



R.C.P.U. NEWSLETTER

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Family Medical History: Why it Matters

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Introduction:

Medical appointments often come with lots of questions, not only about the patient, but about the patient's family. Why is this? How can medical information about parents and siblings, or even grandparents or cousins, be important? The answer lies in our genes. Each of us is a unique individual, but at the same time, we share genetic information with every person that is biologically related to us. Just as we share (genetic) traits such as the way we look with family members, we share genes that can contribute to disease, or even prediction of disease risk.

What is a gene?:

Genes are the molecular instructions for how our bodies develop, grow, function and respond to the world around us. We inherit them from our parents in packages called chromosomes, one full set from each parent, so that under normal circumstances, we have two copies of almost every gene (genes on the X and Y, or sex chromosomes, are the exception because females have two X chromosomes and males have one X and one Y). When a cell divides, these instructions are copied and then split equally between the two daughter cells. This process is repeated over and over, during every cell division from conception until death. While there are proofreading mechanisms that act during every division cycle to recognize and repair copying errors or damaged instructions, these safeguards are not perfect. Occasionally a change in a gene's sequence, also known as a mutation, slips through.

Just like the words on this page, every gene has a correct "spelling" or sequence that is required for the gene to do its job. Changes to that sequence might be neutral (as for

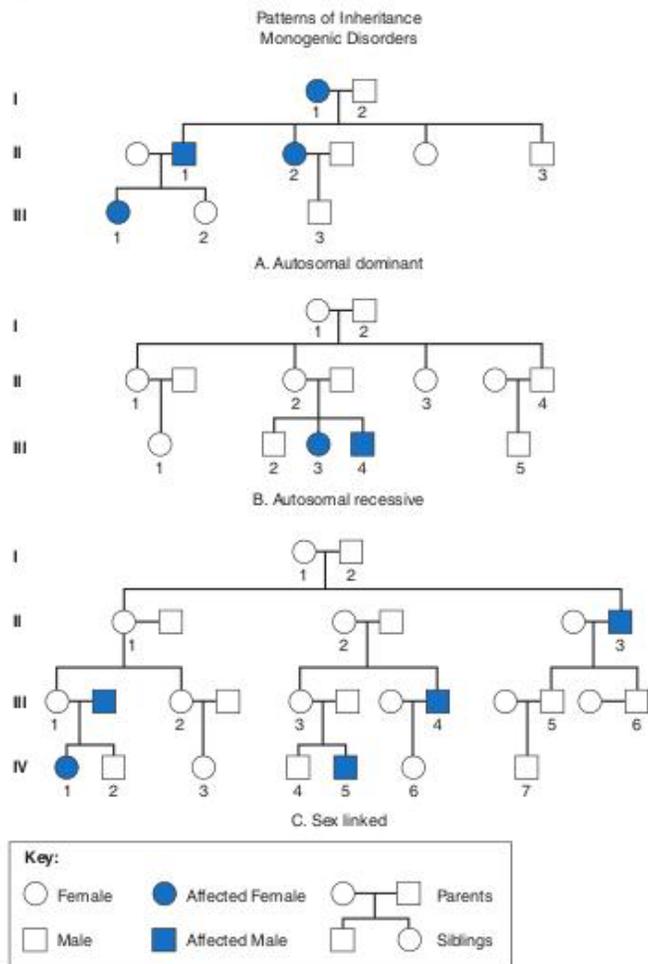
instance, the color of an elephant may be written as "gray" or "grey" without changing the word's meaning), or a mutation may completely alter the word (like "gray" to "grab" or "gry"). Regardless of its effect, once a mutation makes it through the round of cell division, it's often there to stay. The change will remain in the cell where it first arises and will be passed on to every one of its daughter cells. This process happens at every stage of life. We accumulate different genetic changes in different cells and tissues of our bodies as a normal part of aging. But if a mutation is present in a sperm or egg cell that goes on to form a new individual, that individual will have the mutation in every cell of their body, known as a constitutional mutation. These are the genetic changes that can be passed from parent to child and run in families.

In fact, every one of us is born with several constitutional mutations; there is no such thing as genetic "perfection". This is known as being a "carrier", and most of the time we never know, because the second copy of a gene is able to compensate for the changed copy. But it gets more complicated than that. Although we often think about genetics as all-or-nothing, in truth there are many different ways that genes behave and many different patterns seen in families with genetic conditions. It can take careful information gathering (that is, all of those probing medical history questions) and trained professionals to recognize the pattern in what may seem like unrelated details.

When two people who carry mutations in the same gene have children together, they may both pass on their altered gene, and a condition will appear for the first time in their child; this is called recessive inheritance. Sometimes, just one changed copy is enough to cause a disease, in which case the inheritance is termed "dominant". A condition may only

develop in some (but not all) people who inherit the changed gene, but can still be passed on to children, so that the condition appears to “skip” generations. Some genes work primarily alone, but most work together with many other genes in order to get a job done. A single gene can have more than one job, or several genes may do the same job. A gene can be active in different body parts at different times. Some mutations stop a gene from working all together, some change how well it works and others give a gene a completely new function. We have genes that are absolutely essential for life, genes for which science has yet to identify any function, and everything in between. Some genetic susceptibilities only come into play when we encounter particular environmental exposures. Human genetics is enormously complicated.

Figure 1. Patterns of Inheritance



What to look for in a (medical) family history:

Everyone gets sick from time to time, and it is natural for a family to share traits. What, then, are the kinds of things to look out for when considering whether family information might have medical importance? Here are a few of the things that might (but don't necessarily) signal a genetic condition in a family:

- Unusual features: small details can be very important. Is there a trait in the family that other people don't seem to have? Or does someone in the family have features that don't resemble those of their biological parents? Does anyone have something

“unique” about their appearance or physical abilities? Traits like birthmarks, distinctive facial features or hyperextensibility (double-jointedness) can give important clues.

- Multiple pregnancy losses: miscarriage is very common in the first trimester of pregnancy. It is not unusual for a woman to have one or two early pregnancy losses and usually this does not suggest a genetic problem. When there are repeated losses, however, it raises the suspicion that something genetic might be going on. A genetic condition that leads to multiple miscarriages might also have health consequences for other family members.
- Birth defects: approximately 3% of all babies are born with birth defects, and these are usually chance events. More than one baby with birth defects, or one baby with more than one significant birth defect raises the suspicion that there might be a genetic cause.
- Lifelong or early onset medical problems: Medical concerns often occur later in life, in part due to aging and lifestyle factors. When a chronic illness is present at birth, begins in childhood, or comes on much earlier than might be expected, lifestyle and aging have not yet had a chance to act. Therefore early-onset conditions are more likely to have a genetic contribution. This is especially true with cancers.

What if information isn't available?

When it comes to family medical history, it is information on biological relatives that counts. Some individuals may know very little about their biological families, most notably in cases of adoption. Although details may have been unavailable in an individual's past, there are several strategies that may help reveal useful information.

Ask your family:

It is understandable that, when a child is adopted, the adoptive parents may choose not to talk about the adoption details. However, the presence of an illness may change the family's perspective. Or perhaps your family is entirely open about the adoption process; every family is different. In any case, it is worth asking your adoptive family whether they have any information on your birth family. Particularly for older adopted individuals, there may be no medical information readily available. However, adoptive family members may know important clues such as ethnicity, city of birth, approximate age of the birth mother, etc. that could be a launch point for searching for biological family.

Ask the adoption agency:

Legal adoptions generate legal records and paper trails. These records may be available to an adopted individual. It has also become increasingly common for adoption agencies to collect relevant information such as medical histories from birth mothers, and to share that information with adoptive parents. If talking to your adoptive family does not yield useful information, it is possible that the adoption agency has what you need in their records. Alternatively, the agency may have

information that you can use to perform your own search.

Use social media:

Widespread access to the internet has made the world a very small place, and word of mouth is one of the most powerful information-sharing tools there is. Photos or videos go "viral" at light speed, particularly if people feel like sharing a post will help someone. If no one around you has the information you need, maybe someone "out there" does. Prepare a brief post explaining that you need help in finding information on birth family for medical reasons. Provide a few details that will help people to know if they may have any information about you (age, gender, city of birth, perhaps general details about your appearance) and provide a secure and confidential way for people to contact you. Be careful not to include anything that would compromise your safety or security, or that you would feel uncomfortable with the whole world knowing about you. Then send it into the ether and see what comes back. A birth family that chose confidentiality decades in the past may open up when they learn your health is at stake.

Have genetic testing:

Even if no information can be found about biological relatives, your own genetic information is always available to you, if you choose to pursue it. However, whether or not genetic testing will be useful depends on several factors, including the specific condition of interest, whether a genetic test exists for that condition, the accuracy of the test and how much can be predicted about a condition using genetic information. There is a wide range of genetic testing options. Direct-to-consumer tests examine ancestry and risk for some common health concerns and do not have to be ordered by a doctor. Targeted clinical testing is a medical test that looks at single genes or panels of genes to look for changes that directly contribute to illness. Whole-genome sequencing reads every letter of a person's genetic code but is not readily accessible to the public. However, the speed and price of whole-genome sequencing are dropping rapidly. Many medical professionals believe that whole-genome sequencing will become a routine medical test in the near future.

Each of these tests has pros and cons in terms of cost, accuracy, and practical application of the information gained. Some of the information discovered may be unexpected, upsetting or difficult to interpret. There is no guarantee, even with whole-genome sequencing that genetic testing will provide any answers. Finally, insurance may not cover the cost of testing, which can range from hundreds to thousands of dollars. If you decide to pursue genetic testing, it is highly recommended that you speak to a trained genetics professional, both before testing and after the results come back. A genetic counselor or clinical geneticist is trained to properly interpret genetic information, but maybe more importantly, is trained in helping individuals manage the psychological and emotional concerns that can arise in response to genetic test results.

An eye towards the future:

How much do you truly know about your grandparents' medical

histories: What about your own parents? As generations pass, it's often true that less and less information gets passed along and that important information may be lost forever. We do so much for our children to protect them and to prepare them for their futures: we ensure that they get annual checkups, vaccinations and braces; we worry about the quality of their education and may begin saving for college when they are babies; we encourage them in self-development through sports and music. But chances are that preserving the legacy of family health information for future generations rarely crosses a parent's mind. Consider constructing a family tree and opening a dialogue with family members to gather information. Include details that will help bring names to life: photographs, hobbies, significant accomplishments and events. In this way, you can begin to document not only ancestry for your children and their children's children, but significant health information so that it is there if and when they need it.

Family history resources:

- American Medical Association: Provides links to family history questions and questionnaires. <http://www.ama-assn.org/ama/pub/physician-resources/medical-science/genetics-molecular-medicine/family-history.page?>
- Find my past: Provides detailed ideas about how to access medical and family history information on distant relatives. <http://www.findmypast.com/content/20-family-history-resources>
- National archives: Research tools for family history research. <http://www.archives.gov/research/genealogy/>
- National Society of Genetic Counselors: resource for information related to genetic family histories and for location of board certified genetic counselors near you. <http://www.nsgc.org/>

About the RCPU:

The Raymond C. Philips Research and Education Unit began in 1978 when the legislature established section 393.20, F.S., of what is now known as the "prevention" legislation. It is named after Raymond C. Philips, who was the Superintendent of Gainesville's Tacachale (formerly Sunland) Center for 38 years, and was an acknowledged state and national leader in services for mentally retarded persons. The Unit is located on the Tacachale campus and is funded through a contract with the Department of Children and Families and the Department of Health.

The purpose of the R.C.P.U. is to treat, prevent, and/or ameliorate intellectual disabilities through medical evaluations, education and research. The unit provides direct evaluations and counseling to families and promotes service, education, and prevention projects.

Some of the conditions currently under study at the RCPU involve Angelman, Velo-Cardio-Facial, Prader-Willi, Fragile X, Williams and Smith-Lemli-Opitz syndromes.

The R.C. Philips Unit is a resource for all Floridians interested in the diagnosis, treatment and prevention of intellectual disabilities. Staff members are available for consultation and for educational programs for health professionals and for the community at large.

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