The Tuberous Sclerosis Association

This document can be found at **www.tuberous-sclerosis.org**

It reports on a presentation at a meeting of the TS Alliance in San Diego in July 2001.

Social and reproductive issues facing adults with TS

The first part of the session was given by Aimee Tucker, Genetic Counellor at Houston's Medical School.

She began by explaining the genetics of TS. TS is a dominant condition which runs in families. In can be inherited via either the TSC1 or TSC2 genes, or it can be a sporadic event (this is the most common). An adult with TS has a 50% chance of passing it on with each pregnancy. Some will have all children with TS, some will have none of their children with TS: it is a statistical chance of 50% for each pregnancy.

Parents who have no signs of TS themselves but who already have one child with TS have a small chance of having another TS child, quoted as a 1-2% risk. This is due to the possibility of germ-line mosaicism. If you have TS, this means that one copy of the TS gene is changed in all cells of your body. If you have a change to the gene in just some cells that is known as mosaicism. If there are just changes to your eggs or sperm cells, this is known as germ-line mosaicism and can result in your children having TSA when you do not.

Reproductive Options

Anyone with TS has a 50% risk of passing TS on with every pregnancy. So what are the options? These include

- having children regardless of the inheritance risk
- choosing not to have children
- making the decision without understanding the implications or risks
- adopting
- using prenatal diagnosis or pre-implantation diagnosis
- or using donated eggs or a surrogate mother.

Prenatal Diagnosis

For prenatal diagnosis to be possible, the person with TS must have had their genetic mutation for TS found before the pregnancy gets under way. This is because it takes time to work up someone's mutation. Their mutation can be found 80-85% of the time. After that, invasive prenatal testing takes place and the developing foetus's cells are analysed to see if the baby has TS. A report of the findings is then given to the family.

The first step to prenatal testing is DNA testing of the affected parent, and this involves taking a blood sample and sending it to the lab for analysis. If the genetic change is found as part of research, it has to be confirmed in a clinical lab and the results reported back. In 15-20% cases the change cannot be found and further work still needs to be done.

The benefits of DNA testing are that definitive testing of other family members is possible and prenatal testing or testing of a new-born baby can be carried out quickly. There are limitations, however, such as the fact that such testing doesn't yet affect the medical care which can be given, nor is gene therapy currently available.

Prenatal testing is invasive and both kinds use ultrasound. Amniocentesis takes place at 15-22 weeks and there is a 1 in 300 risk of miscarriage. Chorionic villus sampling takes place at 10-12 weeks and there is a 1 in 100 risk of miscarriage. An earlier report has suggested that there is also a risk of damaging a limb, but this has been disputed. With the amniocentesis, the baby pee is tested. CVS is done vaginally and cells from the placenta are tested. The benefit is that you can know as early as 10-12 weeks whether the baby is affected or not. But even if you find TS, you cannot cure it and you cannot tell how severe it will be.

Non-invasive pre-natal testing includes high resolution ultrasound scan of the baby's heart, brain and kidney, plus foetal MRI which may help confirm suspected cases – but you still can't rule out TS this way.

<u>Other Options</u>

Donor eggs or donor sperm (for IVF treatment) can be considered, but the pregnancy rate is quite low and you should discuss the embryo transfer rate with the physician. Pre-implantation genetic diagnosis has not been done for TS yet, and when it is available will be expensive. First the person with TS will need to be genetically tested and their individual TS mutation found. The prospective mother will need to take fertility drugs before having a number of eggs removed and if the mother has TS herself she should ask whether these fertility drugs might exascerbate any of her TS symptoms. The eggs will then be fertilised in a laboratory and grown to less than 8 cells, with one being removed and tested. If it's OK, it can be reimplanted into the mother's womb. The advantage of pre-implantation diagnosis is that testing is done prior to implantation.

<u>Other issues</u>

- DNA testing helps couples with their reproductive decision making. It can also help other family members to know about their genetic status and to make their decisions.
- Anti-convulsants tend to make the birth control pill more ineffective.
- Oestrogen promotes seizures as well as tumours.
- There is anecdotal evidence that hormonal imbalance can promote renal and lung tumours.