Tuberous sclerosis complex (TSC) is a genetic predisposition to growths in different parts of the body, and is caused by pathogenic (or harmful) variants in the *TSC1* or *TSC2* genes. Most often these growths are benign (non-cancerous) and occur on the skin, kidneys, heart, lung, and brain. Both men and women can be diagnosed with TSC. While signs of the condition can usually appear in childhood, some individuals do not know they have TSC until they are adults because they have mild symptoms, or because TSC is relatively uncommon.

Individuals with TSC can live normal lifespans, but they may develop serious health problems if they are not closely monitored by a healthcare provider experienced with the condition. TSC can potentially affect multiple body systems, however it affects individuals differently, even those within the same family.

## Genetics and Inheritance

Pathogenic variants in the *TSC1* and *TSC2* genes are inherited in an autosomal dominant pattern, meaning that children of someone who carries a pathogenic variant each have a 50% risk to inherit the variant and associated cancer risks. In one third (33%) of cases of TSC, someone has inherited a pathogenic variant in the *TSC1* or *TSC2* gene from a parent. In the other two thirds (66%) of cases, the variant was not inherited from a parent, and is something that is new to that person in the family (called de novo). Notably, women and men both have the *TSC1* and *TSC2* genes and have the same chances to inherit and pass down variants in these genes. Therefore, both sides of the family are important when assessing inherited risk.

There can be many different findings throughout many parts of the body in someone who has TSC. Here are some things that a doctor may look for to diagnose someone with TSC:

#### Skin

- Multiple angiofibromas (skin colored, pink, or red bumps) of the face
- Multiple hypomelanotic macules (light colored spots)
- “Confetti” hypomelanotic macules
- Fibrous plaque on the forehead, cheeks, or scalp
- Shagreen patches (elevated area of orange peel-like skin) on the back, buttocks, or thighs
- Fibromas (benign tumor) around or under the fingernails or toenails

**Mouth**

- Fibromas in the gums of the mouth
- Multiple pits in the tooth enamel

**Heart**

- Cardiac rhabdomyoma (tumor of the heart in childhood)

**Brain**

- Seizures
- Cortical tubers (benign lesions) found on a brain MRI
- Subependymal nodules (mass in the brain) found on brain MRI
- Subependymal giant cell astrocytoma (SEGA), a brain tumor that is noncancerous but can block of flow of cerebrospinal fluid in the brain (which is supposed to flow around you brain and down to you spinal cord)

**Eyes**

- Hamartoma (benign flat lesion) of the retina or optic nerve

**Lung**

- Lymphangioleiomyomatosis (LAM), which is when an unusual muscle cell invades the lungs, causing cysts and increasing risk for a collapsed lung. LAM mainly affects women

**Kidneys**

- Angiomyolipomas (benign tumors) of the kidneys
- Fluid filled cysts
- Renal cell cancer (3% chance)

## GENETIC TESTING FOR TSC

Genetic testing for pathogenic variants in *TSC1* and *TSC2* are currently available, but there are a few different ways to approach testing:

- *Single site analysis*: Testing specific to a known pathogenic variant in the family

- Full gene sequencing and rearrangement analysis: Comprehensive testing to search for all currently detectable variants in the gene
- Gene panels: Newer, more broadly based gene tests that would include not only the *TSC1* and *TSC2* genes, but other genes known or suspected to be associated with an increased risk for tumors or cancer.

Determining whether an individual meets criteria for genetic testing for TSC is very complex, and would likely be best left to a genetic counselor or other healthcare provider. TSC can be diagnosed by a clinical exam performed by a physician familiar with TSC, or by genetic testing for pathogenic variants in the *TSC1* and *TSC2* genes. About 95% of people who have a clinical diagnosis will be found to have a pathogenic variant in either the *TSC1* or *TSC2* genes. The remaining 5% may have a change in another gene that causes TSC that we have not yet discovered.

**Medical Management for TSC**

Medical management for someone with TSC can be complex, and should be overseen by a medical provider who is familiar with TSC. Because TSC affects people in very different ways, medical management should be tailored to an individual's specific needs. Some options for treatment include:

- Medications to help treat seizures
- Surgery to remove problematic tumors
- Brain MRI every 1-3 years (more frequently if tumors are found)
- Abdominal MRI every 1-3 years
- Annual renal function assessment
- Annual dermatologic exam
- Dental exam every 6 months

This is not a comprehensive list of recommendations, as many of these are tailored to meet someone's specific needs and current health concerns.

Click here to learn more about scheduling a genetic counseling appointment for questions about hereditary cancer predisposition.

**Resources**

Tuberous Sclerosis Alliance

[Tuberous Sclerosis International]