Tuberous Sclerosis Syndrome [1]

What is tuberous sclerosis complex?

Tuberous sclerosis complex (TSC) is a hereditary condition associated with changes in the skin, brain, kidney, and heart. Seizures are a frequent complication, and some people with TSC have learning disabilities.

Skin changes are the most noticeable sign of TSC and are present in nearly all people with the condition. While the skin changes do not have serious medical consequences, they can affect a person?s appearance. There are multiple features that have been associated with TSC. The number of features present and the severity of symptoms can vary among people with TSC, even within the same family. More information about the features of TSC is below.

Although the overall cancer risk associated with TSC is low, people with TSC do have an increased risk of a specific type of brain cancer [2] called giant cell astrocytoma and an increased risk of kidney cancer [3].

What causes TSC?

TSC is a genetic condition. This means that the cancer risk and other features of TSC can be passed from generation to generation in a family. So far, two genes have been associated with TSC; they are called *TSC1* and *TSC2*. A mutation (alteration) in either of these genes gives a person an increased risk of developing kidney cancer and other symptoms of TSC. Research is ongoing to learn more about TSC.

How is TSC inherited?

Normally, every cell has two copies of each gene: one inherited from the mother and one inherited from the father. TSC follows an autosomal dominant inheritance pattern, in which case a mutation happens in only one copy of the gene. This means that a parent with a gene mutation may pass along a copy of their normal gene or a copy of the gene with the mutation. Therefore, a child who has a parent with a mutation has a 50% chance of inheriting that mutation. A brother, sister, or parent of a person who has a mutation also has a 50% chance of having the same mutation.

How common is TSC?

It is estimated that about one in 10,000 people has TSC. As many as 60% of people with TSC do not have any family history of the condition; they have a de novo (new) mutation in the *TSC1* or *TSC2* gene.

How is TSC diagnosed?

TSC is suspected when a person has at least one major feature and one minor feature of TSC. The features are very specific, and a careful evaluation by a doctor familiar with TSC is necessary to make the diagnosis.

Major Features:

- Angiofibromas (skin-colored growths of blood vessels and fibrous tissue) on the face
- Fibromas (hard growths) around or under the fingernails or toenails
- Multiple light-colored areas on the skin, known as hypomelanotic macules or ash leaf spots
- Shagreen patch (rough growth of tissue on the surface of the skin)
- Tubers (thickened areas) found in the brain
- Nodules (round growths) found in the brain
- Giant cell astrocytoma [4] (a type of brain cancer)
- Cardiac rhabdomyoma (benign [noncancerous] heart tumor)
- Angiomyolipoma of the kidney (These are benign growths but can cause serious medical problems; there is a low risk that these tumors could become cancerous.)
- Lymphangiomyomatosis (multiple cysts or fluid-filled growths along the lymphatic system)
- Multiple hemangioblastomas (growths made of newly formed blood vessels) of the brain, spinal cord, or eye
- One or more hemangioblastomas in addition to kidney cysts, pancreatic cysts, pheochromocytoma [5] (rare tumor that usually starts in the cells of one of the adrenal glands), or kidney cancer

Minor Features:

- Multiple pits in the teeth
- Bone cysts (fluid-filled growths)
- Hamartomatous rectal polyps (overgrowths of normal tissue)
- Changes in the pattern of the white matter of the brain
- Fibromas (growths) of the gums
- Multiple kidney cysts
- ?Confetti? skin lesions (small, whitish discoloration)
- Changes in the retina (inside the eye)
- Other hamartomas (benign growths of tissue)

If a person has a family history of TSC, that person is also suspected of having TSC if they have any features of the condition. Genetic testing for mutations in the *TSC1* and *TSC2* gene is available for people suspected to have TSC. However, as many as 30% of people with TSC will not have a mutation detected in one of these genes.

What are the estimated cancer risks associated with TSC?

Both kidney [3] and brain [2] cancers have been seen in people with TSC. The risk of kidney cancer is estimated to be about 4%. The risk of giant cell astrocytoma [4] (brain cancer) is estimated to be up to 14%. A medication called everolimus (afinitor) has been approved to treat people with giant cell astrocytoma associated with TSC. This new treatment is a pill which targets a protein (mTOR) in the activated TSC pathway. Talk with your doctor for more information about treatment options.

What are the screening options for TSC?

Suggested screenings for people with TSC or at risk for TSC include:

- Ultrasound [6] of the kidneys every one to three years (or more frequently if necessary). An ultrasound uses sound waves to create a picture of the internal organs.
- Magnetic resonance imaging (MRI) [7] or computed tomography (CT or CAT) scans [8] of the kidneys, if necessary, to follow-up after the ultrasound evaluation. An MRI uses magnetic fields, not x-rays, to produce detailed images of the body. A CT scan creates a three-dimensional picture of the inside of the body with an x-ray machine.
- MRI or CT scan of the head every one to three years, through the teenage years
- Electroencephalogram (EEG), as needed, for seizure management. An EEG is a test in which electrodes are attached to the outside of a person?s head to measure electrical activity of the brain.
- Developmental and behavioral evaluations of children before they begin school and repeated as necessary
- Echocardiogram (heart evaluation) if symptoms suggest a need
- Chest CT scan if symptoms suggest a need

Screening recommendations may change over time as new technologies are developed and more is learned about TSC. It is important to talk with your doctor about appropriate screening tests.

Learn more about what to expect when having common tests, procedures, and scans [9].

Questions to ask the doctor

If you are concerned about your risk of cancer, talk with your doctor. Consider asking the following questions:

- What is my risk of brain cancer [2]?
- What is my risk of kidney cancer [3]?
- What can I do to reduce my risk of cancer?
- What are my options for cancer screening?
- What can I do about skin changes?

If you are concerned about your family history and think you or other family members may have TSC, consider asking the following questions:

- Does my family history increase my risk of brain or kidney cancers?
- Should I meet with a genetic counselor?
- Should I consider genetic testing [10]?

Additional resources

Guide to Brain Tumors [2]

Guide to Kidney Cancer [3]

The Genetics of Kidney Cancer [11]

What to Expect When Meeting With a Genetic Counselor [12]

Tuberous Sclerosis Alliance
www.tsalliance.org [13]

National Cancer Institute
www.cancer.gov [14]

American Cancer Society
www.cancer.org [15]

Cancer*Care*
www.cancercare.org [16]

To find a genetic counselor in your area, ask your doctor or visit these websites:

National Society of Genetic Counselors
www.nsgc.org [17]

National Cancer Institute: Cancer Genetics Services Directory
www.cancer.gov/cancertopics/genetics/directory [18]

Links:
[1] http://www.cancer.net/cancer-types/tuberous-sclerosis-syndrome
[2] http://www.cancer.net/node/18562
[3] http://www.cancer.net/node/18969
[4] http://www.cancer.net/node/18488
[5] http://www.cancer.net/node/19437
[6] http://www.cancer.net/node/24714
[7] http://www.cancer.net/node/24578
[8] http://www.cancer.net/node/24486
[9] http://www.cancer.net/node/24959
[10] http://www.cancer.net/node/24895
[11] http://www.cancer.net/node/24897

[12] http://www.cancer.net/node/24907
[13] http://www.tsalliance.org/
[14] http://www.cancer.gov/
[15] http://www.cancer.org
[16] http://www.cancercare.org
[17] http://www.nsgc.org/
[18] http://www.cancer.gov/cancertopics/genetics/directory