



The multiple manifestations of TSC

Tuberous sclerosis complex (TSC) is a multisystem genetic disorder^{1,2}

Mammalian target of rapamycin (mTOR) overactivation is a core issue in organ abnormalities of the brain, kidneys, skin, heart, and lungs.¹

- › TSC1/TSC2, the hamartin/tuberin complex, is a protein complex produced by the genes *TSC1* and *TSC2*^{1,3}
- › In normal cells, the function of the TSC1/TSC2 complex is to inhibit mTOR, an important intracellular signaling molecule¹
- › *TSC1* or *TSC2* genetic mutations lead to hyperactivation of mTOR signaling¹

An Overview of TSC Manifestations



BRAIN

- Seizures are the most common neurologic symptom of TSC⁴
 - › TSC-related seizures are associated with significant disease morbidity and mortality⁴
 - › Patients with TSC have a significantly increased risk of seizures throughout their lifetime⁴
 - >80% have seizures in the first 3 years⁵
 - >12% of adults who had no history of childhood seizures develop seizures⁴
 - Nearly 100% likelihood of recurrent seizures after a single seizure⁴
- Neurologic problems, including seizure, cause the greatest morbidity and mortality in TSC patients²
 - › Subependymal giant cell astrocytoma (SEGA)²
 - › Subependymal nodules²
 - › Cortical dysplasias²



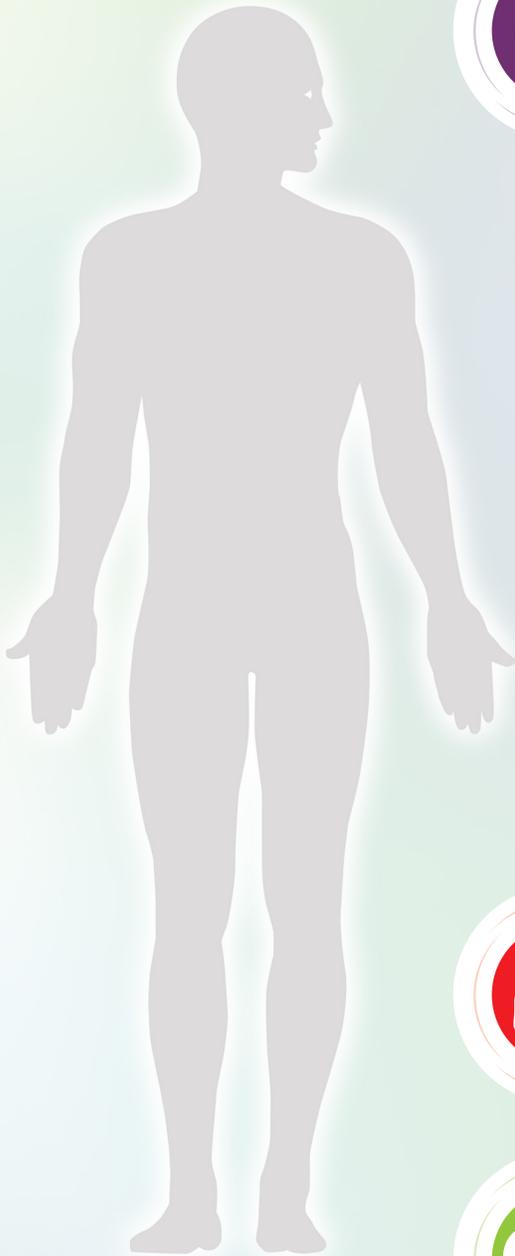
LUNGS

- Lymphangiomyomatosis occurs in 80% of females aged 40 years or older²



KIDNEYS

- Angiomyolipomas²
 - › Second leading cause of premature death after severe intellectual disability²
- Multiple renal cysts²



An Overview of TSC Manifestations



EYES

- Multiple retinal hamartomas occur in 30% to 50% of patients²
- Retinal achromic patch²



TEETH

- Dental enamel pits²



HEART

- Cardiac rhabdomyomas²

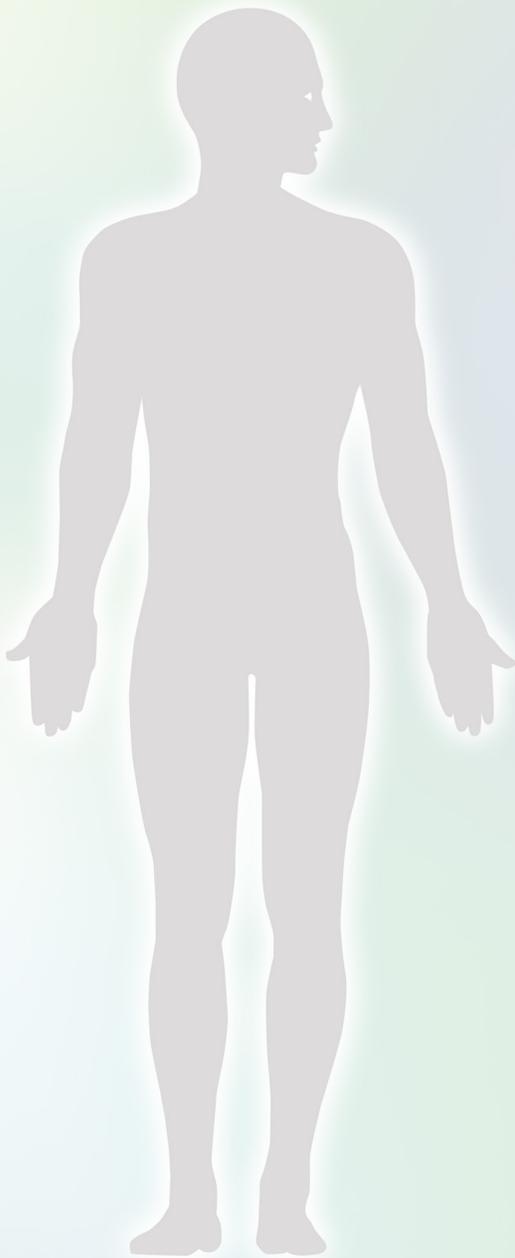


SKIN

- Hypomelanotic macules²
- Angiofibromas occur in 75% of TSC patients, usually between 2 and 5 years of age²:
 - ▶ Fibrous cephalic plaque²
 - ▶ Ungual fibromas²
 - ▶ Shagreen patch²
 - ▶ “Confetti” skin lesions²
 - ▶ Intraoral fibromas²

OTHER

- Nonrenal hamartomas²



Most common TSC manifestations

There are several manifestations present in at least 80% of the TSC population



Dental enamel pits

■ Occur in up to **100%** of patients with TSC (vs 7% of the general population)²



Hypomelanotic macules

■ Occur in **90%** of TSC patients, typically at birth or in infancy²



Seizures

■ More than **80%** of patients with TSC have seizures in the first 3 years⁵

■ **66%** of patients with TSC have refractory seizures (vs 23% of patients with seizures in the general population)^{4,6}



Renal angiomyolipomas

■ Occur in **80%** of TSC patients,² typically developing in late childhood and beyond

References:

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2. Northrup H, Krueger D, for the International Tuberous Sclerosis Complex Consensus Group. Tuberous sclerosis complex diagnostic criteria update: recommendations of the 2012 International Tuberous Sclerosis Complex Consensus Conference. *Pediatric Neurol*. 2013;49:243-254.
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4. Chu-Shore CJ, Major P, Camposano S, Muzykewicz D, Thiele EA. The natural history of epilepsy in tuberous sclerosis complex. *Epilepsia*. 2010;51:1236-1241.
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6. Berg AT, Vickrey BG, Testa TM, et al. How long does it take for epilepsy to become intractable? A prospective investigation. *Ann Neurol*. 2006;60:73-79.