Tuberous Sclerosis Australia

Tuberous Sclerosis Complex (TSC)

Tuberous sclerosis complex (TSC) is a genetic disorder that affects many organs and causes non-malignant tumors in the skin, kidney, brain, heart, eyes, lungs, teeth or oral cavity, and other organs. It is estimated that TSC affects 1 in 6,000 live births. Nearly 1 million people worldwide are estimated to have TSC, with approximately 2,000 in Australia. TSC shows no gender bias and occurs in all races and ethnic groups.

Individuals of all ages may receive the diagnosis of TSC depending on the signs and symptoms they have. The diagnosis of TSC may occur after the development of facial angiofibromas in an adolescent, because of the presence of heart tumours (cardiac rhabdomyomas) in a newborn or the onset of kidney problems in an adult. However, in the majority of cases, the diagnosis of TSC comes after the start of seizures.

TSC affects people in many different ways and with differing degrees of severity. Signs and symptoms of TSC can also progress at different rates in different individuals. This diversity and variation make it challenging to determine what healthcare is needed achieve the best quality of life for a person with TSC.

The diagnosis of TSC and further evaluation of people at risk for TSC involve careful examination of the skin, heart, eyes, brain, lungs and kidneys, as well as genetic testing. It is important to know the disorder's signs and symptoms and to follow the recommendations for screening and evaluating TSC.

Healthcare professionals from around the world with expertise managing TSC have developed diagnosis criteria and guidelines for the surveillance and management of TSC. These have been published in a series of peer-reviewed papers. This booklet summarises these diagnostic criteria and guidelines to help people with TSC, their families and health professionals. Much of this material is published with the kind permission of TSC Alliance. You can find out more about TSC at tsa.org.au/information

About Tuberous Sclerosis Australia (TSA)

TSA is the only organisation dedicated to TSC in Australia. We help in the following ways:

- Provide one-on-one phone and email support with our TSA Nurse for TSC affected families
- Publish *Reach Out*, a regular magazine
- Maintain an up-to-date detailed website of TSC related information and resources
- Connect a network of TSC families across Australia, including an online discussion group
- Hold conferences and seminars for families and health professionals
- Manage the TSC Professionals Network for health professionals involved in managing TSC
- Advocate to improve access to best practice care
- Fund and stimulate TSC research in Australia

Find out more at **tsa.org.au**

Diagnostic criteria for Tuberous Sclerosis Complex (updated 2021)

The clinical and genetics diagnostic criteria of 2021 are summarized in the table below.

Major Features	Minor Features
Hypomelanotic macules (≥3; at least 5mm diameter)	"Confetti" skin lesions
Angiofibroma (≥3) or fibrous cephalic plaque	Dental enamel pits (>3)
Ungual fibromas (≥2)	Intraoral fibromas (>2)
Shagreen patch	Retinal achromatic patch
Multiple retinal hamartomas	Multiple renal cysts
Multiple cortical tubers and/or radial migration lines*	Nonrenal hamartomas
Subependymal nodule (≥2)	Sclerotic bone lesions
Subependymal giant cell astrocytoma	
Cardiac rhabdomyoma	
Lymphangioleiomyomatosis (LAM)**	
Angiomyolipomas (>2)**	

Definite TSC: 2 major features or 1 major feature with 2 minor features.
Possible TSC: either 1 major feature or >2 minor features.
* includes tubers and cerebral white matter radial migration lines.
** a combination of the 2 Major clinical features LAM and angiomyolipomas without other features does not meet criteria for a definite diagnosis.

Genetic diagnosis: A pathogenic variant in *TSC1* or *TSC2* is diagnostic for TSC. Most TSC-causing variants are sequence variants that clearly prevent TSC1 or TSC2 protein production. Some variants compatible with protein production (e.g., some missense changes) are well established as disease-causing. Other variant types should be considered with caution.

Surveillance and management guidelines for Tuberous Sclerosis Complex (updated 2021)

PROCEDURE	FOR INDIVIDUALS NEWLY DIAGNOSED OR WITH SUSPECTED TSC	FOR INDIVIDUALS ALREADY DIAGNOSED WITH TSC
Brain		
Brain MRI with and without gadolinium	Yes	Every 1-3 years up to age 25; periodically as adults if SEGAs present in childhood
Electroencephalogram (EEG)	Yes; if abnormal, follow-up with 24-hour video EEG	Routine EEG determined by clinical need; video EEG when seizure occurrence is unclear or when unexplained behavioral or neurological changes occur
TAND checklist	Yes	At least annually at each clinical visit
Comprehensive evaluation for TAND	If warranted by TAND checklist analysis	At key development time points (years): 0-3, 3-6, 6-9, 12-16, 28-35, and as needed thereafter
Counsel parents of infants	Educate parents to recognize infantile spasms*	Not applicable
Skin, Eyes, Teeth		
Complete eye exam with dilated fundoscopy	Yes	Annually if lesions or symptoms identified at baseline
Detailed skin exam	Yes	Annually
Detailed dental exam	Yes	Every 6 months
Panoramic radiographs of teeth	If age 7 or older	At age 7 if not done previously
Heart		
Fetal echocardiography	only if rhabdomyomas identified by prenatal ultrasound	Not applicable
Echocardiogram	Yes in children, especially if younger than 3 years	Every 1-3 years if rhabdomyoma present in asymptomatic children; more frequently in symptomatic individuals
Electrocardiogram (ECG/EKG)	Yes	Every 3-5 years; more frequently if symptomatic

Kidneys

Blood pressure	Yes	Annually
Abdominal MRI**	Yes	Every 1-3 years
Glomerular filtration rate (GFR) test	Yes	Annually

Lungs

Clinical screening for LAM symptoms***	Yes	At each clinic visit
Pulmonary function test and 6-minute walk test	In all females age 18 or older; in adult males only if symptomatic	Annually if lung cysts detected by high resolution computed tomography (HCRT)
High resolution computed tomography (HCRT) of chest	In females 18 years and older; in adult males only if symptomatic	Every 2-3 years if lung cysts detected on HRCT; otherwise every 5-10 years
Counsel on risks of smoking and estrogen use	In adolescent and adult females	At each clinic visit for individuals at risk of LAM

Genetics

Genetics consultation	Obtain 3-generation family history	Offer genetic testing of TSC1/2 and counseling if not done previously in individuals of reproductive age

*Treat infantile spasms with vigabatrin as first-line therapy. Adrenocorticotropic hormone (ACTH) can be used as a second-line therapy if vigabatrin treatment is unsuccessful.
**Currently in Australia, an ultrasound/imaging of the kidneys is much more commonly used in place of an MRI of the abdomen.
***Evaluate for LAM when symptoms such as unexplained chronic cough, chest pain, or breathing difficulties are present including exertional dyspnea and shortness of breath.

References

The consensus guidelines have been published in these peerreviewed papers:

Northrup, H., et al., Updated International Tuberous Sclerosis Complex Diagnostic Criteria Surveillance and Management Recommendations. Pediatric Neurology (July 2021)

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Hinton RB et al. Cardiovascular manifestations of tuberous sclerosis complex and summary of the revised diagnostic criteria and surveillance and management recommendations from the international tuberous sclerosis consensus group, Journal of the American Heart Association (November 2014).

Teng JMC et al. Dermatologic and Dental Aspects of the 2012 International Tuberous Sclerosis Complex Consensus Statements, JAMA Dermatology (October 2014)