GENETIC TESTING CAN HELP

- The results of genetic testing can provide individuals and their families with important information by:
  - Confirming a diagnosis, particularly when clinical findings are unclear
  - Guiding treatment decisions, thereby improving outcome
  - Providing important information about prognosis and future health concerns
  - Clarifying risks to family members
  - Empowering individuals to make family planning decisions
- Genetic testing can seem complicated. Our team of certified genetic counsellors and client-care specialists are available to support you along the way

CLINICAL DIAGNOSIS AND MANAGEMENT OF TSC

With respect to the features listed in Table 2

- **A Definite Diagnosis of TSC** is made when two major features, or one major feature and 2 or more minor features are identified.
- **A Possible Diagnosis of TSC** is made when one major feature, or 2 or more minor features are identified.
- Screening recommendations are listed in Table 1 for individuals with a definitive or possible diagnosis of TSC.

Table 2. Major and minor features of TSC

MAJOR FEATURES	MINOR FEATURES
• Hypomelanotic macules (>3, at least 5-mm diameter) • Angiofibromas (>3) or fibrous cephalic plaque • Ungual fibromas (>2) • Shagreen patch • Multiple retinal hamartomas • Cortical dysplasias • Subependymal nodules • Subependymal giant cell astrocytoma • Cardiac rhabdomyoma • Lymphangioleiomyomatosis (LAM)* • Angiomyolipomas (>2)*	• Confetti skin lesions • Dental enamel pits (>3) • Intraoral fibromas (>2) • Retinal achromatic patch • Multiple renal cysts • Nonrenal hamartomas

* A combination of the two major clinical features (LAM and angiomyolipomas) without other features does not meet criteria for a definite diagnosis

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RESOURCES

Genetics professionals such as medical geneticists and genetic counsellors can discuss conditions like TSC in more detail and answer any questions you may have about genetic results. To find a genetics clinic near you visit the Canadian Association of Genetic Counsellors website www.cagc-accg.ca.

There are many online resources for individuals and families coping with the diagnosis and management of TSC, some of which are listed below.

- Tuberous Sclerosis Canada: http://www.tscanada.ca/
- Tuberous Sclerosis Alliance: http://www.tsalliance.org/
- TSC on GeneReviews: http://www.ncbi.nlm.nih.gov/books/NBK1220/
- TSC Canadian Clinics:
  - Ste. Justine Hospital, Montreal QC
  - BC Children's Hospital, Vancouver BC
  - Toronto General Hospital, Toronto ON

The Field Of Genetics Is Always Evolving And So Are We Please Visit Our Website For A Current Test List

Ask.Genetics@LifeLabs.com www.lifelabsgenetics.com 1-844-363-4357

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Tuberous Sclerosis Complex (TSC)

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THE FACTS ABOUT TSC

WHAT YOU NEED TO KNOW

- **Affects over 3500 Canadians.**
- TSC causes tumours to develop in vital organs, such as the brain, eyes, heart, kidneys, skin and lungs.
  - Most tumours are benign.
  - When heart tumours are present, they may be seen on prenatal ultrasound, providing an early diagnosis of TSC.
- **TSC is the leading genetic cause of autism and epilepsy.**
  - 90%-95% have seizures.
  - Up to 60% are diagnosed with autism.
- Individuals with TSC most often have normal life spans.
- TSC can be diagnosed at any age and occurs equally regardless of gender, race or ethnicity.

GENETICS PLAYS AN IMPORTANT ROLE

- 85-90% of individuals will have a genetic change (or mutation) in genes TSC1 or TSC2.
  - In the other 10-15% of cases, a negative genetic test does not mean that someone does not have TSC.
- Two thirds of cases result from a new mutation (first case in the family) and one third of the time, TSC is inherited from an affected parent.
- TSC is 100% penetrant, meaning that if someone has a genetic mutation in TSC1 or TSC2, the individual will have clinical features of TSC. The severity and the age of onset of TSC features can vary from person to person and even within families.
- Early diagnosis is key to early intervention, which is important to treat tumors, control seizures, and improve learning and development.
- TSC is an autosomal dominant condition. An affected person will have a 50% risk of transmitting the condition to each of their children.

1 in 6000 babies are born with Tuberous Sclerosis Complex (TSC)

CONTACT INFORMATION

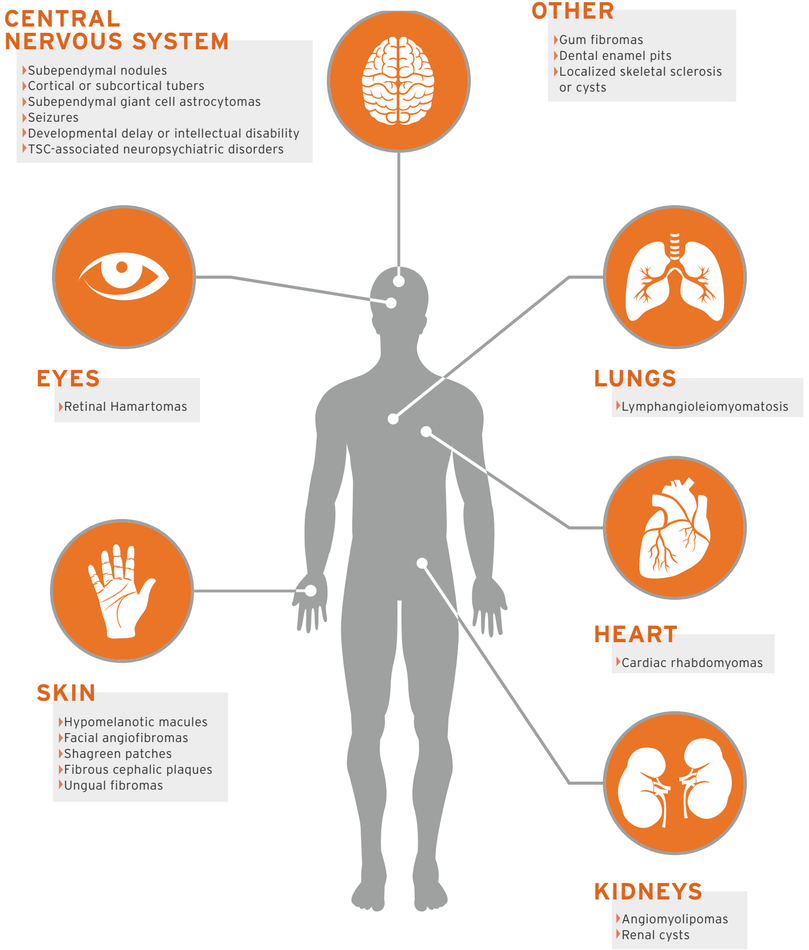
For more information about the genetic tests offered by LifeLabs Genetics, please visit our website at www.LifeLabsGenetics.ca. You may also contact us by phone **Tel: 1-84-GENE-HELP** | **(1-844-363-4357)** | **email Ask.Genetics@lifelabs.com**

CENTRAL NERVOUS SYSTEM

- Subependymal nodules
- Cortical or subcortical tubers
- Subependymal giant cell astrocytomas
- Seizures
- Developmental delay or intellectual disability
- TSC-associated neuropsychiatric disorders

OTHER

- Gum fibromas
- Dental enamel pits
- Localized skeletal sclerosis or cysts



EYES

- Retinal Hamartomas

LUNGS

- Lymphangioleiomyomatosis

HEART

- Cardiac rhabdomyomas

SKIN

- Hypomelanotic macules
- Facial angiofibromas
- Shagreen patches
- Fibrous cephalic plaques
- Ungual fibromas

KIDNEYS

- Angiomyolipomas
- Renal cysts

Table 1. Surveillance and management recommendations for newly diagnosed or suspected diagnosis

ORGAN SYSTEM	SCREENING
Genetics	• Obtain a three-generation family history to assess for additional family members at risk of TSC • Offer genetic testing for family member or when TSC diagnosis cannot be clinically confirmed • All patients/families with a clinical or molecular diagnosis of TSC should be offered genetic counselling
Brain	• Magnetic resonance imaging (MRI) of the brain • Evaluation for TSC-associated neuropsychiatric disorder (TAND), which involves the interrelated behavioral, intellectual, and neuropsychiatric features common in TSC • During infancy, educate parents to recognize infantile spasms, even if none have occurred at time of first diagnosis • Baseline routine electroencephalogram (EEG). If abnormal, follow-up with a 24-hr video EEG to assess for subclinical seizure activity
Kidney	• MRI of the abdomen • Screen for hypertension by obtaining an accurateblood pressure • Evaluate renal function by determination of glomerular filtration rate
Lungs	• Baseline pulmonary function testing (pulmonary function testing and 6-minute walk test) and high-resolution chest computed tomography, even if asymptomatic, in patients at risk of developing lymphangioleiomyomatosis (LAM), typically females 18 years or older. Adult males, if symptomatic, should also undergo testing • Counselling of adolescent and adult females on risks of smoking and estrogen use
Skin	• Detailed clinical dermatologic inspection/exam
Teeth	• Detailed clinical dental inspection/exam
Heart	• Fetal echocardiography (ECG) to detect individuals with high risk of heart failure after delivery when rhabdomyomas are identified via prenatal ultrasound • ECG in pediatric patients, especially if younger than 3 yrs of age • ECG in all ages to assess for underlying conduction defects
Eye	• Complete ophthalmologic evaluation, including dilated funduscopy, to assess for retinal lesions and visual field deficits