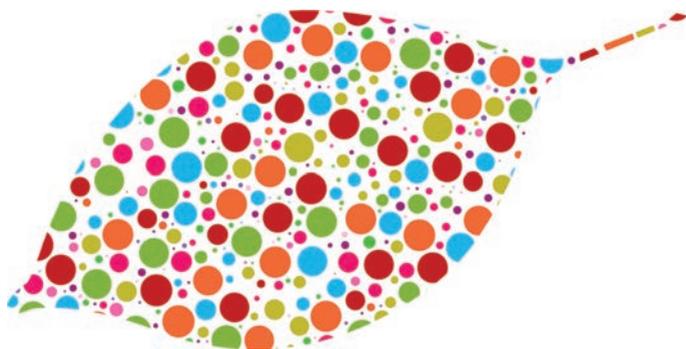


An introduction to tuberous sclerosis complex



tsa

tuberous sclerosis
association

An introduction to tuberous sclerosis complex

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Introduction

Every month about 10 babies are born in the UK with TSC. An estimated 1 million people worldwide have TSC. Some will be diagnosed very early in life while others may not be diagnosed until later childhood, adolescence or adulthood.

This booklet has been produced by the Tuberosus Sclerosis Association (TSA) to help the families and individuals newly diagnosed, and professionals caring for them, to understand more about TSC. In this booklet we describe the various ways in which a person with TSC might be affected.

It is important to keep in mind that TSC varies from person to person and that most people with the condition do not have all of the features described.



What is TSC?

TSC is a genetic condition that can lead to growths in various organs of the body, but those most commonly affected are the brain, eyes, heart, kidney, skin and lungs. These growths may be referred to as benign (non-cancerous) tumours. When they cause problems it is mainly because of their size and where they are in the body. TSC growths have different names depending on which organ they are found in. The severity of TSC varies greatly. Some people are so mildly affected that they experience very few problems. Others may be more severely affected and this can become apparent in childhood or adulthood.

It is important to know the possible effects of TSC on different areas of the body and to follow the recommendations for screening and evaluating TSC. Professionals and parents/carers should be able to identify the early complications to ensure prompt and effective treatment.

Thanks to research findings and with improved medical care, the majority of people with TSC can expect to live healthier lives with a normal life expectancy.

“ The diagnosis of TSC is based on a careful physical examination in combination with imaging studies (scans) ”

Diagnosis

People with TSC may be diagnosed in the course of investigation, during treatment for problems with specific organs or during genetic screening of family members. For example, diagnosis may follow the finding of heart tumours prenatally (during pregnancy) or in newborns, the onset of infantile spasms in babies, a diagnosis of autism in children, the development of skin problems in adolescents or the onset of kidney problems in adults. It is important to know that TSC affects each individual differently, even within a family.

There is no single clinical feature that is absolutely specific to TSC. Instead, a diagnosis of TSC is based on a careful physical examination in combination with imaging studies (scans). This testing does not cause pain to the patient. Published diagnostic criteria exists for professionals to check against and certain features need to be present or in combination to have a definite diagnosis of TSC.

A small number of NHS TSC clinics exist throughout the UK. TSC guidelines provide guidance from TSC specialists on the screening, monitoring and treatment of different aspects of TSC.

The specific tests that are performed depend on the age of the individual who is suspected of having TSC and may include the following:

-  MRI (magnetic resonance imaging) scan of the brain
-  CT (computed tomography) scan of the lungs liver and kidneys
-  Ultrasound scan of the kidneys
-  Echocardiogram (ECG) ultrasound to examine the structures of the heart
-  Eye examination to look for abnormalities of the retina
-  Skin examination under ultraviolet light
-  Genetic testing to diagnose and/or confirm a diagnosis of TSC

How a person with TSC might be affected

Several types of brain abnormalities may be seen in people with TSC. Some people will have all of these changes, and others will have none. However, the majority of people with TSC have one of these abnormalities. It is important to screen all individuals with TSC then tailor the monitoring plan for each person so that any problems can be treated should they arise.

The TSC guidelines include information on what age people should be monitored and how often, this is then broken down by abnormality and size, and also includes recommendations and actions.

Cortical Tubers Cortical tubers are disorganised areas of the brain that contain abnormal cells and are best visualised by an MRI scan of the brain. Some people may have several tubers whereas others may have one or none. Although these tubers may become easier to see on scans over time, no new tubers develop after a child is born.

Researchers used to think that neurological difficulties were caused by a combination of these:

-  The number and position of tumours (tubers) in the brain.
-  The types of seizures, age of onset and whether the seizures can be controlled.

However, as researchers have done more work, it has become clear that the molecular abnormalities caused by the TSC mutation can directly lead to learning, behavioural and mental health problems.

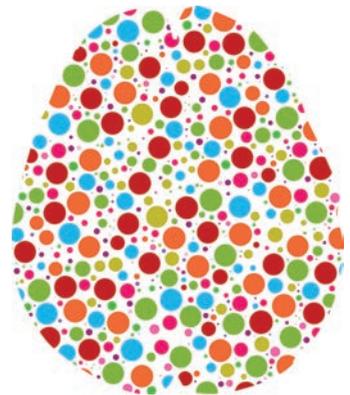
SENSs and SEGAs Subependymal nodules (SENSs) are small accumulations of cells located on the walls of the cerebral ventricles (the spaces in the brain that contain cerebrospinal fluid). The nodules often accumulate calcium, and are then easily identified on CT imaging of the brain.

Subependymal giant cell astrocytoma (SEGA, also known as SGCT) are growths that occur in up to 15% of people with TSC. SEGAs do not usually grow until later childhood, teenage years and young adulthood. They rarely grow beyond the mid 20s. The growth may be removed by surgery, or in certain circumstances it may be possible to shrink the growth using a drug treatment. More information about this drug treatment can be found by contacting the TSA.

Epilepsy

Epilepsy is the most common neurological feature of TSC.

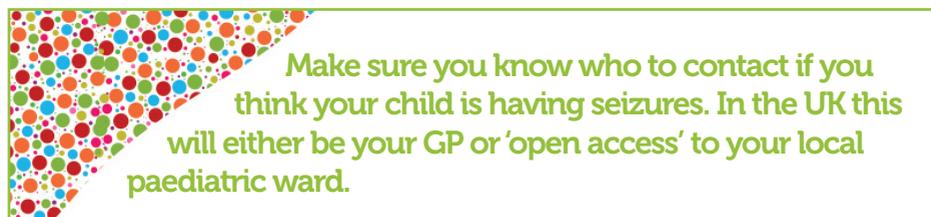
About 40% of children, usually under the age of two with TSC will have a type of epilepsy called 'infantile spasms'. It is important that carers are aware of the symptoms of infantile spasms and seek medical advice early if they have concerns. They can be difficult to identify at first and are often mistaken for other conditions such as colic or reflux by both parents and healthcare professionals.



At first the seizures may be as subtle as a gentle head nod or thrust of the chin. Over time these tend to become more obvious jerking movements. The movements themselves are usually brief and occur several to many times in a row. Most commonly these happen either first thing in the morning or on waking from a nap. The child will often seem sleepy again afterwards despite having only just woken up.

Once children begin to have infantile spasms you may notice that their development slows down. They may lose skills they

had previously learned and become less interested in people and their surroundings. Their sleep pattern may become disrupted and they may seem irritable, distant or just different from their usual self. Spasms are different from child to child, but as a parent/carer you are the best person to notice changes in your child and it is important that your concerns are taken seriously.



Older children and adults may develop other types of seizures. In some children with TSC developmental progress may depend on how severe their epilepsy is and how well it is controlled. In order to reduce the potential impacts of epilepsy it is vital that it is promptly diagnosed and treated. Throughout the UK there are specialist epilepsy centres and several epilepsy organisations that have comprehensive advice and support on all aspects of epilepsy. Some NHS TSC clinics have a particular speciality in TSC and epilepsy.

More than 50% of people with TSC who have epilepsy will not respond to standard antiepileptic medicines and may need an alternative form of treatment. Specialist epilepsy centres exist in the UK that are able to support families with complex epilepsy and advise on drug treatment, dietary options and surgery.

“ In order to reduce the potential impacts of epilepsy it is vital that it is promptly diagnosed and treated. ”

Intellectual ability, learning and academic skills in TSC

In TSC there is a very large range of intellectual abilities, from very high to extremely low.

About 30% of people with TSC will fall within the profoundly impaired range, approximately 20% of people with TSC will have an IQ slightly below the normal range and about 50% of individuals with TSC will have an IQ in the same range as the general population.



There are two main recommendations regarding assessments in TSC:

1. Perform regular assessment of cognitive development and behaviour to identify and treat emerging difficulties and to establish a baseline for evaluating any later changes.
2. Perform a comprehensive assessment when there are changes in cognitive development or behaviour to identify and treat the underlying causes of neurobehavioral change.

Refer to the **'Behaviour and learning in TSC'** to guide you on the type of assessments, monitoring and support available. They are available on the TSA's website here:

www.tuberous-sclerosis.org/factsheets.html

Behavioural difficulties

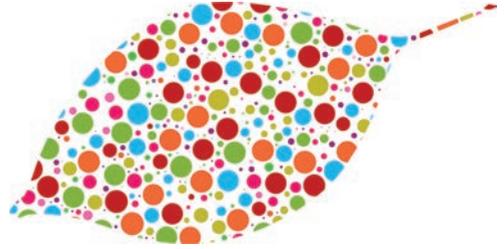
This refers to the problems that can be observed at home, at school or in a clinic. Some of these behavioural difficulties are more common in people with TSC who also have an intellectual disability. Some examples of difficult behaviours that are common in people with TSC are:

- Poor eye contact
- Aggression
- Temper tantrums
- Self-injury
- Sleep difficulties
- Anxiety
- Repetitive and ritualistic behaviour
- Speech and language delay
- Overactivity
- Restlessness
- Impulsivity
- Depressed mood
- Extreme shyness

Developmental delay is the term used when a younger children are slower to reach milestones than other children. Delay may occur in the way a child moves, communicates, thinks and learns, or behaves with others. If the delay is ongoing, the child may be diagnosed with a developmental disability. Specific developmental disabilities include autism and ADHD (attention deficit and hyperactivity disorder)

Skin

A range of skin features may develop as a result of TSC. A person with TSC may have none, some or all of the following:



- **Hypomelanotic macules**

(also known as ash leaf spots) are areas of skin that contain less

pigment than surrounding skin and therefore they appear lighter in colour. Ultraviolet light is used to identify these as they may otherwise be hard to see in babies or people with fair skin.

- **The Shagreen Patch** is a patch of skin similar in colour to surrounding skin but which is rough and dimpled like orange peel. It is usually found on the back but may be seen on other parts of the body.

- **Facial angiofibromas** can appear across the cheeks, nose and chin. These small reddish bumps often appear at the age of 4 or 5 and may increase in size with age. If facial angiofibromas become problematic, a dermatologist can treat them.

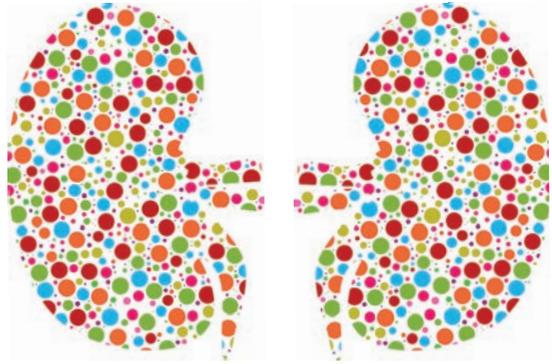
- **A forehead plaque** is flesh-coloured and are soft or compressible or doughy to hard lesion. They are found on the forehead and scalp. At the initial examination, a Wood's lamp (an ultraviolet light) will be used to better visualise the plaque, especially on infants and people with pale skin. At the same time, the skin should be carefully examined for other manifestations of TSC.

- **Ungual fibromas** are smooth, firm, flesh-coloured growths that arise next to or from underneath the nails.

Kidneys

Although many kidney abnormalities in people with TSC cause no problems, some can have an effect on the proper functioning of the kidney. The most common kidney problems in people with TSC are angiomyolipomas (AMLs). These occur in up to 80% of people with TSC. Regular monitoring by a consultant nephrologist (kidney specialist) is essential to the care of people with TSC.

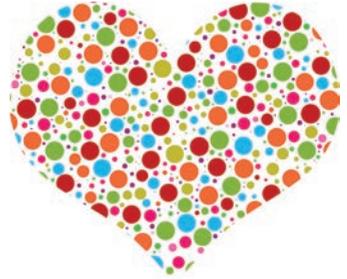
AMLs begin to grow in childhood but may not cause a problem until early adulthood. Once identified AMLs require monitoring. More information on renal AMLs and treatment options can be found by contacting the TSA.



People with TSC may also have simple cysts (fluid-filled bumps) in one or both kidneys. Usually these cause no problems. A small number (2%) of people with TSC also have polycystic kidney disease (PKD), which can cause high blood pressure and impairment of kidney function. It is important that people with TSC and PKD are under the care of a kidney specialist and centre.

Heart

Heart tumours (cardiac rhabdomyomas) occur in about 50% of babies born with TSC. Specialists recommend that everyone diagnosed with TSC have an echocardiogram and an electrocardiogram (ECG) when they are diagnosed with TSC or if TSC is suspected. This will help them see their size, location and number. These tumours are at their largest at the time of the baby's birth and get smaller over time, eventually disappearing. A few individuals will have long-term problems with heart rhythm that will need to be monitored throughout their lives.



Lungs

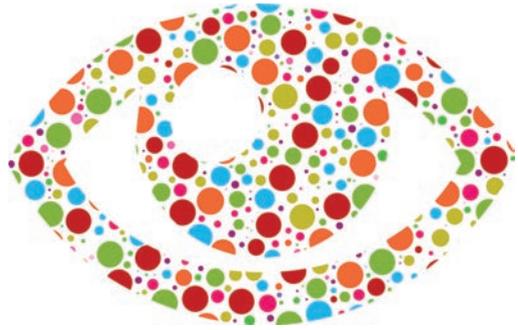
Lymphangiomyomatosis (LAM) is a lung complication of TSC caused by an overgrowth of cells in the airways, blood vessels and lymph vessels. LAM is more common in women than in men and so the female hormone oestrogen is thought to play a part in its development. Therefore LAM occurs between puberty and the menopause. LAM occurs in approximately 30% of women with TSC but only causes breathing problems in a small number of women. Women with TSC and LAM who are considering pregnancy should discuss this with their doctor first.

Recommendations from TSC experts include a high resolution CT scan followed closely by an assessment by a respiratory consultant familiar with TSC/LAM. Contact the TSA for more information on LAM screening, monitoring and treatment.



Eyes

Nearly 50% of individuals with TSC have benign (non-cancerous) tumours affecting the eyes. However, growth and change is rare so usually no treatment is required. Ophthalmologists (eye doctor) are able to check for these growths.



Teeth and mouth

People with TSC may have an overgrowth of the gums (fibromas) and dental pits (weakened enamel of the teeth). As a result, the teeth and gum tissue are slightly different and require a little more care to keep healthy. The tooth enamel will have random pits that occur on any surface and can be the spot where decay can start. The enamel pits can be easily seen by the dentist. Meticulous dental hygiene, including regular brushing and flossing are important.

Other organs

Cysts and AMLs may occur in other organs such as the pancreas, ovaries or liver. They usually do not cause any problems and therefore do not need treatment. If they do cause symptoms they need to be treated by the appropriate specialist.

Genetics of TSC

Two genes, TSC1 and TSC2 have been identified and changes in these can cause TSC. If one parent has TSC, their children will have a 50:50 chance of inheriting the faulty gene. About one in three people who have TSC have inherited a faulty gene from an affected parent. In two out of three children with TSC, neither parent is affected. In these cases it is thought the cause is a 'spontaneous' or new mutation, with this child being the first person in the family to have TSC. The cause of these new mutations is not known.



A small number of physically unaffected parents of a child with TSC have a mutation only in their egg or sperm cells; this is called germline mosaicism.

The chance of unaffected parents of a child with TSC having a second child with TSC is approximately 3% (or three in 100).

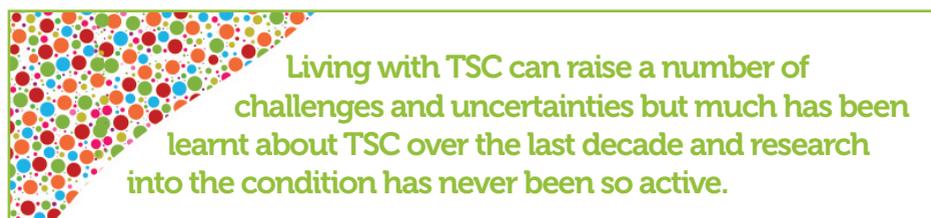
Genetic testing can be used to identify which mutation in either the TSC1 or TSC2 gene is causing a person's TSC. Testing can only be undertaken at genetics centres who will provide advice and counselling before any testing is performed. The gene can be identified in approximately 80% of cases. This information may be helpful in certain circumstances. Regional genetics centres are available throughout the UK and all are familiar with TSC, its variability and complexity.

Information and support

The TSA is here to help and support you.

The first thing to understand is that TSC is a very complex disease. TSC affects all individuals differently, so what you might read about one person and how TSC impacts his or her life may be quite different from how it impacts your life.

Another thing to remember is that different aspects of TSC affect an individual's life at different times. For example, you may be concerned about the heart tumours in a newborn baby who has just been diagnosed with TSC, but people in their 40s may only need to be concerned about the kidney tumours.



The TSA can help you access the accurate and reliable information that you need, as and when you need it. The TSA can liaise with, and signpost you to, specialist services and help raise awareness and understanding of TSC among professionals.

Please get in touch with the TSA at www.tuberous-sclerosis.org or by calling **0207 922 7731**.

TSA Advisers

We have a team of TSA Advisers across the UK.

Examples of the ways in which we can help:

- Supporting people attending meetings with professionals, school review meetings, health care meetings, complaints processes and specialist hospital visits
- Helping individuals liaising with social services and health care professionals
- Liaising on your behalf with our professional medical advisers regarding complex TSC queries
- Providing TSC awareness sessions to staff in residential homes, supported living accommodation, schools and to professional staff such as nurses, where appropriate
- Helping to set up local regional support groups
- Holding events and gatherings to exchange information, share experiences and meet others in similar situations

For more information please contact:

support@tuberous-sclerosis.org

Find your regional TSA Adviser here:

www.tuberous-sclerosis.org/tsa_advisers

The Tuberous Sclerosis Association

“To provide hope for today
and a cure for tomorrow”

References

A list of TSC scientific references, TSC clinics and TSC professional advisers is available on request.

We value your feedback

Please help us improve the information we offer by sharing your comments on this publication.

Please email information@tuberous-sclerosis.org or write to us at the address below.

Supporting the TSA

The TSA provides this information free of charge but if you would like to help cover the cost please visit the fundraising section of our website to make a donation:

www.tuberous-sclerosis.org/fundraising.html

Or send a cheque or postal order to:

**Tuberous Sclerosis Association, CAN Mezzanine,
32-36 Loman Street, Southwark, London SE1 0EH.**

Contact Us

If you would like support or further information about any aspect of TSC, please contact us at:

**Tuberous Sclerosis Association, CAN Mezzanine,
32-36 Loman Street, Southwark, London SE1 0EH**

By email: admin@tuberous-sclerosis.org

On our website: www.tuberous-sclerosis.org

By telephone: **0207 922 7731**

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www.youtube.com/TSAssociationUK

Notes

About the TSA

We're the only UK charity dedicated to supporting people affected by TSC.

Our aim is to ensure that everyone affected by TSC has the care and support they need.

 **TSCampaign:** Our commitment to raising awareness and driving forward positive change

 **TSCare:** Our commitment to enhancing quality of life for all people affected by TSC

 **TSCure:** Our commitment to research

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