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Clinician Management Resource for Tuberous Sclerosis Complex (TSC)

This overview of clinical management guidelines is based on this patient's positive test result for a pathogenic or likely pathogenic variant in the *TSC1* or *TSC2* gene. Unless otherwise stated, medical management guidelines used here are limited to those published in the Updated International Tuberous Sclerosis Complex Diagnostic Criteria and Surveillance and Management Recommendations[1]. Please consult the referenced guideline for complete details and further information.

Clinical correlation with the patient's past medical history, treatments, surgeries, and family history may lead to changes in clinical management decisions; therefore, other management recommendations may be considered. Genetic testing results and medical society guidelines help inform medical management decision but do not constitute formal recommendations. Discussions of medical management decisions and individualized treatment plans should be made in consultation between each patient and his or her healthcare provider and may change.

SURVEILLANCE/SURGICAL CONSIDERATIONS*,[1]	AGE TO START	FREQUENCY
Brain		
Brain MRI to assess for the presence of tubers, subependymal nodules, migration defects, and subependymal giant cell astrocytomas (SEGA).	Following diagnosis	Every 1-3 years in patients without SEGA under age 25, or more often and throughout adulthood for patients with SEGA**
Surgical resection should be performed for acutely symptomatic SEGA. Cerebrospinal fluid diversion may also be necessary.	Individualized	N/A
Education of parents to recognize infantile spasms and focal seizures, even if none have occurred at the time of first diagnosis.	Following diagnosis	Individualized
EEG in asymptomatic individuals: Obtain while awake and asleep. If abnormal, especially if features of TSC-associated neuropsychiatric disorder are also present, follow-up with 8-12 hour video EEG to assess for seizure activity.	Following diagnosis	Every 6 weeks up to age 12 months, then every 3 months up to age 24 months
EEG in individuals with known or suspected seizure activity: Obtain routine EEG. Prolonged video-EEG, 24 hour or longer, is appropriate when seizure occurrence is unclear or when unexplained sleep, behavioral changes, or other alteration in cognitive or neurological function is present.	Onset of symptoms	Determined by clinical need
Epilepsy surgery should be considered for TSC patients with refractory seizures and seizures, particularly after failing three medications.	Individualized. Special consideration should be given to children at younger ages experiencing neurological regression.	N/A
TSC-associated neuropsychiatric disorder (TAND)		
Screening for TAND using validated screening tools.	Following diagnosis	Annually, or more frequently depending on clinical needs
Comprehensive assessment for all levels of potential TAND manifestations at key developmental time points.	Following diagnosis	Infancy (0-3 years) Preschool (3-6 years) Premiddle school (6-9 years) Adolescence (12-16 years) Early adult (18-25 years) As needed thereafter
Refer to appropriate professionals for the management/ intervention of relevant TAND manifestations.	Onset of symptoms	Individualized
A sudden and unexpected change in behavior should prompt a physical evaluation to look at potential medical causes (e.g. SEGA, seizures, renal disease, medications).	Individualized	Individualized
Provide parent/caregiver education and training about TAND to ensure families know what to look for in emerging TAND manifestations across the lifespan (e.g. autism spectrum disorder, language disorders, attention-deficit/hyperactivity disorder, anxiety disorders).	Following diagnosis	Individualized

SURVEILLANCE/SURGICAL CONSIDERATIONS*,1	AGE TO START	FREQUENCY
Kidney		
MRI of the abdomen to assess for the presence of angiomyolipomas and renal cysts.	Following diagnosis	Every 1-3 years
Hypertension screening by an accurate blood pressure measurement.	Following diagnosis	At least annually
Renal function evaluation by determination of glomerular filtration rate and screening for proteinuria.	Following diagnosis	At least annually
Lung		
Inquire about tobacco exposure, occupational exposures, connective tissue disease manifestations, signs of chyle leak, and pulmonary manifestations such as dyspnea, cough, and spontaneous pneumothorax in all adult patients with *TSC*.	Age 18 years	At each clinic visit
Baseline chest CT to assess for lymphangiomyomatosis (LAM).	Age 18 years or older	Every 5-7 years for all adult females with a negative screening chest CT who remain asymptomatic Individualized for symptomatic males
Follow-up chest CT in patients with evidence of cystic lung disease consistent with LAM on screening.	Individualized	Individualized
Serial pulmonary function tests (baseline and routine) in patients with evidence of cystic lung disease consistent with LAM on the screening chest CT.	Following diagnosis	At least annually; more frequently in patients who are progressing rapidly
Baseline 6-minute walk test in patients with evidence of cystic lung disease consistent with LAM on the screening chest CT.	Following diagnosis	Individualized
Education of patients and families about the signs and symptoms of pneumothorax.	Individualized	Individualized
Skin		
Dermatologic examination and ongoing education on sun protection.	Following diagnosis	Annually in children, Individualized in adults
Teeth		
Dental examination.	At the time of the eruption of the first tooth or no later than age 12 months	At least every 6 months
Panoramic radiograph to evaluate dental development.	Following diagnosis	Individualized, or if asymmetry, asymptomatic swelling or delayed/abnormal tooth eruption occurs
Heart		
Fetal echocardiography: consider to detect individuals with high risk of heart failure after delivery.	Prenatally when rhabdomyomas are identified via prenatal ultrasound	Individualized
Echocardiography	Pediatric patients following diagnosis, especially if younger than age 3 years	Every 1-3 years if asymptomatic, more frequently if symptomatic, throughout childhood.
Electrocardiography to assess for underlying conduction defects.	Following diagnosis	Every 3-5 years if asymptomatic, more frequently if symptomatic
Eye		
Ophthalmologic evaluation, including dilated fundoscopic evaluation, to assess for retinal astrocytic hamartomas, retinal achromic patches, and visual field deficits.	Following diagnosis	Annually

* The table above provides a brief summary of the surveillance guidelines published in the Updated International Tuberous Sclerosis Complex Diagnostic Criteria and Surveillance and Management Recommendations[1]. Please review the publication for complete counseling, treatment, and follow-up recommendations.

** Patients with large or growing SEGA, or with SEGA causing ventricular enlargement who are asymptomatic, should undergo MRI scans more frequently, and the patients and their families should be educated regarding the potential of new symptoms. Patients with asymptomatic SEGA in childhood should continue to be imaged periodically as adults to ensure there is no growth.

1. Northrup H, *et al.* "Updated international tuberous sclerosis complex diagnostic criteria and surveillance and management recommendations." *Pediatric Neurology* 123 (2021): 50-66.

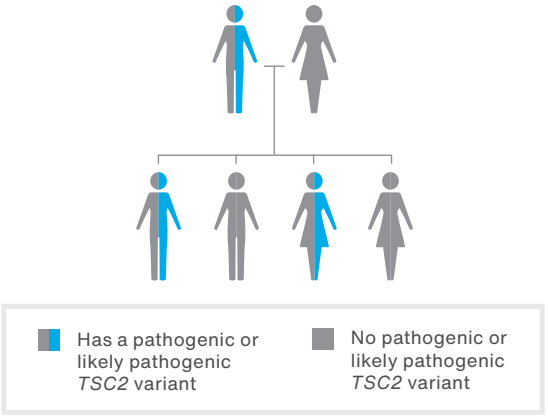
Understanding Your Positive *TSC2* Genetic Test Result

INFORMATION FOR PATIENTS WITH A PATHOGENIC OR LIKELY PATHOGENIC VARIANT

1	Result	Your testing shows that you have a pathogenic or likely pathogenic variant in the *TSC2* gene.
2	Tuberous sclerosis complex	People with a pathogenic or likely pathogenic variant in this gene have tuberous sclerosis complex (TSC).
3	Cancer and noncancerous tumor risks	You have an increased chance (2-5%) to develop kidney (renal) cancer, as well as non-cancerous tumors of the skin, brain, kidneys, heart, liver, and lungs.
4	Other Medical Concerns	People may also have additional signs of TSC, which can include: • Patches of lighter skin color, or patches of overly bumpy or smooth skin • Small bumps on the face (facial angiofibromas) • Learning problems or delays • An increased risk for seizures You should discuss the characteristics of TSC in more detail with your healthcare provider.
5	What you can do	Risk management decisions are very personal. There are options to detect cancer early or lower the risk to develop cancer. It is important to discuss these options with your healthcare provider and decide on a plan that works for you.
6	Family	Family members may also be at risk – they can be tested for the pathogenic or likely pathogenic *TSC2* variant that was found in you. It is recommended that you share this information with your family members so they can learn more and discuss with their healthcare providers.

TSC2 in the Family

There is up to a 50/50 random chance to pass on the pathogenic or likely pathogenic *TSC2* variant to each of your children.



RESOURCES

- Tuberous Sclerosis Alliance tscalliance.org
- National Society of Genetic Counselors nsgc.org
- Canadian Association of Genetic Counsellors cagc-accg.ca

Please discuss this information with your healthcare provider. The cancer genetics field is continuously evolving, so updates related to your *TSC2* result, medical recommendations, and/or potential treatments may be available over time. This information is not meant to replace a discussion with a healthcare provider, and should not be considered or interpreted as medical advice.

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MKT-ONCO-FLYR-10095-EN v6 05.05.26