UPDATED DIAGNOSTIC CRITERIA FOR 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 the diagnosis of 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*.

The International Tuberous Sclerosis Complex Consensus Conference reviewed prevalence and specificity of TSC-associated clinical manifestations and updated the TSC diagnostic criteria from 1998.

Clinical features of TSC continue to be a principal means of diagnosis but include additional clarification and simplification in the updated diagnostic criteria.

In addition, tuberous sclerosis complex may now be diagnosed in most cases via genetic testing.

The new clinical and genetic diagnostic criteria of 2012 are summarized below.

Conference attendees also updated the **consensus recommendations for surveillance and management of tuberous sclerosis complex**, available on TSCanada's website www.tscanada.ca under *Resources: New International Consensus Guidelines for TSC* .

Clinical Criteria

MAJOR FEATURES		MINOR FEATURES	
1	Hypomelanotic macules (≥3, at least 5mm diameter)	1	"Confetti" skin lesions
2	Angiofibromas (≥3) or fibrous cephalic plaque	2	Dental enamel pits (≥3)
3	Ungual fibromas (≥2)	3	Intraoral fibromas (≥2)
4	Shagreen patch	4	Retinal achromic patch
5	Multiple retinal hamartomas	5	Multiple renal cysts
6	Cortical dysplasias (≥3)*	6	Nonrenal hamartomas
7	Subependymal nodules (≥2)		
8	Subependymal giant cell astrocytomas		
9	Cardiac rhabdomyoma		
10	Lymphangioleiomyomatosis (LAM)**		
11	Anigiomyolipomas (≥2)**		
	* Includes tubers and cerebral white matter radial migration lines. ** A combination of the two major clinical features LAM and angiomyolipomas without other features does not meet criteria for a Definite Diagnosis. DEFINITE DIAGNOSIS: 2 major features or 1 major feature with 2 minor features POSSIBLE DIAGNOSIS: Either 1 major feature, 1 major and 1 minor, or ≥ 2 minor features		

Thank you to the TS Alliance for preparing this chart.

Genetic Criteria

The identification of either a TSC1 or TSC2 pathogenic mutation in DNA from normal tissue is sufficient to make a Definite Diagnosis of tuberous sclerosis complex.

A pathogenic mutation is defined as a mutation that clearly inactivates the function of the TSC1 or TSC2 proteins (e.g., out of frame insertion or deletion or nonsense mutation), prevents protein synthesis (e.g., large genomic deletion), or is a missense mutation whose effect on protein function has been established by functional assessment.

Other TSC1 or TSC2 variants whose effect on function is less certain do not meet these criteria and are not sufficient to make a Definite Diagnosis of TSC.

Note that approximately 15% of individuals with TSC have no mutation identified by conventional genetic testing, and a normal result does not exclude TSC or have any effect on the use of Clinical Diagnostic Criteria to diagnose TSC.