# Genetics and Pregnancy in TSC

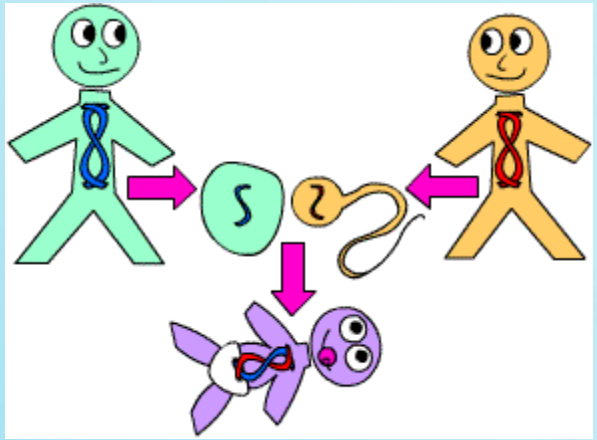
*Hope Northrup, MD*

*McGovern Medical School*

*University of Texas Health Science Center at Houston*

"To find a cure for tuberous sclerosis complex, while improving the lives of those affected"
TS Alliance

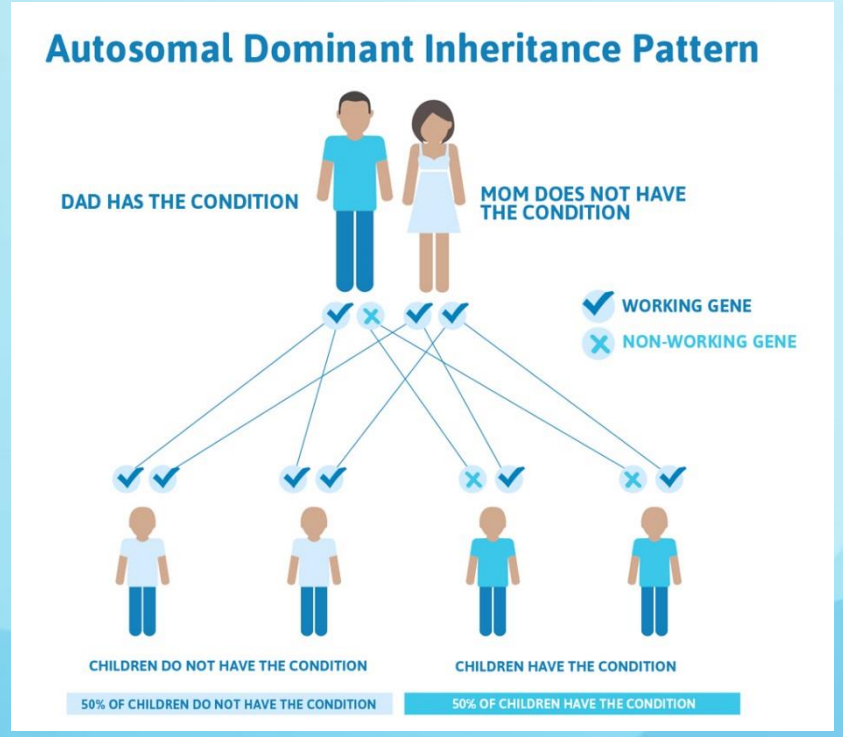
# Reproductive Options in Tuberous Sclerosis



http://www.sperimentando.com/?p=572

# To Review:

- With each pregnancy, a person with TSC has a 50% chance to have a child with TSC, and a 50% chance to have a child without TSC
- There is no way to predict which findings of TSC the child will have




https://www.geneticsupportfoundation.org/genetics-and-you/autosomal-dominant-inheritance

# Reproductive Options

- Decision to have children; accepting of the inheritance
- Decision not to have children; personal health, not accepting of inheritance, other reasons
- Decision to adopt
- Decision to have children; elect to undergo prenatal diagnosis or pre-implantation genetic diagnosis
- Decision to utilize donor sperm, donor egg, or surrogate mother

# Prenatal Diagnosis

1. Genetic testing in person with TSC to determine gene pathogenic variant/change
2. Invasive prenatal testing
3. Analysis of fetal cells for known TSC change
4. Results reported back

# Genetic Testing

1. Submit blood sample from person with TSC to testing lab
2. Gene change causing TSC detected
3. Change not found, individual contacted, further research studies

# Genetic Testing for TSC

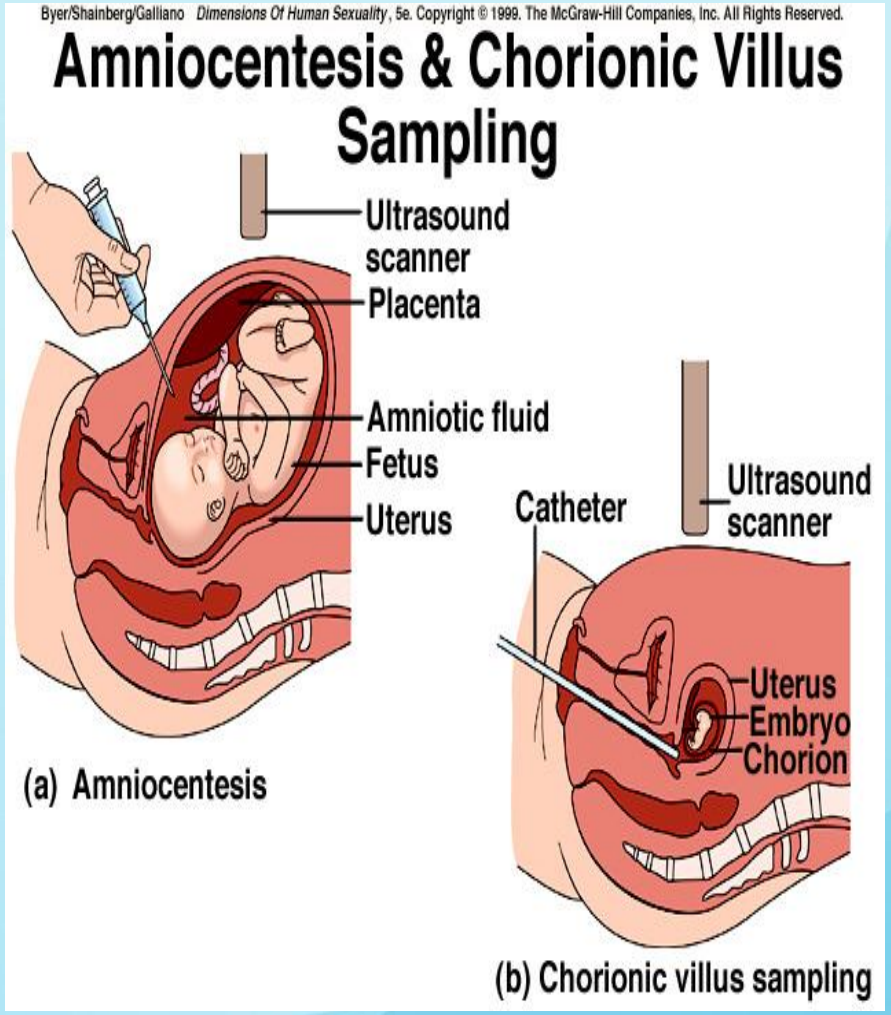
- In persons with a definite diagnosis of TSC, pathogenic variants can be found in approximately 90-95%
- The remaining persons with a definite diagnosis may have pathogenic variants in the promoter or intronic regions of the *TSC1* or *TSC2* genes, mosaicism for a pathogenic variant or there may be an additional gene(s) that causes TSC

# Genetic Testing Options

| Laboratory | Website/E-mail/Telephone | Cost/Pricing |
|---|---|---|
| Invitae<br>(San Francisco, CA) | Website: www.invitae.com<br>Email: clientservices@invitae.com<br>Ph:1-800-436-3037 | • Offers comprehensive *TSC1*/*TSC2* testing and targeted testing.<br>• Self pay option – max a patient will pay is $250 for any TSC testing.<br>• Average out-of-pocket cost >$100.<br>• Accepts most private Ins. & Medicaid.<br>• Free first degree relative testing if variant found.<br>• 1-3 weeks turnaround. |
| Ambry Genetics<br>(Aliso Viejo, CA) | Website: www.ambrygen.com<br>Email: website@ambrygen.com<br>Ph: 1-1949-900-5794 | • Offers comprehensive *TSC1*/*TSC2* testing and targeted testing.<br>• Self pay option - $399 for comprehensive TSC testing.<br>• Average out-of-pocket cost $82.<br>• Accepts most private Ins. & some Medicaid plans.<br>• Free first degree relative testing on a case by case basis.<br>• 2-3 weeks turnaround. |
| GeneDX, Inc.<br>(Gaithersburg, MD) | Website: www.genedx.com<br>Email: genedx@genedx.com<br>Ph: 1-301-519-2100 | • Offers comprehensive *TSC1*/*TSC2* testing and targeted testing.<br>• Self pay option - $600 for comprehensive TSC testing.<br>• Accepts most private Ins. & some Medicaid plans.<br>• Free first degree relative testing on a case by case basis.<br>• 4 weeks turnaround. |
| Fulgent<br>(Temple City, CA) | Website: www.fulgentgenetics.com<br>Email: info@fulgentgenetics.com<br>Ph: 1-626-350-0537 | • Offers comprehensive *TSC1*/*TSC2* testing and targeted testing.<br>• Self pay option - $950 for comprehensive TSC testing.<br>• Average out-of-pocket cost >$900.<br>• Accepts private Ins. & some Medicaid plans.<br>• Free first degree relative testing on a case by case basis.<br>• 3-5 weeks turnaround. |

# Invasive Prenatal Testing

- Amniocentesis
  - 15 to 22 weeks
  - 0.33-0.5% risk of a complication
- Chorionic Villus Sampling (CVS)
  - 10 to 13 weeks
  - 1% risk miscarriage
  - Risk of detecting confined placental mosaicism



# Invasive Prenatal Testing

- Benefits of testing
  - Ability to know as early as 10 to 12 weeks gestation about fetal status
  - Can test for a handful of other conditions
- Limitations of testing
  - Risk for miscarriage
  - We cannot cure the conditions we can detect

# Non-Invasive Prenatal Screening by Imaging

- Hi resolution ultrasound-heart, brain, rarely kidney signs
- 3-dimensional ultrasound-unknown impact
- Fetal MRI-helps confirm diagnosis in suspected cases

# Non-Invasive Prenatal Screening by Imaging

- Benefits of screening using imaging
  - Helpful in cases where parent has TSC, and wants to look for signs of TSC in a pregnancy
  - No risk to pregnancy
- Limitations of screening using imaging
  - Cannot rule out TSC
  - Most signs of TSC can be detected only in late pregnancy

# What if you don’t want to undergo prenatal diagnosis?

- Assisted Reproductive Technologies (ART)
  - Donor egg or donor sperm for use in place of egg/sperm from parent with TSC
  - Surrogacy utilizing either surrogate’s egg, donor egg, mother’s egg
  - Pre-implantation Genetic Diagnosis

# Pre-implantation Genetic Diagnosis (PGD)

1. Genetic testing in person with TSC
2. Mother takes fertility drugs, eggs are removed
3. Eggs are fertilized with sperm from father in laboratory
4. Fertilized eggs allowed to grow to ~8-16 cell stage, then one cell is removed and tested for known mutation
5. Only embryos without TSC placed into mother's/surrogate's uterus for implantation

# Pre-implantation Genetic Diagnosis (PGD)

- Benefits of PGD
  - Testing occurs prior to conception/implantation
- Cons of PGD
  - Expensive ($20,000+)
  - In its early stages
  - Usually encouraged to undergo prenatal diagnosis, regardless

# Questions?