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WHY DO SOME PEOPLE HAVE DOWN SYNDROME?

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Down syndrome is a health condition in which there is an extra copy of the genetic material found on chromosome number 21. This can cause unrelated people with Down syndrome to share certain features such as being shorter and having small ears. Kids with Down syndrome often need extra help with some things, and may learn better in special classrooms. In this article, we will tell you about DS, sharing its key features. Then, to explain how people get DS, we will describe what normally happens when cells divide, specifically what special structures called chromosomes are supposed to do. Next, we will discuss what can go wrong during cell division and how these mistakes can lead to DS. Finally, we will talk about how DS is diagnosed.

WHAT IS DOWN SYNDROME?

Down syndrome (DS) affects how people think, relate to others, and even the way they look. For example, many people with DS

have upward-slanted eyes, flattish noses, and are shorter than people without Down syndrome [1]. Way back in 1862, John Langdon Down noticed a bunch of unrelated people who shared these features, leading him to be the first to describe DS. You might know someone with DS or you may have seen someone with DS on television, because it is common. DS affects about 1 in every 700 people. People with DS can live happy lives but may need some extra help, such as special classrooms. No one knew what caused DS until two scientists observed that people with Down syndrome have an extra copy of one of their **chromosomes**, called chromosome 21 [2]. Scientists called DS **trisomy 21**, which means that there are three copies of chromosome 21 in the cells.

CHROMOSOMES

Small, threadlike structures of DNA that are found in most cells and function to carry genetic information on to new cells as they are made.

TRISOMY 21

A term used by scientists and doctors to refer the cause of Down Syndrome, which is having three (tri) copies of chromosome 21 in each sell (somy).

WHAT ARE CELLS AND WHAT IS INSIDE OF THEM?

Cells are the building blocks that make up the body's tissues and organs. Each cell contains the genetic material, called deoxyribonucleic acid (DNA), which is divided up into structures called chromosomes. To help make this clear, think of each chromosome as its own cookbook. Humans have 23 chromosomes, so you can imagine 23 different cookbooks, each with its own set of recipes. In this analogy, each individual recipe is called a **gene**, which is a segment of DNA that tells the cell how to make a specific protein. Proteins do many important jobs in the body. To make things a little more complicated, imagine that your mom and your dad each gave you their own versions of each of the 23 cookbooks. Thus, you have 46 total cookbooks in total, with 2 slightly different versions of each recipe, one from each parent. Similarly, humans typically have 46 chromosomes, with 23 chromosomes coming from each parent.

GENE

A stretch of DNA bases that serve as instructions for how to make a specific protein by stringing together the correct amino acids in the appropriate order.

WHEN CELLS DIVIDE...

When a person is growing or healing from an injury, one cell can split into two cells, in a process called cell division. When cells are dividing, chromosomes can be seen under the microscope. The chromosomes are copied and then divided up so that the old and new cells each get a set. This splitting up of chromosomes ensures each cell has all the recipes to make all the proteins it will need.

There are two types of cell division. **Meiosis** happens in reproductive cells (sperm or egg) and **mitosis** happens in the rest of the body's cells. Meiosis makes cells with half the total number of chromosomes. So, each egg or sperm cell ends up with 23 chromosomes. This way, when a sperm and an egg cell combine, they make a new cell with a total of 46 chromosomes, which goes on to make a baby with the same number of chromosomes as each parent. When body cells divide by mitosis, one cell will double its number of chromosomes first (so 92

MEIOSIS

The process by which sex cells (sperm and egg) are created. In humans, these cells normally have half the regular number of chromosomes (23).

MITOSIS

The process by which a body cell divides into two identical cells, each with the same number of chromosomes (46 in the normal human).

chromosomes), and then it will split in half, resulting in two cells, each with 46 chromosomes. Cells are amazing!

DOWN SYNDROME: AN EXTRA CHROMOSOME

Generally, our cells are great at cell division but sometimes they do not follow the plan! Having more than the expected 46 chromosomes can result in health problems. For most chromosomes, having an extra copy will prevent a fertilized egg from developing into a live baby. In DS, people are born with an extra copy of chromosome 21. The extra copy of chromosome 21 can come from one of three processes.

Extra Copy from Sperm or Egg

Remember how we said eggs and sperm normally have 23 chromosomes? Sometimes, when egg or sperm cells are made, they can end up with an extra copy of chromosome 21. So, instead of having just one chromosome 21, the egg or sperm will actually have two copies. This extra chromosome results from a process called **nondisjunction**, in which the original pair of chromosomes does not split up as expected during meiosis [3, 4]. If an egg or sperm cell has an extra chromosome 21 and then joins up with another reproductive cell, the result will be a cell with 47 chromosomes instead of the expected 46.

NONDISJUNCTION

When a pair of chromosomes does not separate properly during mitosis or meiosis.

Extra Copy from Mitosis

Sometimes, the egg and sperm cells both carry 23 chromosomes, but the baby still ends up with an extra copy of chromosome 21. This is because nondisjunction can also happen in mitosis, when the cells are dividing as the fertilized egg grows. Nondisjunction during mitosis happens only rarely, but the body cell that ends up with 47 chromosomes will keep dividing to make more body cells that also have 47 chromosomes. If the nondisjunction happens early in development, many cells will have an extra copy of chromosome 21, and the person will likely be diagnosed with DS. This is called mosaic DS because some of the body's cells have the expected 46 chromosomes, while others have an extra chromosome, for a total of 47 (Figure 1) [3]. Individuals with mosaic DS may have different symptoms depending on how many of their cells have the extra chromosome. You can find out more on the National Down Syndrome Society's website!

Extra Copy Stuck to Another Chromosome

In about 3% of DS cases, an extra copy of chromosome 21 can be passed on in a sperm or an egg cell due to **translocation**, which is when all or part of chromosome 21 becomes stuck to another chromosome. This usually happens when two chromosomes have breaks in them, and instead of being repaired correctly, the two broken chromosomes are mistakenly joined together [5]. The translocated

TRANSLOCATION

When part of a chromosome breaks off and sticks onto another chromosome.

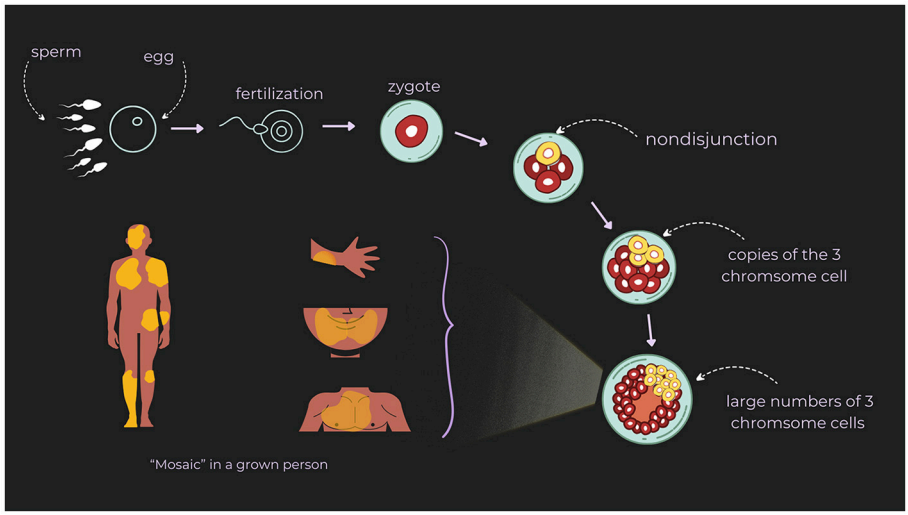

Figure 1

Mosaic down syndrome. Mosaic DS happens when nondisjunction occurs in mitosis, when a baby's cells are dividing before it is born. The yellow cell indicates a cell that had nondisjunction during mitosis. It has three copies of chromosome 21. This cell continues to divide, and the new cells made from it also have three copies of chromosome 21. When this happens early in development, a large portion of cells have trisomy 21. In the grown person, there is a "mosaic" of cells—some with an extra chromosome 21 and some without.

extra copy of chromosome 21 can be passed on from a parent to their child. For this reason, this type of DS is called **familial**.

DIAGNOSING DOWN SYNDROME

Although many people with DS share physical features, you cannot be sure if someone has DS just by looking at them. Diagnosing DS requires special testing. A simple test called a **karyotype** can be used to visualize and count the chromosomes inside of a single cell. Whether nondisjunction happens during meiosis or mitosis, a doctor would see *three* copies of chromosome 21 in the affected cells. The only difference would be that if trisomy 21 arose during meiosis, all cells would have *three* copies of chromosome 21 (Figure 2). Conversely,

FAMILIAL

A term for all things relating to a family. A familial condition is one that gets passed down through families via genes, as is the case in translocation down syndrome.

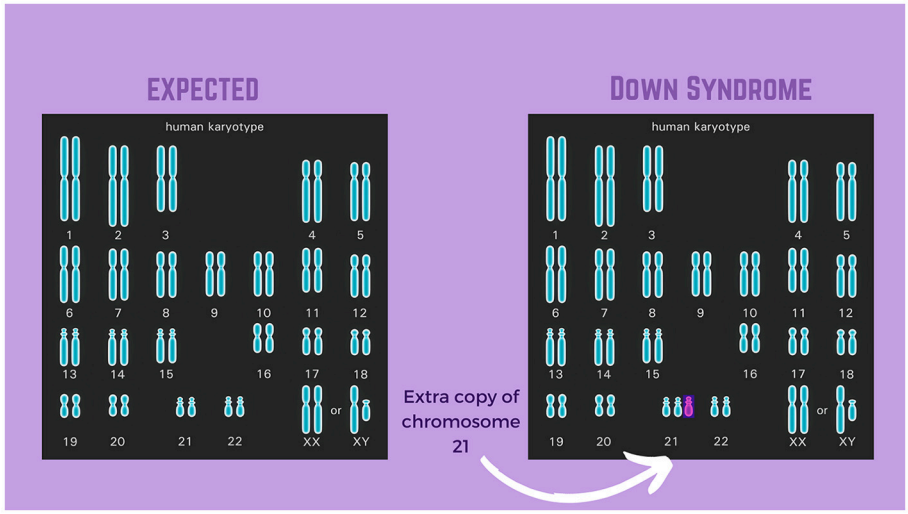

Figure 2

Down syndrome due to nondisjunction during meiosis or mitosis. DS is also called trisomy 21 because the cells of a person with DS contain three copies of chromosome 21 instead of the usual two. The karyotype on the left shows the chromosomes of a person without DS and the one on the right shows a person with DS. The extra copy of chromosome 21 is shown in pink.

the extra copy would only be found in some cells if the DS arose during mitosis. In cases of DS due to translocation, there would be *two* expected copies of chromosome 21 but another chromosome (usually 14 or 15) would be extra-long because an extra copy of all or part of chromosome 21 is attached (Figure 3).

Figure 3

Down syndrome due to translocation. Sometimes, trisomy 21 can result from translocation—when all or part of chromosome 21 breaks off and becomes stuck to another chromosome, often chromosome 14 or 15. In the karyotype on the right, an extra piece of chromosome 21 (pink) is attached to the top of chromosome 14.

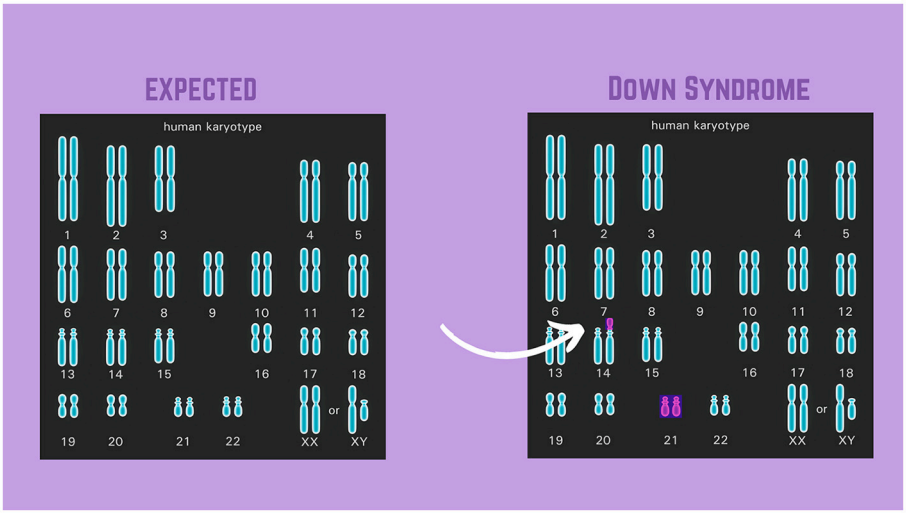

Figure 3

KARYOTYPE

A picture of a person's complete set of chromosomes used to identify health conditions like down syndrome that are caused by the wrong number of chromosomes or a translocation.

CONCLUSION

Down Syndrome was first described 1876, and the condition continues to be studied by scientists and doctors today. DS happens when cell division does not occur as expected. Science in the field of DS has advanced quite a bit. We can even diagnose DS before birth, just from a sample of the mom's blood [6]. We hope that, by reading this paper, you have learned a lot about DS and how people get an extra copy of chromosome 21. Maybe your new understanding will help you to be extra kind to people you meet who have DS or similar conditions.

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ANJA, AGE: 14
Anja enjoys science and volleyball. She spent a year working as the science TA in her middle school, her favorite part of which was preparing hundreds of pickles (adding googly eyes, a plastic "heart" and more!) for a dissection lab.

JONATHAN, AGE: 13
Jonathan is a high school student who became interested in science after participating in science fairs, climate change camps, child research conferences and local brain awareness activities. After school, you can also find him either at the gym or the pool—training and teaching—as a black-belt martial artist and competitive swimmer. Jonathan aspires to become a medical pharmacist or a physician. He believes that motivation cannot only come from seeing someone else's success. He understands that motivation must come from within especially when things become hard.

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