Dear Colleagues,

with this flyer we would like to put a rare disease, the tuberous sclerosis complex (TSC) into focus.

TSC has many faces. Like petals of a flower this condition has facettes which are obvious. But this alleged clarity might obscure underlying crucial aspects impeding the right diagnosis.

In Switzerland only about 10% of individuals with TSC are diagnosed.

The Swiss TSC network was founded to provide a platform for the different stakeholders involved in TSC, as well as to adapt international management recommendations and guidelines according to Swiss needs.

We hope this flyer will serve well as a brief outline of TSC and help to identify more affected patients. Together we might enable a more timely diagnosis and better care for them.

Sincerely,
Your team of the Swiss TSC network

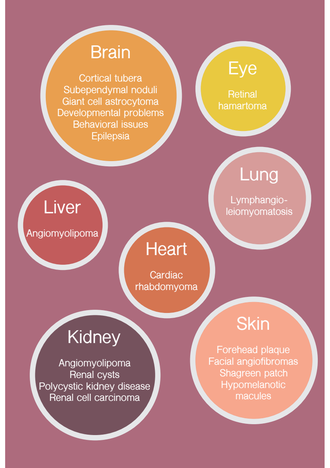
IN A NUT SHELL TSC

The tuberous sclerosis complex (TSC) is a rare genetic multi-organ disease with a prevalence of approximately 1:6000. Thus, more than 1000 individuals are possibly affected in Switzerland, but only about 10 % are diagnosed.

Due to a mutation of either the TSC1 or TSC2 gene, the mTOR (mammalian target of rapamycin) pathway is disinhibited, which may lead to uncontrolled cell and tumor growth in virtually every organ.

The clinical manifestations are highly variable, which makes the diagnosis of TSC a challenge in some cases.

If TSC remains unrecognized, affected individuals may develop acute life threatening complications such as hydrocephalus due to a giant cell astrocytoma or hemorrhage due to a ruptured renal angiomyolipoma.



DIAGNOSIS TSC

The diagnosis of TSC is based on the Gomez criteria which were updated 2012.

Hope Northrup, Darcy A. Krueger: Tuberous Sclerosis Complex Diagnostic Criteria Update: Recommendations of the 2012 International Tuberous Sclerosis Complex Consensus Conference. Pediatric Neurology 49 (2013)

MAJOR FEATURES

1 Hypomelanotic macules (≥3, at least 5 mm diameter)
2 Facial angiofibromas (≥3) or fibrous cephalic plaque
3 Ungual fibromas (≥2)
4 Shagreen patch
5 Multiple retinal hamartomas
6 Cortical dysplasias *
7 Subependymal nodules (SEN)
8 Subependymal giant cell astrocytoma (SEGA)
9 Cardiac rhabdomyoma
10 Lymphangioleiomyomatosis (LAM) **
11 Renal angiomyolipomas (AML) (≥2) **

* Includes tubers and cerebral white matter radial migration lines.

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

MINOR FEATURES

1 "Confetti" skin lesions
2 Dental enamel pits (>3)
3 Intraoral fibromas (≥2)
4 Retinal achromic patch
5 Multiple renal cysts
6 Nonrenal hamartomas

DEFINITE DIAGNOSIS

2 major features or
1 major with ≥ 2 minor features

POSSIBLE DIAGNOSIS

1 major feature or
≥ 2 minor features

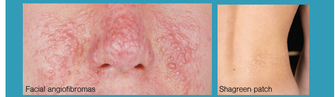
GENETIC DIAGNOSTIC CRITERIA

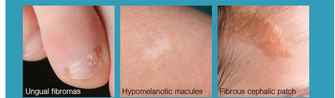
The identification of either a TSC1 or TSC2 pathogenic mutation in DNA from normal tissue is sufficient to make a definite diagnosis of TSC.

VISUAL CUES

In spite of the complexity of this condition there are characteristic symptomes or findings which allow a tentative diagnosis of TSC.

TSC can be diagnosed prenatally, when fetal ultrasound (US) reveals cardiac rhabdomyomas, and additional fetal MRI shows cranial findings such as subependymal nodules (SEN).

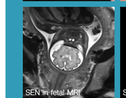

Facial angiofibromas

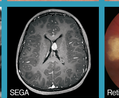

Shagreen patch

Ungual fibromas

Hypomelanotic macules

Fibrous cephalic patch


SEN in fetal MRI


SEGA


Retinal hamartomas


Rhabdomyoma in fet. US[1]


Renal AML


Dental enamel pits

Photo courtesy of: [1] Dr. Shideh Schönfeld, Berlin [2] Prof. Dr. Sevgi Tercanli, Basel

INFO TSC

A national registry has been established to record patients affected with TSC (Swiss TSC Registry).

Further information regarding this registry or concerning TSC specialists and centers in your region are available at

www.swisstscnetwork.ch

Responsible for content and design:
Dr. med. Patricia Dill for the Swiss TSC Network

The print of this flyer was financially supported by Novartis, Switzerland without influence on content and design.

TSC TIME LINE

The natural history of TSC is characterized by an age dependent development and growth of particular organ manifestations.

- Cardiac rhabdomyomas
- Renal Cysts
- Cortical tubers
- Subependymal Nodules
- Hypomelanotic macules
- Epilepsy
- Fibrous cephalic plaque
- Shagreen patch
- SEGA
- Facial angiofibromas
- Renal AML
- Ungual fibromas
- LAM (females)

Modified from Sema A, Bonny O, Bürki S, Dorn T, Fuster D, Guzmann R, Hofbauer GFL, Jenny B, Kaltner C, Plecko-Startinig B, Weibel L, Roth P, Steinlin M, Wohlrab G, Dill PE. Tuberöse Sklerose: Pathogenese, Klinik und neue Therapieansätze. Schweiz Med Forum 2013;13(36):696–702

THE RAPY TSC

Until a few years ago the therapeutic options were limited to a symptomatic and/or surgical approach.

The recent use of mTOR-inhibitors has enabled treatment of the underlying pathophysiological mechanism in TSC.

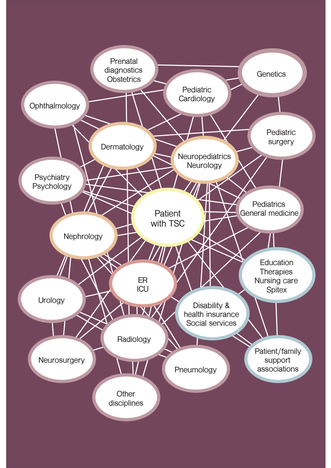
Please think of TSC in the presence of

- more than one renal angiomyolipoma
- white spots on the skin
- autistic spectrum disorder with or without epilepsy
- acne-like facial lesions refractory to therapy

TEAM TSC

The complexity of TSC requires a multi-facetted support network by an interdisciplinary team with a main contact person. According to the frequency of organ manifestations brain, skin and kidney these are often colleagues in pediatric neurology, neurology, dermatology, as well as nephrology.

Potentially any discipline can be the first point of contact of a patient with TSC.



Update Tuberous Sclerosis Complex

A condition with many facettes