

Tuberous Sclerosis Association



An information leaflet for nurses



Tuberous sclerosis complex (TSC)* is a dominantly inherited multi-system disorder. It affects approximately 1 in 7,000 new-born infants, making it one of the more common genetic diseases.

The name **Tuberous Sclerosis** is derived from one type of hamartoma (benign tumour due to failure of cell development) that occurs in the brain (cortical tuber), which looks potato or tuber like and is hard or sclerotic.

The disease most commonly affects the central nervous system, the skin and the kidneys and less commonly the heart and lungs, giving rise to a combination of symptoms which may include epilepsy, developmental delay, behavioural problems, facial skin rash (angiofibroma), depigmented skin patches and kidney disease.

** Older textbooks refer to tuberous sclerosis as Epiloia or Bourneville's disease.*



"Inspired Images", Petts, Wood Kent

Genetics

Tuberous sclerosis follows an **autosomal dominant** mode of inheritance, each affected individual having a 50% risk of passing the disorder on to the next generation.

Over 60% of cases are new mutations, the genetic fault having first occurred in the individual rather than having been passed from the generation above.

The disease is very variable in its presentation. This causes difficulties both with the diagnosis of the disease and with the genetic counselling of affected families - it may be difficult to determine whether the parents of an affected child are or are not affected themselves. A mildly affected parent (with perhaps minor skin changes) may have a child who is very severely disabled by tuberous sclerosis.

There are 2 genes responsible for TSC

- TSC1 on chromosome 9, discovered in 1997
- TSC2 on chromosome 16, discovered in 1993

Presentation of the Disease

Tuberous sclerosis can present itself with various combinations of signs and symptoms, depending which organs are involved in that particular individual. Some of the more common problems are listed below.

Skin Involvement

There is a wide variety of skin features which occur in various frequencies. Many of them cause no problems to the affected individual but are useful in the diagnosis of the condition.

- **Hypomelanotic Macules** - occur in 80 – 90% of patients, but may not be present in the first year of life and may disappear later. They can be seen without ultraviolet light but are more obvious under it. (They can however, present in infants who do not have TSC, 8 /1000).



- **Facial Angiofibroma** - areas that look like tiny blood blisters at first but are composed of blood vessels and fibrous tissue. They are rarely seen before the age of 2 years and sometimes don't appear until middle age. They appear in up to 85% of those affected and the rash occurs in a butterfly distribution over the cheeks and nose, involving the nasal folds. The area between the chin and lower lip can also be affected. It can be very disfiguring, causing the individual considerable distress.



- **Forehead Fibrous Plaques** - raised areas of discoloured skin on the forehead, occurring in up to 25% of affected individuals. They can be present in the first few weeks of life. Unique to TSC, they are a good diagnostic sign.

- **Shagreen Patches** - areas of thickened leathery skin, present in 40% of affected individuals, usually over the lower lumbar region, slightly to one side of the mid-line.



- **Ungual Fibromas** - small fleshy fibromas which grow on the nailbed, occurring in 50% of sufferers. They may be seen on the toenails or finger nails and may require to be surgically removed if they enlarge or if bleeding is a problem. Nail ridges are due to unguinal fibromas (which may not be visible) in the nail bed.



- **Molluscum Fibrosum** - skin tags can be profuse and typically occur across the back of the neck and shoulders. They can also be found in individuals who do not have TSC.

Eyes

- **Phakomas** - examination of the dilated pupils with a fundoscope may reveal phakomas (benign growths seen as white patches on the retina) in up to 50% of affected patients.

Neurological Involvement

A CT or MRI scan is used to determine the presence of cortical tubers in the brain. These cortical tubers can be multiple but do not tend to enlarge after the age of five years. A CT scan is more sensitive than MRI in finding the calcified subependymal nodules which are characteristic of TSC and are present in 80% of affected individuals.

The subependymal glial nodules have the potential to grow and can cause raised intracranial pressure. They usually occur along the walls of the lateral ventricles or 3rd ventricle, causing secondary hydrocephalus as they grow. This occurs in 5 – 14% of TSC patients.

More commonly the neurological involvement results in epilepsy, learning or behavioural disabilities.

- **Epilepsy** - occurs in 60-70% of affected individuals. Onset is often in the first year of life, presenting with infantile spasms. However, a full spectrum of seizures can occur, including myoclonic seizures, complex partial and generalised seizures. It is thought that the early treatment of seizures (and of infantile spasms in particular) is an emergency and can help prevent the child developing learning problems. The onset of seizures after the age of 12 – 18 months is likely to result in fewer children developing learning disabilities and those that do are likely to be less severe than in those with early onset of seizures, unless the epilepsy is poorly controlled. Unfortunately there is often a poor response to antiepileptic therapy and it is estimated that a large proportion of children are still fitting at the age of 5 years.

- **Learning Disability** - occurs in 40% of individuals and tends to be associated with seizure disorder. Lack of speech is a common feature of the TSC learning problems, occurring in 50% of the severely affected group.
- **Behavioural Difficulties** - tend to be associated with learning disabilities. Autistic features are evident in 50% of cases and other problems are hyperactivity, attention deficit, sleep problems, destructive behaviour and self harm. The behaviour problems can be the most difficult of all the TSC problems for the carers to manage.

Renal Involvement

The kidneys are affected in 80% of individuals with TSC by their 20's or 30's. Renal ultrasound is routinely used to look for abnormalities, and sometimes it may be necessary to follow this up with a CT scan.

- **Angiomyolipoma (AML)** - these are abnormal growths of fatty and muscle tissue in the kidneys. Many are asymptomatic but they can cause problems if they continue to enlarge, including flank pain and haemorrhage. Haemorrhaging can be profuse causing shock and necessitating surgical intervention - embolisation or nephrectomy.
- **Cysts** - they are less common than AMLs. They can be indistinguishable from autosomal dominant polycystic kidney disease. They may result in hypertension and renal failure.
- **Renal Cell Carcinoma** - a small number have been reported in less than 5% of sufferers.

Cardiac Involvement

Rhabdomyoma - these may be seen on the 2nd trimester ultrasound scan during pregnancy or on cardiac ultrasound. They are most commonly found in early childhood, regressing with time. The reason for this is at present unknown. They may cause arrhythmia or Wolfe-Parkinson-White Syndrome.

Pulmonary Involvement

Lymphangiomyomatosis - this occurs in less than 5% of affected individuals and is generally confined to females.

Liver Involvement

Angiomyolipoma (25%) and cysts - they are mostly asymptomatic and can be seen on ultrasound.

Teeth and Gums

Dental pits - the teeth can be pitted due to areas of enamel hypoplasia. These are more frequent in TS when they are often multiple. Gum fibromas may also occur.

Diagnosis

Two TSC genes have now been discovered (TSC1 and TSC2 on chromosomes 9 and 16 respectively), and molecular genetic testing will gradually become available. Until then diagnosis depends upon the individual having two or more types of lesions (NB this is taken from the Revised Clinical Diagnostic Criteria published in the Journal of Child Neurology, December 1998). A careful clinical examination is essential in combination with a CT or MRI of the brain and an ultrasound of the liver and kidneys. The examination should include

- Examination of the skin with and without an ultra violet light for the wide variety of skin signs

- Examination of the finger and toenails for unguis fibroma or grooves
- Examination of the teeth and gums for teeth pits or gum fibroma
- Fundoscopy of the dilated pupils

Prognosis

The prognosis in TSC is usually normal and even severely handicapped individuals may nowadays live to become elderly, provided they are monitored regularly and treated symptomatically. Tuberosus sclerosis is not generally classed as a progressive disorder. The chief early problems may be epilepsy, learning difficulties and behavioural problems due to brain lesions and the severity of these problems is apparent by the age of 5-10 years. Late complications include kidney problems (such as haemorrhage from AMLs, hypertension, or renal failure from polycystic kidneys or carcinoma), or more rarely lymphangiomyomatosis or hydrocephalus.



"Inspired Images", Petts, Wood Kent

Treatment

Treatment of the disease concentrates on controlling the symptoms and monitoring the complications. The main screening presently includes regular renal ultrasounds, BP monitoring and brain scanning when indicated. Carers should be aware of the warning signs of complications and have access to professionals who are familiar with the disorder.

Professionals involved may include

Geneticist - for genetic counselling which would include information about the disorder and prognosis and also wider family investigations.

Neurologist or epilepsy specialist - for management of anticonvulsant therapy.

Neurosurgeon - if epilepsy surgery is being considered or if a tumour obstructs the ventricles, causing hydrocephalus.

Psychiatrist or Psychologist - for behaviour management. Early intervention in behaviour problems can be useful and the TSC Clinic at Cambridge has a special interest in this field.

Dermatologist - a variety of treatments, including laser therapy, can be used to treat the facial angiofibroma and the unguis fibromas.

Nephrologist - if renal pathology is symptomatic. Haemorrhage can often be treated with embolisation or conservative surgery.

Cardiologist - for investigation or if antiarrhythmic treatment is necessary. Occasionally surgery may be required.

Chest physician - if pulmonary problems develop. If repeated or bilateral pneumothoraces occur, pleurectomy may be required. Treatment with hormones may be appropriate.

Social Worker - to assist in other areas, including respite and benefit needs.

Therapists and Teachers - referral to speech, occupational or physiotherapists may be necessary. Education provision will depend upon the presence or degree of learning disabilities.

Warning Signs to Look Out For

- worsening fits
- increased headaches, vomiting, sudden walking or sight problems
- changes in behaviour
- anaemia
- haematuria
- urinary tract infections
- unexplained fevers
- tummy or flank pain
- shortness of breath or poor skin colour

Hospitalisation

Children or adults who have learning and or behavioural problems are often very upset by the change of environment and routine that hospital admission brings. Their needs can be very different from others admitted for the same investigations or treatment. Family and/or carers are often in the best position to advise on the ways to approach new situations, such as investigations. The establishment of trust and relationships are important. Extra time and effort will be required, often on a one to one basis.

Tuberous Sclerosis Association (TSA)

The Association provides accurate and up-to-date information about tuberous sclerosis and advice for professionals as well as families. It also organises study days for professionals. For details of our extensive range of literature, including our medical brochure and Warning Signs leaflet, please contact the National Secretary at the address below.

Specialist Tuberous Sclerosis Clinics have been established and supported by the TSA. The clinics are situated in Leeds, Bath, Cambridge, London, Edinburgh and Belfast and offer support and advice in the various problems arising from tuberous sclerosis.

The TSA is currently funding research into the development of a genetic test for tuberous sclerosis. This will hopefully be available in the next few years, offering a diagnostic test and also the option of prenatal testing.

*Further information on TSC and the work of the TSA
can be obtained from: Mrs. Diane Sanson, Head of Administration,
PO Box 12979, Barnt Green, Birmingham B45 5AN
Tel/Fax: 0121 445 6970
Email: diane.sanson@tuberous-sclerosis.org
Web: www.tuberous-sclerosis.org*

Tuberous Sclerosis Association



The Tuberous Sclerosis Association is a Company Limited by Guarantee
Registered in England No. 2900107. Registered Charity No. 1039549

March 1999