Tuberous Sclerosis Complex New Zealand

Surveillance and management guidelines for **tuberous sclerosis**

Tuberous sclerosis complex (TSC) is a genetic disorder that may affect nearly every organ system. 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.

Healthcare professionals from around the world with expertise managing TSC have developed guidelines for the surveillance and management of TSC. These have been published in a series of peer-reviewed papers. This publication summarises these consensus guidelines to help people with TSC, their families and health professionals.

WHAT IS 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. Individuals with TSC may be initially diagnosed because of involvement in any or all of these organs, often depending on the age at which a person receives the diagnosis.

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.

The severity of TSC can range from mild to severe, even within the same family if more than one person has 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.

It is estimated that TSC affects 1 in 6,000 live births. Nearly 1 million people worldwide are estimated to have TSC, with approximately 750 in New Zealand. TSC shows no gender bias and occurs in all races and ethnic groups.

You can read more about the signs and symptoms of TSC at **www.tsa.org.au/information**

Recommendations for **Newly Diagnosed** Individuals

Recommendations for Newly Diagnosed Individuals of **Any Age**

Review the newly diagnosed individual's nearest three generations (siblings, parents, and either children or grandparents). Genetic testing for family counseling or when TSC diagnosis is in question should be offered.

Undergo magnetic resonance imaging (MRI) of the brain to look for possible sub-ependymal giant cell astrocytomas (SEGAs), subependymal nodules (SENs), and tubers.

Have an assessment for TSC-associated neuropsychiatric disorders (TAND), a new terminology to describe the interrelated behavioral, intellectual, and neuropsychiatric features common in TSC. Download the TAND Checklist designed to be completed by a clinician.

Obtain a baseline routine electroencephalogram (EEG); if EEG is abnormal, and particularly if features of TAND are present, follow this with 24-hour video EEG to look for subtle seizure activity.

Perform MRI of the abdomen to check for possible renal angiomyolipomas or cysts. Kidney function (glomerular filtration rate, or GFR) and blood pressure should be measured.

Undergo dermatological and dental examinations to check for abnormalities of the skin and teeth that are frequently associated with TSC.

Obtain a routine electrocardiogram (ECG) to check for abnormal heart rhythm.

Obtain an echocardiogram to assess cardiac function and presence of rhabdomyomas (especially in children under 3 years of age).

Undergo an exam by an ophthalmologist for possible vision problems or abnormalities of the retina.

Additional Recommendations for Newly Diagnosed **Infants and Children (Under 3 Years of Age)**

Teach parents and other caregivers of children under 3 years of age about how to recognize infantile spasms and what to do if they suspect the child is having infantile spasms. A description and video are available at www.tsalliance.org/infantilespasms.

Additional Recommendations for Newly Diagnosed **Adults (18 Years of Age or Older)**

Perform baseline pulmonary function testing and high-resolution computed tomography (HRCT) in adult females 18 years of age or older to check for possible lymphangioleiomyomatosis (LAM). Younger females and adult males should only be evaluated for LAM when clinical symptoms are present that heighten suspicion (such as unexplained chronic cough, chest pain, or breathing difficulties).

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Recommendations for individuals **Already Diagnosed** with TSC

Once the diagnosis of TSC is established and initial diagnostic evaluations completed, continued surveillance is necessary to monitor progression of known signs and symptoms of TSC and emergence of new ones.

Recommendations for Individuals **of Any Age**

Offer genetic testing (if not done previously) and family counseling to affected individuals upon reaching reproductive age.

Obtain EEG in individuals with known or suspected seizures. The duration and frequency of EEG should be determined by clinical need rather than set or defined ages or intervals.

Treat seizures other than infantile spasms similarly to that for other types of epilepsy. In individuals with TSC whose seizures are resistant to commonly used anti-seizure medications, the ketogenic/low-glycemic diet, vagus nerve stimulation, and epilepsy surgery can be of benefit.

Screen for TSC-associated neuropsychiatric disorders (TAND) symptoms at each clinical visit. Any findings of concern should prompt more detailed evaluation and treatment. In addition, formal behavioral, intellectual, and neuropsychiatric evaluation should be performed at least once during each key developmental stage: 0-3 years old, 3-6 years old, 6-9 years old, 12-16 years old, and 18-25 years old. TAND symptoms should be treated with a combination strategy of pharmacologic and non-pharmacologic interventions, individualized for the specific TAND profile of each patient.

Perform MRI of the brain every 1-3 years until age 25 years even in asymptomatic individuals to monitor for emergence or progression of SEGA. The frequency of MRI should be increased if SEGA is large or growing. Adults with SEGA in childhood may continue to require periodic MRIs. When a SEGA is causing symptoms of fluid accumulation in the brain, surgical removal of the SEGA is the preferred treatment when possible. Growing SEGA that are not causing symptoms can be treated with surgery or mTOR inhibitors.

Obtain abdominal MRI every 1-3 years to monitor renal and non-renal TSC disease progression.

Check blood pressure and glomerular filtration rate at least annually.

Treat angiomyolipomas associated with acute bleeding by vascular embolization and corticosteroids. Angiomyolipomas without acute bleeding that are larger than 3 cm in diameter should be treated with an mTOR inhibitor as first-line therapy to prevent continued growth and bleeding; embolization and corticosteroids or kidney-sparing resection are appropriate second-line therapies.

Examine skin annually for new or worsening TSC-associated lesions. Severe or problematic lesions may be treated by surgery, laser, or topical mTOR inhibitors.

Perform a dental examination twice per year by a dentist experienced with recognition and management of dental issues common in TSC.

Undergo a detailed eye and vision examination annually in individuals with previously identified retinal lesions or new vision complaints or concerns. Individuals treated with vigabatrin should also undergo periodic ophthalmologic evaluations.

Obtain an echocardiogram every 1-3 years in individuals with previously identified cardiac rhabdomyomas until regression/stabilization of cardiac rhabdomyomas is established.

Obtain an ECG every 3-5 years to check for problems with electrical activity in the heart.

Continued overleaf

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Recommendations for individuals **Already Diagnosed** with TSC

Recommendations for **Infants and Children (Under 3 Years of Age)**

Treat infantile spasms with vigabatrin as first-line therapy. Adrenocorticotropic hormone (ACTH) can be used as second-line therapy if vigabatrin treatment is unsuccessful.

Recommendations for **Adults (18 Years of Age or Older)**

Perform clinical screening for LAM symptoms, including exertional dyspnea and shortness of breath, at each clinical visit.

Obtain HRCT every 5-10 years in asymptomatic persons at risk for LAM (all adult females 18 years of age or older and males or females of any age with clinical symptoms present that heighten suspicion). Patients with previously identified LAM should obtain HRCT more frequently (every 2-3 years) to monitor for disease progression.

Obtain pulmonary function testing annually in patients with previously identified LAM or if new respiratory difficulties or concerns arise in previously asymptomatic persons at risk for LAM.

References

The consensus guidelines have been published in these peer-reviewed papers:

Northrup, H., et al., Tuberous Sclerosis Complex Diagnostic Criteria Update: Recommendations of the 2012 International Tuberous Sclerosis Complex Consensus Conference Pediatric Neurology (October 2013)

Krueger, D.A., et al., Tuberous Sclerosis Complex Surveillance and Management: Recommendations of the 2012 International Tuberous Sclerosis Complex Consensus Conference Pediatric Neurology (October 2013)

Roth, J., et al., Subependymal Giant Cell Astrocytoma: Diagnosis, Screening, and Treatment. Recommendations From the International Tuberous Sclerosis Complex Consensus Conference 2012 Pediatric Neurology (December 2013)

Leclezio L et al. Pilot Validation of the Tuberous Sclerosis-Associated Neuropsychiatric Disorders (TAND) Checklist, Pediatric Neurology (January 2015)

deVries PJ et al. Tuberous Sclerosis Associated Neuropsychiatric Disorders (TAND) and the TAND Checklist, Pediatric Neurology (January 2015)

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)

You can view the full list of references and links to the papers online at www.tsa.org.au/guidelines-tsc

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About Tuberous Sclerosis New Zealand (TSCNZ)

TSCNZ is the only organisation dedicated to TSC in New Zealand. We are run by a dedicated team of volunteers. We work closely with Tuberous Sclerosis Australia and are a member organisation of Tuberous Sclerosis Complex International. We help in the following ways:

- Provide email and phone support for TSC affected individuals and families
- Maintain a website of TSC related information and resources
- Connect a network of TSC families across New Zealand, including an online discussion group and facebook page www.facebook.com/TSCNZ
- Publish a quarterly newsletter and contribute to ReachOut – a regular magazine published by Tuberous Sclerosis Australia
- Hold conferences and seminars for families and healthcare professionals
- Advocate to improve access to best practice care
- Support TSC research activity in New Zealand

Find out more at **www.tsc.org.nz**

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