CONSENSUS GUIDELINES FOR DIAGNOSIS, SURVEILLANCE AND MANAGEMENT OF TUBEROUS SCLEROSIS COMPLEX

Tuberous sclerosis complex (TSC) is a genetic disorder that may affect nearly every organ system, but disease manifestations vary widely among affected individuals and some can be life threatening. The diverse and varied presentations and progression of TSC are a challenge for optimal health care management with significant impact on cost and quality of life. This page provides a brief summary of the latest consensus recommendations for monitoring and treating individuals with tuberous sclerosis complex.

Healthcare professionals from around the world with expertise managing TSC met in June 2012 to update guidelines for the diagnosis, surveillance and management of tuberous sclerosis complex. The consensus reached as a result of the work before, during and after that conference has been published in the October 2013 edition of *Pediatric Neurology*.

Peer-Reviewed, Published Consensus Papers

The following papers are available free of charge with open access to anyone in the world. TSCanadaST encourages patients and caregivers to share these articles, linked on our website under *Resources: New International Consensus Guidelines for TSC* along with this summary document, with their healthcare providers, including family doctors and specialists. Future updates will also be posted on our website.

- Northrup, H., et al., **Tuberous sclerosis complex diagnostic criteria update: recommendations of the 2012 international tuberous sclerosis complex consensus conference** *Pediatric Neurology* (October 2013)

  http://download.journals.elsevierhealth.com/pdfs/journals/0887-8994/PIIS0887899413004906.pdf

- 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)

  http://download.journals.elsevierhealth.com/pdfs/journals/0887-8994/PIIS0887899413004918.pdf

RECOMMENDATIONS FOR NEWLY DIAGNOSED INDIVIDUALS

For individuals who are not healthcare professionals, below is a brief summary of the consensus recommendations for monitoring and treating individuals with TSC. A summary of updated diagnostic criteria for TSC is available here.

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 counselling 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 disorder (TAND), a new terminology to describe the interrelated behavioural, intellectual, and neuropsychiatric features common in TSC.

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 – thanks to the TS Alliance for making this video available to all.

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).

RECOMMENDATIONS FOR INDIVIDUALS ALREADY DIAGNOSED WITH TSC

Recommendations for Individuals of Any Age

Offer genetic testing (if not done previously) and family counselling 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 TAND symptoms at each clinical visit. Any findings of concern should prompt more detailed evaluation and treatment. In addition, formal behavioural, 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.

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.