Chronic Kidney Disease in WAGR Syndrome

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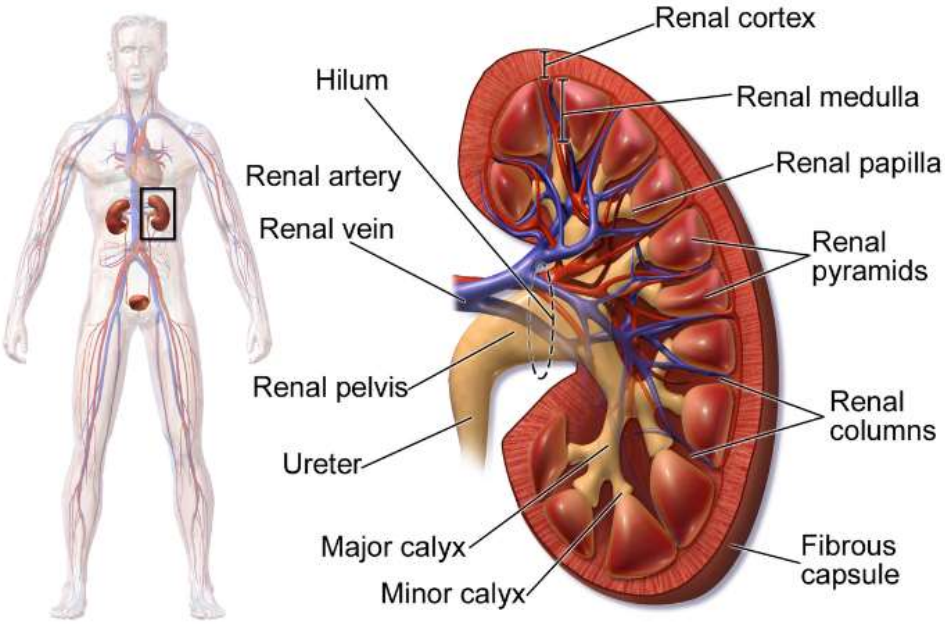
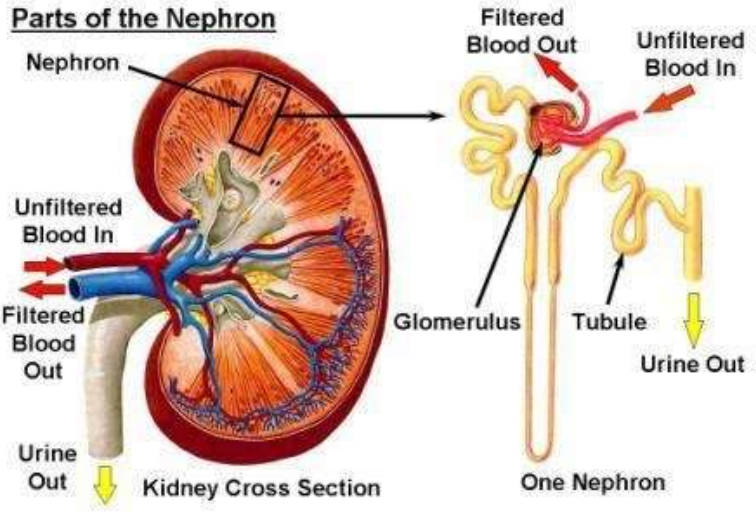
Introduction

One of the conditions associated with WAGR syndrome is a type of chronic kidney disease called FSGS, or Focal Segmental Glomerulosclerosis. Approximately 60% of individuals with WAGR syndrome will develop FSGS at some point in their lives, most often during adolescence or early adulthood.

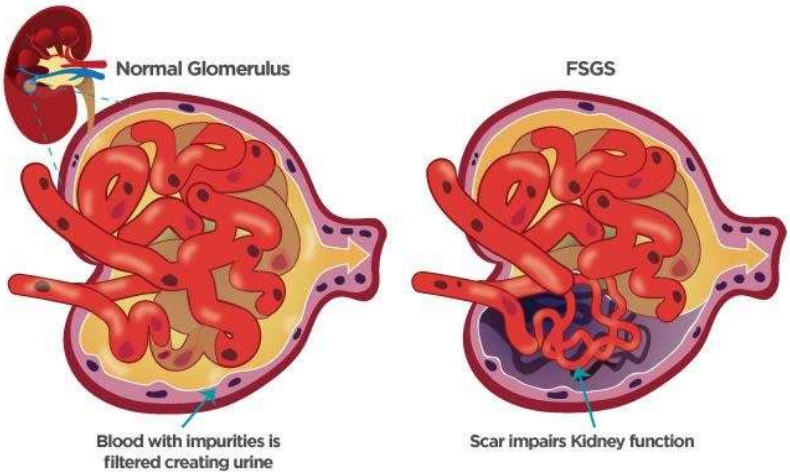
The risk for FSGS is elevated in individuals with WAGR syndrome regardless of whether they have had Wilms tumor. Symptoms may include high blood pressure, high levels of cholesterol (fat) in the blood, or protein in the urine. FSGS may progress to kidney failure, requiring dialysis or kidney transplant. Early detection of FSGS is important, because prompt treatment of FSGS can prolong the life of the kidney(s), in some cases for many years.



Kidney Anatomy



Nephrons of the Kidney



Glomerulus

The functional part of the kidney is the **nephron**. There are about 1 million nephrons in each kidney. Within each nephron, there are about 1 million clusters of vessels called "**glomeruli**." These glomeruli filter toxins out of the blood as it passes through the kidneys.

In Focal Segmental Glomerulosclerosis (FSGS), some of the glomeruli become scarred. This reduces their ability to filter out toxins. As FSGS progresses, more of the glomeruli become scarred, and the kidney begins to lose its ability to function.

Q: Do all individuals with WAGR syndrome need to be screened for FSGS?

A: Yes. We recommend that all individuals with WAGR syndrome have regular screening to detect kidney disease.

Q: My child never had Wilms tumor -- does he/she need to be screened for kidney disease?

A: Yes. Even if your child never had Wilms tumor, your child is still at risk for developing kidney problems.

Q: What is the cause of kidney disease in WAGR syndrome?

A: Patients with WAGR syndrome may have several factors that increase their risk of developing FSGS:

- The WT1 gene is critical for normal function of the podocyte, which is a glomerular cell type. WAGR patients have only one normal copy of the WT1

gene. It is thought that in many cases, this is insufficient for the podocyte to function normally.

- WAGR patients are prone to obesity, which puts a metabolic stress on the kidneys by compelling them to work harder. An analogy would be that a car engine that is driven at high speed for a long period of time will not last as long an engine that is driven moderately.

- WAGR patients who have had a Wilms tumor often have just one remaining kidney, and that kidney then is called upon to do the work of two kidneys - again, this represents stress to the kidney. By itself one kidney is unlikely to be problem (remember that people can safely donate one kidney to another person) but having only one kidney can make other kidney diseases worse.

- If high blood pressure develops, this may accelerate the progressive scarring of FSGS that was initiated by one of the other factors above.

- WAGR patients who have had radiation treatment for Wilms tumor may have radiation damage to their remaining kidney.

- WAGR patients who develop diabetes are at risk to develop diabetic kidney disease, which is a different disease from FSGS, but has in common glomerular scarring (glomerulosclerosis).

Q: At what age should the testing begin for WAGR kidney disease?

A: We recommend that testing for kidney problems begin at birth. During infancy and early childhood, individuals with WAGR syndrome are at high risk for developing Wilms tumor. During late childhood and early adolescence, the risk for kidney disease increases. Therefore, lifelong monitoring is recommended.

Q: What tests can be done to detect early kidney disease?

A: For FSGS screening, children should have at least annual measurement of blood pressure, cholesterol levels in the blood, and measurement of urine protein. Abnormalities in these tests should prompt more frequent monitoring. **Treatment for FSGS should begin at the onset of high blood pressure or elevated protein in the urine.**

There are three ways to measure urine protein:

- Dipstick test, done as part of a routine urinalysis - this can be useful but is not very sensitive (in other words, it can miss small amounts of protein in the urine that can still be a sign of kidney disease).

- Measurement of the urine protein/creatinine ratio, which is more sensitive and can detect early kidney disease.

- Measurement of the urine albumin/creatinine ratio.

Q: How is kidney disease in WAGR syndrome treated?

A: There are three therapies that slow progression of other scarring kidney diseases, and although they have not been studied specifically in WAGR patients, these therapies are likely to be effective. **Treatment for FSGS should begin at the onset of high blood pressure or elevated protein in the urine.**

1. Control of blood pressure to the age-appropriate normal level.

2. Use particular blood pressure medicines, called ACE inhibitors. These medications have three beneficial effects: they lower systemic blood pressure, they lower blood pressure within the glomerulus, and they prevent or slow the process of glomerular scarring.

3. Limit dietary sodium (salt) intake, as this lowers blood pressure and also increases the effectiveness of ACE inhibitors to reduce kidney scarring.