The Tuberous Sclerosis Alliance (TS Alliance) -- the only national voluntary health organization for the genetic disorder known as tuberous sclerosis complex (TSC) -- is a membership-based organization; members have voting privileges at the organization's annual meeting. It is also the lead organization for the funding of medical research related to TSC. Such medical research has included the breakthrough discovery of two genes (TSC1 and TSC2) that are known to cause the disorder.

WHAT IS TSC?
Tuberous sclerosis complex (TSC) is a genetic disorder that causes tumors to form in many different organs, primarily in the brain, eyes, heart, kidney, skin and lungs. You will see it referred to both as tuberous sclerosis (TS) and tuberous sclerosis complex (TSC). The term TSC is used in scientific literature to distinguish tuberous sclerosis from Tourette's syndrome.
The true prevalence of TSC is unknown, but its incidence has recently been estimated to be 1 in 6,000 live births. This means approximately 50,000 individuals in the United States and more than 1 million worldwide have TSC. It occurs in both sexes and in all races and ethnic groups.
Because TSC is a genetic disorder, it is not contagious. It is the result of a genetic mutation over which a parent has no control. It is often first recognized in children who have two neurological symptoms—epileptic seizures and/or varying degrees of mental handicap. However, the clinical symptoms of TSC vary greatly and may often not appear until later in life. There are presently no cures and there is no way to predict how severely or mildly an individual may be affected by TSC.

QUESTIONS AND ANSWERS
What is tuberous sclerosis complex (TSC)?
Tuberous sclerosis complex is a genetic condition characterized by lesions of the skin and central nervous system, tumor growth and seizures. The disease affects some people severely, while others are so mildly affected that it often goes undiagnosed. Some people with tuberous sclerosis experience developmental delay, mental retardation and autism. However, there are also many people with tuberous sclerosis living independent, healthy lives who are enjoying challenging professions such as doctors, lawyers, educators and researchers.

How many people have tuberous sclerosis?
At least two children born each day will have tuberous sclerosis. Current estimates place tuberous sclerosis affected births at one in 6,000. Nearly 1 million people worldwide are known to have tuberous sclerosis, with approximately 50,000 in the United States. There are many undiagnosed cases due to the obscurity of the disease and the mild form symptoms may take in some people. TSC is as common as ALS (Lou Gehrig's Disease) but virtually unknown by the general population.

How does a person develop tuberous sclerosis?
Tuberous sclerosis is transmitted either through genetic inheritance or as a spontaneous genetic mutation. Children have a 50 percent chance of inheriting TSC if one of their parents has this condition. At this point, only one-third of TSC cases are known to be inherited. The other two-thirds are believed to be a result of spontaneous mutation. The cause of these mutations is still a mystery.
If a parent has a mild form of tuberous sclerosis, will their child with tuberous sclerosis also be mildly affected?

People with mild cases of tuberous sclerosis can produce a child who is more severely affected. In fact, some people are so mildly affected that they may only find out they also have TSC after their more severely affected child receives a diagnosis of TSC.

How is tuberous sclerosis diagnosed?
Diagnosis of tuberous sclerosis is currently made after the following tests are performed: a brain MRI or CT Scan, renal ultrasound, echocardiogram of the heart, EKG, eye exam and a Wood’s Lamp evaluation of the skin.

What genes are responsible for tuberous sclerosis?
Two genes have been identified that can cause tuberous sclerosis. Each person carries two identical genes, to develop TSC one of the genes needs to be affected. The TSC1 gene is located on chromosome 9 and is called the hamartin gene. The other gene, TSC2, is located on chromosome 16 and is called the tuberin gene. Researchers are now trying to determine what these genes do and how a defect in these genes causes tuberous sclerosis.

How can so many different organs be affected by tuberous sclerosis?
Both the TSC1 and TSC2 genes are believed to suppress tumor growth in the body. When either of these genes is defective, tumors are not suppressed and tuberous sclerosis results. The genes also play a role in the early fetal development of the brain and skin.

Are the tumors cancerous?
The tumors resulting from tuberous sclerosis are non-cancerous, but may still cause problems. Tumors that grow in the brain can block the flow of cerebral spinal fluid in the spaces (ventricles) in the brain. This can lead to behavior changes, nausea, headaches or a number of other symptoms. In the heart, the tumors are usually at their largest at birth, and then decrease in size, as the individual gets older. These heart tumors, called cardiac rhabdomyomas, can cause problems at birth if they are blocking the flow of blood or causing severe arrhythmia problems. The tumors in the eyes are not as common, but can present problems if they grow and block too much of the retina. The tumors in the kidney (renal angiomyolipoma) can become so large they eventually take over all of the normal kidney function. In the past, the patient was left until they developed kidney failure. Today, doctors are more aggressive and remove individual tumors before they get too large and compromise healthy kidney tissue. Very rarely (less than 2 percent of) individuals with TSC develop malignant (cancerous) kidney tumors.

What is the normal life expectancy of an individual with tuberous sclerosis?
Most people with TSC will live a normal life span. There can be complications in some organs such as the kidneys and brain that can lead to severe difficulties and even death if left untreated. To reduce these dangers, people with TSC should be monitored by their physician throughout their life, for potential complications. Thanks to research findings and improved medical therapies, people with tuberous sclerosis can expect improved health care.

Since there is no cure, what can be done?
Early intervention is helping to overcome developmental delays. Advancements in research are bringing new and improved therapeutic options. Surgery to remove tumors or stop tumor growth is helping to preserve the function of affected organs. Technology is pinpointing the exact portions of the brain stimulating seizures and creating new therapies to help control seizures. With every new day we are one step closer to finding improved treatments.

GENETICS OF TSC
Tuberous sclerosis complex (TSC) is a genetic condition, meaning that it is caused by a change, or mutation, in one gene. Genes are the instructions for the normal growth and maintenance of our bodies. Each of us has thousands of genes, and each gene is responsible for the direction of a specific protein or component of our bodies. A gene that carries a mutation is unable to instruct the body to grow correctly, causing a disruption in normal development and functioning.
Mutations in one of two genes, TSC1 and TSC2, have been identified as causes for tuberous sclerosis. All genes, including those involved in TSC, come in pairs, with one copy inherited from (or passed down by) the mother, and the other copy inherited from the father. In some genetic conditions, like TSC, a mutation in one copy of the gene is enough to cause the condition. These conditions are called dominant conditions because the mutation in one copy "dominates" over the normal copy, causing the condition and its symptoms. In other genetic conditions, both copies of the gene must have mutations before the symptoms occur. These are known as recessive conditions. One well-known recessive condition is cystic fibrosis. Approximately 33 percent, or one-third, of people with TSC inherits it from a parent who also has tuberous sclerosis. This occurs via dominant inheritance. When you have children, you pass on one copy of each of your gene pairs to the child, and your partner passes on one copy. The passage of one gene copy from each parent ensures that the child is a genetic "mix" of both parents. If a parent has TSC and passes on the copy of the gene with the mutation, then the child will also have TSC. If the parent passes on the copy of the gene without the mutation, the child will not have TSC. Thus, there is a 50 percent chance with each pregnancy for a parent with TSC to have a child with TSC. This is true regardless of the sex of the parent or the sex of the child.

In the remaining 66 percent, or two-thirds, of people with TSC, neither parent shows any symptoms or signs of TSC. It appears that one of the normal genes from either parent changes to the abnormal form, leading to a new (or sporadic) occurrence of TSC in the child. Normally, these parents do not have another child with TSC because the mutation was sporadic, not inherited. However, some families have more than one child with tuberous sclerosis, even though neither parent showed symptoms or findings of TSC.

How does this occur? Scientists have determined that a small number of physically unaffected parents of a child with TSC actually have TSC mutations in some of their cells. Because the mutation is limited to a small portion of all of the body's cells, these individuals show no signs of TSC. But if a portion of the egg or sperm cells of a parent carries the TSC mutation, that parent can have more than one affected child, possibly at the same 50/50 chance that people with TSC have. A person who carries cells with TSC mutations in her egg or his sperm supply has germline mosaicism. "Mosaicism" means that the person's body is made up of a combination of cells with and cells without a TSC mutation. "Germline" refers to the presence of cells with TSC mutations in the egg or sperm cell supply. Germline mosaicism is relatively rare, and this explanation does not apply to most families with a sporadically affected child. However, the occurrence of germline mosaicism has led geneticists to estimate a recurrence risk (or chance that a family with a sporadically affected child will have another child with TSC) ranging from 1 percent to 3 percent. At this time, there is no simple way to determine whether an unaffected parent of a child with TSC has germline mosaicism.

CLINICAL MANIFESTATIONS

- Heart Involvement
- Brain Involvement
- Psychiatric and Behavioral Involvement
- Lung Involvement
- Kidney Involvement
- Skin Involvement
- Eye Involvement
- Other Organ Involvement

First described in the 1880s, tuberous sclerosis complex (TSC), also known as Bourneville's Disease, is a genetic disease that affects multiple organs. It can cause tumors in the skin, kidneys, brain, heart, eyes, lungs, teeth as well as other organ systems. In most individuals, the disease affects only some of these organs. The severity of TSC can range from mild skin abnormalities to, in severe cases, mental retardation or renal failure. Many TSC manifestations also develop later in life. Most individuals who are mildly affected by TSC lead active and productive lives, but it is important to realize that TSC is a life-long companion and individuals should receive continuous follow-up care.
Due to better testing methods, estimates of TSC frequency have risen dramatically in recent years as individuals with less-severe manifestations of TSC are identified. Population-based studies suggest a prevalence of 1 in 9,407 individuals, but recent estimates place the prevalence to be 1 in 6,000 live births. It is estimated that approximately 50,000 Americans and 1 million individuals worldwide have TSC.

HEART INVOLVEMENT

MANIFESTATIONS

Testing of the heart using echocardiography is performed to visualize cardiac rhabdomyomas, the most common primary cardiac tumor of tuberous sclerosis complex (TSC) in infancy and childhood. The incidence of these tumors in TSC has been reported to vary from 47 percent to 67 percent. Childhood tumor regression is the rule. In other words, in most cases, cardiac tumors are their largest at birth and may shrink or disappear, as the individuals grow older. A second peak in the incidence of these tumors may occur during puberty.

Electrocardiograms (EKGs) are used to detect abnormal heart rhythms or arrhythmias. Any symptoms should be monitored by a cardiologist who is aware of the risks involved for individuals with TSC.

TREATMENT

Cardiac rhabdomyomas are more likely to be the cause of heart failure in a newborn infant or young child than in an adult with TSC. Most rhabdomyomas of the heart are asymptomatic, but an experienced cardiologist should treat them if an arrhythmia or other cardiac problem is present. Cardiac arrhythmias infrequently have developed in children just after starting carbamazepine (Tegretol), used for the treatment of epilepsy. Reports have also shown a significant increase in the size of cardiac rhabdomyomas in infants with TSC with infantile spasms who are treated with adrenocorticotropic hormone (ACTH). Therefore, echocardiograms and EKG baseline measurements should be obtained before initiating these treatments.

BRAIN INVOLVEMENT

Brain and Neurologic Function: Several types of brain lesions are seen in individuals with tuberous sclerosis complex (TSC); some people will have all the lesions, whereas others will have no brain involvement at all.

- Cortical tubers (from which TSC is named) can be thought of as a "birth defect" on the brain. They are small areas in the cortex (the outer layer of the brain) that do not develop normally. It is thought that the presence of cortical tubers, which disrupts the normal "wiring" of the brain, is what causes seizures in individuals with TSC.

- Subependymal nodules develop near the walls of the cerebral ventricles (the cavities in the brain that contain cerebrospinal fluid). Typically, these nodules accumulate calcium within the first few months or years of life. Because of this calcification, they can be easily detected with a computed tomography (CT) scan. The subependymal nodules are not directly responsible for neurological problems.

- Subependymal giant cell astrocytomas (SEGAs). This type of tumor develops in approximately 15 percent of individuals with tuberous sclerosis. Typically, SEGAs do not occur in very young children, and the chance for their growth decreases after age 20.

If a giant cell astrocytoma grows large enough, it can block the flow of fluid inside the ventricles of the brain, and the tumor will have to be removed and/or the ventricles shunted to relieve fluid buildup and pressure. Symptoms include vomiting, nausea, and headaches as well as changes in appetite, behavior, and mood. These symptoms may or may not signal growth of a tumor, but they do signify that there may be a problem and that a physician should see the child.

Brain imaging should be done at the time of diagnosis to get a baseline image and then every 1 to 3 years afterward. A brain scan can sometimes show growth of a tumor even before symptoms develop.

The most common affect of brain manifestation is epilepsy or seizures. Seizures occur in 60 percent to 90 percent of individuals diagnosed with TSC.

PSYCHIATRIC AND BEHAVIORAL INVOLVEMENT

The behavior of a child with tuberous sclerosis complex (TSC) can often be the most difficult and trying problem for parents and family. Aggression, sudden rage, hyperactivity, attention deficit, acting out, obsessive-compulsive
behavior, repetitive behaviors, staying in their “own world,” being nonverbal even at an age when most children are speaking, and other autistic behaviors have all occurred in children with TSC. Such behavior does not mean you are a bad parent; it is due to TSC.

Some children with TSC, usually those who have a mental disability, are also diagnosed with autism. There appears to be a connection between TSC and autism that is not understood, and active research is exploring this link. It is important for you to keep notes on your child’s behavior and on whether or not he or she reaches the developmental milestones, and bring them to the attention of your child’s physicians. The earlier these behaviors are identified and special programs outlined for your child, the better. Occasionally, individuals with TSC are also diagnosed with schizophrenia, bipolar disease (manic depression), depression, or other psychiatric disorders. Again, bring any unusual, disruptive behaviors to the attention of your child’s physicians and be your child’s advocate so that he or she can obtain optimal medical and psychiatric treatment.

LUNG INVOLVEMENT MANIFESTATIONS
The three main pulmonary lesions found in tuberous sclerosis complex (TSC) are lymphangioleiomyomatosis (LAM), multifocal micronodular pneumocyte hyperplasia, and clear cell tumor of the lung. LAM is the most common. The average age of onset is 32–34 years of age, and lung involvement is essentially, although not exclusively, a manifestation of TSC in women.

The first symptoms of lung involvement in an individual with TSC may be shortness of breath after mild exercise, spontaneous pneumothorax, or coughing. Progression to pulmonary failure may develop, but not usually until the third or fourth decade of life, if at all. Pulmonary involvement in TSC can be severe, and some individuals will require lung transplantation.

DIAGNOSTIC SCREENING AND FOLLOW-UP
Recent studies have shown that many women with TSC have minor, asymptomatic lung involvement. The Consensus Conference Panel on Lung Involvement recommended that female patients should have a chest CT scan (not an x-ray) sometime before age 18 or at the time of diagnosis for women older than 18. A CT scan of the lung is superior to an X-ray because the early signs of lung involvement may easily be missed on an X-ray. If pulmonary involvement is noted, the individual should be monitored closely and should have repeated chest CT scans as needed.

TREATMENT
Pulmonary involvement in TSC can be severe, even fatal. Recently, tamoxifen and progesterone have been used to treat pulmonary TSC with encouraging results. Any individual with TSC with lung involvement should see a pulmonologist who is knowledgeable about LAM. The National Institutes of Health is also conducting clinical research of LAM and you may also apply to participate in the study. Call the Tuberous Sclerosis Alliance or the LAM Foundation for more information.

KIDNEY INVOLVEMENT MANIFESTATIONS
Tuberous sclerosis complex (TSC) can present itself as five different lesions in the kidneys: angiomyolipomas, cysts, malignant angiomyolipomas, oncocytomas, and renal cell carcinoma.

BENIGN ANGIOMYOLIPOMAS
Benign angiomyolipomas are the most common TSC lesion, occurring in 70 percent to 80 percent of adults and older children. Accurate noninvasive ultrasound, CT, or MRI diagnosis of these lesions is highly dependent on their fat content. It can sometimes be difficult to tell the difference between a small or low-fat-content benign angiomyolipoma and a malignant tumor. When tumors become larger than 4 cm, bleeding of the angiomyolipoma, the primary complication of this lesion increases in frequency. Pain may also become a significant problem with angiomyolipomas. Renal angiomyolipomas—made up of vascular tissue (angio), smooth muscle (myo), and fat (lipoma)—are benign hamartomas. These hamartomas are well-circumscribed groups of cells that multiply excessively, growing as tumors that may or may not cause symptoms. The prevalence of TSC-related renal angiomyolipomas increases with age, and in adults bilateral tumors or multiple tumors in one kidney are common. Angiomyolipomas begin in childhood in many individuals with TSC, but they usually grow very slowly and may not
TUBEROUS SCLEROSIS COMPLEX

be problematic until young adulthood. Individuals with TSC should have their kidneys imaged at the time of diagnosis and then regularly throughout their lives.

CYSTS
TSC renal cysts are commonly multiple and bilateral. They are the second most frequently occurring kidney manifestation of TSC. Single or multiple renal cysts occur less often in individuals with TSC than do angiomyolipomas, but they may appear earlier. Some cysts may collapse and disappear. One important research finding was the discovery of the TSC2 gene in close proximity to the gene for polycystic kidney disease (PKD1) on chromosome 16. A small group of individuals with TS have a large segment of chromosome 16 deleted that means that both the TSC2 and PKD1 genes are also removed. These individuals most often will have polycystic kidneys from birth and will require close monitoring and treatment throughout the childhood years.

MALIGNANT ANGIOMYOLIPOMAS
Individuals with TSC and renal angiomyolipomas have a greater risk of developing malignant kidney tumors than do individuals with renal angiomyolipomas who do not have TSC. As a result, patients with TSC must have their kidney images carefully reviewed by a physician who is knowledgeable about TSC and who can differentiate between angiomyolipomas and other types of kidney tumors. The physician should work closely with a radiologist who can differentiate between malignant and benign angiomyolipomas. Malignant angiomyolipomas should be removed as soon as possible after their detection.

ONCOCYTMAS
Oncocytomas are tumors only occasionally seen in individuals with TSC.

RENAL CELL CARCINOMA
Renal cell carcinoma, or cancer in the kidney, is also rarely seen in individuals with TSC, but when these tumors are present, they often are multi-centric and bilateral. These tumors should also be removed as soon as possible after their detection to prevent metastasis.

DIAGNOSTIC SCREENING AND FOLLOW-UP
Both renal angiomyolipomas and cysts are often asymptomatic and may not require treatment; however, both should be followed closely with imaging every 1 to 2 years because aggressive treatment can preserve kidney function with minimal trauma to the individual or the kidney. If the tumors are allowed to grow, they may lead to obstructive uropathy or displacement of much of the normal kidney tissue. There is also a significant risk of hemorrhage if the angiomyolipomas or cysts grow larger than 4 cm. Hematuria, back or abdominal pain, or internal hemorrhage may be the initial signs of kidney problems.

TREATMENT
The renal lesions that appear in many individuals with TSC may remain stable and require no specific treatment. Renal tumors must sometimes be removed, however, if they grow rapidly, if there is an indication that they may be malignant (i.e., a solid tumor with little or no fat content), or to alleviate obstruction. Less-invasive methods of removing the angiomyolipomas, such as embolization, reduces kidney trauma and helps preserve as much normal kidney as possible. With more frequent imaging of the kidneys and good clinical care, an individual with TSC should not have to lose an entire kidney or experience hemorrhaging from an angiomyolipoma. Early and aggressive treatment is much better for most individuals with TSC.

Unfortunately, some individuals with TSC who also have polycystic kidney disease will also have problems maintaining normal blood pressure levels. Their blood pressure usually can be controlled with medication early in the disease process; however, dialysis, and sometimes even renal transplantations, may eventually be necessary. Renal transplantation has been performed successfully in individuals with TSC; there does not appear to be a recurrence of angiomyolipomas in transplanted kidneys.

SKIN INVOLVEMENT
Individuals with tuberous sclerosis complex (TSC) often see the disease manifested in the skin, including on the face, body and nails. In some cases, skin growths can become obstructive but in most cases, the growths themselves are harmless. However manifestations such as facial angiofibromas can have a social impact and treatments are available.

MANIFESTATIONS
Skin lesions resulting from TSC include:

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hypomelanotic macules—patches of skin lighter than the surrounding skin (can be any size or shape or may be the classic "ash-leaf" shape)

- shagreen patch—a patch of skin that is tough and dimpled like an orange peel
- periangual or subungual fibromas—fibrous growths that appear around the fingernails and toenails; and
- facial angiofibromas—tumors of the face

Fibrous plaques sometimes appear on the forehead of individuals with TSC. There may also be fibrous, hairless scalp plaques surrounded by thin, white tufts of hair. Occasionally an individual with TSC coincidentally will have café au lait spots (areas of skin darker than the surrounding skin, but lighter and usually larger than a mole), but these skin lesions are not diagnostic of TSC. A child with three or more or an adult with five or more café au lait spots may be diagnosed with neurofibromatosis, another genetic condition.

**DIAGNOSTIC SCREENING AND FOLLOW-UP TREATMENT**

At the initial testing, the physician uses a Wood's lamp (an ultraviolet light) to better visualize the hypomelanotic macules—white patches on the skin that often are difficult to see, especially on infants and people with very pale skin. The entire body should be examined. The skin should be carefully examined for the other skin manifestations of TSC as well. Some of the skin signs may not be present at birth; the facial angiofibromas do not usually appear until between the ages of 3 and 5 at the earliest, and the periangual and subungual fibromas do not usually occur until much later in life. Lesions that appear later should be noted and brought to the attention of the physician.

**TREATMENT OPTIONS FOR SKIN INVOLVEMENT**

The most often treated skin manifestations of tuberous sclerosis complex (TSC) are the facial angiofibromas and periungual and subungual fibromas. The facial angiofibromas can be removed using dermabrasion or laser treatment; these procedures should not be considered cosmetic surgery because they treat tumors resulting from a genetic condition. Research has suggested that the facial angiofibromas should be removed (using laser treatment) when they are small, before they enlarge and become fibrous. They most likely will recur and need further treatment, but they will be milder than if left untreated. Individuals with TSC, who are interested in treatment, should see a dermatologist or a plastic surgeon that specializes in laser surgery. When screening for doctors, make sure they are qualified surgeons who have experience dealing with medical skin conditions. Some cosmetic companies also manufacture makeup to cover hypomelanotic macules if they are large or in exposed areas of the skin. For some individuals, the hypomelanotic macules are not problematic, whereas others will chose to cover them with clothing or makeup.

**EYE INVOLVEMENT MANIFESTATIONS**

The appearance of retinal lesions varies from the classic mulberry lesions adjacent to the optic disk to the more common plaque-like hamartoma. Retinal hamartomas are occasionally noted in individuals without other manifestations of tuberous sclerosis complex (TSC) and in individuals with other disorders. Therefore, although they are suggestive of TSC, single lesions are not diagnostic of TSC. The frequency of retinal hamartomas in individuals with TSC has varied in reports from almost negligible to 87 percent of individuals, a difference probably reflecting the technique used and the expertise of the examiner. Although less common than the retinal hamartoma, a defect in the pigment of the iris has also been observed in some individuals with TSC. In addition, white depigmented patches, reminiscent of the hypopigmented macules on the skin, have also been observed on the retina of some individuals with TSC.

**DIAGNOSTIC TESTING AND FOLLOW-UP**

Retinal lesions may be difficult to identify without pupillary dilation and indirect ophthalmoscopy, particularly difficult to examine in uncooperative children. Most retinal hamartomas remain dormant, although occasionally individuals with TSC have visual impairment resulting from a large hamartoma in the macular region. Instances of visual loss following retinal detachment, vitreous hemorrhage, or hamartoma enlargement are rare.

**TREATMENT**

For the most part, treatment of the retinal lesions and repeated ophthalmologic examinations are unnecessary. Normal eye care should be maintained.
OTHER ORGAN INVOLVEMENT
Cysts and tumors similar to those observed in the kidney sometimes appear in the liver, lung, pancreas, and other organs. These lesions are not usually seen until later in life and are rarely symptomatic. Bone cysts can also develop but usually do not cause problems until later in life. In addition, pits have been noted in both baby and adult teeth in over 90 percent of individuals with tuberous sclerosis complex (TSC), but their significance is not known. Rectal polyps have also been reported but do not appear to cause problems.

DIAGNOSTIC CRITERIA
At the time of diagnosis, many medical tests are performed. Patients and parents should also be aware of routine testing that needs to be performed. Patients are advised to share the following diagram with their physicians: Suggested Routine Diagnostic and Surveillance Screening in TSC.

In July 1998 the Tuberous Sclerosis Alliance, then known as the National Tuberous Sclerosis Association, convened a consensus conference of international experts to review the literature and the status of knowledge and research about tuberous sclerosis complex (TSC). The event was funded by the National Institutes of Health, a federal agency dedicated to medical research. One of the consensus panels developed a revised scheme for the TSC diagnostic criteria (see Table 1) based on new information from clinical and molecular genetic studies.

The new diagnostic criteria eliminated any single finding as specifically distinctive or characteristic of the disorder; this represents a change of thought in the diagnostic process. Originally, cortical tubers were believed to be pathognomonic, or specifically characteristic of TSC. However, evidence now suggests that radiographic brain imaging and histologic studies are unable to distinguish these tubers from isolated cortical dysplasia. Histology is the science of the minute structure of cells, tissues and organs. Two other types of brain lesions—subependymal giant cell astrocytomas and subependymal nodules—can be distinguished from cortical tubers and from each other, however. In particular, the two-subependymal lesions have a histologic and radiographic appearance that differs from the cortical tuber, whereas the giant cell astrocytoma is the only one that tends to enlarge. It is important to distinguish between the three different brain lesions for identification and monitoring purposes (See Table 1).

An especially important tool in diagnosing TSC is its dermatologic manifestation, which comprises four major and one minor feature of TSC. Hypomelanotic macules are considered a new grouping, whereas the histologically similar forehead plaque, facial angiofibroma, and renal and retinal hamartomas, continue to be considered major features used in diagnosis. Liver, spleen, rectal or other lesions—preferably histologically confirmed hamartomatous lesions—constitute minor features. As we learn more about TSC and as diagnostic genetic testing becomes more widely available, the diagnostic criteria will again be revised.

| TABLE 1 |

Revised Diagnostic Criteria for Tuberous Sclerosis Complex (REF)

**Major Features**
1. Facial angiofibromas or forehead plaque
2. Non-traumatic ungual or periungual fibroma
3. Hypomelanotic macules (more than three)
4. Shagreen patch (connective tissue nevus)
5. Multiple retinal nodular hamartomas
6. Cortical tuber
7. Subependymal nodule
8. Subependymal giant cell astrocytoma
9. Cardiac rhabdomyoma, single or multiple
10. Lymphangiomatosis
11. Renal angiomyolipoma

**Minor Features**
1. Multiple randomly distributed pits in dental enamel
2. Hamartomatous rectal polyps

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3. Bone cysts
4. Cerebral white matter migration lines
5. Gingival fibromas
6. Non-renal hamartoma
7. Retinal achromic patch
8. "Confetti" skin lesions
9. Multiple renal cysts

Definite TSC: Either 2 major features or 1 major feature with 2 minor features
Probable TSC: One major feature and one minor feature
Possible TSC: Either 1 major feature or 2 or more minor features

**KEY**

a When cerebral cortical dysplasia and cerebral white matter migration tracts occur together, they should be counted as one rather than two features of TSC.

b When both lymphangiomyomatosis and renal angiomyolipomas are present, other features of TSC should be present before a definitive diagnosis is assigned.

c Histologic confirmation is suggested.

d Radiographic confirmation is sufficient.

e One panel member recommended three or more radial migration lines constitute a major feature.

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**LIVING WITH TUBEROUS SCLEROSIS COMPLEX**

Tuberous sclerosis complex (TSC) manifests itself in many different ways, but one factor individuals with TSC have in common is that they must live with the disorder their entire lives. As children, it means that their parents must face issues regarding education, health insurance and socialization, among others. As young adults, some of those affected by TSC may have to deal with a transition to independent living and employment while others may deal with dating issues and reproductive concerns. Throughout their lives, those affected with TSC must live with a permanent medical condition. This section provides resources and information for such issues.

- Education
- Family Support
- Teen to Adult Options
- Financial Planning
- Guardianship
- Independent Living Options
- Self-Advocacy

**EDUCATION**

Children with disabilities are entitled to a school program that will meet their educational needs. Special education programs are governed by a combination of state and federal laws. Under these laws, school districts must provide each student with a disability with a free appropriate public education (FAPE). FAPE means that special education and related services that are provided at public expense and without charge must meet appropriate standards, include preschool through secondary education, and conform to an Individual Education Program (IEP). A student that qualifies for educational services must be provided these accommodations in the least restrictive environment. Below are some links that will provide information about the educational rights of those with disabilities.
TEEN TO ADULT OPTIONS
Teens and adults with TSC may be faced with many challenges as they strive for independence and explore their options. It's important for each of us to discover who we are, what our needs are and what choices are available. Because an individual is challenged with a disability does not mean that his or her needs are any different than other teenagers and adults. Everyone needs goals to reach for and a plan to achieve the goals. A transitional plan is a guide for individuals. The plan must include goals and services needed, based on the individuals needs, preferences and skills. The transition process is a complex one with many decisions to be made. In conclusion, a student with a disability can increase her or his options by having a good transitional plan. The plan must involve the parents and the student, school officials and community agencies that can help facilitate a smooth passing from one phase of life to the next.

COLLEGE, VOCATIONAL & CAREER CHOICES
Career choices for individuals with disabilities are more plentiful today than any other time in our history. The career path begins in high school by selecting the courses that match your future goals.
TUBEROUS SCLEROSIS COMPLEX

While education beyond high school in the U.S. is optional, it has become a necessary investment in future employment and life satisfaction for many people. Over the years, public and private sources of money have been developed specifically to meet this need. College bound students with disabilities may qualify for financial aid through both federal and state programs. The needs of individuals with disabilities mirror the needs of people in the general community; however, people with disabilities usually have needs that go beyond the normal services provided for the non-disabled individual. They may need unique, specialized supportive services that are provided through state and federal programs. These types of programs provide the disabled individual with expanded access to employment and vocational rehabilitation services, and other related services. The intent of the programs is to enable the beneficiaries to obtain, regain or maintain employment and to reduce their dependency on cash assistance in the future.

SELF-ADVOCACY
Self-advocacy means that a person makes an informed decision about a matter of importance to her or him, and then takes responsibility for bringing about the change necessary to make that choice a reality. Some ideas for establishing relationships with agencies in the process of self-advocating are as follows:

• Be respectful but firm with your needs.
• Treat agency staff the way you want to be treated.
• Be persistent and ask for clarification.
• While most agencies must respond to requests within a certain time limit, it does take time for the process to occur. Be patient and ask for clarification if you don’t understand the process or need more information about the matter.
• Know your rights.
• Keep good records.
• Request written confirmation of kept promises, timeline or denial.

Self-advocacy is an act of directly representing yourself in a way that will be perceived as assertive and not passive or aggressive. In the past, it has not been customary for people with disabilities to challenge the power of authorities; thus being a self-advocate and asserting rights and needs can be quite alien. However, all people have the right to self-determination, even if it goes against professional judgment. Ultimately, each person is the expert in what is needed and useful, so go ahead and ask for it.

MAKING THE MOST OF YOUR DOCTOR VISITS
When planning to visit a physician about you or your child’s symptoms of tuberous sclerosis complex (TSC), there are some things you can do, and know, to be better prepared.

KEEP A JOURNAL:
• of troublesome symptoms.
• of all medications currently being used, and those that were changed (include dosage size and time).
Include any side effects of previous drugs.
• of all vitamins, supplements, over the counter medications and alternative therapies you are using, or have used.
• of symptoms, concerns or new observations (ie. seizures, sleeping difficulties, or behavior changes). Try to be as descriptive as possible, especially when describing seizures.

PLAN TO TAKE THESE ITEMS ALONG:
• Health insurance card
• Social security card
• Addresses and phone numbers of family physicians
• Pen and paper to write down any new information, or answers to questions you take with you
• A copy of the latest TSC treatment recommendations (i.e. "Revised Diagnostic Criteria" or "Diagnostic Evaluation," available from the TS Alliance)

ASK QUESTIONS:
There are NO dumb questions. Inquire until you are comfortable and satisfied. Some questions you may want to ask your physician are:
• Do you have experience treating people with TSC?
• What is the treatment plan you offer or suggest?
• What tests should be done next?
• How long should we wait to see if this medication/therapy works before we try a new one?
• Is this the only option available?
• What other options are used to treat these symptoms?
• What do we need to look for or be aware of?
• When should we visit you again?
• What additional information can I provide that will help you offer the best care?

REMEMBER:
• that your physician is your consultant, and part of the team you need to organize to obtain the best care possible.
• to be respectful, but do not be intimidated.
• to be wary of any medical professional that tells you, "Don't worry, you just don't understand."
• to educate yourself as much as possible about TSC.
• not to underestimate the value of networking with other people who have been through similar situations.
• to always consult with your doctor prior to making any medical care changes.
• that you are always entitled to a second opinion.

TRACKING MEDICAL CARE: TS JOURNAL
The first edition of the "Tuberous Sclerosis Journal" made its official debut at the Second National Family Conference (NFC) in San Diego. The journal, presented in a loose-leaf notebook format, is available upon request through the TS Alliance at no charge. The journal's first edition is designed to provide those affected by TSC with help in organizing their medical history, as well as their TSC-related doctor visits and scheduling issues. The journal, if used properly, can help clarify significant relationships between various TSC manifestations, such as seizures and their medications and treatments. To further this goal, each patient should take a filled out journal to their doctor's appointments to aid their physicians in providing more efficient and effective medical care. To order your free copy of the "Tuberous Sclerosis Journal", call the TS Alliance today at (800) 225-6872.

GETTING A MEDICAL BRACELET
Individuals with TSC who are taking medication or who have medical conditions that require special care in emergency situations should think about getting a medical bracelet. A medical bracelet provides paramedics with pertinent medical information if/when you are unable to speak clearly about medical conditions, allergies or special needs. Identification bracelets can help you or your child receive fast, accurate treatment in emergencies. Medical tags are also available in the form of a charm, anklet or watch, although the bracelet is the most common form. The following Web sites can provide you with more information:
• MedicAlert (www.medicalert.org).
• Medic Assist (www.medicassist.com)
• Medic ID’s International (www.medicid.com)
• Oneida Nameplate Company (www.oneida-medical-jewelry.com)

You can seek more information from our Family Resource Center located on the 2nd floor of the Taggart Pavilion or from the following web sites:
http://www.nlm.nih.gov/medlineplus
http://www.niddk.nih.gov/