as a primary infection or a secondary infection. When this occurs, the person is exposed to a pathogen and is considered a **primary infection**. A **secondary bacterial infection** occurs when there is some type of other disease present. It can be viral disease or mechanical factor, which may result in a bacterial infection afterwards. For example, a person has a nasal obstruction of some kind. This leads to sinusitis, and because of bacterial influx, it is secondary infection. Eustachian tubes obstruction mechanically, or again secondary to other infective organisms, and may lead to otitis media.

Normal flora is the bacteria that occupies the skin, lives on the skin, and is usually harmless. It is also found in the intestinal tract, genital tract, and mucous membranes in mouth and nose. The bacteria that is harmless and creates normal flora can become pathogenic under certain conditions. When the resistance or body defenses are weakened, these bacteria can take over.

Staphylococcus is an infection on the skin and can be a very devastating. If the skin barrier is broken, the microorganism can enter, and may infect any organ. **Staphylococcus aureus** is a bacterium that can be very devastating and harmful, especially the Methicillin resistant forms such as MRSA or MRSA. **MRSA** is resistant to penicillin and other antibiotics. It is a consequence of widespread antibiotic use, treatment, and overuse of antibiotics mostly in primary care, as well as in acute care. A significant number of people with viral diseases, such as bronchitis are treated by antibiotics, in which there is no indication for that. Bronchitis often has a viral origin, and signs and symptoms aren't recognized. For instance, if patient has productive cough, and a yellow greenish sputum, the chest x-ray will be negative for pneumonia, a patient is febrile, and everything points on viral infection. However, a primary care provider may go ahead and prescribe antibiotics. This creates the resistance of the normal flora, that can be invasive and become an invasive pathogen and MRSA.

In regions that the over-prescription of the antibiotics is very low, the MRSA and other type of **Streptococcal bacteria** can normally live on the skin and in the throat, Common infections caused by streptococcus will include streptococcal laryngopharyngitis, or commonly called strep throat, scarlet fever, pneumonia and even meningitis. Some people may develop as the sequel of streptococcal laryngopharyngitis, rheumatic fever and glomerulonephritis. **Enteric bacteria** in the intestines includes E.coli, Klebsiella, Pseudomonas, Shigella, and Salmonella. E.coli can cause enteritis in infants and adults. It is also associated with "travelers diarrhea" because when people travel to different regions the are infected with an E.coli strain the local

dwellers are susceptible against, but the travels are not and results to some type of colitis. Pseudomonas is notorious for infecting wounds.

Pseudomonas infection will result in a green exudate, pus exudate production, and a foul odor. Although, Shigella and Salmonella, are not usually found in the intestinal tract, Shigellosis can still happen, and Salmonella infection can occur. **Salmonella** can cause severe food poisoning especially if the cause is from eggs.

Viruses are the smallest infective particle. Viruses have properties of a living organism; however, it needs another living organism to replicate. In the healthcare field, it is important to recognize and treat viral infections. Viruses need a host cell to reproduce and are not easily treated. Antibiotics again are not effective, but when pneumonia is a sequel of a viral infection antibiotics will be needed to combat secondary infection. Immunizations are still an effective way to prevent certain viral infections, such as measles, mumps, rubella, smallpox, chicken pox. Latent viruses may lay dormant in cells and replicate. Varicella can present later in life as the shingles infection. Shingles is not only disease of elderly people but can affect younger people in their twenties and thirties who present with shingles.

Fungi are different in that fungus is bigger than bacteria but is not as deadly or harmful as bacteria- only very few types are pathogenic. Most of the fungal growth is harmless, and fungus plays a significant role in nature. It helps to restore the balance in nature by destroying already dead tissues and debris. They are a few fungal infections or types of fungus that can be harmful to humans. **Tinea infections** are fungal infections on the skin; the skin is a cooler environment than inside the body and fungus often choose cold environments. Tinea infections are commonly described as ringworm, athlete's foot, or jock itch. They are common and very infective and can be transferred from one person to another. Another type of fungal infection is **Candida infections**. It is a superficial infection of skin and mucous membranes. In an adult, Candidal infection in the oral cavity or thrush is not an expected finding, but in this case, oral Candida in an adult or thrush may signify immunocompromised status. Children may often develop Candida and it may be considered quite an expected finding. Adult candidiasis may signify an HIV infection. Also, candidal infection can cause vaginitis and/or yeast infection which is easily treatable. Other fungal infections may cause histoplasmosis; histoplasmosis can be tied to certain geographic locations and certain behavioral factors, such as 'having the cat and emptying the litter box,' and is not common in general population, but still the damage can be devastating. Fungal infections can be treated with antibiotics and certain fungal medications. Some fungal infections are extremely difficult to cure, such as nail fungus, or even ringworm infections; they may require long-term therapy. For example, nail fungus may require the Sporanox-pulse therapy and other type of antifungal medication. Antifungal medications may cause liver damage in some cases, but other fungal infections like vaginitis or even candidiasis are easy to treat and cure.

Ricketsiae is a microscopic organism, that is an intermediate between bacteria and viruses. Like a virus, it needs a living host so to multiply. It can be spread by a vector organism

like flea, tick mites' lice, something that can bite. The most common disease that may have devastating consequences is **Rocky Mountain spotted fever** which is spread by the tick. A regular tick that you may find on a dog is not the carrier of Rocky Mountain spotted fever. The carrier will be much smaller brown tick. If there is suspicion of the infection of Rocky Mountain spotted fever caused by a tick, the tick should be preserved in some way and presented a healthcare provider for identification and treatment.

Protozoan infections are caused by a single-cell microscopic organism and can be found in the soil in dead or decaying material. Ingestion of spores or infection can be caused by insect bites. **Malaria** can be spread by mosquitoes and is a protozoal infection It is the most prevalent of the protozoa infections worldwide. However, in the United States, it is very uncommon. The malarial infection is a result of the protozoa living in the red blood cells of the host and causing destruction of red blood cells.

Giardia is another type of protozoal infection and usually is not as devastating as malaria. It can be caused by drinking infected water and can results diarrhea. It is often can resolve by itself or if detected early can be treated by antibiotic therapy.

Helminths is another class of infection that includes roundworms, flatworms, tapeworms. The helminths are very common worldwide, but not common in developed countries. Pinworms or tapeworms are the most common helminths in the United States. Pinworms are usually causing anal itching. Tapeworms may cause certain symptoms such as pain and diarrhea; they usually are a result of consuming inadequately cooked meat especially in hamburger meat. Treatment can include anti helminthic agents; this type of treatment is very effective, and is one of the reasons that these infections were under control in the United States. However, with the influx of immigrants from developing countries, it is typical to have the reemergence of these infections, but these types of infections are easily treatable.

Testing for bacterial or viral infections may include testing blood for increase white blood cells. Bacterial infections will cause a left shift and viral infection-right shift. The left shift is most commonly observed. The left shift signifies the increase in numbers of neutrophils while the right shift signifies an increase in the number of lymphocytes. Another test that can be done, is a culture and sensitivity for blood or urine. This involves culturing the invading organisms and then check the sensitivity of that organism against certain antibodies.

Skin testing is also used to determine antibody presence for a pathogen. It is one of the common tests done as well as the **Mantoux test** to determine tuberculosis presence. The tests involve intradermal injections- injections of antigens of tuberculosis. If the patient is exposed to TB and developed tuberculosis antibody, the antibody will attack the antigen and cause induration. In severely immunocompromised patients, the size of induration is smaller because they cannot mount an immune response. The size of induration for different categories of population is constantly changing, but currently 15 millimeters is for people who do not have any potential for exposure for TB. 10 millimeters is for healthcare workers, and 5 millimeters for

immunocompromised people with HIV. There are many other types of testing for the infections, but there are three major types.

In general, the immune system will be able to control the invasion of foreign organisms or foreign particles. When the barriers of defense are broken and inflammation doesn't occur, infection may occur. Many different organisms can cause infection, but most common types are bacteria and virus. These two can be diagnosed and treated in many different ways. Immunization is an important consideration for the prevention of viral infection, and beneficial for treatment in many types of viral infections.

Cancer

Neoplasms and **cancers** are very important topics for everyone involved in healthcare, either someone in clinical practice, clinical education, or research. Thousands or even millions of people worldwide are diagnosed with neoplasms every year. To many, the news can be the equivalent to death sentence, however, many neoplasms and cancers are treatable. Research is continuing to find ways to treat most of the common neoplasms. Neoplasm and tumor are terms that may be used interchangeably. Tumor is a more colloquial term and neoplasm refers to a new growth; the new growth can be cancerous or benign. Not all the tumors and neoplasms are deadly or malignancies.

Common Cancers

For men, **prostate cancer** is the most commonly diagnosed. Women are most commonly diagnosed with **breast cancer**. Cancers are diagnosed in many different ways, and the earlier the cancer is detected the treatment outcomes increase. Cancers are classified according to their appearance, growth patterns, type of body tissue, and where is started.

Benign neoplasms are the neoplasms that are confined to a certain localized area and will not spread. The term *tumor* most often refers to benign neoplasms, however some can refer to malignant tumors. One important characteristic of benign neoplasm is that they are *encapsulated, localized, don't metastasize or spread*. Most of the time, these types of tumors are harmless unless they grow in some type of confined space such as the cranium or proved pressure on important blood vessels and cut off the blood supply, nutrients, and oxygen to the certain areas of the body. Benign neoplasms are usually harmless and can be considered a cosmetic defect that can be removed.

Malignant neoplasms or c**ancers** present with two main characteristics - invasions and metastasis. **Invasion** will involve spreading of the neoplasm into local or surrounding tissue. **Metastasis** will be involve spreading of the neoplasm to distant sides. Metastasis can happen

via lymphatic venule or via the blood stream. When differentiating the neoplasm, focus should involve the tissue of origin. Neoplasms are classified into tissue type related classification or classification based on the tissue from which they grow. Depending on the location of the tumor and origination site of the tumor, the tumors may have different names. Benign tumors usually take the tissue name and the suffix-*oma* for tumor. For example, lipoma is a tumor of fatty tissue. Malignancies will have terms carcinoma or sarcoma added to the type of the tissue.

Epithelial vs Connective Tissue Malignancies

If an epithelial tissue is harboring a neoplasm, it is a non-malignant tumor and will be named **adenoma**. If it is a malignant tumor, the name will be **adenocarcinoma**. In general, the epithelial tissue neoplasm, a malignant neoplasm will be named **carcinoma**. Depending on the original tumor site and tissues where tumor originated the name of the tumor changes. A benign tumor of connective tissue such as bone will be named **osteoma**. If the tumor becomes malignant, the name will change **osteosarcoma**. **Sarcoma** is a term is used in connective tissue disorders such as muscle, fat, and bone; sarcomas are less common than carcinomas and will also spread more rapidly.

Lymphatic and blood forming organs and lymphatic tissues do not produce benign neoplasms, neoplasms in these tissues are always malignant. Malignancies do not have to have a benign variety or benign counterparts, for malignant transformation to occur. **Lymphomas and leukemias** are malignant neoplasms of lymphatic and blood forming organs and lymphatic tissues. The leukemias and lymphomas, can be deadly and have a high degree of mortality, but depending on the variety they may be predictable and may result in a favorable course of treatment and remission dependent on the type of cancer.

In other tissues, the naming process is different. For example, **melanoma** is a malignancy of melanocytes. The tern carcinoma is not added to the name; melanoma is the specific term used. Also in brain tumors, which originate in the glial cells of the brain, is referred to as gliomas. **Gliomas** are benign in appearance and do not metastasize, but they are still considered malignant because most gliomas are fatal. Adenoma will come up from the granular epithelium and will be a benign neoplasm. If something comes out from the squamous epithelium it is an epithelioma, and if something comes from the fat tissues it is a lipoma. If fat tissue turns into a malignant neoplasm, it is **liposarcoma**. When malignant neoplasm appears, usually some type of genetic mutation is to blame. Genetic mutation can take place secondary to disruption of genetic code by radiation, viruses, different carcinogens, or different chemicals. There is a big list of household chemicals, pesticides, herbicides, insecticides, they all may be presenting themselves as carcinogens. Research has also determined many other possibilities of carcinogens, such as burnt cooking oils, excess in certain dietary, certain dietary ingredients such as fat and trans fats and all.

Carcinogen refers to chemical structures that are considered cancer-causing. Viruses and radiations are separate entities because they are not chemical structures and cause genetic

mutation by a different mechanism that results in a disruption of the genetic code and development of a malignant neoplasms. Malignant neoplasms do not have the structure and the purpose of the normal cells. Normal cells have a purpose and have controlled division, but cancer cells do not follow any pattern. This can cause difficulties in determining the location of the metastasis and the tissue of origin.

Oncogenesis occurs when cancer tissues grow and is a genetic mechanism where normal cells are transformed into cancerous cells. Carcinogenic agents affect the DNA of the cell and leads to DNA damage which eventually will result in malignancy. Unregulated cell differentiation and growth is main problem with cancer. The malignant neoplasm steals nutrients, oxygen, and blood supply form other places in the body and grow uncontrollably. A malignant tumor can take over the body and result in death if not treated. Another concern with cancerous tissues is invasion and metastasis. Invasion into the surrounding tissue may damage vital organs and vital function. Invasion occurs by the process of growing endings from the original tumor as well as the process of metastasis. Metastasis involves seeding the cancer cells into remote location by using lymphatic supply or blood supply. **Proto-oncogenes** are normal genes that regulate cell growth. **Oncogenes** are mutations that lead to uncontrolled cell growth; the growth is autonomous because the cell grows by itself. The growth is not regulated by any factors from the body and does not obey the uniform program that entire body obeys. Oncogenes include growth factors, receptors, different enzymes and transcription factors.

Growth factors will bind to receptors on cell structure which will activate signaling enzymes inside the cell. This activates special proteins called **transcription factors** inside of cell nucleus. The activated transcription factor will facilitate the turning on of the genes required for cell growth and proliferation. This will also promote autonomous cell growth in cancer cells in the absence of normal growth promoting signals because of the point mutations, chromosome translocations, or chromosome applications. For the cell to grow autonomously and uncontrollably, the oncogenes must be present, and these oncogenes are factors such as growth factors signaling enzymes, transcription and factors that would disrupt or turn on the genes are required for growth and proliferation. The whole process promotes uncontrolled growth. Tumor suppressor genes are “brakes” that the body uses stop the cancerous or malignant growth. There are numerous suppressor genes that have been identifies. One example is the p53 gene; mutation in the gene can result in lung, breast, an colon cancer. This specific gene mutation is blamed for the three leading types of cancer. A single genetic event can activate an oncogene. There are two copies of each gen from each parent, if both genes are mutated, both copies of the suppressor gene will become inactive. Two mutations must occur for the loss of both alleles of a gene to be inactive- this is referred to as a **loss of heterozygosity**. Loss of heterozygosity (LOH) must occur for the process of genetic mutation of suppressor gene to occur. DNA repair occurs secondary to the presence of cyclins. **Cyclins** are important for making sure that the cell has produced the proteins needed for separation of the chromosomes. Cyclins will check that the DNA has been correctly duplicated and the cyclin proteins to measure whether cells have grown large enough to divide. Cyclins regulate the

process as a whole and serve as checkpoints. They check the presence of the proteins necessary for chromosome separations and check the duplication of the DNA to make sure it is correct, and they measure if the cell is large enough to divide.

The earlier the cancer is detected the likelihood of better treatment outcomes increases. Cancers are classified according to their appearance, growth patterns, type of body tissue, and origin. Normal cells undergo apoptosis while cancerous cells divide indefinitely. Apoptosis does not occur in cancerous cells; these cells not only survive but replicate. When the telomers shorten with each replication in a normal cell, it eventually the cell will no longer be able to divide. In cancerous cells, the enzyme telomerase is activated, and it keeps repairing the telomers until indefinitely; the cancerous cells are able to replicate because the telomers are maintaining their length. HeLa cells are cancerous cells that were obtained from a young woman, a 31-year-old named Henrietta Lacks, upon her death from cervical cancer. The cells were collected in 1951 and the cells are still living and multiplying. These HeLa cells were used for polio research, and in 1955 the vaccine was created that was helped to nearly erase the polio disease. The HeLa cells are slightly different from other cancer cells. When the cancer cell samples were obtained in the early fifties, they would replicate for a short time and then die outside of the host organism. However, the HeLa cells would multiply uncontrollably, and some scientists speculated that the total weight of all cells that multiplied from the original HeLa cell sample is about 20 tons. This experiment raises an issue of bioethics. The tissue samples were obtained from Henrietta Lacks without her consent.

When the telomerase is activated in cancer cells, they continue to divide. Normally with all genetic abnormalities, tumors cannot grow without blood supply. Blood supply is needed for tumor growth and metastasis. In a healthy body, **angiogenesis** **(development of new blood vessels)** only occurs in two cases- wound healing, secondary and primary wound healing, and in the uterus during the proliferation state of the menstrual cycle. With the expectation of these two processes, angiogenesis will be one of the signs of tumors and tumor growth. In one research study, Thiabendazole (TBZ), a common antifungal drug, was shown to inhibit angiogenesis in vivo, and Xenopus embryos.

Malignant Transformation

The first step in the malignant transformation process involves the initiation phase. In this phase, cell damage occurs resulting in changes to the tumor suppressor genes. Apoptosis agents transform to a promotion period or a latency period. The latency period is the time between the cell initiation into a detectable tumor. During this phase, the growth is still occurring, but cannot be detected. The last phase includes the occurrence or emergence of the detectable tumor. The tumor is still small, approximately one centimeter in size. Even though the tumor is small, 1 billion cells have already been replicated; the growth is exponential, and the cells rapidly divide. In reference to the HeLa cells, their growth doubled in only 24 hours compared to the growth of normal cells in 36 hours. The malignant cells have, in addition to uncontrolled growth, a faster growth time compared to normal cell.

Grading and Staging are two important concepts in cancer diagnostics and treatment. The factors allow for the determination of the development of the disease, the extent to which the disease is developed, how to plan treatment accordingly, and predict the possibility of a cure.

Grading is the degree of differentiation. If tissue is well differentiated, like a normal tissue, there is a lower grade. If tissue is very similar to normal tissue, it is a grade 1. When differentiation starts to disappear, the grading will increase. Grade 4 will be less differentiated than grade 2. Grading is typically numbered by Roman numerals from one to four. However, in regard to prostate cancer, five gradings of malignancy may be used; these are obtained by using the Gleason grading.

Staging of the cancer determines the extent of spread of neoplasm. Stating can be developing from clinical examination, imaging studies, biopsies, and even surgical exploration with biopsies. Staging is also categorized by numerical numbers, from one to four, and the system is very similar to grading, but is spread. Staging will show how well spread the cancer is. The TNM system can be used for staging; in this system, tumors are staged according to the size of expand of primary tumor, number of lymph nodes involved, and metastases present in the other remote sites. The staging depends on an extent of metastasis and invasion of the tissues. In this staging system, stage zero will signify carcinoma in situ, stage 1, and stage 2 and stage 3, basically reflect the extent of the disease. Things to consider when determining the stage include how big or small the tumor is, if it spread beyond the organ in which it first developed and is it in lymph nodes and organs that are adjacent to the location of primary tumor. Stage 4 cancer will be a result of the cancer spreading to the other organs.

The TNM system is an important classification system, and it provides a better idea of what's going on compared to a simple staging system. For TNM, under T, the primary tumor is being examined. If its size prevents the tumor from being evaluated or there is no evidence of a primary tumor like carcinoma in situ, the stage will be T'0'. N stands for regional lymph nodes; if a carcinoma is present in situ, the state will be T '0' N '0'. CIS will also be added to this stage if abnormal cells are present but have not spread. When carcinoma in situ becomes cancer, the size of the primary tumor is described by as T 1, T 2, T 3, T 4 size, and extent of primary tumor. So, T always presents the primary tumor, and N also refers to the lymph nodes. If there is nothing in the lymph nodes, you may N0 may be used; if there is some involvement, number like N 1 , N 2, may be used to reflect the number of lymph nodes and the extent of spread.

Distant metastasis has no way of being evaluated, so it is represented by M0 there is no way to evaluate this, it's M0. For example, breast cancer may be represented by T3 N2 M0. T3 reflects a relatively large tumor that has spread to nearing lymph nodes, but not to other parts of the body- there is no metastasis. Another example includes prostate cancer represented by T2 N0 M0. This involves a tumor that is located only in the prostate, has is no signs of lymphatic spread or metastatic spread. The result in a good prognosis for the patient. No set standard is used for measuring staging and grading. They are both interpretations that reflect the condition

of what happens and the condition of the patient. Staging refers to what has happened to the tumor, and grading refers to how bad the tumor has become. Zeros in TNM system are good, and the greater the numerical values the worse the prognosis usually is.

Neurologic System Disorders

Seizures are abnormal and sudden; they are an uncontrolled electrical discharge that occurs in the brains. The neurons are the particles that release the charge. A seizure may result of alteration and consciousness, motor and sensory ability, or even behaviors. There is a differentiation between seizures and epilepsy**.** **Epilepsy** is a chronic disorder and the seizures are unprovoked. Every individual has a seizure threshold. Seizures are the result of resting potential instability and is a burst of action potential. It is a significant discharge of electrical energy and determines hyper synchronization. Seizures do not start and affect the entire brain; however, they start at an **epileptogenic focus**. The term **focus** refers to a certain group of neurons that are sensitive to a trigger. The trigger can be depolarization, an external or internal agent, or an intervention that may cause a seizure.

Clonic seizures are generalized seizures with area of hyper excitable neurons that define the epileptogenic focus. The epileptogenic focus will be the source or the place where seizure starts taking place. The **tonic phase** is accompanied by laryngeal spasm. The autonomic reaction may occur at this time; pulse and blood pressure may change, and the patient may have increased mucus secretion. The tonic phase will last approximately 15-20 seconds. The clonic phase will follow and is characterized by Antonia and spasms. During the clonic phase, the patient may become incontinent and my have urination and defecation. Normally, tonic-clonic seizures will not exceed 1 to 2 minutes. The postictal phase will follow the seizure. During this phase, the patient is questioned, and patients may experience amnesia of the seizure event, confusion, lethargy, muscle cramping. Psychosocial side effects may also occur, such as embarrassment. Consideration of the person who has history of seizures must occur. The patient may be embarrassed of the episode if they seizure happened in a public or hospital setting. Muscle pain is the result of the severe spasming of the muscles. The consequences of seizures may be severe. The **status epilepticus** is due to a tremendous increase in adenosine triphosphate (ATP). The cerebral oxygen consumption and blood flow increases, and the available sources of glucose and oxygen are depleted. The severe seizure may also produce hypoxia, acidosis, and lactic acid or lactate accumulation. This may result in brain injury and destruction and cellular exhaustion and destruction. Other consequences of status epilepticus, besides injury to the brain, injury to the body may occur from trauma. Patients may unconsciously bite lips or tongue and may experience vertebral fracture. Psychosocial consequences of the disease may result in strain on the relationship and alienation of the patient because of their disorder. Epilepsy can be classified into three different types.

Idiopathic epilepsy is characterized by neurogenic abnormalities or genetic abnormalities; however, the exact cause is not identified. Patients with idiopathic epilepsy may

have a family history or family members with this type of epilepsy **Symptomatic epilepsy** is related to some type of lesion and cryptogenic. Epilepsy is characteristic with an aura. An **aura** is a sensation that the patient may experience that predicts that an epileptic episode may occur soon. Some patients may not experience the aura and the seizure may start quite suddenly. The aura is some type of warning to the patient and some patients will choose to take protective measures especially if they are alone to avoid the seizure. This could include medication to safe positions.

Mental Confusion and Dementia. Acute confusional states occur secondary to external factors such as drug intoxication, some type of metabolic disorders, or a neurologic system disease. Confusion may also present with a urinary tract infection. When a disruption of the reticular activating system of upper brainstem occurs, the patient may experience acute confusion. The **acute confusional** state may have abrupt onset and is a differentiation from a disease that manifests itself over long period of time such as dementia. The acute confusional state may happen to a patient who has no previous history or have no symptoms. The abrupt onset is one of the main characteristics of that concludes no organic disease, but a secondary consequence such as a urinary tract infection or metabolic disturbance. When talking about dementia, this is a progressive failure or progressive disturbance of cerebral functions. There is no impaired level of consciousness or altered mental status at this point may not be so significant. In the beginning of the disease especially there is no impaired level of consciousness. There is cortical classification that include Alzheimer's and Picks disease, and subcortical classifications such as Parkinson's Disease and Huntington disease. A mix type of cortical and subcortical classification includes infection and Creutzfeldt Jakob disease. For individuals with cortical dementia such as Pick disease, they may have abnormal tangles or substances called Pick bodies or Pick cells inside neurons in the areas of the brain that sustained damage. Pick cells are cells that contain abnormal protein called tau- this can be found in all types of cells. However, persons with Pick's disease has and abnormal production of this protein. Pick disease is very rare and is much more devastating than Alzheimer's because it affects younger group of population. The disease can start as early at 20, but the average age is around mid-50's and has progressive characteristics. The patients may experience symptoms or behaviors that may be typical for Alzheimer's disease as well as difficulty in social settings, keeping a job, inappropriate behavior. Unlike Alzheimer's disease, Picks disease results in personality changes while Alzheimer's results in memory loss.

Alzheimer's disease can be divided into familial, early and late onset, and non-hereditary sporadic or late onset. In a familial type of disease, there is a strong genetic component compared to a non-hereditary there is no evidence that anyone in family had onset of the disease, but the genetic component is still present. Alzheimer's disease is a combination of genetics, lifestyle, and environmental factors unlike to popular belief that Alzheimer's is only the reflection of genetic predisposition. Popular belief is that Alzheimer's is a combination of the above factors, such as environment, lifestyle and genetic composition. The chances of developing Alzheimer's, despite genetic predisposition, is relatively low at a 5%. Patient also will

have a lifestyle, history, and also environmental factors or combination. To develop Alzheimer's disease, an accumulation of clumps of **beta amyloid protein** will occur. These proteins will destroy cells resulting in an interference with intracellular communication and will cause destruction to the cell communication link. The tangles of the **tau protein** will also occur and lead to the cell death. The trademark of Alzheimer's disease is the presence of the beta amyloid proteins. Theories regarding the alteration of apolipoprotein E and pathologic activation at MNDA exist.

Senile plaques and neurofibrillary tangles from tau proteins, and plaques, beta amyloid plaques can hinder the functioning of the brain and result in the development of forgetfulness. In Alzheimer's disease, the first symptom is the memory changes, memory loss, and then personality change, problem-solving abilities, and judgment will decline. A classic example of a declining task is *balancing a checkbook*. When balancing a checkbook, a person must use complex thought to complete the task, even if it is a task that they have done before. If a patient cannot balance a checkbook, this may be a sign of the onset of Alzheimer's disease. However, with the development of online banking, the universal balancing a checkbook test, may not be an appropriate screening for testing the onset of Alzheimer's disease. Alzheimer's disease is a diagnosis of exclusion and can be made by ruling out other causes of dementia. However, a true diagnosis can be made only by **autopsy** when the neurofibrillary tangles are present in the brain. It can be easy to describe a patient as having Alzheimer's disease because of their age. However, the cause can be several different things especially when the onset of mental confusion is rapid. The patient deserves and warrants a thorough evaluation of other causes that can be metabolic or other neurologic diseases such as Parkinson's disease.

Another type of dementia is **HIV related dementia**. This type of dementia may affect anyone who has history of HIV. This disease runs somewhat similar to Alzheimer's disease in the way that it is very unpredictable. While in Alzheimer's disease, there is stages of development and a timeline of progression, but with HIV related dementia the development may be very rapid, but the result will be the same- the patient will present with cognitive system deficits. Memory is one of the deficits, and it is similar to memory loss in Alzheimer's disease as well as the loss of balance, ataxia, and generalized hyperreflexia. Parkinson disease is a result of degeneration of basal ganglia and corpus striatum and involves a dopamine deficiency. The patient will have a **dopamine deficiency** and treatment may be focused on several different agents that may replenish the dopamine deficiency or make dopamine production or availability higher. The patient will present with rigidity, brady kinesia, tremor, postural abnormalities, shuffling gait, autonomic and neuro endocrine disorder. The endocrine disorder is one of the autonomic disorders that may result in abnormal sweating and cognitive affective symptoms.

Patients with Parkinson's are also very prone to developing depression. Treatment involves treating the dopamine deficiency and trying to alleviate the symptoms. Parkinson may lead to development of dementia. Approximately half of the people who are diagnosed with

Parkinson's disease may have depression. Depression may not improve because some of antidepressants may work on dopamine re-uptake, and other patients may develop dementia. Some patients are institutionalized in skilled nursing facilities. The progression of the disease leads to disorientation, confusion, and memory changes. Patients can be distracted, have difficulty with the concept of judgment, and thinking. The dementia related to Parkinson's disease may be similar to Alzheimer's disease. When a patient with Parkinson's disease develops dementia, there is no steady progression to a worse state, but eventually, symptoms will worsen. The patient may have better days or worse days. The patient may also have anxiety disorders or impulse control disorders. These disorders may be related to dopamine deficiency. Motor behavior is also impaired, and patients will develop stereotypic motor behavior that includes a fascination with repetitive handling and examining mechanical objects. Daytime sleepiness can also be a symptom. Gait can also be affected.

Cerebral vascular accidents (CVA) can be divided into three main categories: Thrombotic stroke, embolic stroke and hemorrhagic stroke. A **thrombotic stroke** occurs within the brain and is due to a blockage formed within the brain, arteries supplying blood to the brain, or in the intracranial vessels. A **transient ischemic attack (TIA)** is a small thrombotic stroke that resolves itself within 24 hours. An **embolic stroke** is very similar to thrombotic stroke, but embolic stroke is the consequence of traveling thrombus or traveling clot which called an embolus. When the thromb is dislodged from another place in the body, such as in deep veins in lower extremities, it travels to the brain. A thrombotic stroke is due to a clot formed inside of brain and an embolic stroke is due to a clot that comes from somewhere else. A **hemorrhagic stroke** is a stroke that is caused by excessive bleeding in the brain and damage to the blood vessels secondary to hypertension, or any other factor that may disturb the blood flow. The main concern with a hemorrhagic stroke is ischemia caused by excessive pressure that can lead to infarction. **Lacunar strokes** are typically small strokes, and the lacunae is a small absent matter in the brain. The lacunar infarcts are silent, but on radiographic examination they are possible to see.

Aneurysms are formed in the vessels in the brain and result in a rupture. Aneurysms are diagnosed by imaging studies and treatment will include prevention of the rupture and stroke. One treatment included using a small clip in attempt to isolate the aneurysm.

Vascular malformations include cavernous angiomas, capillary tangel ectasias, venous angiomas and arteriovenous malformations or AVM s. Vascular malformation is not as common an occurrence as aneurysms, cavernous angiomas, or collections of blood vessel. Cavernous angiomas has n o interference with normal brain tissue and rarely results in a hemorrhage. **Telangiectasiasis** is dilated capillaries; it can be seen on the integumentary covering on the skins, and when in the brain it may interfere or intercept with normal brain tissue, however, hemorrhage is rare.

Venous angioma can present as a vascular malformation and rarely will result in a hemorrhage. This is one of the most commonly found disorder or venous malformations or

vascular malformation when an autopsy is performed. AVM, arteriovenous malformation, can occur in the brain or in other parts of the body such as gastrointestinal tract. The arterial vascular malformation is arteries tangled into the vein and is malformed vessels. There is no capillary network, but the veins are fed into the artery or vice versa. This formation may rupture and cause a hemorrhagic stroke. On evaluations, AVMs will be remarkable for systolic bruit and when the carotid arteries are auscultated bruit may be experienced. Other sources recommend to acetate the eyeball; if you hear the bruit, this may be a sign of AVM. Treatment includes surgical excision, embolization and radiotherapy. Treatments are effective and reduce risk of a hemorrhage. A **subarachnoid hemorrhage** is a condition that should be treated rapidly. If a rupture of the blood vessel occurs, blood can escape into the subarachnoid space and settle causing an inflammation response by irritating the meningeal and other tissues in the brain. Intracranial pressure (ICP) will also significantly increase because of the pumping action of the heart. At some point the ICP will reach diastolic levels which is high and will eventually return to normal. Patients with a subarachnoid hemorrhage may present with infarctions in the brain on a radio graphic examination. The patient may have an altered mental status, nausea, vomiting, neurologic deficits, knuckle rigidity and complaints of a throbbing or explosive headache. The patient may also present with positive Kernig sign and Brudzinski sign. The **Kernig sign** refers to the producing pain in the back neck from straightening the knee with the hip. The **Brudzinski sign** is a passive flexion of the neck that produces neck pain and rigidity. Treatment of a subarachnoid hemorrhage is directed to prevention of a cerebral ischemia and may include surgical treatment to correct the vessel dysfunction or abnormality. Risk factors may include familial history.

Headaches are one of the most commonly diagnosed condition. There are four types of headaches. **Migraine headaches** present with trigger factors and may have an aura or warning. Migraines are usually unilateral and may be severe. They can also be sensitive to noise and light, and patient may also have nausea and vomiting. **Cluster headaches** are most common in male patients, while migraines are most common in females. Cluster headaches are typically unilateral and may also have a trigger. However, cluster headaches will not have an aura and may spontaneously resolve; the patient may have several attacks in one day and then experience a period of remission. Some of the most common triggers of cluster headaches include hunger. **Chonic paoxysmal hemicrania** is a type of cluster headache that occur in a higher frequency, but it will have shorter duration, and unlike a typical cluster headache this may be experienced more often by women. Tension type headaches are the most common and are bilateral. If a patient complains of having a headache or migraine in which the whole head or forehead hurts, it is most likely a tension headache. Triggers may be present and have chronic characteristics. Chronic characteristics are diagnosed if the headache occurs at least 15 days a month or half of the time during the month. A patient can be diagnosed with a chronic condition if it occurs over a long duration of time. Headaches can be treated by NSAIDS, over-the-counter medications, and prescription preparation. Tension headaches have a relation to the contraction of the jaw and neck muscles. The exact mechanism is unknown, but some

treatments include Botox to paralyze the muscle and prevent headaches. Many medications available over the counter and prescriptions on the market to treat headaches, but again this is one of the most common conditions diagnosed. In review, migraine headaches are usually unilateral have an aura, sensitivity to light, nausea, and vomiting. Cluster headaches are unilateral and have no aura. **Tension headaches** are bilateral and usually related to some type of muscle tension.

Meningitis is an acute inflammation of arachnoid and Pia matter that surrounds the brain and spinal cord. It may lead to increased cerebrospinal fluid production and increase in intracranial pressure. **Bacterial meningitis or meningococcal** may be considered a medical emergency; the mortality rate is relatively high at 25 percent. **Viral meningitis** is a limiting condition that will not require treatment. Meningitis can be caused by again bacteria, viruses, micro bacterial fungal infections, amoebas, cancer, or other known infectious sources. The most common entry way is respiratory system. Symptoms that may occur include headache, nausea, vomiting, and constitutional symptoms like fever, loss of appetite, and phobia. Headaches are a result of an increase in intracranial pressure. Patients may also have nuchal rigidity and resistance to flexion of the neck; these are the positive Kernig and Brudzinski's sign. The patient may even develop seizures and petechiae with meningococcal meningitis. Meningococcal meningitis is one of the less common types of meningitis but has a high rate of mortality. Treatment should include a cure for the meningitis and treating the Brudzinski sign. If a patient presents with a headache, nuchal rigidity, and carrying Brudzinski's signs positive, they have petechiae. The brain can tolerate this for some time, but unfortunately, if the treatment isn't initiated fast enough the patient may have devastating consequences. Changes in level of consciousness may also occur; this may be the first initial sign followed by headache, nuchal rigidity, and petechiae. These symptoms can occur simultaneously and result in strange behavior form the patients or levels of consciousness affected. Vaccination is important and recommended for bacterial meningitis especially for individuals living in crowded conditions. For bacterial meningitis, antibiotics and antipyretics may be required depending on the cause. Some patients may need treatment for pain management. Surgical intervention including drainage is rarely needed.

Encephalitis is an inflammation of the brain parenchyma. Often, the meninges are also involved as well as the cerebrum, brain stem, and cerebellum. In the case of encephalitis, hemorrhage edema and necrosis may occur in cerebral hemispheres. Encephalitis is different from meningitis because the cerebral function changes. Encephalitis is most commonly caused by arthropod borne viruses, herpes, simplex viruses. Viral encephalitis is due to the vector, and the patient may experience fever, headache, nausea, vomiting, altered cerebral functioning, altered mental status, motor deficits, and weakness or paralysis. Encephalitis may result in an altered mental status confusion but does not affect the level of consciousness like meningitis. Patients with encephalitis may need antipyretics, analgesics, sedatives, and corticosteroids. The patient will require ICP monitoring and may need other invasive methods to introduce antiviral treatments if a viral infection is the cause. If a viral infection is present, it is most likely the West

Nile virus infection. The patent may present with brain herniation as a complication and needs to be treated rapidly. The patient will require continuous monitoring of intracranial pressure, lab values such as CBC and ICP measures, may need extensive interventions. Patient may have a severe or mild case. This may also result in a rather challenging period for the family and patient while the rapid decrease in cerebral function and altered mental status occur.

Lyme disease is a disease that was discovered in 1975 in the town of Lyme, Connecticut. The disease is most prevalent in the Northeast. It has become the most common tick-borne disease in the United States. When diagnosed it is often a consequence of tick bite. The tick does not cause the disease, but the tick is a vector and carrier of the Borrelia burgdorferi bacterium. The tick transmits the borrelia burgdorferi to humans. The time it takes for the bacteria to incubate can be on average 3 to 32 days. The bacteria can affect any organ and can cause a variety of symptoms such as flu like symptoms, constitutional symptoms such as chills, fever, and malaise. The patient may also develop arthralgia. The most common sign of Lyme disease is the bullseye which is a reddened circle with a light-colored center that appears within days or weeks of the bacteria incubating. The bullseye rash is the first state of the disease. During the second stage, the patient may develop cardiac and neurological manifestation and complain of chest pain or soreness, rib soreness, and shortness of breath. The patient may also complain of palpitation, develop arrhythmias, cardiac blocks, murmurs, and valvular prolapse. Cardiac echocardiogram may be necessary for diagnosis. Neurological symptoms such as twitching of the face, spontaneous tremors, Bell's palsy development of facial paralysis, paresthesias, headaches, confusion, cognitive difficulties, difficulty in concentrating, reading, poor short-term memory, and disorientation may occur.

Multiple sclerosis is a disease characterized by the degeneration of the myelin sheath in the central neural system. It is the most common case of neurologic disability among young and middle-aged adults; typical onset is between ages 20 and 45. There is some genetic component in multiple sclerosis inheritance, however, there is no direct inheritance. It has been suggested that second- and third-degree relatives of person with multiple sclerosis are at increased risk of developing MS. When the **demyelination** of subsequent degeneration of neural fibers in SNS happens, the patient may start experiencing symptoms. Symptoms are a result of the nerve being demyelinated and resulting in the improper conduction of electrical signals. Different conduction abnormalities can occur and are measured by testing changes or decreases in conduction velocity and conduction blocks. The location and size of the lesion can also have an effect. The abnormality of demyelination causes a disappearing or decreased sped of the neuron's signal. The signal either will slow down or be completely will be blocked.

Multiple sclerosis is an autoimmune disorder. A lymphocytic invasion of the lesion occurs as well as demyelination. Lymphocytes may invade the lesions resulting in evidence of antibody mediated damage and damage to the myelin proteins. When examining the nerve, hard or sclerotic patches are visible in the white matter even without a microscope. The patches are called plaque, and they can appear anywhere in the brain, brain stem, cerebellum,

and spinal cord. If the plaque is fresh, evidence for an active myelin breakdown may be present. An **MRI** is one way to diagnose and evaluate for MS. It may show two types or two states of lesions. It may also show the inflammatory component found in stage one and they formation of scars from the demyelinated nerve that occurs in the second stage. The **demyelination** prevents nerves from conducting a signal normally. This results in neurologic symptoms as well as speech and swallowing problems, visual problems, abnormalities in gait, paresthesia's, disturbance of visual field, and diplopia. The patient will progressively worsen. There are several types of multiple sclerosis. **Remitting** of the disease is characterized by episodes. The patient present with acutely worsening symptoms and then experience a relapse or fairly stable period of time. In the **secondary progressive disease**, gradual deterioration, neurologic deterioration, and possibility of relapse may occur. In the **primary progressive disease,** there is a continuous neurologic deterioration from the time the symptoms start. Remitting includes a patient having episodes of acute worsening symptoms and then returning to a stable phase, and then worsening. Secondary progressive disease is a gradual worsening with the possibility of a relapse. Primary progressive disease is the continuous neurologic progressive worsening from the time that symptoms appear.

Amyotrophic lateral sclerosis is a devastating neurodegenerative disease. It is also referred to Lou Gehrig's disease, and named after the famous baseball player. This disease effects individuals in their late adult years around 50 to 60 years of age. The disease is very progressive and from the time of onset of symptoms the life expectancy is approximately two to five years. The disease is characterized by the death of the lower motor neurons. As the lower motor neuron is dying, innervation occurs and results in no nerve connection to the muscles. This causes muscle mas or the muscle fibers to shrink and results in atrophy. This type of atrophy is secondary to the death of the nerves. Denervation is referred to as Amyotrophy, and therefore the disease's name is Amyotrophic lateral sclerosis. The term lateral sclerosis reflects the structure of the nerve fibers in lateral columns of white matter of the spinal cord which are affected and lost. The disease does not affect intellectual abilities, regulatory mechanisms of coordination, or control of movement and sensory systems. The neurons of the ocular system are also parasympathetic neurons. The ocular mobility in the parasympathetic neurons in the spinal column is also spared. The cause of this disease is uncertain; some evidence of familial history has been shown. There are several mechanisms of ALS that occur and lead to a possibility of injury to the nerves through the glutamate gated ion channels. These channels are distinguished by sensitivity to the N-Methyl D aspartic acid. One theory disclaims this a cause of the disease, but other immune sources describe or suggest evidence that disease will not respond to a suppressant and may not be autoimmune. However, there is no cure for the disease. Care is palliative and includes rehabilitation techniques. Patients who cope and maintain independence as long as possible will prolong survival. An anti glutamate drug such as Riluzol is FDA approved for treatment of the disease, but the drug only prolongs survival by three to six months. Patients will experience atrophy of the muscles, but intellectual abilities will not be affected. Symptoms of ALS will result in muscle deficits and patient develop

dysphasia or dysarthria. Dysarthria is an inability to talk or articulate speech movement due to too weak muscle tone or too high. In rehabilitation, during evaluation and treatment it is important to involve an entire healthcare team that includes auxiliary services such as speech therapy and physical therapy. The goal of treatment is to prolong the survival time and improve or maintain quality of life.

Neuropathies are peripheral nervous system disorders. Neuropathy is not a single disorder, but a collection or cluster of disorders that result in neuropathy. **Guillain-Barre syndrome** is an acquired inflammatory disease that can be described as an acute immune mediated polyneuropathy. It is clinically defined as a rapid progressive weakness of the limbs and loss of tendon reflexes. The syndrome is the most common cause of acute paralysis. There are several types of Guillain-Barre syndrome, but the most common has an immune component. It is due to some type of exposure to virus or an offending. To determine diagnosis, a epidemiology study is done to link the infection to Campylobacter, Cytomegalovirus Epstein-Barr, and Mycoplasma. Often, patients will report having flu-like illness. Prior to the onset of symptoms, some patients will have antibodies against gangliosides which may be consistent with infections or campylobacter. The disease results in a progressive ascending muscle weakness of the limbs that produces symmetric flaccid paralysis. Paresthesia will occur as well as a rapid loss of motor function, however, progress of progression may vary. Disproportionate involvement of upper or lower extremities may occur. Paralysis in ascending cases will progress upwards. This can present with symptoms involving the respiratory muscles. The autonomic nervous system may also be affected and result in cardiac arrhythmias. Autonomic dysfunction symptoms such as sweating and facial flushing, urinary retention, postural hypertension may also occur. Patients may have a significant amount of pain. Guillain-Barre syndrome is a medical emergency, but it is treatable. Approximately 90% of individual effected achieve a full recovery. Recovery may take up to a full year to recover. The patient may require ventilator support and support of other vital functions as treatment.

Myasthenia Gravis is a chronic autoimmune disease that effects neuromuscular junction. This disease results in a breakdown in communication between motor neuron and the innervated muscle cells. The disease effect individuals who are in their twenties and thirties and is more common in women. Because it is an autoimmune disease, it is caused by antibody mediated destruction of acetylcholine receptors. The receptors are located in neuromuscular junction. The exact mechanism is unknown, but the cause is believed to be related to abnormal T lymphocyte function. Often individuals will also present wit thymus abnormalities. The symptoms of Myasthenia Gravis will involve the patients having less acetylcholine receptors in postsynaptic membrane. The release of acetylcholine from the presynaptic membrane will result in lower end plate potential. The muscle will present with weakness and fatigue when the patient I trying to make a movement or use the muscle. First symptoms may occur in the ocular muscle. Myasthenia Gravis may present with sudden exacerbation of symptoms. This is referred to as a **Myasthenia Crisis**. A **crisis** is a condition when the ventilation is affected due to stress. This can include emotional stress, infection, excessive alcohol, or surgical intervention.

Treatment involves a replenishment of acetylcholine. If stress is too high, acetyl-choline esterase drugs may not be enough. If the patient receives an acetyl-choline esterase test, Tensilon will be used. **Tensilon** is a drug that inhibits acetyl cholinesterase. It is used for treatment of Myasthenia Gravis and clears symptoms completely. A positive Tensilon test is a diagnostic method for Myasthenia Gravis. Electrophysiology studies can also be done to demonstrate how muscles do not respond to stimulation of motor nerves to diagnosis. Pharmaceutical treatments involve immunosuppressive therapy and corticosteroids. This involves using mediation that affect cholinesterase such as Tensilon. Removal of the thymus gland may be a treatment method; however, it is controversial due to its unproven link to the disease.

Mental Health Disorders

Schizophrenia is a type of psychosis and is a collection of thought disorders. Psychotic individuals may have delusions, hallucinations, impaired coping skills, and impaired communication. Swiss psychiatrist Eugen Bleuler used the term schizophrenia first time in 1911, but the disease itself was first described and distinguished as separate mental illness by Dr. Emil Kraepelin in 1887. During that period, the term was Dementia Praecox, and Kraepelin described the symptoms of Schizophrenia. Through the centuries, people have described symptoms of Schizophrenia. Sources begin with ancient Egypt, and there are descriptions of symptoms that are similar to symptoms of Schizophrenia. Symptoms often appear in an individual's teenage years to mid-twenties. However, it is not uncommon if a patient in diagnosed with Schizophrenia at an older age. The patient develops the disease and will lose touch with reality. Individuals will replace reality with an imagined or fantasy realty. The patient truly believes in this reality and will have mood or affective disorders.

Affective disorders involve emotions and the outward representation of emotions. When discussing and person's emotions that is referred to as a **mood**, but the representation of those emotions if the **effect**. **Effective states** are brief emotional feelings that are somewhat visible and manifest within the patient. Effective states can be observed in the patient, but their mood is a result form the sustained emotional state. Often healthcare professionals fail to recognize that people experience times of sadness and extreme happiness during appropriate events and may misdiagnosis. For instance sadness after the death of beloved family member. However, if an individual's displays emotions that are not appropriate for an event, or the mood lasts for very long duration of time, or mood changes are extreme in nature then a mood disorder may be suspected. Every individual reacts differently, but **extremes** in mood changes can be diagnostic for mood disorders. An example of a mood disorder is manic depressive disorder or bipolar disorder which alternates between a manic and depressive state.

Depression is a prolonged feeling of extreme sadness, and unhappiness, despair, and discouragement. Healthcare providers need to differentiate depression from grief. Grief is a realistic sadness related to a loss. This can include a personal loss of another person or animal. A patient may grieve because of a loss of function or loss of limb. Prolonged grief may become

depression, and if a person is not able to cope with their loss, they may experience symptoms of depression. Genetic manifestations may also be a factor as well as biological and environmental factors. In some cases, depression can be caused by a single factor and in others it is multiple factors. The exact cause of why an individual develops depression is unknown. Heredity personality may be a cause along with environmental factors.

Situational depression is a different type of depression. It occurs as a reaction to a situation. If an individual's reaction to a situation is prolonged, this could be due to situational depression. Medical conditions can affect development of depression. Hypothyroidism is an example. When people develop this condition, they often develop depression and suicidal thoughts are common. The symptoms are reversed with levothyroxine or Synthroid is used treatment. There is a strong correlation between hypothyroid state and depression.

Substance abuse can be another source of **depression.** Dietary deficiencies such as Folic acid and B12 and gender is a risk factor for depression. Females are at more risk to developing depression than males. Elderly-age, socioeconomic status, income level may also be factors of depression. Extreme weight loss can result in depression as well as social isolation. The cause and consequence of social isolation are hard to identify but may accompany individuals who live alone. Individuals who experience depression have feelings of rejection, helplessness, and worthlessness. These individuals will be uninterested in their surrounding or in events that were once pleasurable.

Anhedonia is a term used to describe the patient's loss of interest in previously pleasurable activities. Irritability, suicidal thoughts, easily crying, and lack of or excessive sleep are symptoms of depression. Depression may occur during critical periods in life. It can occur and affect puberty in adolescence, during menopause, retirement, or entering into new work environment. Diagnosis of depression includes a medical physical examination, a questionnaire, and lab work. Depression is a *Diagnosis is of Exception*, and any organic source of depression must be ruled out.

Besides the depression, the cohort of mood disorders can include **seasonal affective disorders**. This is speculated to be related to circadian rhythms of the person, and treatment usually is the same as depression. Some activities for treatment may involve mimicking the longer duration of daylight, especially during the winter months. Bipolar disorders are due to a genetic component, and treatment may include mood stabilizers as well as antidepressants. The use of antidepressants in bipolar treatment is somewhat controversial because they may exacerbate the manic episode.

The **antidepressant medications** work by altering a pathway of communication between the synaptic cleft and as a result different neurotransmitter may be affected. The SSRI interrupt neurotransmitters' reuptake in the synaptic cleft. The sufficient amount of neurotransmitter provides the halting of the depressive symptoms. There are three major classes of antidepressants. Medications that are Monoxidase inhibitors are very seldom prescribed

because of the side effects and possibility of adverse effect such as overdose. Amitriptyline is a medication that is often not prescribed. This medication is often prescribed for sleep disorders. **Selective serotonin reuptake inhibitors (SSRI**) is the main treatment for anti-depressive therapy. These medication work in a single synaptic cleft and inhibit the reuptake of serotonin. SNRI is a subcategory of SSRIs, but it is a drug that acts similarly by affecting the reuptake of the neurotransmitter, but this drug affects several neurotransmitters. SNRI can cover norepinephrine serotonin as well as dopamine. As a result, they are used to treat not only depression but also anxiety.

Anxiety disorders is the condition that can be considered as a deviation from a normal anxiety presentation. Normally anxiety is a response to stress which induces a fight-or-flight response in some individuals, but for others, anxiety may become a chronic problem. The individual may experience anxiety that is exaggerated or inappropriate to the situation. Anxiety disorder was previously referred to as neurosis. Anxiety affects the largest number of people of any mental health disorder It's truly the largest mental health disorder in the United States. The cause of the anxiety disorder is unknown, but genetic factors, stress, environment, chemical alterations, and physical factors may be causes. Physical causes of anxiety can be better studied. For example, Hyperthyroidism can have an effect on the development of anxiety in a patient. Anxiety has several types and different manifestations. An extreme manifestation of anxiety disorder is panic disorder.

Panic disorder is a state of extreme and uncontrollable fever which may be referred to as a panic attack. It is usually a very sudden onset and peaks in minutes. The patient may experience a feeling of impending doom and may want to escape of run away. **Psychosomatic manifestation** may also be present and present with diaphoresis, chest pain, and tachycardia. The patient may also have a sense nausea and disassociation. In a **generalized anxiety disorder (GAD)**, feelings of excessive worry are a continuous state of mind. Intense anxiety is not related to a specific event. GAD is characterized by a state of constant anxiety that may lead to somatic manifestations such as nausea, vomiting, diarrhea, dryness of mouth, tachycardia. In these exaggerated states, patients live on the edge and are always anticipating some impending drastic event.

Post-traumatic stress disorder (PTSD) is the development of the reaction as a response to psychologically stressful event or an event that the person could not control and was outside of normal human experiences. PTSD is a relatively new addition to the classification of anxiety disorders. It may be observed in war veterans, victims of rape abuse, or survivors of natural disaster. Individuals who are often in extreme situations such as policemen and firemen are at a higher risk for developing PTSD. Symptoms may occur immediately after the event or dormant until several months after the trauma. Diagnosis in a post-traumatic stress disorder includes a thorough physical examination to rule out other physical or organic conditions that may result in the development of similar symptoms. Diagnosis is established also by confirming the history of symptoms and confirming no other conditions are present. Treatment may include stress

reduction, hypnosis, relaxation, exercise therapy, biofeedback, and medications. Treatment with antidepressants may be beneficial. Some studies suggest that rapid debridement after being exposed to a traumatic event, will have higher results versus debridement after a few days when the event occurred.

Obsessive-compulsive disorder is an anxiety disorder with two major components. **Obsession** is a repetition of a thought or emotion and **compulsion** is repetitive act. This disorder affects the individual in a way that person cannot resist not performing that act or get rid of the thought. With OCD, the person is unable to stop the thought, or the action resulting in the behavior becoming some type of ritual. Thoughts or attempts to stop the ritual may result in extreme anxiety. The behavior may become time consuming. In some health care providers, handwashing can become obsessive compulsive behavior, and may become disruptive to job activities. Treatment will include anti-anxiety agents, and sometimes SSRIs or even SNRI'S may be prescribed. The results can be reassuring with treatment of SSRIs. Psychotherapy may also be beneficial.

Musculoskeletal Disorders

Trauma is the leading cause of death among young people, ages one to forty-four years old. Trauma is not discriminative based on race, socio-economic status, or national origin. Other alternation can happen in the bones, joints, and muscles. These disorders are not caused by external factors like trauma and other musculoskeletal injuries but are caused by internal factors. These factors may include distorted metabolism, infections, inflammatory, non-inflammatory disease, malignancies, tumors, and non-malignant tumors. A **fracture** is a break in the continuity of the bone; the bone is not completely broken, but there is complete detachment. A **break** can be a greenstick fracture where part of the bone is still attached with some type of crack. In some types of breaks, a distortion or disruption may be present in the continuity of the bone. A diagnosis of a cracked bone is colloquially an incomplete fracture. A fracture will occur when force is applied that exceeds the tensile or compressive strength of the bone. The term tensile refers to tension or compression that the bone cannot sustain. Elderly individuals may develop features than those who are younger. The causes may be benign like falling that may result in a femoral fracture. Younger athletes may sustain numerous falls and have no trauma. This is attributed to the aging process. Different age population will have different strengths in bone and a different ability to sustain trauma. Fractures can be classified in several ways. They can be classified as conditions based on the condition of the overlying skin- closed, open, complete, or incomplete.

A **closed fracture** is when no visible bone is puncturing the skin. If the bone is protruding through the skin or if an object has punctured the skin resulting in an opening that hits the fracture site, it is an **open fracture**. An open fracture is not just characterized by a bone coming out. Open fractures are also referred to as compound fractures because they are not only a

fracture but open skin. When the skin is no longer intact, it is a compound fracture. A **complete fracture** occurs when the fracture goes completely through the bone. An **incomplete fracture** is when the bone is not fractured in two and is still connected. If there are more than two ends of the fragments, the break is a **comminuted fracture.** If the bone is somehow sustained, like a nice clear-cut break, it is a **linear fracture**. An **oblique fracture** runs in a transverse pattern, a **spiral fracture** will twist around the bone. A spiral fracture is a disturbing sing if found on an infant or toddler; it typically is a sign of abuse. Fractions can also be classified by differentiate of location and how the fracture goes through the bone.

A **transverse fracture** will cut across at a 90-degree angle. It is opposite of a **longitudinal fracture** that runs the length of the bone. A greenstick fracture or call it Torus fracture is an incomplete bone break and is a bowing of the bone without visible breaks. Cracks and changes occur in the bone. Torus fracture is a greenstick fracture that usually occurs in children because of their soft, non-completely calcified bones. It is more difficult to break a bone completely resulting in a transverse fracture.

Pathologic fractures are typically related to a pathologic process such as hypercalcemia. This condition results in calcium being stolen from the bones and can result in a deficiency of vitamins such as vitamin D. Pathologic fractures have some underlying cause such as a cancer, tumor, or other conditions. Stress fractures are another class of fractures that are repetitive. With repetitive use, tiny cracks will occur in the bone. **Transchondral fractures** are a type of stress fracture of the articular surface of the bone. It is a result of force that is transmitted from the articular surface of the bone, across the joint, through the articular cartilage, and to the subchondral trabecula of the fractured bone.

Open fractures are an important physiological or paraphysiological phenomenon because the continuity of the skin is disturbed and allows open access to the bone. This can result in an osteomyelitis if not treated rapidly. A pathologic fracture is due to some type of tumor or degeneration of the bone. When segment of the bone is present, it may be more difficult to repair the fracture. The healing process is dependent upon the number of segments present, but because of modern technology such as open reduction and internal fixation repair is possible. Spiral fractures, transverse fractures, greenstick fractures, and impact fractures are the most difficult fractures to heal because the femoral head is affected. In the past, these types of fractures resulted in a severe handicap or loss of mobility, but because of modern technology treatment is possible. Treatment may include a partial or total hip replacement that can result in a sufficient degree of mobility; however, baseline level of mobility may not be achieved.

Bone fractures may also cause **damage to surrounding tissues**, periosteum blood vessels, and the cortex and bone marrow. This damage can result in hematoma formation and initiation of the inflammatory response. Procallus formation may also occur and result in incorrect healing. For healing, the bone or fractures needs to be set correctly by a cast splint or surgical procedures such as open reduction internal fixation. A patient with bone fractures may

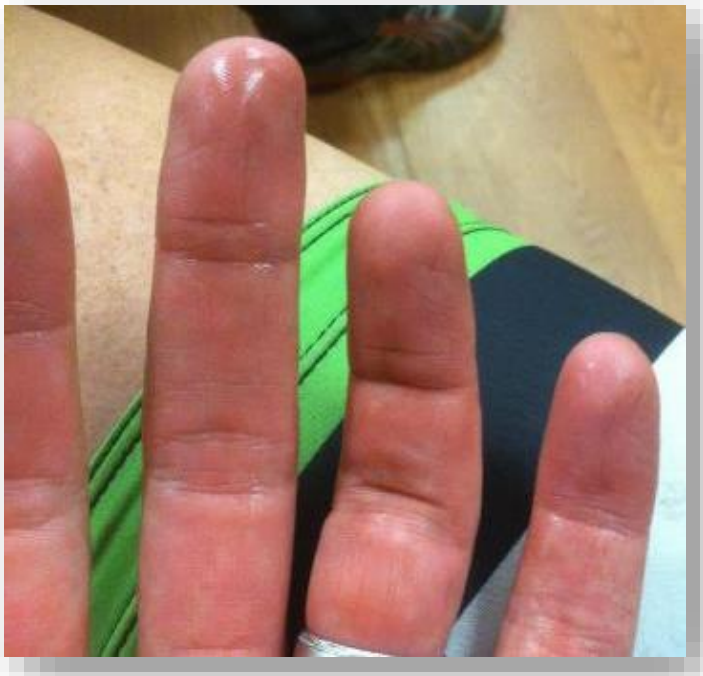
present with unnatural alignment, edema, swelling, muscle spasms, tenderness, pain, impaired sensation. Impaired sensation is a consequence of nerve compression. Nerve compression is the consequence of edema or trauma to the nerve from a broken bone.

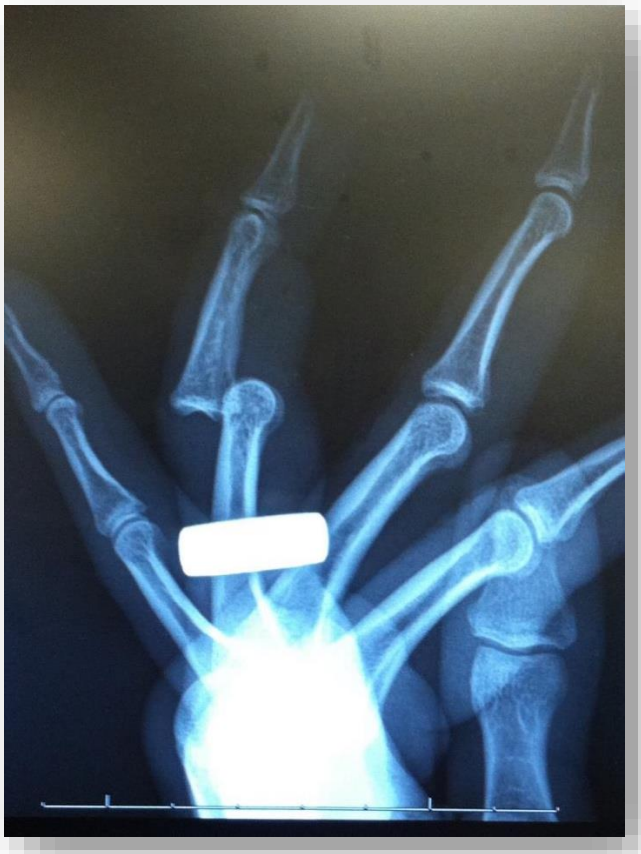
Treatments for a bone fracture may involve manipulation or closed manipulation which includes aligning the bone, with a cast or splint. When the bones are severely misaligned, the bones may need to be pulled apart due to a union in an inappropriate angle.

Open reduction is another treatment option that involves creating and incision and fixating the bone with an internal device such as plates, screws, or rods. Open reduction typically results in a quicker recovery time and improved functionality after surgery. If the reduction is improper, complications such as non-union, delayed union, or malunion may occur. All these complications may result in severe impairment of mobility and severe reduction of the quality of life of the patient. When **non-union** occurs, the edges of the bone fail to grow together. This results in a gap between the broken ends of the bone that will fill with fibrous and cartilaginous tissue. The gap will not be functional. A fluid-filled sac may also fill the space and create a pseudo joint, pseudarthrosis, or false joint. A fiber will be created, and the fluid will act as a synovial fluid and fill the space. Because it is not a joint, it will not have a function, but will cause complications. Malunion occurs when a fracture results in the bones uniting an inappropriate angle. Malunion will result in no function of sustaining mobility. A delayed union of the bone occurs when the time of the union takes longer than usual.

Dislocation and Subluxation are displacements of the bones, but dislocation results in displacement and loss of contact between articular cartilage and articular surfaces. Subluxation results in a partial loss contact between articular cartilage and articular surfaces. Both, dislocation and subluxation occur with fractures, muscle imbalance, joint instability, Rheumatoid arthritis, and other causes of joints becoming more or less lax. Trauma, a fall, and excessive force in an individual, who otherwise has strong bones and not prone to fractures, may cause dislocation.

The picture and x-ray below are of an individual who sustained trauma on his ring finger. The picture was taken in the emergency room and does not look like a severe trauma. However, the x-ray shows the complete dislocation of the joint. The bone is completely dislocated and there is no connection of the articular cartilage and bones. From the lateral view, the dislocation is easily seen compared to the posterior view. On the lateral view of the x-ray, there is a significant amount of swelling.





Images are cortesy of M. Parsons, Esq.

Support structure injuries include sprains, strains and avulsions. A **strain** is a tear or injury to a tendon and a **sprain** is a tear or injury to a ligament. These terms are sometimes used interchangeably. **Avulsion** is the complete separation of the tendon or ligament from wherever the bone. A strain is one of the most common injuries and is an over stretching injury of the muscles. For example, a patient may have a lumbar strain from lifting too much weight, inappropriate lifting techniques, or repetitive lifting. The back is the most common muscle strain. A complete sprain or complete tear will be avulsion. Sprains most commonly occur during sports activities because of an intense overload of the joints incurs overload of the ligament. The ankle joint is most commonly affected. The pain can become unbearable and result in the ankle not being used. The pain is a protective mechanism that prevents the use of the injured extremity or body part to facilitate healing. Swelling, pain, erythema, ecchymosis due to damage to the capillaries, and hemorrhaging are signs and symptoms of a sprain.

X-rays are used not as a tool for diagnosis of support structure injuries, but to rule out a fracture. A sprain will be diagnosed by exclusion. If there is a suspicion of something else or a complicated sprain, an **MRI or arthroscopy** may be ordered. If an arthroscopy is ordered it will most likely be a repair procedure. Sprains and strains can be treated, especially when mild, by using the RICE principle (Rest Ice Compression and Elevation). Compression is typically an Ace bandage. All these interventions benefit the patient by reducing or eliminating the use of the affected ligament and result in healing. In severe cases, surgical intervention may be needed. It is important to evaluate for fracture if patient presents with sprain because the presentation will be similar with same edema, pain, ecchymosis, and tenderness on touch. So, it's all the same. An x-ray should be done if the patient does not have a severe sprain. If the patient has typical function in the extremity, the **RICE** principle may be applied. If there is suspicion of a complete avulsion, a referral to an orthopedics or emergency services is needed for further evaluation and treatment.

Disorders of the tendons may vary from **tendinitis**, which is inflammation of the tendon, to **bursitis** which is inflammation of the bursa. **Tendinosis** is a painful degradation of collagen fibers. When the tendon by itself is degrading, it may also cause pain. Tendinitis is inflammation of the tendon. The tendon is a connective tissue that may attach the muscle to the bone. Any of these conditions can occur in any tendon, but tendinitis most commonly occurs in the shoulder. It may be caused from overuse, age, and calcium deposits. It may also be associated with bursitis. A patient with tendinitis will present with tenderness over the affected tendon and pain when the muscle is in use or against resistance. Treatment includes RICE, analgesic medications, anti-inflammatory, and NSAID. The patient will benefit from physical therapy and range of motion exercises once the pain is under control. Some individuals will develop adhesions in joints that often require surgical interventions to destroy the adhesions. Strengthening exercises that avoid overuse will prevent this type of injury and tendonitis. Bursitis is inflammation of bursal sac. It is caused by a repetitive motion or overuse.

The joint will be affected. This also most often occurs in the shoulder. Severe pain, immobility due to pain, location, tenderness on palpation are symptoms of bursitis. X-ray testing is used to do a diagnosis of exclusion. The same rules for a fracture apply, but heat is recommended in place of rest. Corticosteroid treatments and surgical treatments can be used in extreme cases. Physical therapy may also strengthen the affected area. Colloquially, bursitis is most commonly referred to as tennis elbow, however, tennis elbow is epicondylitis. Epicondylitis is a type of tendinitis and is inflammation of the tendon in the place where it is attached to the bone. This is an overuse injury and same principles may apply. Rest, physical therapy, steroid injections, and muscle strengthening may help.

Muscle strain is one of the most common injuries and is a severe stretch that stretches beyond normal capacity. It is local muscle damage. It is difficult to distinguish between muscle or tendon strain. A muscle relaxant may or may not be prescribed. Principles of rest, correct techniques of use or movement and lifting can avoid muscle strains.

Rhabdomyolysis is a life-threatening condition that may be related to severe muscle trauma and cell loss. When the content of the damaged muscle is released into circulation (Myoglobin), it will clog the kidneys and tubules resulting in kidney damage. Once reaching this stage, it is an emergency and requires immediate treatment. For individuals who are prone to injuries, such as falls, it is important to reduce the risk for prevention. Other risk factors include alcoholism, use of cocaine, heat stroke, and ischemia.

Osteoporosis is a metabolic bone disease that causes porous bone appearance. The bone loses mineralization and strength and bone density decreases. Osteoporosis is a disease of multifactorial origin. It is also an age-related bone loss will happen in men and women, but mostly women experiencing severe negative consequences of osteoporosis. These consequences include fractures, and during post menopause the risk for a fracture increase. Immobility is another factor that can affect the development of osteoporosis. If patient has a decreased activity level, they may experience osteoporosis. When a woman becomes estrogen deficient after menopause, it may result in loss of density and the inability to retain and absorb calcium resulting in osteoporosis. Hormone therapy is a controversial therapy; however, weight-bearing exercise can slow the progression of osteoporosis. When osteoporosis occurs, the patient may experience consequences related to compression and vertebral fracture in the spine may occur as well as tiny wrist fractures. Compression fractures are common. Compression fractures in the spine may result in a decrease of height or the development of a hump.

A **Dowager's hump** is an abnormal curvature in the upper thoracic spine. Wrist fractures may occur as the disease progresses. Patients may also experience an increased risk for fractures of the hip, femur, and distal radius. Approximately 1 million hip fractures occur annually in the United States despite the introduction of medications such as Boniva and Fosamax. Hip fractures will occur in older women and increase mortality. Advanced techniques of hip replacement may result in regaining mobility and preserving and providing quality of life.

Treatment includes leveling the bone mass to maintain adequate levels of bone mass. Medications such as Fosamax, Actonel, Boniva, and Reclast may be used for treatment. Reclast is a once a year injection and Boniva can be done every three months. Fosamax and Actonel are dependent on a daily or weekly regimen. Treatment can prevent osteoporosis development. Adequate consumption of calcium is also important for prevention and treatment. Besides calcium, adequate vitamin D intake and weight bearing exercise is needed. Estrogen therapy may be a benefit but is controversial because of the strong correlation to breast cancer. The decision for hormone therapy should be made case-by-case and the patient should be involved in the decision-making process.

Postmenopausal osteoporosis is one of the most common types. Postmenopausal women are more commonly affected the males of the same age. Serum androgens will affect bone density and cause it to increase. Androgens such as Testosterone or Dihydrotestosterone will stimulate bone formation. A decrease level of Estrogen will cause an increase of Aromatase which is the enzyme that converts testosterone to estradiol. This will result in losing the intensity of bond formation compared to a female who does not have significant amounts of aromatase. Another cause of osteoporosis is a progesterone deficiency. This may be due to changes in osteroprotegerin and insulin growth factor (IGF). Osteoporosis is a combination of deficiency in osteoprotegerin, deficiency of calcium intake, deficiency in vitamin D, magnesium deficiency, and not enough weight-bearing exercise. Dropping estrogen levels and family history are also factors. Excessive consumption of sodas is also linked to osteoporosis. Sodas are laced with phosphorous that will interfere with the calcium phosphorus balance and result in osteoporosis.

Osteomalacia is a softening of the bone due to a calcium deficiency. A deficiency of vitamin D may lower the absorption of calcium from the gut. Osteomalacia will occur if not enough vitamin D is present. Vitamin D is needed to facilitate the bone mineralization that gives structural integrity and hardness to the bone. Without appropriate mineralization or delayed mineralization, the bone formation will not advance. During the bone formation, the bone will progress to osteoid formation, but if calcification does not occur is will result in a soft bone. A vitamin D deficiency in an adult may be secondary to low nutrition intake or malabsorption problem. A patient with osteomalacia will have bone pain, may develop small fractures, may have vertebral collapse and bone malformation. Bones that have weight-bearing roles will be affected the most and will show deformity if in the spine, vertebra bones, pelvic, girdle, or bones in the lower extremities. Treatment will include the correction of the deficiency, vitamin D. The patient may be required to consume significant amounts, approximately two hundred thousand international units weekly of vitamin D, for a month or month and a half. This may be followed by daily doses of vitamin D. If damage such as bowing of the bones, shortening, flattening, these treatments will not help, and baseline will not be achieved. Recommendations for prevention included sunlight. It is important to discuss the minimal risk of skin related malignancies due to UV ray exposure. Dietary intake of vitamin D is important for prevention.

Fish such as salmon, eggs like egg yolks are rich in vitamin D. Supplements may also be recommend.

Paget's disease is a relatively rare disorder and is also known as Osteitis Deformans. It is a chronic metabolic disorder that affects bone formation. Excessive resorption of spongy bone will cause accelerated formation of softened bone. So, normally bone is broken down and replaced. Osteoclasts and osteoblasts work together. Remodeling is the constant rate in which this occurs. Paget's disease is characterized by an overgrowth of a new bone that out places the breakdown of the old bone. The new bone is thicker than the old but is weaker resulting in an increased possibility of rupture. There is a change in the bone into something spongy and brittle while becoming a new structure that is thicker but not as strong. When an x-ray is done, the **mosaic bone pattern is revealed**, and Paget's disease can be diagnosed. Paget's disease will affect the axial skeleton, and it will affect the pelvis and long bones of lower extremities. It typically occurs after the age of 40 and becomes more common with advancing age. Thickened bones can cause abnormal bone shapes which can be a cosmetic defect or functional defect. They can also result in brain compression, impairment of motor function, deafness, and atrophy of the optic nerve. Deafness occurs because the bones in the ear are affected. The development of osteosarcoma is more prevalent in individuals with Paget's disease. The etiology of Paget's disease is unstudied, but there is a theory of an idiopathic source. Treatment includes calcium and vitamin D supplements.

Osteomyelitis is an infection of the bone. Th most common causative organism is Staphylococcus. If the infection is due to an open wound it is exogenous osteomyelitis. The infection can also be due to blood-borne and is considered endogenous. The infection will be acute and chronic inflammation will cause symptoms such as fever, weight loss, severe pain, and bone pain. If not treated, a necrotic bone may be the result causing necrosis of the bone. Treatment may include antibiotics, debridement, surgical removal of the affected bone, and hyperbaric oxygen therapy. Hyperbaric oxygen therapy is a rather new technique that uses a capsule to release antibiotic that may be placed surgically in the spot or enclave where osteomyelitis in present. The antibiotics will be releases over a span of months. A severe infection is difficult to teat. Exogenous osteomyelitis is more common and preventable. It can occur nosocomial as a consequence of manipulation of the bone for surgeries and with injections to the joint. A strict sterile technique is important for procedures done to the bones. Treatment may be successful but Is taxing to the patient.

Joint disease can be inflammatory or non-inflammatory and can be differentiated between easily. In theory, if no synovial membrane inflammation is present then the disease is non-inflammatory. The inside of the synovial capsule cannot be directly observed, but if no signs and symptoms are present is non-inflammatory. A synovial fluid analysis can be done to also determine inflammation. Inflammatory is a more systemic while non-inflammatory is localized. **Osteoarthritis** is one of the degenerative joint diseases and disease of the bone that results in severe mobility. The occurrence may increase with age and use of assistive devices.

The quality of life for the patient may become impaired and patient will eventually require assistance or placed in a skilled nursing facility. When osteoarthritis occurs, it is inflammation of the joint that may result in the loss of the articular cartilage and formation of bone spurs. In the past, the patient most likely had arthritis. Arthritis is joint inflammation. Osteoarthritis is a degenerative joint disease that is characterized by the process of wear and tear on the joint. Most people acquire osteoarthritis to some degree and it typically starts in early adulthood and continues with age. The etiology is unknown, but it I a primary disease which is idiopathic. Sporting injuries will increase the onset of the disease. During osteoarthritis, the local areas of damage will occur and result in a loss of cartilage. A new bone will start forming at the joint margin. Subchondral bones will change and patient will develop mild synovitis and have a thickening of the joint capsule. The patient may experience muscle pain, pressure, and an increase in the subchondral bone. This increase will result in the capsule stretching and causing the ligaments and tendons to be strained and the periosteum will become elevated. Patients may also experience pain, stiffness, enlargement of the joint, tenderness to touch, mobility issues, and deformity. With severe osteoarthritis in the knee, the size of the knee will significantly increase. Inflammatory joint disease is often called arthritis and is different from osteoarthritis.

Arthritis is inflammatory damage and destruction of synovial membrane, cartilage or articular cartilage, and has systemic signs of inflammation. When a patient experiences a fever, the will also experience elevated white blood cell count, malaise, loss of appetite due to an infectious or non-infectious in origin. If some type of inflammation of joint occurs with systemic changes, this may be due inflammatory damage secondary to infection.

Rheumatoid arthritis is a separate disorder that is a systemic, inflammatory, autoimmune disease the results in an autoimmune attack to the self-connective tissues in the synovial membrane. The patient will have many of the same symptoms as osteoarthritis with a few differences. The difference between osteoarthritis and rheumatoid arthritis is how the joints are affected in the hands. Osteoarthritis affects the working joints in the hands such as the primary, distal, and proximal interphalangeal joints causing swelling and pain. Rheumatoid arthritis effects all the joints in the hand. A patient with rheumatoid arthritis will have significant deformity and ulnar deviation. This is a characteristic sing of rheumatoid arthritis. Osteoarthritis usually does not affect the small bones but is a big joint disease. Lab results will reveal if rheumatoid factors are present as well as antibodies IgG and IgM. When the synovial fluid is aspirated, it must be significant for the presence of the inflammatory exudate. However, if small joints are affected, it is likely rheumatoid arthritis. If big joints are affected, it is likely osteoarthritis. If there is symmetrical involvement with both hands, it is likely rheumatoid arthritis. If there is asymmetric involvement, it is osteoarthritis. Historical evaluation for rheumatoid arthritis includes a list to diagnose with four symptoms present. Morning joint stiffness that last at least one hour, arthritis in three or ore joint areas, arthritis in the hand joint, symmetric arthritis, rheumatoid nodules or subcutaneous nodules, are the symptoms that present in patients with rheumatoid arthritis. The elevation of the Rheumatoid factor can be

detected through a blood test. X-rays can show ulnar deviation or ulnar drifts. If four of these factors are present, then they are used to diagnose rheumatoid arthritis.

Ankylosing spondylitis is an inflammatory joint disease that can cause stiffening and diffusion of the joints. It is a systemic, autoimmune, inflammatory disease. Inflammation in the spine or sacroiliac joints occurs causing stiffening and fusion of the joint. The primary sites affected include sites where ligaments, tendons, and joint capsules are inserted into the bone. The site may cause enthesis. No known cause is distinguished, but there is association of the disease with HLA B27 antigen. This disease is one of symptomatology and diagnostic evaluation. The patient may experience inflammation of the fibrocartilage in the vertebral and sacroiliac joint. When this occurs, inflammation cells will start infiltrating and destroy or erode fibrocartilage. The cells will then try to repair the damage, but scar tissue will form and ossify and calcify resulting in the joints to fuse. The patient will have early symptoms of low back pain, stiffness, pain decreased mobility, and the lumbar curvature is lost. Patient will have a flat back due to the fusion.

Gout is a metabolic disorder that results in a impaired uric acid production or excretion disorder. High levels of uric acid can be found in the blood and other bodily fluids. If the concentration of uric acid is too high, it will crystallize. The crystallization will result in deposits in connective tissues such as joints and synovial fluid leading to inflammation. The inflammation can cause gouty arthritis or gout. Gout is related to purine metabolism. **Purine metabolism** refers to the adenine and guanine metabolism. Individuals who have a rapid purine metabolism synthesize too much purines causing in the purine to start breaking down. The breakdown could also be due to poor uric acid excretion by the kidneys. The concentration of uric acid will increase resulting in crystals to deposit. The crystals will deposit in lower extremities and cause gouty arthritis. The crystals typically deposit in the metatarsal phalangeal joint or big toe. The crystals that are formed have very sharp edges and may irritate or damage the joint causing a inflammatory response. Erythema, edema, and tenderness to the touch may be occur. The patient will have symptoms of deposits of the uric acid crystals in other places with connective tissues. When the deposits are in the cartilage of the ears it is known as **tophis**. The symptoms of Gout do not appear overnight, and the patient will be in a long period of asymptomatic hyperuricemia. The tophi can deposit in any type of connective tissue such as the ear cartilage or metatarsal phalangeal joint. The crystals attempt phagocytosis by leucocytes. Eventually the crystals will be excreted from the phagolysosome and leucocyte will be disturbed resulting in inflammation.

Fibromyalgia is a disorder that is often misdiagnosed. Patients with this disorder will present with vague symptoms such as sensitivity to touch. Inflammation will not occur. Fatigue and sleep disturbances may also occur. There are no objective factors that may confirm the presence of the disease. Fibromyalgia is a chronic widespread joint and muscle pain. Chronic fatigue syndrome is often a misdiagnosis of fibromyalgia. Other misdiagnosis include flu like viral illness. Some patients with HIV or Lyme disease are misdiagnosed with fibromyalgia which

delays needed treatment. Some medications, such as beta blockers, may cause the symptoms of fatigue. Other medications like statins may cause muscular tenderness or myalgias. Physical and emotional trauma can also result in aches and pains. There is no scientific study that clearly defines the cause or etiology of Fibromyalgia. When a practitioner diagnoses patient with fibromyalgia a through musculoskeletal examination should be performed. To have a positive diagnosis practitioner must apply pressure to certain pressure point and that manipulation may elicit pain. The pain should be symmetrical, and should be present in most of these points.

A brief Overview of Integumentary Disorders

Psoriasis may be viewed as a consequence of the T cell activation, which in turn results in an attraction to neutrophils and monocytes to the site of the future plaque. Simultaneously, these growth factors will attack the keratinocytes and create papules or plaques.

Hyperkeratosis is the scaliness and inflammation of the erythema. The neutrophils and monocytes cause the inflammation growth factor to instruct cells to rapidly divide. An individual's immunity type will be dependent upon the t-cells. Sun exposure and skin damage creates risk for cancers.

Skin cancers. The basal cells, squamous cells and malignant melanoma are three cancers that are caused by skin damage. The easiest of the three to treat is basal cell. Malignant melanoma has the most severe consequences. The **basal cell** is a self-contained cancer and its chances of metastasizing are low. **Squamous cell** is in between. **Malignant melanoma** should be removed immediately after being found. Basal cell can be treated through ointments. Sunlight creates ultraviolet radiation which causes the damage. Tanning is a response reduce ultraviolet radiation. The melanin is oxidized, and the skin gets darker restricting the amount of light that can go in. When ultraviolet lights go deep into the tissue, it causes DNA damage, inflammation, and immune damage. Malignant melanoma is caused by melanocytes.

How to describe lesions on the skin:

For any skin cancer or lesion, use the A (asymmetrical), B (border irregularity), C (color variegation), and D (diameter; >0.6 mm). Another factor that can be used for 'B' is bleeding. If a cancerous mole bleeds by itself, it is **angiogenesis**. It bleeds because it develops a new vessel to feed itself. This trait is typical of cancers. Immediate removal by a specialist in recommended. 'E' can be added to the "A, B, C, D" and examines if the lesion is elevated or evolves over time. Basal cell is the least dangerous and is characterized an indentation or umbilicated lesion with no inflammation. A biopsy is used for diagnosis. The lesion will be treated by being cut out or using an ointment call Aldara. The ointment is antiviral cream that stops the basal cell for growing. Squamous cell is invasive, and it will go to dermis and lymph nodes. A shallow border and ulcer bleeding will be present. A difference between basal cell and squamous cell, it that squamous cell typically bleeds unlike basal cell.

Actinic Keratosis (AK) is a pre-malignant lesion that includes liver spots or lentigines from sun damage. Vascular lesions such as angiomas, telangiectasias, and venous lakes are also considered AK.

Seborrheic Keratosis (SK) is not cancerous. AK has a different appearance that includes a wider asymmetrical appearance. Liver spots are benign like pigmentation. AK is a risk for progression to squamous cell carcinoma. Imiquimod cream or Aldara is the antiviral ointment that is used for treatment.

Xanthelasma is cholesterol or fat deposits over the lids. The clinical significance of this is cosmetic but also may signify atherosclerotic disease. These cholesterol deposits are permanent if not surgically removed.

Hematologic Disorders

Hematologic Cancers

Leukemia is a malignant neoplasm of hematopoietic cells. Leukemia involves immature lymphocytes and their progenitors in bone marrow. **Myelocytic or myelogenous** involves pluripotent myeloid stem cells. This includes all the blood cells from the myeloid stem cells. This characteristic differentiates lymphocytic and myelogenous. The lymphocytic will affect B cells and T cell natural killer cells. Myelogenous will affect eosinophils, neutrophils, basophils, platelets and even erythrocytes. **Myelocytic leukemia** occurs when the multipotent stem cell produces lymphoid stem cells and neoplastic myeloid stem cells. The lymphoid stem cells may be normal, but the myeloid stem cells will have neoplastic precursor cells. These will result in abnormal monocytes or leukocytes. This is related to some type of mutation in which it will result in an overproduction of abnormal cell. The overproduction of cells results in spending resources as energy on the production. Other cell types that are not malignant will not keep up with this production. Normal cell production will decrease because of overproduction of abnormal myeloid cells. When the mutation occurs in the lymphoid cells, it is **lymphocytic leukemia**. The committed precursor cells will be neoplastic because they originate from the neoplastic lymphoid stem cells. This will result in neoplastic B cells, T cells, or natural killer cells. Abnormal cell production will increase while the normal cell production will decrease because the abnormal malignant cells require more energy.

Lymphomas are malignancies that arise from lymphoid tissue cells. They will either be lymphocytes or histocytes. There are two main types- Hodgkin's lymphoma and Non-Hodgkin's lymphoma. During **Hodgkin's lymphoma,** malignant B cells will invade lymphatic tissues. In Non-Hodgkin's lymphoma, the B cells and T cells will be affected. The presence of Reed Steinberg cells is a sign of Hodgkin's lymphoma. Hodgkin's lymphoma usually will come from a single lymph node and often is a localized disease. It may be treated with radiation. If multiple nodes are involved chemotherapy and radiation may be used as treatment. The disease may be presented with lymph node enlargement, the development of a lump in a single lymph node or group of lymph nodes. The most common concern is the involvement cervical lymph nodes or

mediastinal lymph, and sometimes the maxillary and inguinal lymph nodes. Constitutional symptoms occur once the patient feels sick, tired, experiences night sweats, fevers, chills and weight loss. Weight loss occurs because of the energy demands of most malignancies. If the patient drinks alcohol, they lymph node may become painful. This is a unique characteristic of the disease and cannot be explained. Treatment may involve radiation and chemotherapy. If the disease is diagnosed early, it is very treatable. This disease typically effects individual in their twenties. There is a decline in patients who are in their fifties. The disease is more prevalent in males. There is no known cause of carcinogen for Hodgkin's lymphoma. There is some evidence that HIV infection or an acquired immunodeficiency syndrome may increase the incidence of Hodgkin's lymphoma. **Non-Hodgkin's lymphoma** or neoplastic tumors is composed of lymphoid cells. The etiology is unknown. It is believed that the presence of the Epstein Barr virus can affect the incidence and HIV. Non-Hodgkin's lymphoma malignant transformation can occur both in T or B cells, while in Hodgkin's it's only B cells. There is potential for the disease to spread to various lymphoid tissue through the body. This may affect many vital organs such as the liver, spleen, and travel through the lymphatic system. The symptoms will depend on the type of lymphoma. Non-Hodgkin's includes a variation of different types of lymphomas. The manifestation of the disease may be slow, fast, or relatively fast. The clinical or natural course of the disease is approximately five to ten years. The patient may live five to ten years without treatment even if lymphoma is low-grade.

Myeloma is a disease that presents with abnormal B-cells and malignancy of terminal differentiated plasma cells. **Multiple Myeloma** is one of the most common types of plasma cell disorders. It is relatively rare and makes up one percent of all cancers, but among the disorders of blood or blood cancers it may increase to 20%. The cause Is unknown, but there is evidence that points to immune deficit radiation. Pesticides and herbicides may increase chances of developing the disease. 'Agent Orange' has also been thought to linked to myeloma along with several other viruses such as HIV. During myeloma, the proliferation of malignant plasma cells occurs resulting in abnormal cells forming a tumor. Multiple myeloma involves the bones and bone marrow. It involves the proliferation of marrow plasma cells resulting in bone disorders such as bone resorption. If the bone resorbs, the bone will be distracted, and fractures will occur. Hypercalcemia may also occur. Bone pain is one of the most common symptoms that occurs in individuals with multiple myeloma. The pain is due to the destruction of the bone which effects the production of other cells. The patient may develop anemia and neutropenia or agranulocytosis. The patient will also experience typical cancer symptoms such as weight loss. Diagnostic procedures included blood tests, bone marrow aspiration and examination, imaging studies, and MRIs. Chemotherapy or a cell transplantation may be appropriate therapy for patients younger than twenty years old. Relapse may occur to individual with multiple myeloma; however, treatment may still suppress the disease.

Hematopoiesis

It is important to know where the cells are coming from. The pluripotent stem cell can go two different directions- a lymphoid stem cell or myeloid stem cell. After lymphoid cell is produced, it may transform into a progenitor cell, t-cell progenitor or b-cell progenitor. These cells will eventually transform into natural killer cells. T-cells will be transformed into a t-cell progenitor cell. A b-cell will mature into a plasma cell. Unlike lymphoid cells, myeloid stem cells give origin to many different cell types and to majority of the cells found cells in circulation, point myeloid stem cell can break down to monocytes. This will result in a monocyte progenitor and then transform into a mono blast, then a monocyte, and then a granulocyte. **Granulocytes** can be transformed into three different type of cells- eosinophils, neutrophils, and basophils cells. These cells are still considered granulocytes because they contain granules. Granules can have substances inside that may have toxic properties for the invading organism. **Megakaryocytes** will be transferred to the platelets, and the erythrocyte progenitor cell will transform to a reticulocyte. A r**eticulocyte** is an immature red blood cells that will transform into an erythrocyte cell. Erythrocytes do not have a nucleus but has an indentation that signifies the location of a nucleus. White blood cells are also called leukocytes, which is a granulocyte.

Neutrophils, Eosinophils, and Basophils

Neutrophils are the primary pathogen fighting cells and are the first responders to an invasion. **Eosinophils** help control allergic responses and fight parasites. They may also evolve into processes such as asthma. **Basophils** release heparin, histamine, and other inflammatory mediators. They may also transform into mast cells when they migrate inside of the tissues. All three of these types of cells have common features that include the presence of granules. Granules contain some type of toxic or inflammation mediator counting granules that make them different. When cells are stained under a microscope, the differentiation is due to the agranulocytes. These do not contain inclusions that contain granules. **Lymphocytes** are the different type of cells. B cells create antibodies, and T cells that control the immune system. B cells create antibodies and they produce antibodies, and T cells are responsible for cell mediated immunity. Lymphocytes originate from lymphoid stem cells and are found in the bone marrow. Lymphocytes constitute approximately 30% of white blood cell counts. Granules are not present, but agranulocytes are present. B lymphocytes are antibody producing cells that are involve din humoral mediated immunity. T lymphocytes create cell mediated immunity. Natural killer cells are lymphocytes that have different receptors. These three types of cells are distinguished by their surface molecules. Molecules refers to markers that are identified by use of advanced methods. Monoclonal antibodies are may be used. These markers are clusters of differentiation that can be grouped into categories that are specific for cells of different origin. For example, helper T cells may have CD4 markers, a cluster of differentiation marker, and the effector T cell CD8 marker. CD markers are widely used to identify the cells.

Monocytes make up the largest portion of white blood cells. They are approximately six percent of white blood cells. This statistic is a median of percentage of monocytes; the number

may fluctuate between three and eight percent. Monocytes are the largest and have a 'U' shape. They also have a relatively long-life span that is approximately one to three days. This lifespan is approximately four times longer than the lifespan of a neutrophils cell. Cells may also survive in the tissues for several months to years. When a **monocyte** migrates to the tissue, it becomes a **macrophage.** These cells have distinct roles such as inflammation roles, antigen presenting roles. Antigen presenting roles entails the cell digesting an invader. The role of monocytes and macrophages is important because they are presenting cells, there long survival rate, and ability to present antigens to T cells. Monocytes have a nucleus with a distinct 'U' shape.

Transformation of myeloid stem cells results in emergence of platelets, monocytes and granulocytes and erythrocytes. The process of transformation of myeloid stem cells involves the pluripotent stem cell transforming into a committed precursor or colony forming units. Colony stimulator factors are chemical substances that are affecting bone marrow to produce certain type of cells. Erythropoietin is the most common factor and is a stimulating factor that will affect the bone marrow. Erythropoietin may be produced in a synthetic form and administered to patients with some type of bone marrow suppression, or blood loss secondary to one or the other factors. Radiation and chemotherapy can suppers the bone marrow production of erythrocytes.

Other colony-stimulating factors such as thrombopoietin may result in the facilitation of platelet production. Pluripotent stem cells may transform into lymphoid stem cells. From the lymphoid stem cells, they may transform into committed precursor cells for T cell progenitor or B cell progenitor. Both T and B cell progenitor will work through thymus and turn to T and B cells. These cells will become plasma cells and natural killer cells. White blood cell deficiencies may result in l**eucopenia**. Leucopenia is a deficiency of leukocytes. Neutropenia refers to agranulocytosis, which may be present. White blood cell disorders can affect the count of white blood cells and may affect other factors such as infectious disease, viral disease or even anemia.

RBC development

Red blood cells contain hemoglobin that's vital for oxygen transport. Hemoglobin molecules in an adult has two alpha chains and two beta. The term chain refers to polymers or polypeptides. Each chain is attached to a heme group which is a protein and a heme unit. A heme unite is an iron atom surrounded by the heme unit. It is vital for the iron atom to connect to the oxygen for transport and release. The oxygen binds to the heme group or iron. There are four chains, and each chain has one heme group. In each molecule of hemoglobin, four molecules of oxygen will be transported. When the blood has consistent low oxygen level, it signals to kidneys to start producing erythropoietin.

Erythropoietin as Thrombopoietin stimulates bone marrow to produce red blood cells. The erythropoietin is for red blood cells, and thrombopoietin is for platelets. When the bone marrow is stimulated it will result in creation of new red blood cells which are initially

reticulocytes and then mature red blood cells. In men who are receiving chemotherapy as cancer treatment, they may become anemic because the chemotherapy can be destructive to bone marrow. Their kidneys will not be able to respond correctly to the erythropoietin need. The kidneys do not respond when a decreased blood oxygen need is present. The kidneys will not produce erythropoietin and the bone marrow is not stimulated. Red blood cell production is needed to sustain needs for oxygen. A patient will become anemic if bone marrow is not stimulated enough.

Bone marrow is the site of red blood cell synthesis, and it can be stored there and released. Immature red blood cells are nucleated. Reticulocytes still have endoplasmic reticulum, although they lost already their nucleus. Mature red blood cells will have nothing except hemoglobin. Red blood cells will live three to four months. The cell membranes become weak due to being squeezed between the tissues in very narrow capillaries. Red blood cells are not able to repair themselves because they do not have a nucleus. After the damage, the cell will be out of circulation. Most red blood cells will break in the spleen. A certain type of leukocytes is found in the spleen that will process the red blood cells and result in the creation of unconjugated bilirubin.

Unconjugated bilirubin is also produced in the liver, bone marrow, and even lymph nodes. Unconjugated bilirubin is a toxic form of bilirubin, and it is processed into the conjugated form that is found in the bile. Men with defective red blood cells will develop hepatosplenomegaly because there is too much to process in the liver and spleen. Bilirubin unconjugated will result in jaundice. Jaundice is when the patient turns yellow or green in extensive cases. The Liver can conjugate the bilirubin by linking it to the glucuronide and is used to produce bile. An individual will develop jaundice because the liver does not process bilirubin, and it stay in the blood and accumulates and is deposited in the tissue. The red blood cells are destroyed outside the spleen in the capillaries. Hemoglobin will be freely floating in the blood resulting in Hemoglobinemia.

Hemostasis

Hemostasis is a protective mechanism or the consequence of the protective mechanism of achieving balance. It is also protecting from the loss of blood. Hemostasis occurs by stopping the blood flow by blood clots. Blood is typically a viscous fluid that flows freely inside vessels under normal circumstances. When damage to vessels occurs, the vessel will break and become sealed by a clot. This is a normal mechanism. An abnormal mechanism occurs when there is an inappropriate clot or insufficient clot. Inappropriate clotting may include hyper-coagulative states, and insufficient clotting may include hypo-coagulated states. If an excessive amount of blood is present in the clot, it is hyper-coagulative or inappropriate clotting. If there is too little blood for a clot, it is a hypo-coagulative or insufficient clotting. For hemostasis to occur, the transient vessel vasospasm occurs allowing briefly to stop or slow down the blood flow outside and then form the platelet pug. A clot will form after. Platelets are one of the key factors for

achieving hemostasis. Platelets are thrombocytes in the blood. Erythrocytes, leukocytes and platelets are thrombocytes. Platelet formation is facilitated by thrombopoietin which is made in the liver, kidney, smooth muscle and the bone marrow. When there is not enough platelets, thrombopoietin is made and signals the bone marrow to produce megakaryocytes. Megakaryocytes are precursors of the platelets. Megakaryocytes are large formations that break down to numerous platelets. Platelets are not long lived as red blood cells and live eight to nine days in circulation. Platelets are stored in the spleen. When a need arises, platelets will be released. Mediators of hemostasis are chemicals produced by platelets. When injury occurs, clotting is initiated by reacting with proteins that float in the blood. They also help platelets to clump or stick together. Clumping is a beneficial process because it facilitates the formation of the clot and facilitate hemostasis at the end. Mediators of hemostasis will also stimulate wound healing and facilitate the clumping of the platelets to vessel walls. Vasoconstriction will also occur.

Coagulation Factors There are numerous coagulation factors. The liver has an important role besides helping with digestion and being part of GI system. It is involved in the production of it has an important plasma proteins and synthetization. The liver supply's the blood with the coagulation factors. The synthetic function of the liver is to produce clotting factors such as plasma protein. The Von Willebrand factor is characterized by endothelium. Von Willi brand is a disease that involves a deficiency of the liver. The plasma proteins or coagulation factors circulate as inactive procoagulant. This is referred to as **coagulation cascade** with intrinsic and extrinsic flow. Factors such as factor 12 may change to factor 12a which may stimulate factor 11 to change to 11a. The result may lead to the formation of fibrin from fibrinogen. **Cyclooxygenase enzymes** are the products of the metabolism of arachidonic acid. The result is the production of the mediator of hemostasis. For example, Celebrex which is a non-steroidal anti-inflammatory drug that is a cox-2 inhibitor which may reduce the inflammation secondary to arthritis. It also may result in a reduction of pain secondary to arthritis. When individuals take Celebrex - cox-1, the thromboxane A2 levels, which is a mediator of hemostasis, may result in the development of hyper coagulative disorders. These disorders include increased risk stroke, heart attack, or thrombus of any other kind. The thromboxane A2 results in an increase the developing of a clot. The prescription of Celebrex is limited and has strict regulations that include informing the patient about possible side effects and increased risk for stroke and heart attack. Clotting factors associated with Thromboxane A2 is a result of cox-1 metabolism which links to the arachidonic acid metabolism.

Plasminogen is a plasma protein that is a pro enzyme in the blood that circulates in relation to clotting or when coagulation is inactive. When it is converted to an active form, it is called plasmin. The plasminogen activators can be formed in the endothelial lining of the vessels, liver and, kidneys. The plasmin will be formed from plasminogen in which plasmin is the active substance. The plasmin will help to digest the fibrin, and the fibrin will affect clotting factors such as fibrinogen, factor 5, factor 8, prothrombin, and factor 12. The plasmin will be inactivated by the plasma inhibitor. The acting of the plasma localized to a certain clot that should be dissolved. Before the plasminogen is transformed into the plasmin, it needs to be

activated by the tissue plasminogen activators. These are naturally synthesized substances that come from different sources including the liver and vascular endothelial lining. The activators will be released in response to events such as an occlusion of the vein, exercise, and other factors such as certain vasoactive drugs. These factors are unstable; however, they signal plasminogen to convert to plasmin. The conversion starts with the fibrin is eaten away and the clot is dissolved. The tissue plasminogen activator can be natural or synthesized or given as a medication for a stroke. Heparin and warfarin are acting on prevention of blood clot formation. The tissue plasminogen activator activates the plasminogen for conversion to the plasmin. The plasmin in the fibrin in the blood clot that is being digested. TPA helps clot digestion while heparin and warfarin are merely preventing it. Heparin molecules are basically cofactors that work on antithrombin.

Antithrombin is the substance that can inactivate thrombin and other clotting factors such as factor 10. Heparin can be synthesized by body. Warfarin affects the synthesis of the vitamin K, which is a coagulation factors, that is synthesized by the liver. Heparin can be digested and cross the GI tract and must be given by injection IV or subcutaneously. TPA will actively facilitate clot dissolution. Hyper coagulation disorders may be the result of several factors. When an increase of the number of the platelet occurs, too many platelets are in the blood causing platelet aggregation. **Platelet aggregation** refers to the platelets clumping too much together. This endothelial damage can result in the decrease of production of several anticlotting factors such as heparin or tissue plasminogen activator or increased procoagulant factors. Von Willebrand factor is considered part of this type of decrease because it is a consequence of endothelial damage.

Thrombocytopenia is a decreased number of platelets. A decrease in productions increases destruction and may result in too many clots forming simultaneously. Impaired platelet function can occur under normal platelet production circumstances.

Disseminated intravascular coagulation may be examined as a disorder despite the paradox. It involves hyper coagulability and hypocoagulability which results in too much clotting or too little clotting will occur simultaneously. Some type of trigger will initiate one of the pathways in coagulation. It may be intrinsic or extrinsic. The intrinsic pathway can be activated with extensive endothelial lining damage acquired through injury, infection, virus, immune disorders, or blood stasis. The extrinsic pathway may be activated when tissue factors become activated. Common extrinsic pathway activators include obstetrics complications, cancer, and trauma. Intrinsic pathway activation is typically due to endothelial or cellular injury. Extrinsic pathway activation is typically due to tissue damage. Thrombin generation will be the result of both pathways being activated. The thrombin generation may be extensive which may result in a clotting thrombosis. If the thrombosis has a large amount of vascular fibrin deposited, ischemia in the tissues will occur along with distraction of the red blood cells. Too much thrombin leads to the plasminogen involvement. Plasminogen or TPAs attached to plasminogen will become activated and result in plasmin generation. This will result in blood clot destruction or fibrinolysis. The products of destruction of the blood clot or fibrin will inhibit thrombin and platelet aggregation. Bleeding may also occur. Thrombin production will result in platelet consumption for the clot, but there are not enough platelets to provide clots which will result in

bleeding. Treatment includes treating underlying disorders. If disseminated intravascular coagulation occurs, the person may exhibit different signs and symptoms secondary to failure of the vital organs, such as kidney, heart, lung, or brain. The clots may deposit, or extensive bleeding may occur. Hemolytic anemia may occur, and patient may have signs of hypoxia. Primary disease management is very important. If a patient presents with excessive bleeding, treatment will include replenishing the plasma proteins and correcting the deficiency. Anticoagulants such as heparin may be considered for treatment.

Red Blood Cells Disorders

Red blood cells are known as **erythrocytes**. Men have higher content of hemoglobin than women. On average, men have 14 to 16 and a half grams per decaliter compared to women who have 12 to 15 grams per decaliter. Hematocrit is the amount of cellular material that comes out from spinning the blood in the tube in centrifuge. No matter the sediment type, men will have approximately 40 to 50% hemoglobin and women will have 37 to 47%. Bilirubin can be measured as byproduct of the hemoglobin breakdown. Red blood cells break down 0 to 1.2 grams per decaliter. This is important in lab work to show liver function or anything else with hemoglobin and body. If the ratio of normal hemoglobin to normal hematocrit is higher or lower, it may signify a change in the blood such as dehydration or excessive fluid volume. If the hemoglobin to hematocrit is higher than 1:3, there are too many blood cells and not enough water. If it is lower, there is too much water and too little red blood cells.

Mean corpuscular volume (MCV) is the size of the cells. The **mean cell hemoglobin** (MCH) and MCHC reflect the color of the cell. The MCHC is more concentrated hemoglobin; it is more red. It is possible to measure by red blood cell distribution width (RDW). Distribution width refers to the difference between sizes of cells. If the cell distribution width is narrow, it is uniform or normal. A wider distribution or increased number will reflect a variety of sizes of cells. This typically means bleeding and a production of small or immature cells to replenish the blood loss.

Anemias relates to size or corpuscular volume. If the cells are normal size, but the patient is still anemic it is due to a low hemoglobin level, and it is **normocytic**. **Macrocytic** refers to the cells being large. **Microcytic** refers to the cell being small. Microcytic anemia Macrocytic anemia, Normochromic, and Hypochromic are related to the color or hemoglobin concentration. **Normochromic** refers to when the hemoglobin is a normal color. **Hyperchromic** refers to when the hemoglobin is not concentrated, or the hemoglobin is pale. An iron deficiency anemia is characterized by cells that are small. The small size is due to not enough iron to make the cells normal size. Megaloblastic anemia is when the cells are large. Megaloblastic anemia is typically a result of a b12 or folic acid deficiency. The large cells are dysfunctional.

When iron deficiency anemia is present, it is often caused by blood loss. A patient with Microcytic hypochromic anemia will have an increased RDW due to blood loss but will still have

normal sized cells. Many new cells will be in circulation that will be relatively small and the RDW will increase resulting in hypochromic anemia because the new cells are pale.

Megaloblastic anemias are b12 anemia which is also referred to as **Pernicious anemia** and folic acid deficiency. Alcoholics are more prone to develop B 12 anemia because of an impaired absorption of B12. Individuals with impaired GI production of intrinsic factors may have a b12 deficiency. This can be resolved by intravenous injections of b12 for an acholic in the acute phase, but for someone who is missing an intrinsic factor it is necessary to absorb b12 from GI tract by intramuscular monthly b12 injections. Folic acid can be corrected by oral administration of folic acid. Both deficiencies will result in increased cell size and b12 deficiency that interferes with DNA production and increased size of the cells which are not effective. Megaloblastic are large cells related to a folic acid deficiency or b12 deficiency. Pernicious anemia is a b12 deficiency that is secondary to the absence of an intrinsic factor. An intrinsic factor is necessary for GI absorption. The cells will present the same way for a folic acid or b12 deficiency. **Aplastic anemia** is a consequence of inability of bone marrow to produce red blood cells, and is related to bone marrow suppression. **Chronic disease anemia** is chronic inflammation and chronic renal failure. **Chronic renal failure** is the result of decreased erythropoietin production and decreased stimulation of the bone. This can result in normochromic anemia because the bone has normal production capacity for producing red blood cells. However, there is not enough signal to start production of the cells. Iron deficiency anemia is hyperchromic and microcytic and is characterized by small pale cells.

Hemolytic anemias are membrane disorders. Hereditary Spherocytosis and Acquired hemolytic anemias may be something like a drug that causes hemolysis and hemolytic disease of the newborn. Hemolytic disease of the newborn may result in excessive deposits of bilirubin under the skin. The excessive drug destruction of fetal hemoglobin will result in the newborn turning yellow. One of the first nursing interventions performed regarding this disorder, was performed in the 19th century in England. One nurse was believed that fresh air and sunlight is a benefit to everyone. She would take all the babies, especially the ones who had turned yellow, and lay them under the sun. The babies be only a benefit to everyone, and she would take all the babies, especially the ones who turned yellow outside, and lay them under the sun. It was noticed that the babies under this nurse's supervision developed better than those in other hospitals or wards. The babies who had the yellowish tint also lost it. Physicians then wrote a paper and presented this phenomenon. However, the use of photo therapy was not widespread until 20th century. Modern technology involves the use of ultraviolet lights in the nursery to destroy excessive bilirubin.

Hemoglobinopathies, Thalassemia and Sickle-Cell Anemia

Sickle cell anemia may result as a change in the shape. Sickle cell disease is a mutation in the beta chain of hemoglobin. If hemoglobin is deoxygenated, the beta chain link may clamp together resulting in a long protein rod. This will make the cell stick and make it stickle. When the cells become stuck it may cause strokes, retinal infarct, stuck in the eyes, in lungs, and they

can block the blood flow to bones, avascular necrosis of femoral head. Painful infarcts in the extremities, fingers and toes, ischemia, pain may also occur due to lack of oxygen supply. Skin ulcers, atrophy of the spleen, and chronic kidney disease may develop. Blocking of the capillaries by sick old cells, will result in acute pain infarctions causing damage to most vital organs. Sickle cells are being destroyed extensively. The patient may develop jaundice as a result. Individuals who have only alpha chains or have fetal hemoglobin, which has only alpha chains and gamma chains, are protected from sickle-cell disease. This is due a lack of beta chains. Beta chains are the only chains that can sickle.

Thalassemia is a defective chain of hemoglobin is due to a defective gene for alpha chain synthesis or defective gene for beta chain synthesis and depends how many genes are involved. Fetal hemoglobin does not contain beta chains. This is the reason that alpha thalassemia will affect both fetal and adult hemoglobin. Beta thalassemia only affects adults. Individuals of Asian descent may develop alpha thalassemia. Beta thalassemia is more prominent in individuals of Mediterranean origin such as Greek and Italian. Severity of clinical manifestations may vary. Alpha thalassemia may result in severe manifestation in newborns when all the alpha chains are deleted, and only gamma chains are present. Fetal hemoglobin in newborns may be a severe manifestation. When all the alpha chains are deleted, only gamma chain chains are present resulting in fetal hemoglobin. This will result in gamma 4 hemoglobin production. Gamma 4 hemoglobin has a strong affinity to oxygen. The oxygen molecule will be captured but will never be released into the tissues. This may result in death in utero or shortly after birth due to the inability to transport oxygen. Beta thalassemia may result in a patient needing a transfusion or phlebotomy therapy to rid defective hemoglobin. A bone marrow transplant may also serve as a cure for some patients. The presence of clinical symptoms of both disorders may vary depending on the number of genes effected and type of anemia. Treatment may vary due to the manifestation.

Cardiovascular Disorders

The cardiovascular system includes the heart, arteries, and veins with blood. The heart is a muscular organ. Typically, it is approximately the size of the individual's fist. It has four chambers. The cardiovascular system is a closed system. The heart and lungs are connected with arteries and veins. The left pulmonary and right pulmonary vein is an artery and have oxygenated blood. Arteries and veins are named based on the direction of blood flow. If the blood flow is toward the heart, it is a **vein**. If the blood flow moves away from the heart, it is an **artery**. The heart has a muscular structure which is different than a skeletal muscle. The heart has automaticity and the ability to transfer the electric impulse rapidly between the cells. The **Purkinje fibers** allow for a rapid transport of an electric impulse. The heart also has layers. The **muscular structure** is one layer. **Myocardium** is the layer inside the muscular structure.

Endocardium is the inside lining of the heart and its chambers. **Epicardium** is the outside lining of the chambers.

Several diagnostic tests can be performed on the heart. Non-invasive procedures are becoming more popular. One non-invasive procedure, *auscultation,* is an older procedure, but other techniques are relatively new. Cardiac catheterization is an invasive procedure. It involves inserting a catheter through the vascular system to further evaluate the heart or for intervention. X-rays having typically are less valuable. Other imaging may include an Angiocardiography venogram. Blood testing for cardiac enzymes are also important tests used for diagnostic procedures. A cardiac exam may also be used to determine onset of cardiac events such as myocardial infarction.

Hypertension is a common disease of the arteries. Hypertension is a chronic disease. It is a slow developing disease, often called "silent killer" because the patient may not experience symptoms while developing hypertension. This disease may be related to the development of cerebral vascular, cardiovascular, arteriosclerotic, and kidney disease. This disease is the leading cause of hypertensive stroke and heart failure. However, this disease is preventable and treatable. **Primary hypertension** has no known cause. It is idiopathic with a gradual onset. It is also known as **essential hypertension**. Risk factors for hypertension include smoking, artero sclerotic disease, obesity, sedentary lifestyle, lack of exercise, and other numerous risk factors. Heredity and age are also risk factors. Age has influence on hypertension because with age-the elasticity and ability of the vessels to adapt to higher volume of the blood decreases. This results in increased blood pressure. Hypertension may be treated by lifestyle changes that include decreasing sodium chloride or table salt intake. Pharmaceuticals may also be used as treatment.

Arteriosclerosis and atherosclerosis are diseases of loss of elasticity and thickening or hardening of artery wall. Both diseases include the development of fibrous plaque that consists of fatty and lipid materials in the wall of the artery. In atherosclerosis, the vessels affected are the coronary arteries, cerebral arteries, aorta and peripheral arteries. Atherosclerosis limits pass capacity of the blood. The arteriosclerotic plaque may rupture causing myocardial infarction or stroke. Atherosclerosis has two type of risk factors- controllable or non-controllable factor. Heredity, age, sex and history of diabetes are non-controllable factors. Diabetes may be modified and result in a lower risk of atherosclerosis development. Controllable factors include diet, exercise, stress reduction, smoking, and hypertension. Atherosclerosis is diagnosis by image studies such as an arteriogram and doppler. An increase in blood pressure may be suggestive of atherosclerosis. If atherosclerosis is becoming advanced, the patient may experience stable angina or unstable angina. CABG surgery may be needed, and the occluded arteries will be removed and replaced. Angioplasty is another treatment option that involves a cardiac cath.

Peripheral vascular disease is a condition that can impair the circulation, quality of life, and intermediate claudication. It is characterized by muscle cramps, leg pain, and lower calf

pain during activities such as walking. The pain is typically relieved at rest. It is due to a buildup of arteriosclerotic plaque in the artery that supplies blood to the legs. Treatment may include a bypass and angioplasty. Endarterectomy is the cleaning of the affected vessel and may also be used as treatment. Treatment should happen quickly to avoid occlusion of the vessel occurs. Tissue loss may occur secondary to necrosis. Amputation may be necessary. When necrosis occurs, pain is not present. Pain is a positive symptom in this situation and may be indicative that treatment may be helpful.

An **aneurysm** is the result of the weakening of the wall of artery and leads to a bulge or rupture. Aneurysms are asymptomatic. They may be bruit or palpated. An abdominal aortic aneurysm may be palpated. Aneurysms need to be repaired before rupture. Treatment is typically successful. If a rupture occurs, treatment cannot be performed due the possibility of a significant amount of blood loss. If rupture occurs in a hospital or other medical setting, there is an increased chance of survival compared to in the home.

Coronary artery disease is a consequence of arteriosclerosis and is the single leading cause of death in the United States. Atherosclerosis will lead to narrowing of arteries that supply the blood to myocardium. If the atherosclerotic plaque ruptures, it may lead to inflammatory response, development of a platelet plug, ischemia and infarction. A sudden decrease of the blood supply to myocardium may lead to infarction, necrosis, and death. The progressive narrowing of vessels will lead to ischemia of the heart muscle.

A **stable angina** is a pattern of repeated symptoms such as chest pain when walking for a certain amount of time or distance. The pain may be relieved by rest or nitroglycerin.

Unstable angina is when the typical intervention does not relieve symptoms (chest pain). For example, when given two nitroglycerin SL tabs the pain does not cease. This is a medical emergency and patient should be rushed to hospital or EMS should me called. Appropriate protocol should be initiated. Occlusion may progress slowly or suddenly secondary to thrombus or embolus. When the plaque ruptures, the thrombus and platelet plug develop resulting in an immediate discontinuation of blood supply. A slow progression is not as dangerous as an immediate, but still needs medical attention. A patient may develop an accessory vascular system in which the body creates a natural bypass. The development of plaque may be prevented by lifestyle changes and anti-cholesterol drugs such as statins. Statin may have side effects such as muscle pain and weakness. Statin may not only prevent the increase in the size of plaque, but also stabilize existing plaque. In rare cases, Statin may lead to myocardial infarction due to the drugs stabilizing properties and anti-inflammatory properties.

A **myocardial infarction** occurs when the blood supply is suddenly decreased or stopped. Diagnosis is by history, EKG or ECG and angiograms. EKG is an old way of writing; the correct term in ECG, however, some providers still write EKG. Laboratory work will include examination of cardiac enzymes such as troponin and CKMB. Troponin is a cardiac *specific* enzyme. The CKMB enzyme is non cardiac specific, it may signify other disease such as

rhabdomyolysis and diseases that result in damage to the skeletal muscles. Treatment will include revascularization by CABG surgery. A cardiac catheter and angioplasty may be used to compress existing plaque or for a stent. Angina is treated with vasodilators such as nitroglycerin. Diet, exercise and reduction of smoking reduce the risk of adverse effects of the disease.

A **thrombus** is a clot that sits and does not move in the vessels. An embolus is a clot that has traveled from another place in the body to the brain or heart. Heparin may be prescribed to reduce the size of the clot or prevention of a clot. If a patient is under risk, a low weight Heparin, like Lovenox, with sequential compression devices in lower extremities may be used as prevention. **Rheumatic heart** disease is a sequel of streptococcal throat infection. Strep A testing is done on patients who present with Laryngopharyngitis or Pharyngitis, to eliminate diagnosis of Streptococcus A. However, when testing is done, there is a change the infection will not be identified. It is important that Strep A is treated promptly. Strep A has a typical pharyngeal appearance that can be diagnosed. The development of rheumatic fever may occur. All layers of the heart, Cardia, Myocardium, and Epicardium may be affected. Valvular deformities and valvular disease are secondary concerns. Treatment includes prevention, treatment of streptococcal infection, and treatment of rheumatic fever. Rest during the acute stage is important for an effective treatment. If valvular damage occurs, a valvuloplasty or valvular replacement may be utilised for treatment.

Congestive heart failure occurs when the heart fails to pump blood adequately. It results in an increase of the workload of the heart. The myocardium will slowly thicken, and symptoms may include gradual increase in dyspnea, tachycardia, tachypnea, and Paroxysmal Nocturnal Dyspnea or PND. PND is the sudden waking up with shortness of breath in the middle of the night. secondary to increased workload. Congestive heart failure will also result in neck vein distension, edema in ankles and lower legs, and pulmonary edema. Different manifestation of edema may occur.

If the **right-side** of the heart is not functioning properly, the edema will be peripheral. If the left-side of the heart is affected, pulmonary edema will occur. Combined right left-side failure may occur and both peripheral and pulmonary edema will be present. A diagnosis by history, physical, chest x-ray, and EKG will reveal an increased size of the heart. Decreasing the workload may reduce vascular volume along with diuretics. A low salt diet, less than two grams, and fluid restriction should also be implemented. Salt reduction may significantly decrease vascular volume and workload on the heart. Cardiotonic such as digitalis or digoxin can strengthen all cardiac muscle and strengthen the contraction. They help the heart to pump more effectively.

If the heart fails to pump blood adequately, the workload of the heart increases resulting in the tissue thickening. The myocardium may thicken and result in symptoms to increase. Symptoms may include a gradual increase in dyspnea. Tachycardia or tachypnea and **Paroxysmal Nocturnal Dyspnea (PND)** may also occur. **Paroxysmal Nocturnal Dyspnea** is

characterized by a sudden awakening during sleep with shortness of breath. Congestive heart failure will also result in neck vein distension, edema in ankles and lower legs, pulmonary edema. Edema may have different presentation whether related to right side heart failure or left side heart failure. If the right-sided heart is not functioning well, the edema will be peripheral. If the left-sided heart is not functioning well, the edema will be pulmonary. A combination of peripheral edema and pulmonary edema may occur if the heart failure has both left and right sided combination. A diagnosis is made through a medical history, a physical, chest x-ray and EKG. A chest x-ray will reveal increased size of the heart. Diuretics will be introduced for treatment. A low salt (low sodium) diet of less than two grams Na and fluid restriction may also be used as treatment. Diet may also play a significant role in treatment. Cardiotonic medications such as digitalis or digoxin can strengthen the cardia muscle and contraction. This may facilitate the heart to pump more effectively.

Cardiomyopathies are disease of the heart muscle. As a result, the heart may become dilated, enlarged and thick, or flabby. There is no cure and it may certainly lead to myocardial infarction, congestive heart failure, and death. **Carditis** is an umbrella term for Pericarditis, Myocarditis, and Endocarditis. The type depends on the onset of the place. **Pericarditis** occurs when the pericardial sac becomes inflamed. This may be a consequence of an infection that affected the pericardium. The infection typically enters through the respiratory, urinary tract or a skin and causes inflammation or infection to the heart. Treatment for all types of carditis is similar. Antibiotics, analgesics, and antipyretics are typically used. A diagnosis is made through imaging studies and ultrasounds. Antibiotics may resolve the disease. Patients with pericarditis may have significant chest pain. *Positional changes may alleviate the pain of pericarditis*. It is different from pain during the Myocardial infarction: myocardial infarction pain is not modifiable by positional change or compression of the chest area.

Valvular heart disease may be a consequence of Rheumatic fever as well as endocarditis. When the endocardial lining is inflamed, deformities of the valves may occur. Diagnosis is made by an auscultation. Murmurs should be present when the heart valves are not completely closed or there is a stenosis of the valve. Arrhythmias are abnormal heart rhythms. However, arrhythmias can be abnormal. Arrhythmias such as ventricular fibrillation can be deadly. Arrhythmias should be diagnosed and treated with medications or by a defibrillator. Defibrillators may be implanted to combat life-threatening arrhythmias. Atrial flutters are characterized by an irregular increase in heart rate. A pattern up to 350 beats per minute may be observed. A **heart block** is a regular irregular pattern of interruption in the conduction system. **Atrial fibrillation** or **flutters** are an irregularly irregular pattern in heart rate. Heart blocks can be classified as first degree, second degree, AV block or a bundle branch block. Treatments may include medication or implantation of a pacemaker defibrillator.

Rheumatic heart disease is a sequela of streptococcal throat infection. For this reason, there is concern when Strep A testing done for patients who present with laryngo-pharyngitis or pharyngitis. Even with the best testing technique, streptococcus A may not be identified. If a

patient is suspected to have strep clinically, treatment of antibiotics may be prescribed despite results of testing. Strep A typically has a significant pharyngeal appearance that may be diagnosed. The sequela of this virus is the development of rheumatic fever. As a consequence, the valves, layers of the heart, and cardia and epicardium may be affected. Valvular deformities are the main concern secondary to valvular disease. Treatment may include prevention and treatment of the streptococcal infection. Rest is the best treatment for rheumatic fever. If valvular damage occurs, valvular replacement or a valvuloplasty may be used for treatment. Treatment of the strep infection is key to avoiding rheumatic heart disease and congestive heart failure.

Cardiomyopathy is a disease of the heart muscle that results in the heart becoming dilated, enlarged, and thin, or flabby. It may lead to cardio myocardial infarction, congestive heart failure, or death. *Carditis* is an umbrella term for pericarditis, myocarditis and endocarditis. The location of onset determines the type. Pericarditis occurs in the pericardial sac and may cause constrictive pericarditis due to an infection.

Adult Respiratory Disorders

Respiratory Symptom Evaluation

Auscultation is used to diagnose respiratory diseases by assessing breathing quality and rates such as labored, tachypnoea, and rapid pace. Rapid respirations may due to hyperventilation related to respiratory alkaloses. When patients are auscultated, different sounds and rhonchi may be heard. **Rhonchi** is rattling sounds due to obstruction. **Rale** is the crackle noise that may signify pulmonary congestion. Rale may also signify a chronic condition; crackle noises are not typical and may be a sign of congestive heart failure. A **wheeze** has a musical like tone unlike rale or rhonchi. Chest x-rays are the first step to diagnosis of a respiratory condition. A sputum culture is an unorthodox diagnostic tool in primary care; however, it is common in the hospital setting. The culture may be used to diagnose tuberculosis. Tissue biopsies for bronchoscopy can be done. Arterial blood gases may reveal the metabolic state and respiratory acidosis or alkalosis. Pulmonary function tests are used to diagnose restrictive and obstructive diseases. Diseases of upper respiratory tract are common conditions. In colder regions, diseases of the upper respiratory tract may be more common. Most respiratory disorders are not life threatening.

Rhinovirus is a common cold virus that can cause an upper respiratory infection. Other viruses such as Adenovirus or influenza may also cause an infection. Hundreds of different organisms may also cause infection and makes it hard to develop immunity. Infection occurs when an organism invades the nasal mucosa resulting in nasal discharge and inflammation. The mucous production will increase, and the epithelial cell will begin to shed. This is a first line of defense that increases the vulnerability to a bacterial invasion. The bacterial superimposed invasions or infections occur when the initial viral infection stars developing. Wet, cold and

unsanitary conditions may increase risk for infection. The weather does not directly impact the development of an infection. However, it does directly impact the risk and spread of sickness because people are in confined spaces closer together and not outside as much during warmer weather. Treatment will include palliative measures such as rest, fluids, antipyretics, and analgesics. Antibiotics may be prescribed if a secondary infection occurs. Acute rhinitis can be contrasted with allergic rhinitis because it does not involve a microorganism infection, but instead Hay fever. Sinusitis, pharyngitis, and laryngitis has a bacterial origin and may warrant treatment target toward a specific bacterium. Patients with sinusitis may have facial pain. Patients with pharyngitis and laryngitis may have a sore throat. Treatment may include antibiotics. Superimposed infections or sequela of upper respiratory infections may cause life threatening situation such as Streptococcal A.

Laryngopharyngitis may result in valvular disease of heart. It may become life threatening. Laryngopharyngitis is not a disease, but the sequela of an infection. Bronchi and the lungs may be affected by an invasive organism. If not watched closely or treated immediately, it can manifest into a severe sequela of upper respiratory infection causing life threatening complications. Disease of bronchi and lungs include asthma and an allergic reaction. A hypersensitivity reaction will lead to bronchial constriction and spasm resulting in a difficulty in breathing. When an asthma attack occurs, wheezing and dyspnea will be the result. Severe episodes may require drastic measure and the treatment. Intervention of asthma will include removing allergens and bronchodilator treatment. Juvenile asthma can be triggered by exercise. This is different from adult asthma. Acute bronchitis is most likely a sequela of an upper respiratory infection. A sequela refers to being able to determine a diagnosis of a viral disease by a sequence of symptoms such as fever, tightness behind the sternum, sternal, substernal tightness, and productive cough. A productive yellow greenish sputum may also occur due to a bacterial infection. Antibiotics should be prescribed. If the diagnosis is acute bronchitis, it is a viral infection even with the cough and sputum. Palliative measures should be prescribed instead of antibiotics.

Treatment for upper respiratory infections will include palliative measures such as rest, increased fluid intake, cough syrups, or Tessalon drops. Cough syrups such as hydrocodone preparation may lead to addiction and the development of dependence on the medication. Prescribing Tessalon pearls may be effective and will not create and dependence or opioid related side effects. If a patient develops a fever, analgesics and antipyretics may be prescribed for comfort care. Antibiotic should be prescribed to treat secondary superimposed infections if those occurs.

Influenza is a viral disease that can start as an upper respiratory infection. It is not a common cold but may have similar symptoms and GI symptoms such as nausea, vomiting, and diarrhea. Influenza can be caused by three different types of viruses. These viruses are highly adaptive and constantly mutant. A, B and C types of influenza virus is the most common. Type A

influenza may have several subtypes and it's the most common type of virus. Influenza can result in pandemics, epidemics, and global pandemics. The HINI type of influenza or swine flu started as a pandemic in the United States, Mexico and Canada in 2009. It was characterized by a dramatic increase in cases and little outcomes of the disease. Type B influenza can also cause epidemics. Type B is mild and type C is sporadic and typically results in local outbreaks. Type C has never resulted in a large epidemic. Most people will recover from influenza; however, it might account for significant number of hospitalizations and even deaths.

If an individual already has an **immunocompromised status**, preexisting chronic diseases, or is a child the consequences of the flu may more significant. Death may also be a result of dehydration or pneumonia from a secondary superimposed pneumonia or flu. Influenza is a viral disease that is spread by coughing, sneezing, droplet infection and may have empiric period of 1 to 4 days. The most contagious period is first day after symptoms occur. Influenza usually lasts approximately 4 to 7 days in adults, and children the infection can be spread up to 6-7 days from onset of symptoms. Treatment will include palliative measures such as rest, analgesics and antivirals such as Tamiflu. The average time of decrease of the duration of the illness is approximately one day with the use of antiviral agents like Tamiflu. For some, a greater time is needed to recover from the illness. Fluid hydration is also important for treatment.

Prevention includes hand washing, avoiding crowding spaces, and vaccination. The effectiveness of the vaccine varies from 60 to 80%. There is also a chance that the vaccine will not be effective for the certain strain that may be popular during the flu period. The vaccine is a prediction of which strain will be more prevalent during the current flu season.

Chronic Obstructive Pulmonary Disease is a cluster of disorders that includes asthma, chronic bronchitis and emphysema. The two major types are chronic bronchitis and emphysema. These two types have a link to cigarette smoking. They are both difficult to treat, and improvement is very rare to impossible. If a patient discontinues the behavior, COPD may occur, but the patient may still maintain the functioning of the of pulmonary system on the level that it was on a given date. By stopping smoking, the patient can prevent the further deterioration of the pulmonary system. COPD is irreversible and progressive.

Tissue degeneration will occur along with airway obstruction. Patients will not be able to work or function independently. Hypoxia and hypocapnia may also occur and result in respiratory failure. Hypocapnia will result in an irregular pattern of breathing. This is a consequence of shifting from normal carbon dioxide breathing drive to oxygen related breathing drive. COPD can lead to Cor Pulmonale, right sided heart failure, and the other rare diseases. Cigarette smoking, inhalation of chemicals, and pollutants may result in COPD. Another type of COPD is a familial type and is a alkaline antitrypsin deficiency. This type of

COPD can be diagnosed by a blood test. This COPD can develop in the early thirties and forties. Chronic bronchitis and emphysema can be the sources of this disorder. It can be present alone or together. Diagnostics ay include gathering a history, a physical, chest x-ray, and pulmonary function tests.

Chronic bronchitis is an obstructive respiratory disorder characterized by inflammation of the bronchi resulting in a productive cough and excessive mucus production. **Acute bronchitis** is related to a viral infection. Chronic bronchitis is an inflammatory response to smoking or other offending agents like chemical exposure. The inflammation will affect the mucous glands, resulting in the development of an increased hyperplasia edema mucous production. Bronchoconstriction cough in a defense against inhaled irritants. When this occurs, the pulmonary defenses are reduced and consequently the cilia is dying as well. Phagocytosis will decrease and the chronic bronchitis respiratory infection will occur. The development of bacterial infections is also common.

Emphysema is an obstructive respiratory disorder that will result in the destruction of the alveoli or the alveolar walls. This will result in a large permanently inflated alveolus. The lung tissue will remodel when it grows and will repair if infection inflammation occurs. Enzymes are involved in this process by influencing or preventing the excessive tissue damage. Smoking may cause an enzyme deficiency. Smoking initiates inflammation that results in changes in enzyme levels and structural damages. Emphysema will gradually affect the alveoli causing them to grow or develop into large irregular pocket. These pockets will have large holes that results in a loss of oxygen. The alveoli will collapse during expiration, and air will be trapped in the lungs. The recoil of the lungs in lost in the hyperinflation of the alveoli. The narrowing of the terminal will lead to distinct shape of the chest. In patient with COPD will open hyperventilate. They will have a pink appearance to their skin and a shallowing breathing pattern. Patients with emphysema and chronic bronchitis use accessory muscles to help with the breathing. To breath more effectively, the patient will develop barrel chest to increase oxygenation. This is a significant finding during a physical examination.

A VQ mismatch is also a sign of COPD. If the ventilation is larger and the perfusion is in normal range, it is a VQ mismatch that is typical of COPD. The end stages of COPD are characterized by the patient losing the reserves of fat resulting in the development of oxygenation maintenance and a high respiratory breathing rate. The patients may develop increased hemoglobin and hematocrit to compensate for a fast-respiratory rate. Symptomatic treatment includes albuterol and mucolytics. Avoidance of exposure to upper respiratory infection may result in exacerbation of COPD cough suppressants. Individuals with COPD may need to take mucolytics like Mucinex all year around.

Pneumonia is the inflammation of the bronchioles and the alveoli. It is caused by a bacterial or viral infection. A viral caused pneumonia will have symptoms such as a non-productive cough, low-grade fever, and a normal count of blood cells. A bacterial caused

pneumonia will have symptoms such as a productive cough, high-grade fever, and a left shift in blood cell count. Bacterial pneumonia or classic pneumonia presents with infiltration. On an x-ray of a viral pneumonia there will be minimal changes. If the pneumonia is viral, antibiotics should not be prescribed. If the pneumonia is bacterial, antibiotics may be prescribed to determine the causative organism. Pneumonia pathophysiology can have a different origin based on offending agent. For example, aspiration pneumonia occurs the gastric content or tube feeding formula can reach the lung tissue causing irritation and triggering the inflammatory response. This will cause an increase in the mucus production resulting in pneumonia. A feeding tube has a mixture of sugar and protein and serves as an ideal medium for bacteria growth. If pneumonia develops, the activities of daily living will become more difficult. The patient will not be able to move or talk normally. Coughing may become disabling for the patient. Hydration may help the secretion to become easier to expel. **Lobular pneumonia** when one or more than one lobe is involved in bronchopneumonia. It is the most frequent type of pneumonia. Interstitial pneumonia is an atypical type of pneumonia. It occurs between the alveoli and may be caused by a virus. **Nosocomial pneumonia** is a hospital related pneumonia.

Tuberculosis (TB) is a very serious infectious disease. In recent years, the incidence rate as declined in the United States, however, the rate of TB is increasing worldwide. Populations typically affected are those who have Acquired Immuno Deficiency Syndrome (AIDS) in underdeveloped countries. The World Health Organization (WHO) reported that more than two million people from this disease every year. TB is an opportunistic infection because it may become active in someone with a weak immune system.

TB is transmitted through infectious aerosol droplets. Many individuals are exposed to the disease because of a weak immune system. TB is a very old disease and present for centuries. Nutritional status, drug abuse, and living conditions may also affect who contracts disease. The offending agent of TB is Mycobacterium Tuberculosis bacillus, which is an aerobic bacillus. The bacillus can survive in dry secretion or sputum. UV light, heat, alcohol, formaldehyde can destroy the bacillus. TB may involve the lungs, liver, brain, bones, bone tissue, and bone marrow. TB pathogenesis has two stages. **Primary TB** occurs when the bacillus enters the body and the macrophages surround it resulting in the microbes to become engulfed. This causes local inflammation. Regardless of inflammation, the bacillus will travel to the lymph nodes. Type four hypersensitivity reaction will occur. The lymphocytes and macrophages will attack and form a granuloma. A **granuloma** is an epithelial nodule that contains the bacilli that will form into a **tuberculum** which contains a little ball and a cottage cheese like substance called caseous necrosis. The immune system will hinder the develop even with TB exposure. The lesion with and the balls will stay small; only the surrounding fibrous tissue that will grow. Calcification may also occur creating another barrier.

This growth process of the fibrous tissue and classification is referred to as **Ghon's complex**, and it prevents the bacillus from spreading to surrounding areas causing TB. The bacilli may remain dormant until the immune system no longer has impact. The TB will enter the secondary or active phase in which the TB breaks through the Ghon's complex and spreads through the lungs into other organs. The patient will develop a cough that progressively

worsens, hemoptysis, night sweats, fever, chills, anorexia. The constitutional symptoms such as fatigue nausea, anorexia, and fever will depend on the location that the TB develops. Symptoms will also depend on the organ affected.

The Mantoux test will be used for diagnosis. A chest x-ray and sputum culture may also be used in addition. Treatment is typically outpatient but requires a long duration from 6 to 9 months or a year in some cases. Treatment includes a combination of techniques, and this may result in a resistance to antibiotic or antitubercular medication to develop. Prevention of transmission mostly affects Health Care providers. Protection includes TB approved mask, adequate ventilation, and negative pressure rooms.

Renal Disorders

Kidney stones often cause urinary tract obstruction. If the stone is dislodged, it may travel down the urinary tract to and obstruct the flow. Kidney stones crystals of substance that typically pass through the urinary system and are excreted. There are certain substances that may inhibit the growth or excite the growth of these crystals. If the stone is not excreted, it will stay in the kidney or urinary tract and grow. Kidney stones can be a small as a grain of sand or as large as the size of a golf ball. The demographics of kidney stones may vary. **Urolithiasis** is more common in white male patients. The calculi typical form in the renal pelvis, ureters, and bladder. A renal stone are not uniform and may be made of a mixture of crystal structures. There are several types of renal stones. **Calcium stones** form secondary to different factors. This type of stone is common and form in the presence of excess calcium intake. **Hyperparathyroidism** may also cause calcium stones. It is characterized by the inability of renal tubules to reabsorb calcium. **Chronic bowel disease** may result in a loss of fat and steatorrhea. If fat is lost, the fat may combine with calcium and be absorbed. This will result in the calcium not binding to oxalate causing stone formation to occur. **Steatorrhea** may be considered a precursor of stone formation because of the calcium inability to bind to the oxalate. Treatment will vary depending on the cause. Phosphate or thiazide diuretics may be administered to decrease the dietary absorption of calcium. If the stone becomes so large that it cannot be removed by traditional methods such as increased fluid intake, surgical intervention may be necessary. If parathyroid dysfunction is present, surgical intervention may be necessary to treat hyperparathyroidism and decrease the calcium stone formation.

Struvite stones are magnesium ammonium phosphate stones that are caused by bacteria. If the urinary pH falls below the level of 7.2, the acidity creates and environment that is nonbeneficial for the bacteria. This creates a narrow pH window for treatment. Unlike calcium stones, struvite stones are large and may have a soft texture. Patients are also more susceptive to UTI because of the bacteria that cause the formation of the stones. These stones are also more common in women than men. Treatment of the UTI may prevent the formation of the struvite stones. Percutaneous nephron lithotomy may be used as treatment for struvite

stones as well as other types of stones. **Cysteine stones** are related to abnormal exertion of amino acids or cysteine, lysine, and arginine. These types of stones are caused by the abnormal conditions related to an amino acid excess. Prevention will include the increase of fluid and pH of urine to create an environment that is not beneficial to the stones. **Uric acid stones** are large stones that is caused by an acidic pH environment around 5.5. Common causes may include rapid and dramas with loss and malignancies. These stones are typically large and may be dissolved by increasing the urine pH with potassium citrate. When potassium citrate is introduced, the pH level will increase from a 5.5 to a 6.5 resulting in the stones to dissolve. pH levels play a significant role in the formation of stones. Stone manifestations cause severe, colicky pain. **Colicky pain** refers to pain that fluctuates in intensity. The colic may last to one hour or ore.

Stone analysis may give clues as to the treatments that should be used. Kidney ureter bladder x-ray, intravenous Pyelogram, and CT scans are test that may be utilized for the analysis. Clinical presentation such as colicky pain are also important factors. Imaging such as KUB compared to IV P and CT scan should be considered. A stone analysis for a uric acid stone may include decided treatment to increase the pH level to dissolve the stone or removal of the stone by percutaneous nephrolithotomy or surgery.

A neurogenic bladder is a complicated and complex condition that occurs in types of neural disorders. These disorders affect the bladder innervation. The bladder innervation becomes destructed or interrupted. The interruption causes a neurogenic bladder. This condition may be secondary to brain or spinal cord injury, neurologic system tumors, a brain or spinal cord infection, dementia, Parkinson disease, spina bifida, stroke, and multiple sclerosis. Other conditions such as alcoholism, lupus, metal poising, herpes zoster, and medications may also cause neurogenic bladder. Neurogenic bladder is a condition most commonly found in the acute setting. Manifestations may include urinary retention and hesitancy. Diagnosis of a neurogenic bladder will include a case history, physical examination, and urinary diary. Urology practices may ask the patient to keep a bladder diary, urinalysis, culture sensitivity, cystoscopy, and imaging procedures such as MRI.

Urinary tract infections (UTI) are one of the most common conditions encountered in primary care. It is characterized by inflammation of the urinary epithelium. When the epithelium is attacked by bacteria or other pathogens within the urinary tract, inflammation occurs, and an infection may develop. A complicated UTI is recurrent and responds vaguely to treatments. An uncomplicated UTI is sporadic and responds to treatment. Complicated and persistent UTIs are very similar. Complicated UTIs can be from a lower urinary tract and can travel to the upper tract resulting in impaired renal function. The duration of treatment depends on the classification of the UTI. Uncomplicated UTIs occur seldom, and treatment is typically short because the patient is responsive. Complicated or persistent UTIs will require a longer duration of treatment. Treatment may last seven to ten das compared to the three-day treatment regime of an uncomplicated UTI. The dosage of antibiotics will also depend on the nature of the

UTI. Because of more common sulfur drug allergies, other drugs such as Ciprox may be considered for treatment. When gather a case history of a UTI, medical personal should focus on the details. **Interstitial cystitis** is a debilitation and complicated condition that is often misdiagnosed as an UTI. There is no known cause for this condition. It is a painful condition that results from the inflammation of the bladder wall. It often takes four years for diagnosis from time of the onset of symptoms. This condition most commonly affects people around 30 to 40 years old. Women are ten times more likely to have interstitial cystitis than men.

Treatment for interstitial cystitis is palliative. Pain management and patient education will be important components of treatment. The disease has no cure but can be managed through treatment and medication. E. coli is very closely located urinary tract infections. The risk for contracting E. coli is higher in women than men. E. coli comes from the GI system and a woman has a shorter urethra causing UTI secondary to E. coli to more common in women. Treatment in the primary care setting will include ciprofloxacin or Bactrim or Cipro if you patient is allergic to sulfur drugs. If treatment is ineffective, the infection may be due to a virulent strain of E. coli. A culture and sensitivity will need to be completed.

Cystitis is inflammation of the bladder. Manifestations such as frequency, dysuria, urgency, lower abdominal pain, and suprapubic pain may present similar to those of a UTI. Antimicrobial therapy may help increase fluid intake for both cystitis and UTI. High concentration of cranberry extract may also be used as treatment provided by a trained professional. Cranberry extract prevents the attachment of the bacteria to the wall of the bladder.

Pyelonephritis is an acute infection of ureter, renal pelvis, and renal parenchyma. This type of infection is commonly cause by Cystitis. It occurs when an obstructive UTI is present resulting in a reflux of urine. The patient will present with flank pain, fever, chills, costovertebral tenderness, costovertebral angle, CVA tenderness, and purulent urine. If urine becomes purulent, further investigation is needed. An uncomplicated UTI will not result in purulent urine. you better do something to further investigate why this. Chronic Pyelonephritis is related to a chronic obstructive source or chronic urinary retentions. Treatment will include antibiotics. Uncomplicated cases may be treated as outpatient, but hospitalization may be considered if the case if considered complicated.

Glomerulonephritis is an inflammation of the glomerulus. Inflammation may be due to immunologic abnormalities, drugs, toxins, vascular abnormalities, systemic diseases, or viral infections. Bilateral inflammation and bilateral disorders that affect the glomeruli may be sequela of streptococcal infection. This is typically more prevalent in men than women and is the leading cause of renal failure in the United States. Inflammation and other symptoms such as congestion and cell proliferation will impair kidney function, the ability to filter, and the ability to excrete excess water and harmful substances. Glomerulonephritis can be acute or chronic. It is subdivided or sub diagnosed into nephrotic and nephritic syndromes. A streptococcal infection may lead to the formation of immune complexes such as antigens and

antibodies. These immune complexes will circulate in the blood and may be deposited in the glomerulus. The antibodies will produce and fight against the streptococcal organism, but the glomerular endothelial cells will cross react with the antibodies. Activations of complement will occur resulting in recruitment activation of immune cells and mediators. This will result in acute glomerulus nephritis. Clinical manifestations of acute glomerulonephritis will occur. Hematuria is a troublesome sign that may be observed. A bloody or brown tinge may be observed. If a cola or beer color or more blood than bilirubin is observed in the urine, it may be a presentation of glomerulonephritis. However, on lab work will confirm the results. Proteinuria and low serum albumin may indicate a loss of protein in the urine. Edema will develop as a result of low serum albumin due to the permeability. Osmolarity is determined in the blood or serum by the albumin concentration as well as other solutes. The albumin plays a critical role. As a result of glomerulonephritis, oliguria will develop. When glomerulonephritis occurs, the kidneys will shut down and the urine output plays a critical role in measurement. Foley catheters may monitor urine output. **Nephrotic syndrome** is manifestation of glomerulonephritis. It occurs when the antibody antigen lodges in the glomerular membrane and triggers the complement system.

Renal Failure

Post renal failure occurs when something obstructs the outflow of the urine and does not allow the urine to flow away from the kidneys. BPH may be benign or cancerous. BPH is more common than prostate cancer and may contribute to the obstruction of urine cause pressure to build up. This will result in a decrease in rate of the glomerular filtration. **Neurogenic bladder** includes bilateral urethral obstruction and bladder outlet obstruction, or anything that obstructs the urine flow from the bladder. If the urine cannot be evacuated, it will become post renal failure. Clinical manifestations of acute renal failure include Oliguria, anuria, elevated BUN, creatinine, hyperkalemia, metabolic acidosis, and hypertension. The volume may overload resulting in a systemic disorder. **Renal failure** causes an inability to produce urine resulting the fluid becoming backed in circulation and hypertension.

Acute renal failure may affect organ systems outside of the renal system. In an acute renal disorder, function may improve quickly compared to chronic renal failure when disfunction manifests to all organ systems. The renal reserve will be lowered, and at some point, the patient will start experiencing renal insufficiency, renal failure, and then end-stage renal disease. All the stages are described and determined using glomerular filtration rate determination.

Chronic renal failure is the irreversible loss of renal function. Chronic renal failure can affect creatinine, urea levels, sodium and water balance, phosphate, calcium, potassium and acid base balance. Because of sodium and phosphate imbalance, skeletal and bone alteration will occur resulting in a loss of calcium, cardiopulmonary manifestation, and neural function. Endocrine reproduction and erythropoietin production will decrease or cease, and hematologic alterations will occur. Chronic renal failure can affect immunologic, GI, integumentary systems,

protein, carb, and lipid metabolism is affected. Because of the loss of proteins and lipids, the liver will try to compensate resulting in hyperlipidemia.

Chronic renal failure is the gradual progression of the disease. Type 1 and Type 2 diabetes is the leading cause of chronic renal failure. It is the sequela of vascular damage and damage to the endothelial lining. The second leading cause is hypertension and then urine obstruction. Urolithiasis and Benign Prostate Hyperplasia may block urine flow and result in postrenal failure that may transform into chronic renal failure. Other renal diseases include Pyelonephritis, glomerulonephritis, and renal artery stenosis. Renal artery stenosis is due to prerenal sources of toxic exposure. Other causes of renal disease include sickle-cell disease, lupus, and smoking. Smoking may cause atherosclerotic changes in blood vessels causing the vessels to become smaller. This will affect the vessels in the kidneys as well. Chronic ischemia and necrosis may occur as a result. Age is also a factor that may play a role in chronic renal failure. Age may affect the GFR and reduce the glomerular filtration rate. The GFR is calculated by a Cockcroft formula or through another formula. A patient may function well at GFR rate of 50%. GFR will describe the renal insufficiency. Failure occurs when there is a significant loss of function and the GFR is less than 20% of normal. The patients may still have function, but signs and symptoms will be present. When the GFR begins to decline, the end-state of renal failure has started.

When considering treatment involving dialysis or a kidney transplant, there are many factors that need to be considered. Factors include the patient's comfort, availability of the donors, availability of the matching kidney, and genetic makeup. A transplant is a complex procedure and may require lifelong immunosuppressive therapy. Some transplants may decrease the quality of life for the patient. The decision for a transplant or dialysis is made on a case by case basis.

Renal insufficiency occurs the GFR is reduced to 25%. The patient will still have mild clinical symptoms related to mild uremia, BUN, and creatinine. The erythropoietin may be affected during stress. This is due to the increased blood circulation through the kidneys and the increase need for filtration. Given a stressful situation, the function of the kidneys will be decreased. Renal failure with a GFR less than 20% causes BUN and creatinine to continue to increase. Oliguria urine output is small resulting in metabolic acidosis to begin. This will cause electrolyte imbalances, hyperkalemia, and hypernatremia, severe anemia, and erythropoietin. Sub cu shots may be very beneficial for the patient. The uremia may not affect non renal organs. Renal disorders can be very debilitating and impair the quality of life for the patient. Renal disorders may result in more complex diseases that effect multiple organs. Diabetes and hypertension are two precursors of renal disorders, chronic renal failure, and the need for dialysis.

Endocrine Disorders

Hormonal Regulation

The **endocrine system** is responsible for hormone production. **Hormones** are chemical messengers that help regulate other systems in the body. The endocrine system is a feedback system with a negative or positive subtype. When there is dysfunction in any of the endocrine glands, there is an excessive production of the hormone associated with the gland. This overproduction may lead to an alteration in the body or an insufficient or inadequate production of the hormone resulting in other alterations. An **altered hormone inactivation** or degradation may also occur. This is characterized by the hormone staying and working too long. **Degradation** refers to when the hormone is destroyed too quickly, and no effects occur. **Ectopic hormone release** may occur from known endocrine sources such as autonomous production with no feedback mechanism. For example, a tumor will produce a hormone with uncontrollable production without any feedback from the body**.** **Target cell failure** may also occur and is most common in type 2 diabetes. This occurs when the receptors decrease in number of their function is impaired. Antibodies can destroy the receptors and attach to the receptors and mimic their action although they are not hormones. The receptor may also have an unusual expression in function, however, that is rare.

The **Hypothalamus-Pituitary system** is important to understanding may disorders in the body such as hypo or hyperthyroidism. The hypothalamus can communicate with the anterior pituitary gland. This results in anterior pituitary gland to release hormones to complete one or more functions. For example, in the thyroid TRH will be released resulting in the anterior pituitary gland producing TSH. This catalyzes the thyroid to produce T3 and T4. The Gonadotrophin releases a hormone that will affect the production of the follicle stimulating hormone or luteinizing hormone. It is important to know that the anterior pituitary gland is not the origin of the hormonal messengers. **Hormonal messengers** originate in the hypothalamus. In regard to pituitary disorders, the anterior portion of the pituitary gland produces majority of hormone in comparison to the posterior portion of the gland. The pituitary gland has many blood vessels and is vascular. It may be vulnerable to ischemia and infarction like the heart. It can also be traumatized easily by a hemorrhage. **Hypopituitarism** may be a consequence of a pituitary infraction related to Sheehan syndrome. Factors such as a hemorrhage, shock, trauma, head trauma, infections, and tumors may result in significant pressure on the pituitary gland causing pituitary dysfunction. **Sheehan syndrome** is a rare syndrome of ischemia related to maternal bleeding during childbirth. Risk factors include having twins or triplets. The ischemia or infarction may result in the inability of the pituitary gland to produces hormones. Treatment include hormone replacement. This may result in **Panhypopituitarism** resulting in an absence of production of all hormones in the pituitary gland. **Hyperpituitarism** is the opposite condition. It is usually a consequence of a benign tumor resulting in an overproduction of hormones. Changes in the feedback mechanism may be observed. Hormones that are produced in the

anterior pituitary gland include the growth hormone. This hormone regulates growth and is associated with two disorders- hypersecretion of the growth hormone and acromegaly. **Acromegaly** occurs when there is an overproduction of the growth hormone during adulthood; this is not a childhood disease. The disease may slowly progress and may result in death from cardiac hypertrophy, hypertension, and arthrosclerosis. Diabetes may result as a consequence of endothelial dysfunction and coronary artery disease may occur due to malignancies. **Giantism** is a similar disorder that occurs in children and adolescents. In giantism, the growth plates are not closed resulting in the child or teen to have a significant growth sprout. In acromegaly, there is no open growth plate. However, sections of the cartilage that is sensitive to the growth hormone may grow significantly. These areas include the ears, nose, and other body parts. Cardiac hypertrophy may also occur. The connective tissue in the ears may proliferate and the tongue may enlarge. The sebaceous and sweat glands will become overly active. Skin and body hair may become coarse and bony proliferation, large joint arthropathy, and periosteal vertebral growth may result from kyphosis. The facial bones, hands, and feed will grow.

Hypersecretion of prolactin may also occur in the anterior pituitary gland. The production of prolactin is a consequence of **prolactinoma**. This is the most common pituitary tumor and is hormonally active. In a female, prolactin may cause amenorrhea, galactorrhea, hirsutism and osteopenia. Males do not respond well to a prolactin increase and the overproduction may result in impaired gonads or hypogonadism. This may result in impaired testosterone production and erectile dysfunction, a libido decrease, oligospermia, and a diminished ejaculated volume. These factors may affect quality of life and fertility in male patients.

Thyroid and Parathyroid Functions

The functions of the thyroid gland are related to thyroid hormone production. If the thyroid gland is impaired the primary function is altered. If hormones form the pituitary gland or TSH production is impaired, this is a secondary production impairment. Most thyroid disorders are related to primary dysfunction. TSH may be use as a diagnostic tool to determine the type of dysfunction. In the case of hyperthyroidism, TSH levels will be change due to an excessive production of the thyroid hormone secondary to the dysfunction of the thyroid gland. In **hyperthyroidism**, the TSH levels will decrease. In **Hypothyroidism**, the thyroid hormone levels will decrease, but the TSH levels will increase. **Thyrotoxicosis** is the result of an excessive amount of the thyroid hormone resulting in toxic consequences. **Graves' disease** is a significant disorder that is the most common manifestation of hyperthyroidism. Hyperthyroidism can also result from **nodular thyroid disease** resulting in the patient presenting with goiter and thyrotoxic crisis. It may be very dangerous and may result in numerous metabolic alterations and life-changing or life-threatening disorders. If a person has some type of hyperthyroidism, they may have an enlarged thyroid gland. Although goiter is not a definitive diagnosis, if someone presents with goiter then a diagnostic workup needs to be considered.

Hyperthyroidism may result in a non-palpable or mildly palpable thyroid. Hyperthyroidism is the consequence of the loss of production of thyroid hormone T3 and T4. It is also a type of sub-acute thyroiditis. **Hashimoto's disease** is an autoimmune thyroiditis that results in the same consequences. Both types will be treated the same, however, once the function of the thyroid is impaired it cannot be restored. Thyroiditis is usually painless. Postpartum thyroiditis may resolve. However, approximately 20% of women who have postpartum thyroiditis will need Thyroid hormone replacement. **Postpartum thyroiditis** may go undiagnosed and may occur 3-4 months after delivery. The patient may experience a thyroid toxic phase in which the levels of the thyroid hormone increases. This phase may go unnoticed due to consequences of taking care of an infant. Hypothyroid phase is the next phase to occur. During this phase the patient will become lethargic, sleepy, anxious, or depressed. This phase is resolved in most women in eighteen months or less. Approximately 1/5 of women will need thyroid replacement. A **myxedema coma** is a loss of brain function that occurs secondary to a long-standing thyroid disease. If hypothyroidism goes undiagnosed, it may result in comatose. **Congenital hypothyroidism** may lead to cretinism in children. Early thyroid hormone replacement may prevent this. **Thyroid carcinomas** may have life-threatening characteristics and result in radical thyroidectomy.

The **parathyroid hormone (PTH)** is produced in one of the four of five parathyroid glands. **Hyperparathyroidism** is typically caused by parathyroid adenomas. This can also occur secondary to chronic disease such as renal failure or vitamin D or calcium deficiency due to a malabsorptive syndrome. A patient who presents with hyperparathyroidism may also have hypercalciuria, alkaline urine, hypophosphaturia, and calcium stones.

Hypoparathyroidism will result in low levels of PTH, a decrease in the serum calcium level, and an increase of the serum phosphate level. This is a consequence of the loss of the parathyroid in radical thyroidectomy due to the glands being attached and not being able to implant. Decreased serum calcium levels cause muscle contraction consequences. A patient with hypocalcemia will also present with Chvostek and trousseau's symptoms and laryngospasm may occur. These symptoms are not diagnostic markers. **Hypocalcemia** will result in decreased or absent PTH levels causing muscular dysfunction. Hypocalcemia begins when the threshold for a nerve and muscle excitation occurs. This may be hyperreflexia tonic clonic convulsion, laryngeal spasm, or asphyxia. Treatment including a calcium gluconate infusion should be given as soon as possible. Phosphate retention may also be another sign.

Adrenal gland disorders

Adrenal gland disorders may affect one or both part of adrenal glands and consequences depending on the part that is affected. If the adrenal cortex is affected, **Cushing disease** may occur. This disease is caused by an excessive production of **anterior pituitary hormone (ACTH)** resulting in excessive amount of glucocorticoids. Excessive levels of cortisol due to glucocorticoids or other external sources may cause Cushing syndrome. Adrenal tumors secrete glucocorticoids and pituitary tumors secrete ACTH and cortisol. This may result in

truncal obesity. Symptoms may include moon face, a buffalo hump, muscle weakness, delayed growth, acne, striae marks on the abdomen, thighs, belly, and breast, edema, and hypokalemia. Mood swings and psychosis may also occur by an iatrogenic cause. To diagnosis, the patient's cortisol level, ACTH, glucose should be checked as well as a complete blood count chemistry, imaging studies and biopsy of the glands may be needed. Treatment will depend on the cause. If the cause of dysfunction is external glucocorticoid related, treatment should be tapered slowly. If the cause is due to an internal glucocorticoid dysfunction due to a tumor, surgical intervention may be needed.

Addison disease is an opposite disorder and is caused primarily by adrenal insufficiency and secondary to adrenal cortical hyper function. Secondary manifestations may include hypertension, changes in heart rate, arrythmias, and hypoglycemia. The patient may also experience lethargy, sluggish movement, and may have GI consequences such as anorexia, nausea and vomiting after eating, and a craving for salt. These consequences are due to a low cortisol level. To diagnose, a cause history and physical exam should be completed. Cortisol, ACTH, and glucose levels should be checked as well as imagining studies of both the adrenal and pituitary glands. Treatment of Addison's disease will include lifelong hormonal replacement via corticosteroids.

Diabetes

Diabetes results from the inability to metabolize glucose resulting in hyperglycemia. It can be classified into Type 1 diabetes, Type 2 diabetes, or gestational diabetes. Gestational diabetes may resolve or developed into Type 2 diabetes. A glucose test is most commonly used to diagnosis diabetes. A glucose challenge test involves checking glucose levels after a length of time. If the patient present with a glucose level of 126 or higher, this may be used for a diagnosis of diabetes. **A1C** is glycated hemoglobin; it is not used to diagnosis diabetes but can be used as a tool to monitor the progression of the disease. **Type 1 diabetes** is theorized to be commonly genetic susceptible. However, it is typically triggered by an illness, viral disease, or autoimmune disorder. It begins with the destruction of beta cells becoming immunologically mediated. Type 1 diabetes is characterized as hyperglycemia due to the rapid loss of function in the beta cells. Diabetes is characterized by three P's: Polydipsia, Polyuria, Polyphagia- no matter the type. **Polyuria** is the direct consequence of having too much glucose in the blood. It involves having an increased osmolarity resulting in intravascular fluid excess and a need to urinate. **Polydipsia** is consequence of polyuria, and **polyphagia** is when the body does not utilize glucose. Patients with Type 1 diabetes will start losing fat to be broken down as a source of energy. This will result in ketosis or ketones in the blood or urine. **Type 2 diabetes** may affect adults and children. It characterized by the resistance of target cells to insulin or the inability to accept insulin and glucose. The risk for developing Type 2 diabetes increases with age. Excessive weight may facilitate the development of Type 2 diabetes as well as genetics and environmental factors. **Metabolic syndrome** is a triad of hypertension, hyperglycemia and hyperlipidemia. A patient with metabolic syndrome will have increased blood pressure. This syndrome is referred to as pre-diabetes. If the fasting glucose is 116 to 125, it is considered

metabolic syndrome and puts the patient at risk for developing diabetes. A patient with type 2 diabetes may experience recurrent infections, vision problems, and neuropathy. These symptoms are a consequence of end organ damage secondary to hyperglycemia. Treatment will include exercise, weight loss if needed, medication, and insulin. **Hypoglycemia** may be a manifestation of diabetes melitus or occur secondary to an overdose of insulin. It should be treated rapidly. It can be treated by an oral glucose or glucose agents such as orange juices or an intravenous injection.

Diabetes ketoacidosis (DKA) is a consequence of a diabetes. It occurs when ketone bodies are excessively accumulated in the Blood. The patient may become acidotic or even comatose. Introduction to intravenous insulin as well as intravenous fluids should be administered in a hospital setting and treated as a medical emergency if DKA occurs.

Hyperosmolar hyperglycemic non-ketonic state is another consequence of diabetes. It most typically occurs with Type 2 diabetes and is characterized by severe dehydration and potassium deficit. This occurs when the glucose or hyperglycemia is not under control. When a patient has continuous hyperglycemia, they may develop a polyol pathway resulting in a sorbitol and fructose increase as well as an increase in the intracellular osmotic pressure. The pressure will attract water and cause the cells to burst. This can occur in the eyes, nerves, and red blood cells. **Protein kinase C** is a kinase enzyme that will be activated by hyperglycemia and is the hyperosmotic effect that results in damage to the nerves and red bloods cells secondary to osmosis.

Patients with diabetes may develop microvascular disease, retinopathy, and diabetes neuropathy. **Retinopathy** is due to hyperglycemia. Patients with nephropathy will have albuminuria secondary to glomerular damage and glomerular unit loss. **Diabetes nephropathy** is the number one cause of dialysis placement in Western countries. Retinopathy is the leading cause of blindness in working age adult sin the United States, secondary to diabetes mellitus. **Primary Retinopathy** is caused by damage to the blood vessels in the retina causing swelling and blockages. Secondary Retinopathy occurs when the patient develops new vascular beds and the vessels try to combat the damage. This may lead to exacerbation of the disease. Diabetes can also cause damage to the end organs. Macro vascular disease and endothelial damage results in coronary artery disease. This is the highest mortality cause for patients with Type 2 diabetes. The longer patients have Type 2 diabetes, the higher the chance of death from a cardiac disease. Endothelial damage may result in the development of vascular disease such as coronary artery disease, stroke, and peripheral artery disease. Neuropathies are quite common and may lead to other negative consequences such as diabetic foot ulcers. They may also be caused by a B12 deficiency and are characterized by numbness or tingling. **Charcot joint** neuropathy should be addressed by medication and frequent physical checks completed by healthcare providers and patients. If a patient has diabetes mellitus, he or she will be more susceptible to neuropathy and infection.

Gastrointestinal Disorders Part 1

Disorders of the Digestive System

One of the most common disorders of the digestive system is **gastrointestinal bleeding.** Bleeding can occur the upper or lower tract. Upper portion of the system include the esophagus, stomach, and duodenum, and the lower portion is anything below the ligament of the Treitz including the jejunum, ileum, colon, and rectum. The brighter blood indicates bleeding in a lower portion of the system. A patient with an upper GI bleed may present with hematemesis. **Hematemesis** is characterized by profuse bright red blood vomit. **Hematochezia** is blood in the stool. Melena in the stool will have a dark tarry appearance. Pepto-Bismol can often make the stool black and tarry. When taking a history of a patient who complains of melena, it is important to ask if they have been taking Pepto-Bismol or other bismuth preparations. **Occult bleeding** will not be observed in the stool but will be present on an occult blood test. Occult bleeding may be due to a bleeding malignancy of colon cancer. Occult bleeding can be a slow upper GI bleed and may even result from dental disorders. Upper and lower GI bleeds should be considered medical emergencies because of the risk of perforation, blood loss, and blood loss anemia. However, occult bleeding is not a medical emergency, however, it may be present in serious conditions such as cancer. In all cases, a lower and upper endoscopy should be performed for further evaluation. A diagnostic workup that includes CBC, RDW, and check for hyperchromic and microcytic anemias, anisocytic cells, MCV, and MCHC.

Dysphasia is difficulty swallowing. It can be caused by mechanical obstruction or functional obstruction. Mechanical obstruction involves a narrowing of the esophagus by some type of structure or ring such as a Schatzki ring. A Schatzki ring is a ring of connective tissue that occurs because of gastroesophageal reflux disease. A malignancy or benign tumor may also cause obstruction and result in dysphasia. A patient may complain of food getting stuck behind the sternum or chest pains related to food ingestion.

Achalasia is a very concerning disorder characterized by the denervation of the smooth muscle in the esophagus and lower esophageal sphincter. The esophagus collapses and turns into a narrow passage or completely closes. During achalasia, the patient may have a built-up food bolus that is vomited. If the patient complains of an inability to swallow, they may also have retch. Fluid may even be difficult to swallow. If untreated, the patient may experience severe nutritional deficiencies. Botox injection may be used as a possible treatment.

Gastroesophageal reflux disorder is a disorder of motility. It occurs when the food bolus cannot go down into the stomach, but instead comes back up. It is the reflux of chyme form the stomach to the esophagus. Chyme is an acidic substance or acidic mix. Reflux may cause stricter rings, damage and inflammation to the esophagus, as well as predispose the patient for esophageal malignancy. Inflammation to the esophagus is known as **esophagitis.** Treatment will include action to reduce acidity as well as recreate lower esophageal sphincter functioning.

A **hiatal hernia** occurs when part of the stomach slides into the chest cavity through the diaphragm. Most patients with EGD will have some degree of hiatal hernia. A **paraoesophageal hernia** occurs when the lower esophageal sphincter does not have a diaphragm around it and becomes loose resulting in acid to come back up. For both, symptoms of gastroesophageal reflux disorder will present. Treatment may include a **Nissen fundoplication** if medication does not work.

Peptic ulcer disease is the breakage or alteration of the mucosal lining in the esophagus stomach or duodenum. It can be acute or chronic. The patient may have superficial erosions or deep through ulcers. Ulcers may perforate and bleed causing peritonitis. In severe cases, the ulcers may also bleed inside causing an acute GI bleed which should be treated as an emergency. All cases of peptic ulcer disease are related to H pylori. The mucosa of the ulcer is destroyed causing some bloody discharge. Ulcers are typically approximately two centimeters in length. If the ulcer is chronic it may exacerbate and perforate. An H pylori infection, NSAID abuse, cigarette smoking, and alcohol can all cause ulcers.

Duodenal ulcers are most common ones and will be in the duodenum. They have several layers. The ulcer crater, mucosa, and submucosa is destroyed and may perforate. **H pylori** is a very resilient bacteria that lives in acid and produces toxins and enzymes that promote inflammation, destruction, and ulceration. Hypersecretion of chloric acid and pepsin may also occur. NSAID and smoking use may promote hypersecretion of acid. An **Esophageal Gastro Duodenoscopy (EGD)** can show the location of the ulcer int eh duodenum. If ulcers appear and then self-heal, connective tissue will appear resulting in a narrowing or obstruction in the duodenum causing an inability to pass food. The patient may have related bowel obstruction that may need surgical intervention.

Gastric ulcers will develop in the antral region due to its adjacent location to the acid secreting mucosa of the body of the stomach. The antrum does not secret acid but is affected by the acid. H pylori is the cause due to its mucosal permeability to hydrogen ions. Gastric secretions will be more normal or less normal. An overproduction of gastrin is due to random acid attack on the stomach mucosa and antrum of the stomach.

Liver disorders

Liver disorders may cause hepatitis, cirrhosis, and portal hypertension. **Portal hypertension** is when the blood pressure in the portal vein or venous system increase due to resistance in the blood flow. The kidneys can be prehepatic, intrahepatic, and post hepatic. Portal hypertension may cause esophageal varices. Portal veins reach to the stomach, intestines, spleen, and branch to the liver. If there is an obstruction in the liver, pressure will build up in all the pre liver portions of the portal system. This will cause esophageal varices. Hemorrhoids may also occur as well as splenic congestion or splenomegaly. Ascites and hepatic encephalopathy may also occur due to the inability to dispose of waste products such as ammonia. **Varices** can occur in the stomach, in the rectum as hemorrhoids, and in the lower esophagus. They most commonly occur n the esophagus. They should be treated as a medical emergency, and open and break

easily. If an esophageal bleed occurs, they patient could bleed out, vomit, or aspirate. An esophageal bleed or variceal bleed can be stopped by cauterization and banding of the varices. Banding techniques may also be applied to treat hemorrhoids in the rectum. Hemorrhoidal bleeding is easier to stop by conventional methods like prednisone suppositories, surge, banding, and banding. Hemorrhoidal bleeds are typically not as severe as esophageal bleeds. A bright red blood will signify an esophageal bleed while a coffee ground emesis will indicate a bleeding ulcer. **Melena (black tarry stools)** may represent bleeding from any part of the GI tract. In addition to banding of the bleeding hemorrhoids and varices, treatment may include prescription of beta blockers to reduce pressure in the portal system. Because of the increased pressure in venous system, fluids may seep through the veins and collect in the abdominal cavity causing ascites. Interventions such as paracentesis may be needed to remove extra the fluid. Treatment for ascites may include diuretic and diuretics such as Aldactone and Lasix. Lasix may reduce ascites. **Hepatic encephalopathy** is a related complication that is secondary to the buildup of ammonia and other waste materials that results in cognitive changes.

Hepatic liver occurs when toxins have built up and ammonia is more abundant in the blood flowing to the brain. These neurotoxins result in hepatic failure. Ammonia is not recycled and will affect brain function. The patient may have changes in personality, confusion, memory loss, unusual behaviors. The patient become comatose or deceased due the ammonia levels. Treatment includes lactulose and antibiotics.

Viral Hepatitis. Hepatitis A, B, and C are the most common types of viral hepatitis that affect the liver. **Hepatitis A** is passed by fecal oral transmission. The virus may be excreted in feces, bile or serum and passed by the fecal oral route. It is the most common type of hepatitis and is more prevalent in areas of crowded unsanitary conditions and places of food and water contamination. Consuming shellfish from a contaminated water sources may cause the virus and well as other restaurant outbreaks. Treatment includes palliative care and typically does not require medication or hospitalization. The disease has a high morbidity rate and a low mortality rate. A patient who has hepatitis A should stay in isolation and their feces should be isolated and decontaminated. Patients typically recover on their own. Approximately 10% of people with liver failure may need further intervention for treatment of hepatitis A. Typically these individuals already have some type of liver condition due to hepatitis C or cirrhosis.

Hepatitis B is transmitted through contact with blood and body fluid. Maternal transmission may occur when giving birth. A prevention vaccine is available. Treatment includes a long antiviral treatment, however, there is no cure of 100% effective treatment for hepatitis B. The transmission of the virus can occur through blood, body fluid, sexual contact, and contaminated needles. The nationwide rate of hepatitis B is much lower than hepatitis C.

Hepatitis C is another blood-borne disease. The virus can be passed through many sources, however sexual contact and body fluids are the most prevalent. The virus may also be passed through a blood transfusion. Approximately 50% to 80% of hepatitis C will result in chronic hepatitis. Genotype plays a role in determining if the disease will be chronic. Only

approximately 20% of individual will develop immunity to hepatitis C on their own. Antiviral preventions and treatment are available. Hepatitis C may lay dormant and accidentally discovered during routine blood test. When a patient presents with elevated liver enzymes, further workup will show that patient has Hepatitis C. A patient with hepatitis C may need to be referred to a hepatology clinic or gastroenterology clinic for further evaluation and treatment.

Hepatitis D is rare and requires the presence of Hepatitis B for replication. If Hepatitis B is not present, Hepatitis D will not develop. **Hepatitis E** is also very rare in the United States but may be increasing due to an influx in immigration. Hepatitis E is caused by fecal-oral transmission. **Hepatitis G** is a newer strand on hepatitis that may be transmitted from parent to offspring or sexually transmitted. When a hepatitis infection occurs, typically the course includes an incubation phase. The **incubation phase** may differ depending on the type of hepatitis. A **Prodromal phase** will also occur. This phase occurs before the patient develops jaundice. The **Preicteric phase** or development of jaundice will occur next. The last phase will include a **recovery phase**. Patients with chronic Hepatitis B or C may not enter the icteric phase because this phase is mostly association with Hepatitis A. Some patients with types B and C may be able to recover without drugs. If these patients due not recover, they risk the development of chronic hepatitis and the deterioration of the liver. **Fulminant hepatitis** may occur due the impaired or neurotic hepatocytes. It may also result form acute liver failure due to a worsening overdose of Tylenol. If a patient presents with hepatic failure and an acetaminophen overdose, a liver transplant may be required due to the liver's small chance to recover.

Cirrhosis is the destruction of the liver function and structure. The function of liver will be lost, and the liver tissue will become nodular, then fibrotic, and then and fibrosis. There will be less, and less biliary channels and the liver will become more obstructed causing portal hypertension. This causes the blood to not travel causing fibrosis to contribute to the development of necrosis. Cirrhosis is a sequela of either hepatitis or alcohol induced hepatitis. Cirrhosis is not reversible, even patient stops drinking. Other complications such as biliary obstruction jaundice, ascites, and hepatic encephalopathy may occur secondary to liver failure. Only cirrhosis patients who have abstained from alcohol or other sub illicit substances for at least six months are qualified for a needed liver transplant. Alcohol and drugs are taxing on the liver and damage hepatocytes. After ingestion of alcohol, the liver enzymes will become elevated. A cirrhotic liver will not have elevated liver enzymes due to damaged hepatocytes.

Primary Biliary cirrhosis is different disease in which the cirrhosis starts in the bile ducts. This is an autoimmune disorder. Treatment may include medication or weight control. The cirrhosis is more common than biliary cirrhosis. Post necrosis is consequence of the chronic disease and is characterized by a loss of blood supply to the liver.

Pancreatic Disorders

Pancreatitis is a disorder of the pancreas that has two major causes: alcohol and gallstone or cholelithiasis. Both causes result in injury to the pancreatic cells and result in duct leakage will occur of the enzyme into the pancreatic tissue. Self-digestion of the pancreas will occur and leak into the blood vessels causing damage locally into other organs. Autoimmune pancreatitis may occur, but it is very uncommon.

Alcohol is a toxic substance to pancreatic cells and duct. If alcohol has an influx into the pancreatic duct, it will cause destruction in the area. When cholelithiasis occurs, small gall stones can go upward through the pancreatic duct and cause a blockage resulting in severe pancreatitis. ERCP procedure may be recommended to remove the duct obstruction and release inflammation of the pancreas. Other related treatment will include NPO status or an effort to not encourage the pancreas to produce any digestive enzymes and intravenous hydration. Counselling may be recommended for patients with extensive history of alcoholism.