

Chapter 2

Selected Genetics Topics

Robertsonian Translocation and Other Travel Options for Your Genes: How Your Genes Can do a Little Sightseeing on the Genome

Some chromosome problems have to do with the number of chromosomes – either too many, or not enough, compared to the usual 23 pairs. Other chromosome problems have to do with loss or gain of genetic material, compared to usual (such as deletion disorders), without any change in the usual organization of the chromosome.

A final category of chromosomal disorders is related to the chromosomal *structure* or placement of the genes, rather than the total number of chromosomes or the total amount of genetic material.

Robertsonian translocations fall into this “structural” category.

How Do Chromosomes Mess up their Structure?

Chromosome structure problems occur when chromosomes break and then reattach. If they rejoin at the same place they left, the process is called “*restitution*.” If they rejoin the chromosome in a new location, the process is called “*reunion*.”

Generally, pieces of broken chromosome attach to places in the chromosomes where a break has occurred. The ends of broken chromosomes are “sticky,” so they tend to attach to each other, whether the other sticky end is their original site or not.

When a *reunion* occurs (new site of attachment), the new arrangement may be “**balanced**,” meaning that the same amount of genetic material normally present in human cells will still be present and no clinical problems are likely to occur for that individual.

Alternatively, the reunion could produce an “**unbalanced**” **translocation**. An unbalanced translocation means that genetic material was either gained or lost. When an unbalanced translocation occurs during meiosis, the individual who develops from that gamete is usually affected by some clinical problems.

Balanced translocations

There are three types of balanced translocations, meaning translocations that preserve the total amount of genetic material correctly but alter the usual structure of the chromosome.

1. Balanced reciprocal translocations

Two nonhomologous (not the same) chromosomes exchange segments. Amount of material is the same, and the individual is usually fine. Gametes produced by an individual with a balanced reciprocal translocation are often abnormal, however. (So, for example, miscarriages are more frequent in this population.)

2. Inversions

A section of a chromosome *flips around* so that it is facing the opposite direction in the chromosome. The individual is usually fine, and gametes are often fine, but occasionally abnormal.

3. Robertsonian translocations

Robertsonian translocations are a special case of *unequal* reciprocal translocation.

Two acrocentric (the centromere joins the two parts close to one end of the chromosome) chromosomes form a new metacentric (joined in the middle) chromosome. They fuse near their original centromere location and lose the very short arms in the process. These short portions of the chromosome are usually non-functional, so the loss doesn't cause problems for the individual who has it. As usual, the offspring are at increased risk for problems.

The new translocation chromosome is made up of the long arms of two fused chromosomes – which means that the individual now has only 45 chromosomes!

Ring chromosomes

Deletion at each end of a chromosome allows the two ends to fuse into a ring! This can happen because the exposed rings are sticky, and sometimes they form a reunion *with each other*.

People born with ring chromosomes can be normal, near normal, or may have a variety of congenital anomalies and/or mental retardation.

For people who are affected by a ring chromosome, their phenotype is similar to individuals with a similar monosomy – depending on the quantity of genetic material lost.

Trisomy 21: Just the Facts, Please!

The majority of Trisomy 21 births are to mothers in what age group?

The 20s – they have more babies than older age groups and are less likely to be screened for trisomies.

What prenatal screening pattern suggests a Trisomy 21 fetus?

↓ AFP
↓ Estriol
↓ HCG

What ultrasound findings suggest Trisomy 21?

Thickened nuchal (neck) skin fold
Short or missing nasal bone
Short femur
+ Cardiac and GI abnormalities, of course (e.g., endocardial cushion defects, duodenal atresia)

Much has been made of translocation as a cause for Down syndrome. What's up with that?

Folks in medicine always get excited when we figure something out, so there is now a lot of talk about translocation as a cause for Down syndrome. It is true that translocation can cause Down syndrome, but the vast majority of Down syndrome patients have trisomy, *not translocation*.

The breakdown of Down syndrome causes is:

- 95 %: Three copies of chromosome 21 (trisomy)
- 1 %: Mosaic
- 4 %: Translocations

Translocation as a cause of Down syndrome is more common in younger mothers (less than 30 years old).

Half of the translocations are inherited – half are new translocations specific to that gamete.

Not all of the translocations that produce Down syndrome involve chromosome 21 alone. Sometimes other chromosomes, such as number 14, are part of the translocation process.

Parents of Down syndrome infants due to translocation should have chromosomal evaluation. Why?

To find out whether they have a translocation or not. The risk of Down recurring in a future pregnancy cannot be calculated unless you first know whether one of the parents has a translocation and which one.

The worst possible translocation to have is a 21q21q translocation. These parents have only two possibilities in offspring – autosomal monosomy (no chromosome 21q arms, which results in a nonviable fetus) or Down syndrome infants due to three copies of the q arm of chromosome 21 (two from the translocation parent and one from the presumably normal parent).

Risk of recurrence due to a parental translocation can vary depending on whether the Mom or the Dad has the translocation (oddly enough).

Pediatric Genetics and Inborn Errors of Metabolism

A Practically Painless Review

Houser, C.M.

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