Genetics in Special Education Series

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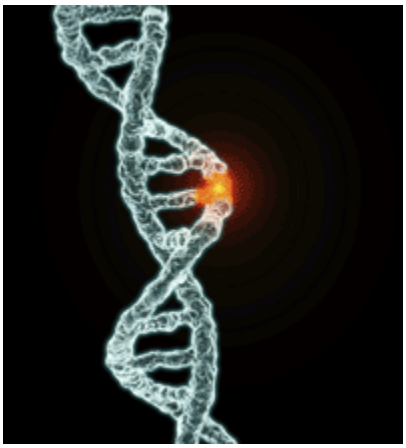

Genetic disorders presented in this issue:

Autosomal dominant polycystic kidney disease

What is autosomal dominant polycystic kidney disease?

Autosomal dominant polycystic kidney disease (ADPKD) is one of the most common forms of polycystic kidney disease. It is present at birth in 1 in 400 to 1 in 1,000 babies, and it affects approximately 400,000 people in the United States. ADPKD occurs in individuals and families worldwide and in all races.
Polycystic kidney disease (PKD) is a genetic disorder characterized by the growth of numerous cysts in both kidneys. The cysts are filled with fluid. The progressive expansion of PKD cysts slowly replaces much of the normal mass of the kidneys, and can reduce kidney function and lead to kidney failure.
When PKD causes kidneys to fail - which usually happens after many years - the patient requires dialysis or kidney transplantation. About one-half of people with the major type of PKD progress to kidney failure, also called end-stage kidney disease. PKD can also cause cysts in the liver and problems in other organs, such as the heart and blood vessels in the brain.

What are the symptoms of autosomal dominant polycystic kidney disease?

ADPKD is usually an adult-onset condition. This means that many people with ADPKD live for decades without developing symptoms of renal functional decline. People who have ADPKD have renal cysts in both kidneys and may also develop cysts in other organs such as the liver and pancreas; abnormalities of blood vessels (vascular system) such as high blood pressure (hypertension) intracranial and aortic aneurysms, heart valve defects , and abdominal wall hernias. Hypertension is the most common problem as a result of ADPKD.
About half of individuals who have ADPKD develop end-stage kidney disease by the age of 60.

How is autosomal dominant polycystic kidney disease diagnosed?

ADPKD can be diagnosed using ultrasound, CT scan or MRI studies of the kidneys. The diagnostic criteria for individuals who have a 50 percent risk of developing ADPKD include:

- At least two unilateral (cysts in one kidney) or bilateral (cysts in both kidneys) cysts in individuals who are younger than age 30.
- At least two cysts in each kidney in individuals who are between 30 and 59 years.
- At least four cysts in each kidney in individuals who are 60 years old or older.

There are two genes known to be associated with ADKPD. *PKD1* is found in approximately 85 percent of individuals who have ADPKD. *PKD2* is found in about 15 percent of individuals who have ADPKD.
A genetic test can detect mutations in the *PKD1* and *PKD2* genes, the genes that, when altered, cause autosomal dominant PKD. Although this test can detect the presence of the autosomal dominant PKD mutations before cysts develop, its usefulness is limited by two factors; it cannot predict the onset or ultimate severity of the disease and no absolute cure is available to prevent the onset of the disease. On the other hand, a young person who knows of a PKD gene mutation may be able to forestall the disease through diet and blood pressure control.
Genetic testing for *PDK1* and *PDK2* is also available for prenatal diagnosis and preimplantation genetic diagnosis. However this testing is not usually requested for ADPKD because it is usually an adult-onset condition.
What is the treatment for autosomal dominant polycystic kidney disease?
The treatment for ADPKD is aimed at treating the kidney and non-kidney symptoms. Blood pressure is followed regularly. High blood pressure is treated with medication.
Pain in the area of the kidneys is treated as needed with pain medications, and for chronic pain, with antidepressants. When standard methods to treat kidney pain do not work, then removing the fluid in the kidney cysts may be done.
When kidney function starts to decline, treatment is aimed at slowing down the progression to kidney failure. This involves controlling high blood pressure, restricting protein in the diet, controlling build up of acid (acidosis) and preventing elevated levels of phosphate (hyperphosphatemia).
When individuals with ADPKD develop renal failure, they need to have dialysis or a renal transplant. Studies have shown that individuals with ADPKD do better on dialysis than individuals with kidney failure from other causes.

Is autosomal dominant polycystic kidney disease inherited?

ADPKD is inherited as an autosomal dominant trait in families. The phrase 'autosomal dominant' means that if one parent has the disease, there is a 50-percent chance that the disease will pass to a child of either gender. In this form, one out of a person's two copies of the gene must be altered in order for the person to develop ADPKD. Most of the time, one parent must have the disease for a child to inherit it. Either the mother or father can pass it along, but new mutations may account for up to one-fifth of new cases.

Charcot-Marie-Tooth disease

What do we know about Charcot-Marie-Tooth disease?

Charcot-Marie-Tooth disease (CMT) is an inherited neurological disease characterized by a slowly progressive degeneration of the muscles in the foot, lower leg, hand, and forearm, and a mild loss of sensation in the limbs, fingers, and toes. The first sign of CMT is generally a high arched foot or gait disturbances.
Other symptoms of the disorder may include foot-bone abnormalities such as high arches and hammer toes, problems with hand function and balance, occasional lower leg and forearm muscle cramping, loss of some normal reflexes, occasional partial sight and/or hearing loss, and, in some individuals, scoliosis (curvature of the spine).
People with CMT disease usually begin to experience symptoms in adolescence or early adulthood. There is no cure for the disease, but there are treatment options, including physical therapy and bracing. Life expectancy is usually normal.
CMT disease can be divided into two classes, depending on where the dysfunction occurs in the peripheral nerves:

- ***In CMT type 1***, the peripheral nerves' axons - the part of the nerve cell that transmits electrical signals to the muscles - lose their protective outer coverings, their myelin sheaths. This disrupts the axons' function.
- ***In CMT type 2***, the axons' responses are diminished due to a defect within the axons themselves. CMT type 2, the less common of the two classes, can be further separated into at least six subtypes, caused by defects in different genes.

Is there a gene implicated in Charcot-Marie-Tooth?

The newly discovered *GARS* gene (see *Gene Discovery Opens Door to Further Research In Inherited Neurological Disorders* [News Release]) is implicated in CMT type 2D, a form of CMT that primarily affects the hands and the forearms. CMT type 2D is inherited in an autosomal dominant fashion.
Even though the *GARS* gene is implicated in only two specific types of CMT, this discovery will guide researchers in studying other forms of these diseases, as well as other neurological disorders.
Because carpal tunnel syndrome affects the hands and the forearms, scientists may now investigate whether the *GARS* gene plays some role in this disorder. And two defective forms of the gene implicated in Lou Gehrig's disease are known to interact with a *GARS* family member.
Ultimately, the *GARS* gene and its family may provide a rich new resource for scientists investigating inherited and non-inherited neurological diseases