

Inheritance of Autosomal Recessive Genetic Diseases

These genetic diseases are diseases caused by an error in a single DNA gene. Autosomal means the errors occurs on chromosome 1..22 rather than on the 23rd sex-linked X chromosome. Recessive means that disease only occurs when a person has two copies of the bad gene. Usually this means they must inherit the disease from both parents.

Some examples of autosomal recessive diseases are **Cystic Fibrosis, Phenylketonuria, Sickle Cell Anemia, Tay Sachs, Albinism, and galactosemia.**

Recessive diseases often occur in genes that produce an enzyme. In a carrier, who has only one bad copy, there is often no disease, because the second gene can pull up the slack, and maintain health. In some recessive diseases, a carrier gets a mild form of the disease.

Autosomal recessive diseases are relatively rare, because to get the disease a person must inherit a bad gene from each parent, not just one. So both parents must have a bad gene. However, parents can be carriers without the disease, since they typically only have one bad gene themselves.

Inheritance patterns: There are various clear patterns common to any autosomal recessive genetic disease:

- Children of an affected person will typically not have the disease (except in the rare case that they too marry someone who is also affected or a carrier of exactly the same disease), but the odds are 100% the child will be a carrier. The affected parent has two bad copies of the gene, so the child gets a bad gene from that parent, but usually a good second copy from the other unaffected parent.
- If only one parent is a carrier (and the other unaffected), the child cannot get the disease, but might still be a carrier (typically 50% chance of being a carrier).
- If both parents are a carrier, there is a 25% chance that their child will have the disease. There is also a 50% chance the child will be a carrier, and only 25% chance the child will be neither diseased nor carrier. The situation where both parents are carriers is the most likely way that children with the disease are born.
- If one parent has the disease, and the other is a carrier, a child has a 50% chance of getting the disease, and 50% chance of being a carrier. The child definitely gets one bad gene from the diseased parent, and has a 50% chance of getting a second one from the carrier parent.

- **Other children:** If parents have one affected child, the odds of a second are usually 25%. If parents have a child with the disease, this almost always means that they are both carriers. The chances a second child will also have the disease are the same as above for two parent carriers: 25% chance of disease, 50% chance the second child is a carrier, and 25% chance of neither disease nor carrier. Note that genetic testing can often detect the rarer case where a child gets a genetic disease without both parents being carriers (perhaps only one is a carrier).
- **Gender bias:** Male or females get the disease equally, because an autosomal error is unrelated to the sex chromosomes.
- Inheritance patterns tend to be "horizontal", which a generation being affected (i.e. many siblings of the same parents), but not their parents nor their own children. Parents and next-generation children will usually be carriers.

Sporadic cases: A genetic disease that occurs when neither parent has any genetic defect is called a [sporadic genetic disease](#). These cases arise via random genetic mutations in the DNA. A sporadic genetic mutation is not likely as a cause of an autosomal recessive disease, because it would require two identical random mutations (one in each copy of the gene) at the same time.

Inheritance of X-Linked Dominant Diseases

These genetic diseases are diseases caused by an error in a single DNA gene. X-linked means the genetic error occurs in a gene on the 23rd sex-linked X chromosome. These diseases are sometimes called "sex-linked" rather than x-linked. This pair of chromosomes is different from all others because male and females are different: males have XY (one X and one Y chromosome), whereas females are XX (two copies of X and no Y).

Rare type of genetic disease: X-linked dominant genetic conditions are rarer than other types of genetic disease. Most X-linked genetic diseases are recessive. The majority of dominant genetic diseases affect the autosomal chromosomes 1..22. However, X-linked dominant genetic disease can occur.

Inheritance patterns for x-linked dominance: The patterns of genetic inheritance for X-linked dominant genetic diseases have the following features:

- **No carriers:** There is no such thing as a carrier in a dominant disease, because you cannot have the bad gene without having the disease.
- **Father (XY) to Son (XY):** 0% chance of disease (because the father's sperm provides only the Y chromosome, the son's good X comes from the mother's egg).

- **Father (XY) to Daughter (XX):** 100% chance of disease (because the father's sperm gives the daughter an X, and the XY father only has one X chromosome to give, i.e. the bad one).
 - **Mother (XX) to Son (XY):** 50% chance of disease because the son gets one X chromosome from the mother, and has a 50% chance of getting the bad one versus the good gene.
 - **Mother (XX) to Daughter (XX):** 50% chance of disease, because it depends on whether the child gets the good or bad X from the mother.
 - **Double dominant mother to child:** The rare case of a mother with double-dominant disease (i.e. both X chromosomes have bad genes), has a 100% chance of passing disease to a child of either gender. Only females can be double-dominant.
 - **Gender bias:** Both males and females can have the disease, since both can have an X chromosome with a bad gene that dominates. However, more females have the disease than men. This is because daughters have 100% inheritance from fathers combined with 50% from mothers, whereas sons only have 50% from mothers. Statistically, there should be 3 times as many women with the disease as men.
 - **Milder female disease:** However, the female version of the disease can be milder for some diseases, because females have a second X chromosome, which should have a good gene that may mitigate somewhat against the dominant bad gene in the other X (i.e. perhaps the bad gene is not totally dominant).
 - **Double dominance:** A female can have the double dominant form of the disease, with two bad copies of the gene. Double dominance can only occur if both the mother and father have the disease. This form is usually more severe than a dominant disease. (However it is unclear whether this is usually the same as the male version, who also has no good genes.)
- Sporadic cases:** A genetic disease that occurs when neither parent has any genetic defect is called a **sporadic genetic disease**. These cases arise via random genetic mutations in the DNA. A sporadic mutation can be the cause of an x-linked dominant disease.

Inheritance of X-Linked Recessive Genetic Diseases

These genetic diseases are diseases caused by an error in a single DNA gene. X-linked means the error occurs on the X chromosome which is the 23rd sex-linked X chromosome. Such diseases are sometimes called "sex-linked" rather than X-linked.

Some examples of X-linked recessive disorders are [Hemophilia](#) and [Duchenne muscular dystrophy](#). These occur only in boys, which is what we expected from an X-linked recessive disorder, as discussed below. For a list of this type of disorders, see [x-linked recessive disorders](#).

Recessive means that disease only occurs when a person has two copies of the bad gene. For [autosomal recessive diseases](#), this usually means they must inherit the disease from both parents, but this is not the case for X-linked recessive diseases. Men have only a single X chromosome, so they have only one copy of any gene on the X chromosome. Thus, a gene error on X definitely caused disease in men (who are XY), but women are XX, and have two copies of the gene. X-linked recessive disorders are more likely to occur than autosomal recessive disorders, because men have only one X chromosome, whereas all people have 2 copies of each autosome.

Recessive diseases often occur in genes that produce an enzyme. In a carrier, who has only one bad copy, there is often no disease, because the second gene can pull up the slack, and maintain health. In some recessive diseases, a carrier gets a mild form of the disease. For example, in X-linked recessive [hemophilia](#), a female carrier has one bad gene on chromosome X, but the good gene on the other X chromosome produces enough of the good clotting enzyme to maintain health. The recessive disease only arises when the male has no good gene on the other chromosome (because they get a Y instead of a second good X).

X-linked recessive inheritance: These diseases arise from an error on the X chromosome, which causes disease only when there is no corresponding paired X chromosome with a good gene. However, since men are XY a man with the bad gene on the X chromosome must get the disease, because there is no second X chromosome. Since women are XX, they usually have a second good X chromosome which suppresses the bad X gene, leaving them disease-free, but as carriers. The following patterns of inheritance are typical:

- **Gender bias:** Typically, males are the ones who get the disease, whereas females are carriers. Men cannot be carriers because they cannot have a bad X chromosome gene without getting the disease. Women cannot get the disease, because they typically have a second good X chromosome. However, in the rare case of a daughter of an affected father and a carrier mother, then the daughter might have two bad X genes and get the disease itself (like an autosomal recessive disease).
- **Father to son transmission:** 0% chance of disease and 100% chance of disease-free unless the mother is also a carrier (males always get their single X from the mother not father and cannot get a bad gene from the father), 0% chance of carrier (males cannot be carriers).

- **Father to daughter transmission:** 0% chance of disease (females can only be carriers), 100% chance the female child is a carrier (because the father gives a bad X gene as there is only the bad one to give). If the mother is also a carrier, the female can be fully afflicted with the rare double-recessive female version of the disease.
- **Mother (carrier) to son transmission:** 50% chance of disease, 50% chance disease-free, 0% chance of carrier (males cannot be carriers).
- **Mother to daughter:** 0% chance of disease (females can only be carriers), 50% chance of female carrier, 50% chance neither affected nor carrier.
- **Other children:** If a couple has one (male) child with the disease, what are the odds for another child having it. Usually this means the mother is a carrier, because the father cannot transmit the disease to a child (and the father would probably have noticeable disease). So the risk for a second child of the same couple is probably the mother-to-son transmission risk, 50% chance of disease, and a female child cannot have the disease but has a 50% chance of being a carrier.

Mild disease in female carriers: Female carriers can have a mild form of disease, because they have a bad gene on one of their two X chromosomes, and a good gene on the other. If the disease is not totally recessive, a partial disease can result even though the woman has one good gene. In other words, if the second gene copy is not a good enough "backup", a partial level of mild disease can still result in carriers. However, most X-linked recessive diseases have symptom-free female carriers.

Sporadic cases: A genetic disease that occurs when neither parent has any genetic defect is called a **sporadic genetic disease**. These cases arise via random genetic mutations in the DNA. A sporadic mutation can be the cause of an x-linked recessive disease (whereas it is unlikely for an autosomal recessive disorder) because only a single mutation is required (in males) to cause the disease. Females can also become carriers owing to random mutations.

Y-linked Genetic Diseases

The Y chromosome is a sex-linked chromosome. Men are XY and women are XX, so only men have a Y chromosome. The Y chromosome is very small and contains few genes.

Y-linked transmission: The Y chromosome has a trivially simple inheritance pattern because women are XX and men are XY. Only men have a Y chromosome and so the Y is only passed from father to son. The Y chromosome is small and does not contain many genes. There are few genetic diseases related to genes on Y.

Male sex determination: The main Y gene is called the SRY gene, which is the master gene that specifies maleness and male features. It is the single gene that sets off the initial cascade of hormone changes that make a person male. It is not the entire Y chromosome, but just this gene that is necessary for maleness. There is evidence of this in rare diseases where the SRY gene is missing. People who are genetically male with XY chromosomes, but with a mutation or deletion of this SRY gene on the Y chromosome, will be female despite having most of the Y chromosome. And people who are genetically female with XX but also have a tiny piece of the Y chromosome with this gene, will become male despite their female-like XX chromosomes.

Sporadic Genetic Diseases

Although most genetic diseases are inherited from parents, this is not always the case. When a genetic disease occurs without any family history or genetic defects in the parents, the disease is called a **sporadic genetic disease**.

The cause of these diseases is usually **arandom mutations** in gene in the DNA that occurred somewhere in the development of the fetus. This is presumably how the diseases arose in the first place throughout history.

It is more common for a sporadic disease to be a **dominant genetic disease**. The obvious reason is that a dominant disease requires only one random mutation, whereas two identically located mutations are required for **recessive diseases**. Hence, a random mutation is more likely to make a person a "**carrier**" of a recessive disease than actually give them the disease.

By this method of random DNA mutations, rare cases of genetic diseases are possible even if neither parent has any genetic history of the particular disease. In such cases, the risk of a reoccurrence in a second child is very low, but genetic testing is required to check whether the parents really do not have the genetic condition.

Introduction to Chromosome Diseases

Chromosome diseases are genetic diseases where a large part of the genetic code has been disrupted. Chromosomes are long sequences of DNA that contain hundreds or thousands of genes. Every person has 2 copies of each of the 23 chromosomes, called chromosomes 1..22 and the 23rd is the sex chromosome, which is either X and Y. Men are XY and women are XX in the 23rd chromosome pair.

Causes of chromosome diseases: Chromosomal diseases arise from huge errors in the DNA that result from having extra chromosomes, large missing sequences, or other major errors. These are usually caused by a random physical error during reproduction and are not inherited diseases (i.e. both parents are usually free of the condition).

Spontaneous chromosome errors: Most chromosomal diseases arise spontaneously from parents where neither has the disease. A large genetic mistake typically occurs in the woman's egg, which may partially explain why older women are more likely to have babies with **Down syndrome**.

Many chromosome errors cause the fetus to be aborted before birth, but some syndromes can be born and survive, though all typically suffer severe mental and physical defects. **Down syndrome** is the most common and well-known chromosome defect, but there are many.

Types of chromosome diseases: There are several common types of chromosome errors that cause disease. The effects of errors in the sex chromosomes (X and Y) differ greatly from errors in the autosomes (chromosomes 1..22). The following major classes of chromosome diseases can occur:

- **Trisomy conditions:** Most people have 2 copies of each chromosome, but some people are born with 3 copies, which is called trisomy. Trisomy can occur in chromosomes 1..22 (autosomal trisomy) and also in the sex chromosome (see below). **Down syndrome** is a trisomy affecting the autosome chromosome 21.
- **Monosomy conditions:** When a person has only one of a given chromosome, rather than a pair, this is called monosomy. These conditions are very rare for autosomes (chromosomes 1..22) because body cells without pairs do not seem to survive, but can occur in the sex chromosome (monosomy X is **Turner syndrome**).
- **Sex chromosome conditions:** Typically men are XY and women are XX in the pair for the 23rd chromosome. However, sometimes people are born with only one sex chromosome (monosomy of the sex chromosome), or with three sex chromosomes (trisomy of the sex chromosome).

Rarer types of chromosome diseases: There are also some other rarer types of chromosome conditions that may lead to diseases:

- **Translocation disorders:** Partial errors in chromosomes can occur, where a person still only has a pair, but accidentally has entire sequences misplaced. These can lead to diseases similar to trisomy. For example, **Translocation Down Syndrome** is a subtype of Down Syndrome caused by translocation of a large sequence of a chromosome.
- **Subtraction disorders:** The process of translocation can also cause large sequences of DNA to be lost from chromosomes. This creates diseases similar to monosomy conditions.
- **Mosaicism:** This refers to the bizarre situation where people have two types of cells in the body. Some cells have normal chromosomes, and some cells have a disorder such as a trisomy.

- **One-sided chromosome disorders:** For these unusual diseases it matters whether the chromosomes were inherited from the father or mother.

Non-contagiousness of chromosome diseases: All types of genetic diseases occur at birth including chromosome diseases. You cannot catch the disease from someone else who has the disease. You are either born with the error in your chromosomes or not. Genetic tests can determine whether or not a person has a chromosome disease, even as early as in the fetus by **antenatal testing** for genetic diseases.

Sex Chromosome Conditions

Sex chromosome defects: There are various defects of the sex chromosomes. Normally a man has XY and a woman XX. But the wrong combinations can arise with extra sex chromosomes or missing ones:

- **Turner syndrome** (XO syndrome, monosomy X, missing Y): This should just be called the "X syndrome" because the person has an X, but no second sex chromosome. Such people are female, as there is no male Y chromosome. It is a 1-in-5000 syndrome, involving some relatively minor conditions, but usually sterility.
- **Klinefelter syndrome** (XXY syndrome, also rarely XXXY): a 1-in-1000 disorder where the person is usually male (because of the Y chromosome), but has lower levels of testosterone and may have some female-like features (because there are two X chromosomes), and is usually sterile. The rarer XXXY syndrome may lead to retardation.
- **Jacobs syndrome** (XYY syndrome): The person has an extra Y male chromosome. He will be male and may be largely normal, or may suffer from minor features such as excess acne and may be very tall, and in some cases behavioral complaints such as aggression. Frequency around 1-in-2000.
- **Triple-X** (XXX, also XXXX or XXXXX): These people are females with an additional X chromosome. In rarer cases, there can even be 4 or 5 X chromosomes. They can be largely normal, or may suffer from problems such as infertility (some but not all), and reduced mental acuity. Occurs with a frequency around 1-in-700.

Note that there is no ordering, and XYX would be the same as XXY.

So there are viable combinations: XX (male), XY (female), XXY (Klinefelter), XXX, XYY, and XO (Turner). They all contain the X chromosome. Interestingly, there has been no combinations found that contain only Y: YO (Y, missing X), YY, or YYY syndromes. Not even aborted fetal embryo cells with this combination have been found. It has been suggested that there is something fundamental on the X chromosome that is needed for life.

Autosomal Trisomy Chromosome Diseases

The 22 non-sex autosome chromosomes (autosomes) can also exhibit disorders, of which the most common is trisomy (having 3 copies rather than a pair). Because these are disorders of the autosomes and not the sex chromosomes, these disorders can occur with males or females. These chromosome diseases arise rather surprisingly from an extra copy of the DNA, which makes you wonder why having 3 copies of the code bad even when the DNA code on the extra chromosome is actually correct. The condition of having 3 chromosomes is called trisomy and the most common example for autosomes is **Down syndrome**.

Here is some details about particular autosome disorders:

- **Down syndrome** (trisomy 21): an extra autosome creating a triplet at chromosome 21. These people are usually mentally retarded, and have physical characteristics such as an enlarged tongue and rounded flattened facial features. Frequency is around 1-in-800 but risk increases with the age of the mother to around 1-in-25 for a 45-year-old mother. The extra chromosome occurs because the mother's egg (or less commonly father's sperm) has wrongly kept both of its autosome 21 pair.
- **Edwards syndrome** (trisomy 18): an extra autosome at chromosome 18. Most fetuses are aborted before term, but a live birth with this condition occurs with a frequency around 1-in-3000. Edwards syndrome is more severe than Down's syndrome, and includes mental retardation and numerous physical defects that often cause an early death.
- **Patau syndrome** (trisomy 13): a very severe disorder leading to mental retardation and physical defects, occurring with a frequency around 1-in-5000. It is so severe that many babies die soon after birth.

Miscarriages caused by trisomy: So we have seen trisomies at autosomes 13, 15, 18, and 21. Trisomy at the other autosomes seems to be fatal in embryos leading to spontaneous miscarriage. The high frequency of natural miscarriages, around 1-in-5, occurs to a large extent because of chromosome errors.

Causes of trisomy: Since Down syndrome occurs more frequently in older women, one might theorize of the reason why. The most likely idea is that the problem is not during the pregnancy, but at the start, with more eggs created with poorly separated chromosomes in older women (about 1-in-5 for young women, compared to 3-in-4 for 40-year-old women). However, another possibility is that the female body gradually loses its ability to recognize wrong cells in a fetus. But it is not an immune issue because the uterus is an immune-privileged site during pregnancy.

Partial trisomy: Down syndrome can be caused not only by a full trisomy, but also by a partial trisomy at autosome 21. Due to errors in a process called "translocation", a part of a chromosome can be wrongly attached to another pair. This creates a partial trisomy.

Another possible variant of Down's syndrome is a translocation between two pairs of chromosomes, usually part of 21 gets added to the 14th. This also causes a variant known as **Translocation Down syndrome**.

Mosaicism: Yet another chromosome oddity is mosaicism, where a person has different sets of chromosomes in different cells. If some cells are normal and others have trisomy 21, then Down syndrome results. Mosaicism can result from two paths. In the first method, the fetus started with trisomy 21, and then one line of cells lost the trisomy. In the second method, the fetus started normal, but somehow a cell line gained trisomy 21.

So why chromosome 21? It is one of the smaller chromosomes, and has relatively few genes (maybe 200-250). Research continues into determining why having too many of these genes, and consequent gene overexpression, leads to Down syndrome's characteristic mental and physical features.

Monosomy and Autosome Subtraction Disorders

Monosomy occurs when there is only one of a pair of chromosomes and is usually non-viable. For example, the opposite of Down syndrome is monosomy-21, which is fatal. More common are "subtraction disorders" which occur due to missing genetic material within chromosomes, typically when a sequence of a chromosome is missing. The creation of reproductive sperm and egg cells involves a complex process that can sometimes misplace parts of a chromosome, such that one cell has an extra sequence (perhaps leading to one of the trisomy disorders if this cell becomes a child), but if a child is generated from the other cell, it may get a subtraction disorder.

- **Cri-du-chat syndrome** (cat's cry): a subtraction disorder at autosome 5, with a missing short arm of chromosome 5, but not an entirely missing chromosome. Extremely rare at 1-in-50,000 and exhibiting severe mental retardation and physical defects including larynx problems giving the characteristic cat-like child's cry.
- **Prader-Willi Syndrome (PWS)** and **Angelman Syndrome (AS)**: These are two separate genetic chromosome subtraction disorders that arise from the deletion of the same sequence on one copy of chromosome 15, specifically the sequence are "15q11-13". Prader-Willi Syndrome arises when it occurs on the father-inherited copy of chromosome 15, and Angelman Syndrome occurs if from the mother-inherited copy. This one-sided distinction between the father and mother's chromosomes is unusual, and quite important, and is discussed in detail later.

One-sided genetic disorders: Prader-Willi Syndrome and Angelman Syndrome

There are several disorders that have an odd characteristic in that it actually matters which of a pair of chromosomes is affected. Different effects arise for the chromosomes from the mother and from the father. This was a totally unexpected discovery since traditional genetic theory, particularly the "law of equivalent crosses", indicated that it did not matter which chromosome a gene was present on. However, it seems that the body does distinguish between the chromosomes that come from the father and the mother within each pair. Some genes are only activated on the chromosome that came from the mother's or father's side. It is like having male and female genes with slightly different effects. They are "imprinted" with some extra information, although exactly how this occurs is as yet unclear.

The best known examples are Prader-Willi Syndrome (PWS) and Angelman Syndrome (AS), which both arise from the same sequence on chromosome 15. They are both rare, arising around 1-in-10,000 to 1-in-15,000 but the two diseases are related in a surprising way. For some reason, the sequence 15q11-13 is likely to be misplaced during reproductive cell creation. Rather than causing a single disease, this error can cause two diseases. If it is deleted from the mother's egg, the child will get Angelman Syndrome; if the deletion occurs in a father's sperm, the child gets Prader-Willi Syndrome.

It is also important to note that both Prader-Willi and Angelman are actually gene disorders, not really chromosome disorders. Although the most common cause is from chromosome deletion (a non-inherited random physical occurrence), both of these diseases can arise rarely from a non-chromosome genetic inheritance. The real cause of the disease is the missing genes, rather than the chromosome-level changes. The gene for Angelman has been identified as the gene that creates the E6AP ubiquitin protein ligase 3A (UBE3A) protein, which is involved in the ubiquitination pathway (whatever that is). Inherited mutations of the UBE3A gene do cause Angelman without any major chromosome error. The exact gene for PWS is not known since there are several genes on the 15q11-13 sequence deleted in PWS and AS. The most likely PWS gene seems to be SNRPN (small nuclear ribonucleoprotein N) gene but it is not yet certain.

PWS and AS are very distinct diseases. They are not two variants of the same disease and have significantly different mental and physical features. This makes sense since they are caused by failures of different genes. The AS gene is mother-sided and the gene(s) causing PWS are father-sided.

PWS has several features, the most notable of which is a total lack of appetite suppression leading sufferers to continual hunger and over-eating. If left uncontrolled, they will literally eat themselves to death via extreme obesity and the consequent heart or organ damage. PWS sufferers may have a slightly reduced mental capacity, but are not usually significantly retarded. Other physical features include some facial features, hypogonadism (testes or ovaries), and short stature.

AS is a more severe mental disorder causing retardation or at least developmental difficulty. There are usually speech problems and an inappropriately happy smiling child.

AS is caused by one gene only, despite losing several genes in chromosome deletion. Presumably, the other missing genes are compensated for by the genes on the other chromosome in the pair, but for some reason the AS gene is one-sided and cannot be activated on the father's chromosome. The UBE3A gene is only one-sided within brain cells, which explains why AS is a mental disease without physical defects. The UBE3A gene is expressed from both chromosomes in other tissues.

Because AS is a single gene disease, there are in fact several ways to get it:

- Chromosome deletion (most common): loss of the 15q11-13 sequence on the mother's copy of chromosome 15, which deletes the UBE3A gene (and many others as well).
- Uniparental disomy: getting both copies of chromosome 15 from the father (i.e. the pair), so there is no mother's copy of chromosome 15 at all.
- Gene mutations: ordinary localized genetic mutations within the UBE3A gene, causing AS in the same way as other genetic non-chromosome diseases. However, the mutation only causes the disease if on the father's chromosome copy. A mutation in UBE3A on the mother's side does not cause AS, nor does it cause PWS, since PWS and AS involve different genes.
- Imprint disorders: mutations in the genetic code that surrounds the gene, inhibiting the activation of the UBE3A gene.

Another point to note is that both male and female children equally get AS and PWS. The one-sided gender-imprinting of the gene is not affected by the gender of the child with the disease.

Does one-sidedness go back to the gender of grandparents? Must it come from the mother's mother or father's father, or can it cross gender in the previous generation?

Some traits inherited from only one side? The one-sidedness of these diseases also raises the question of what other traits are inherited from only one parent.

Uniparental disomy: Another strange way to get both PWS or AS is called uniparental disomy. This means getting from one parent (uniparental) both pairs of chromosome (disomy). In a pair, you get two chromosomes from one parent, none from the other. Although the majority of PWS and AS are caused by simple deletions within a chromosome, some cases arise because both copies of chromosome 15 come from the same parent. Somewhere along the path, the egg or sperm kept both of its pair

of chromosome 15, and the other parent's copy was discarded. People with two mother-inherited copies of chromosome 15 get PWS and two father-inherited copies cause AS.

Uniparental disomy is interesting because the person theoretically has two good copies of chromosome 15 with no genes missing. However, it doesn't work that way. For full health, you need copies from both parents.

Also interesting is that having the entire chromosome 15 from the mother's side seems to only cause PWS, despite there being hundreds or thousands of genes on the entirety of chromosome 15. Hence, it would seem that very few genes are one-sided. If lots of genes are one-sided, then numerous diseases would arise from uniparental disomy of chromosome 15 rather than just one.

Note that uniparental disomy has been seen on several chromosomes: 4, 6, 7, 11, 14, 15, 16, and 21. Like trisomy, it also occurs more often for an older mother.

One-sided disease genes compared to X-linked recessive carriers: But how is this different from X-linked recessive disorders? Isn't inheriting Prader-Willi as an error from the mother's side the same as inheriting a recessive hemophilia gene from a mother carrier? The answer is no, not really, there are several differences. Firstly, the gender differences in hemophilia arise because it involves a gene on the X sex chromosome, whereas one-sided genes occur on autosomes. Secondly, although X-linked recessive disorders are similar to a maternal one-sided disorder, there is no analogous X-linked or autosomal recessive inheritance pattern that matches paternal one-sided disorders.

Polygenic Diseases

Polygenic means "multiple genes" and polygenic diseases are affected by many genes. In a sense, saying that a disease is polygenic almost means "not genetic". Polygenic diseases usually have a small genetic basis, often less than 10% chance of inheritance from parents. This is often described by saying that a child inherited a "genetic predisposition" to getting a disease, but will not always get the disease (unless some other trigger occurs).

Examples of polygenetic diseases: Many of the big name diseases are in this class of diseases including **cancers, heart disease, autoimmune diseases**, and many others. With most of these conditions, they are not regarded as being caused by genetics, nor are they directly inherited from parents. However, a family history of disease is a risk factor for the disease, indicating that there is some inherited risk in the genes. The genetics of this type of disease is an area of current research for all of the major diseases.

Inborn Errors of Metabolism

Inborn errors of [metabolism](#) are inherited disorders in which the body cannot **metabolize** the components of food ([carbohydrates](#) , **proteins** , and lipids

Metabolism is the **biochemical** process that changes food components into **energy** and other required **molecules** . These disorders may be caused by the altered activity of essential **enzymes** , deficiencies of the substances that activate the enzymes, or faulty transport compounds. **Metabolic** disorders can be devastating if appropriate treatment is not initiated promptly and monitored frequently

Inborn errors of metabolism often require [diet](#) changes, with the type and extent of the changes dependant on the specific metabolic disorder. The particular enzyme absence or inactivity for each inborn error of metabolism dictates which components are restricted and which are supplemented. Registered dietitians and physicians can help an individual assess the diet changes needed for each disease. The goals of [nutrition](#) therapy are to correct the metabolic imbalance and promote growth and **development** by providing adequate nutrition, while also restricting (or supplementing) one or more [nutrients](#) or dietary components. Additional goals in some disorders include reducing the risk of brain damage, other organ damage, episodes of metabolic crisis and coma, and even death. These restrictions and supplementations are specific for each disorder, and they may include the restriction of total fats, simple sugars, or total carbohydrates.

Listed below are several of the metabolic disorders that respond to nutrition therapy. The appropriate dietary restrictions and modifications that are necessary for treatment are also listed.

Disorders of Amino Acid Metabolism

Phenylketonuria (PKU) is the most common disorder of amino acid metabolism. In this disorder the body cannot use the amino acid phenylalanine normally, and excess amounts build up in the blood. If untreated, PKU can cause mental retardation, seizures, behavior problems, and **eczema** . With treatment, persons with PKU have normal development and intelligence. The treatment for PKU consists of a special phenylalanine-restricted diet designed to maintain blood phenylalanine levels within an acceptable range. Medical formulas and foods, which do not contain phenylalanine, are used to provide the necessary intake of protein and other nutrients. Foods containing natural protein are prescribed in limited amounts to meet the body's requirement for phenylalanine, without providing too much.

Maple syrup urine disease (MSUD) is a disorder in which the body is unable to use the amino acids isoleucine, leucine, and valine in a normal way. Excessive amounts of these amino acids and their **metabolites** will build up in the blood and spill into the urine and perspiration, giving them the odor of maple syrup (which is how this disorder got its name). An untreated infant with MSUD may have some or all of the following symptoms: difficulty breathing, sleepiness, vomiting, irregular muscle movement, seizures, or coma, and the disease can cause death. Basic treatment involves restricting foods and infant formula that contain leucine, isoleucine, and valine. Medical formulas and foods, which contain very small amounts of leucine, isoleucine, and valine, are used to provide the necessary intake of protein and other nutrients.

Disorders of Carbohydrate Metabolism

Galactosemia is a disorder in which the body cannot break down the sugar called galactose. Galactose can be found in food, and the body can break down lactose (milk sugar) to galactose and **glucose** . The body uses glucose for energy. People with galactosemia lack the enzyme to break down galactose, so it builds up and becomes toxic. In reaction to this buildup of galactose the body makes some abnormal chemicals. The buildup of galactose and these chemicals can cause liver damage, kidney failure, stunted growth, mental retardation, and **cataracts** in the eyes.

If not treated, galactosemia can cause death. Over time, children and young adults with galactosemia can have problems with speech, language, hearing, stunted growth, and certain learning disabilities. Children who do not follow a strict diet have an increased risk of having one or more of the problems listed above. Even when a strict diet is followed, some children do not do as well as others. Most girls with galactosemia have ovarian failure. The treatment for galactosemia is to restrict galactose and lactose from the diet for life. Since galactose is a part of lactose, all milk and all foods that contain milk must be eliminated

from the diet, including foods that contain small amounts of milk products such as whey and casein. In addition, organ meats should not be eaten because they contain stored galactose.

Glycogen storage diseases require different treatments depending on the specific enzyme alteration. The most common type of glycogen storage disease is classified as type 1A. In this disorder the body is missing the enzyme that converts the storage form of sugar (glycogen) into energy (glucose). If food is not eaten for two to four hours, blood glucose levels drop to a low level, leading to serious health problems such as seizures, poor growth, enlarged liver, high levels of some fats circulating in the blood, and high levels of **uric** and lactic acids in the blood. Dietary management of GSD-1A eliminates table sugar (sucrose) and fruit sugar (fructose) and limits milk sugar (lactose), as the body cannot use some sugars in these foods. Frequent meals and snacks that are high in complex carbohydrates are recommended. In addition, often supplements of uncooked cornstarch are often eaten between meals to keep blood sugar levels stable. Eating a diet that prevents low blood sugar will promote normal growth, decrease liver enlargement, and the high blood levels of uric and lactic acids.

Disorders of fatty acid metabolism occur when the body is not able to break down **fat** to use as energy. The body's main source of energy is glucose, but when the body runs out of glucose, fats are used for energy. If untreated, these disorders can lead to serious complications affecting the liver, heart, eyes, and muscles. Treatment includes altering the kind and the amount of fat in the diet and frequent feedings of carbohydrate-containing foods.

Urea cycle disorders are inherited disorders of **nitrogen** metabolism. When protein is digested it breaks down into amino acids, and nitrogen is found in all the amino acids. Those who have these disorders cannot use nitrogen in a normal way. Dietary treatment for these disorders is to provide only the amount of protein that the body can safely use. The diet consists mostly of fruits, grains, and vegetables that contain low amounts of protein and, therefore, low amounts of nitrogen.

There are more than nineteen metabolic disorders that respond to nutrition therapy. The role of proper nutrition in the treatment of these disorders is crucial. Because these disorders are rare and require careful monitoring, affected individuals are best served by clinics specializing in metabolic disorders.