Genetics of TTR Amyloidosis

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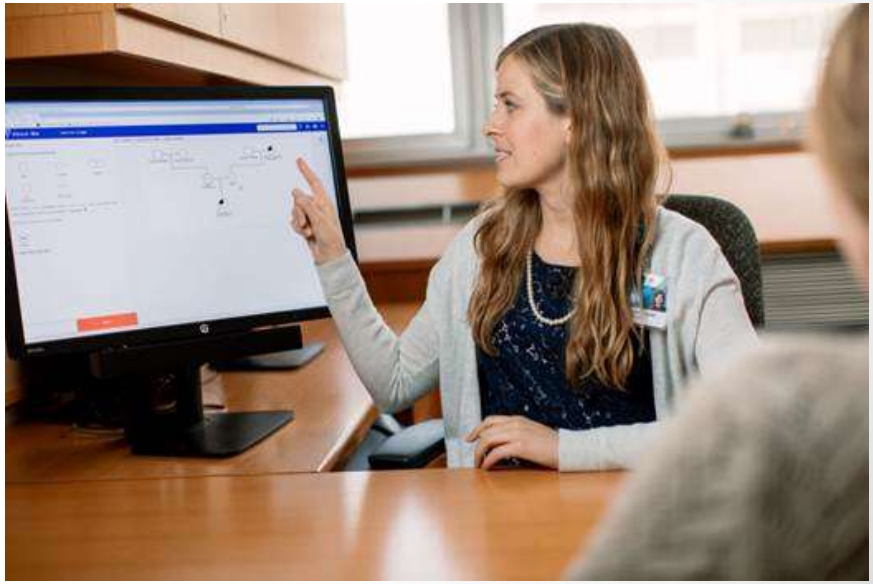
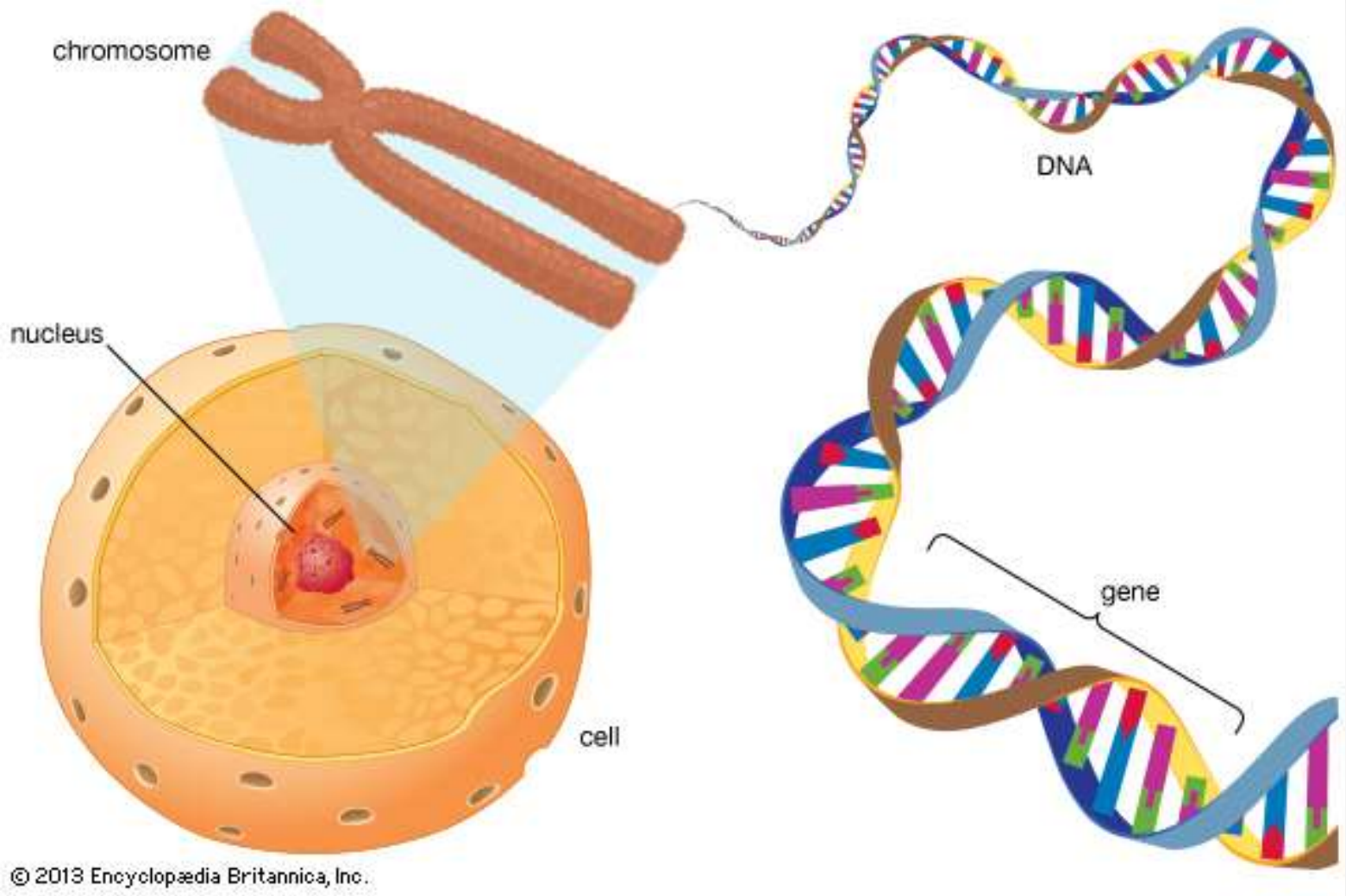
What is a Genetic Counselor?

- Genetic counselors are professionals who have specialized education in genetics and counseling
- More than 4,000 certified genetic counselors nationwide
- See patients for wide variety of indications:
  - Prenatal
  - Reproductive planning
  - Cancer
  - Cardiac disease
  - Neurologic diseases
  - Predictive
  - Pediatric
  - Research
  - Public Health
  - And More!
- Genetic counselors are also employed by commercial laboratories and in industry!



Genetic Counseling for TTR Amyloidosis

- Patient contracting
- Personal history
- Family history
- Discussion of genetics of condition
- Inheritance of condition
- Discussion of family testing
- Resources and support


chromosome
DNA
nucleus
gene
cell
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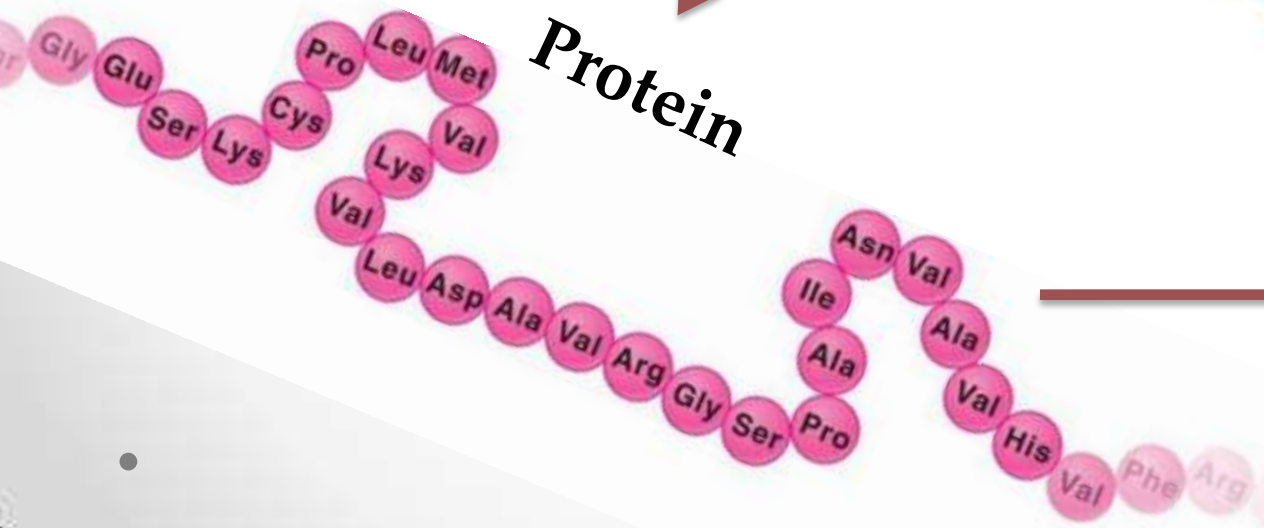
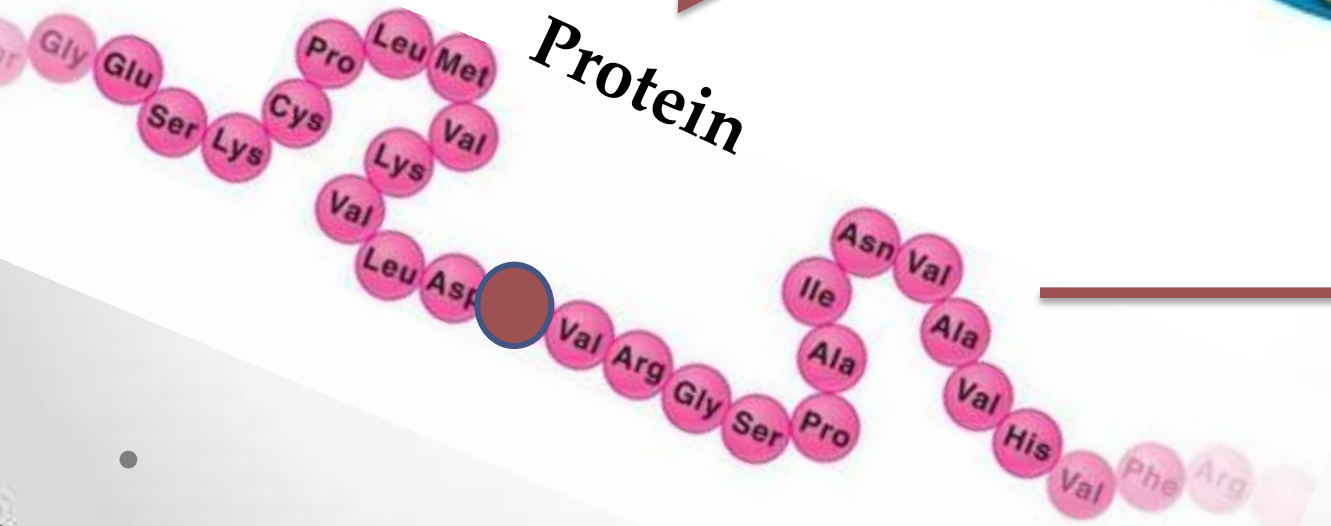
Gene

Protein

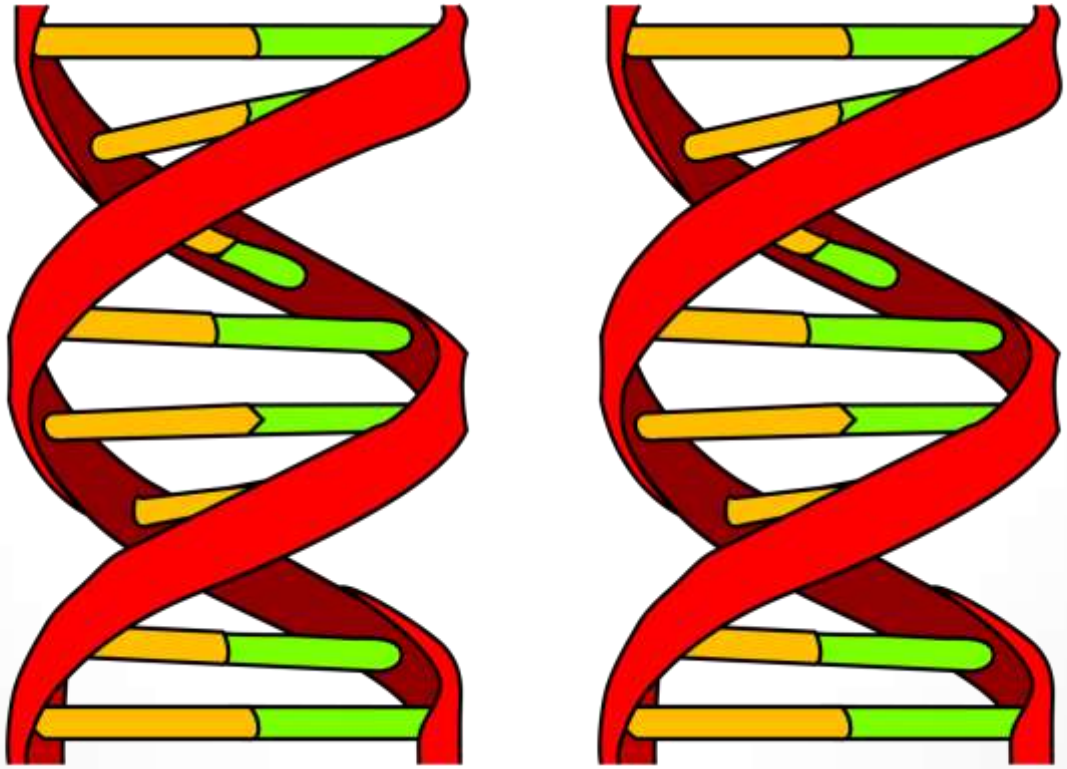


Gene

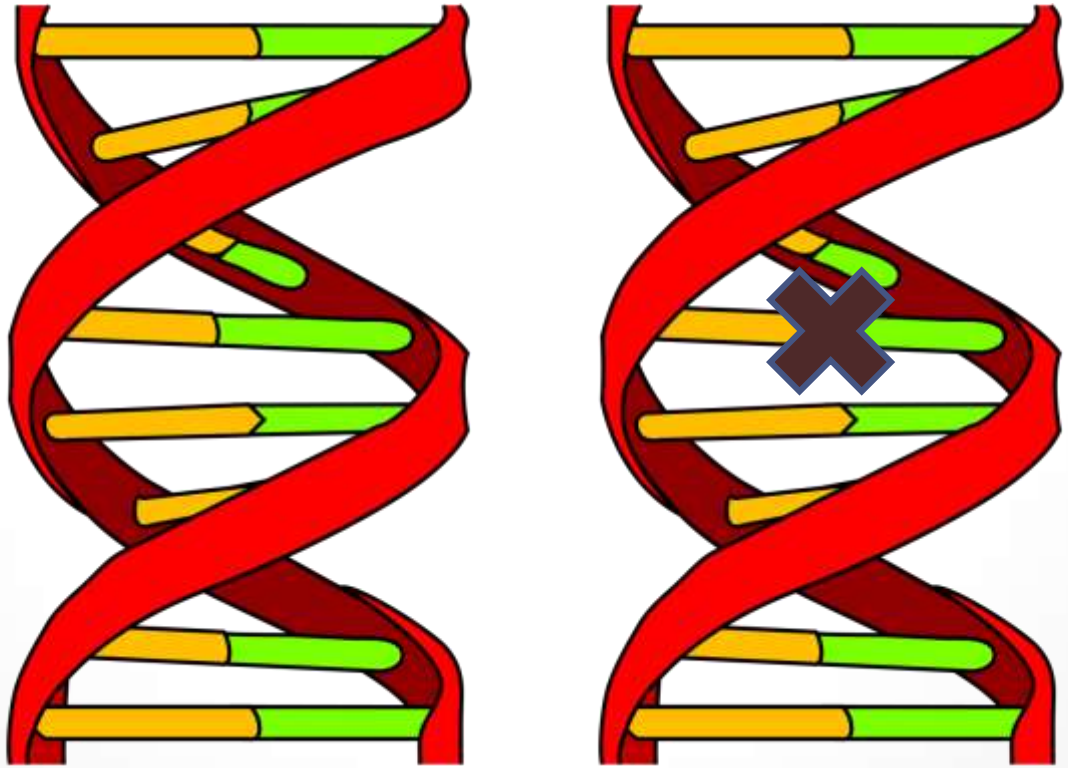
Protein



Everyone has two copies of the TTR gene

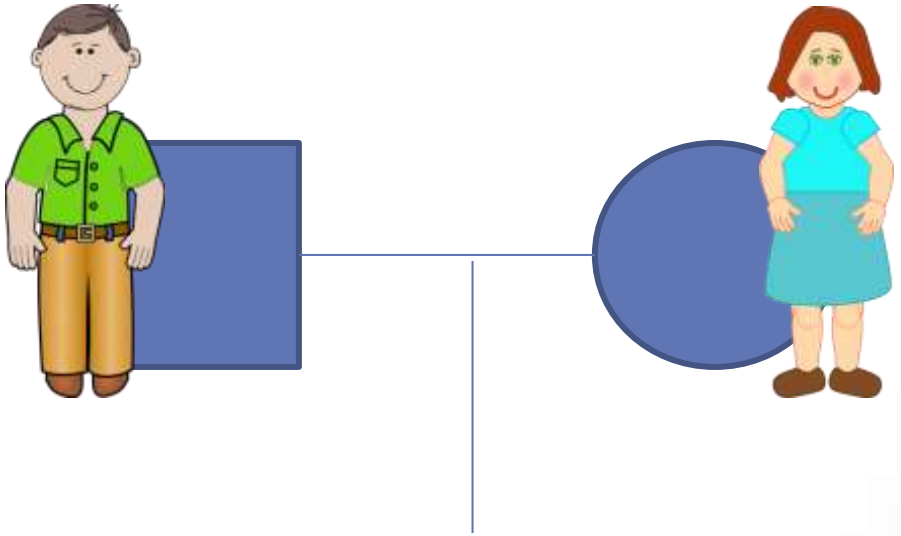


TTR Amyloidosis follows an "autosomal dominant" inheritance pattern



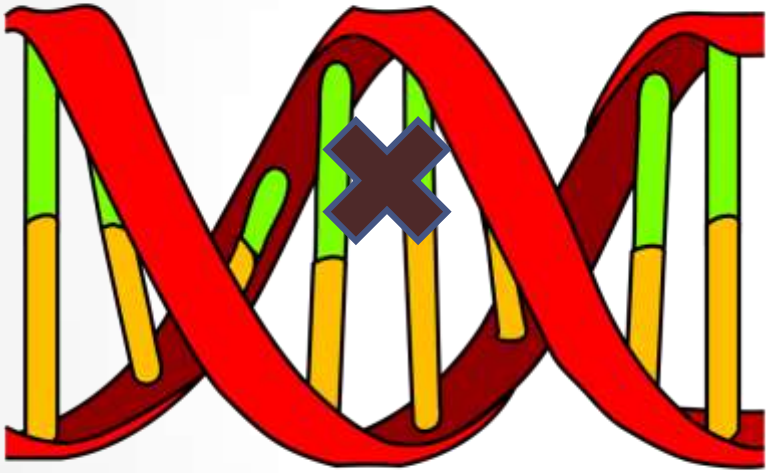
- Cardiomyopathy
- Carpal Tunnel Syndrome
- Neuropathy

New diagnosis of TTR Amyloidosis



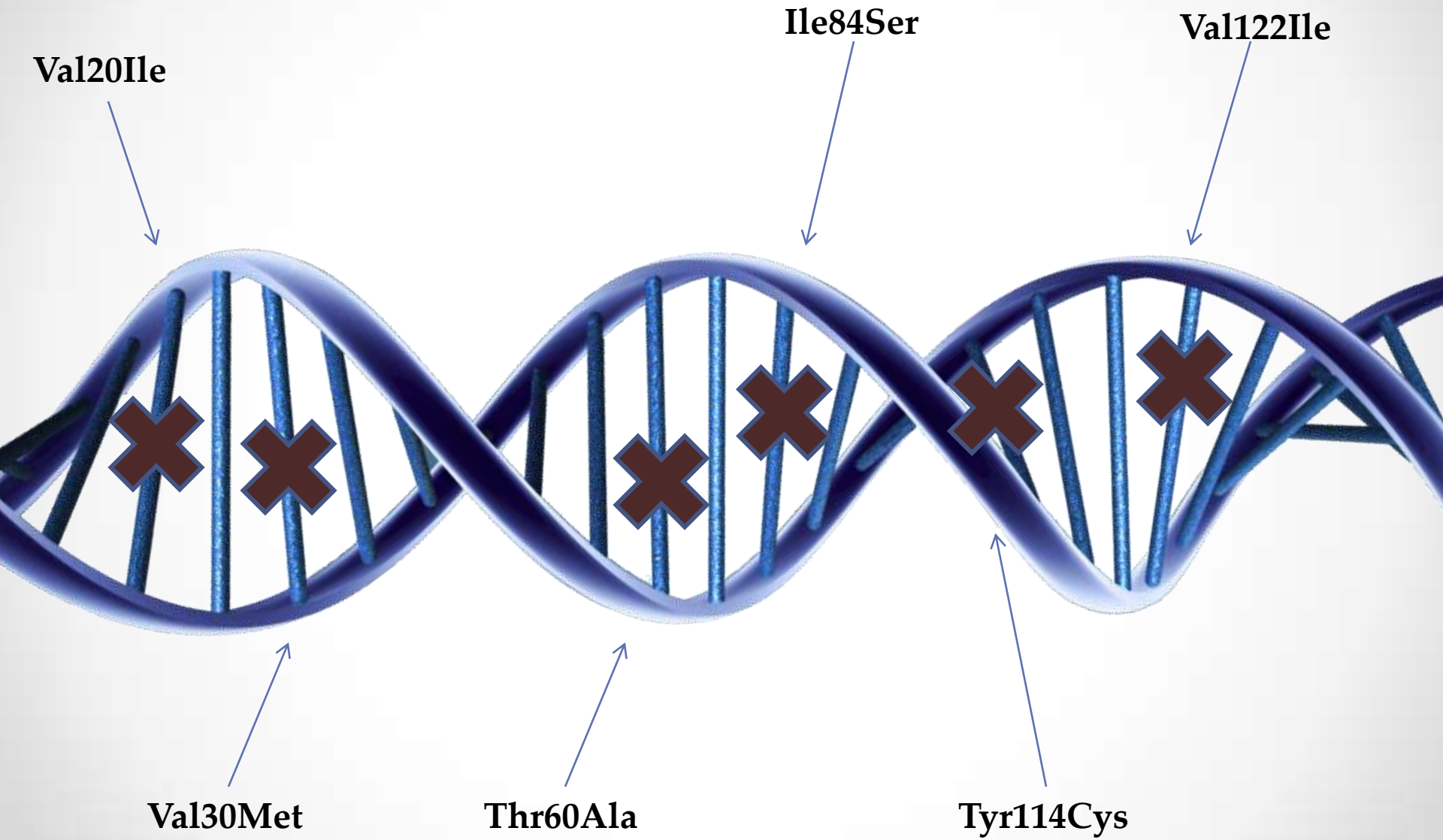
Genetic Testing: Why do we do it?

- Confirm whether the amyloidosis in your family is genetic vs. wildtype
- Impacts treatment and eligibility to clinical trials
- Necessary for testing of family members
- Can provide information about what to expect medically

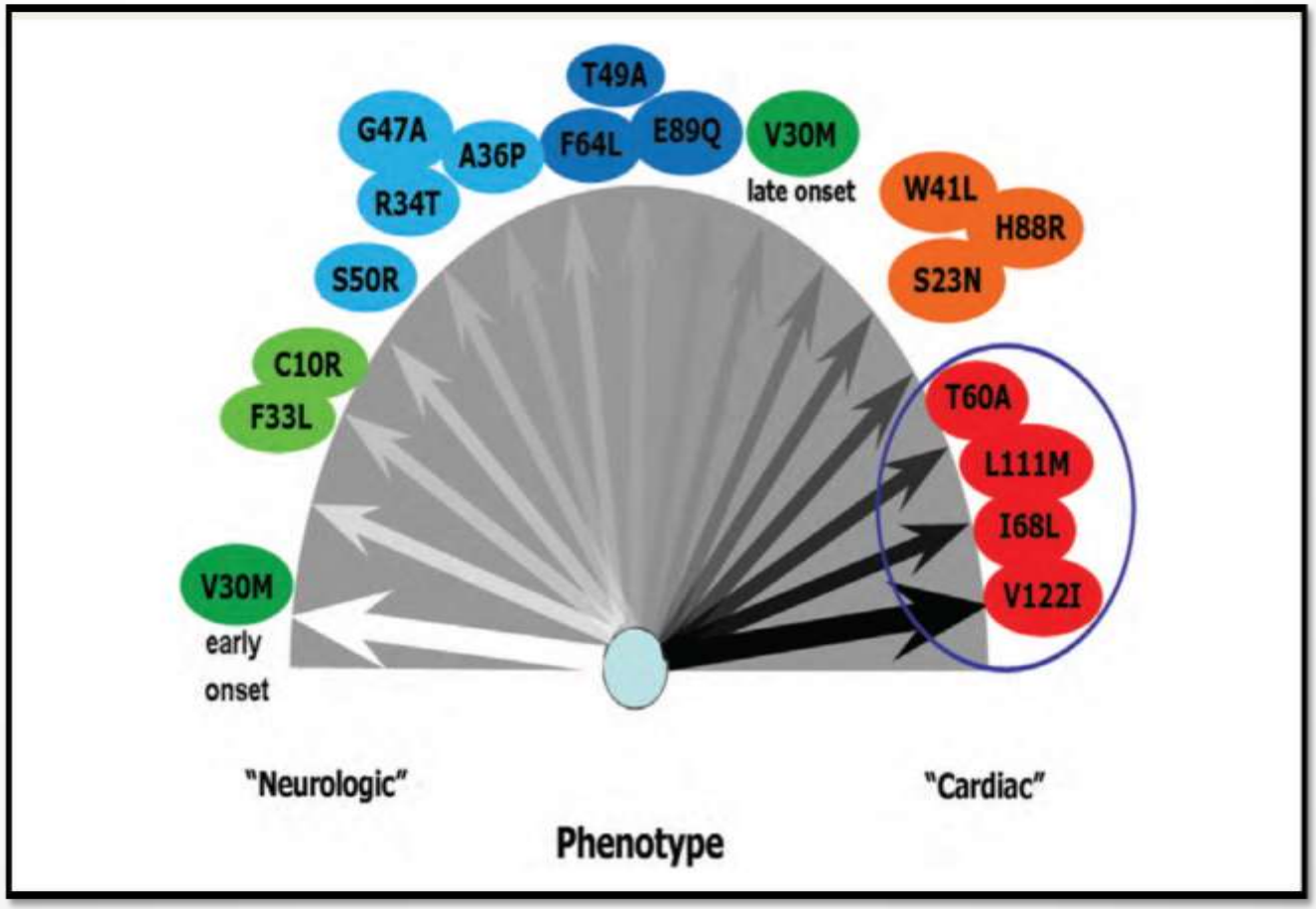


Different mutations have different names

TTR GENE


Val20Ile
Ile84Ser
Val122Ile
Val30Met
Thr60Ala
Tyr114Cys

Mutations can cause different common symptoms

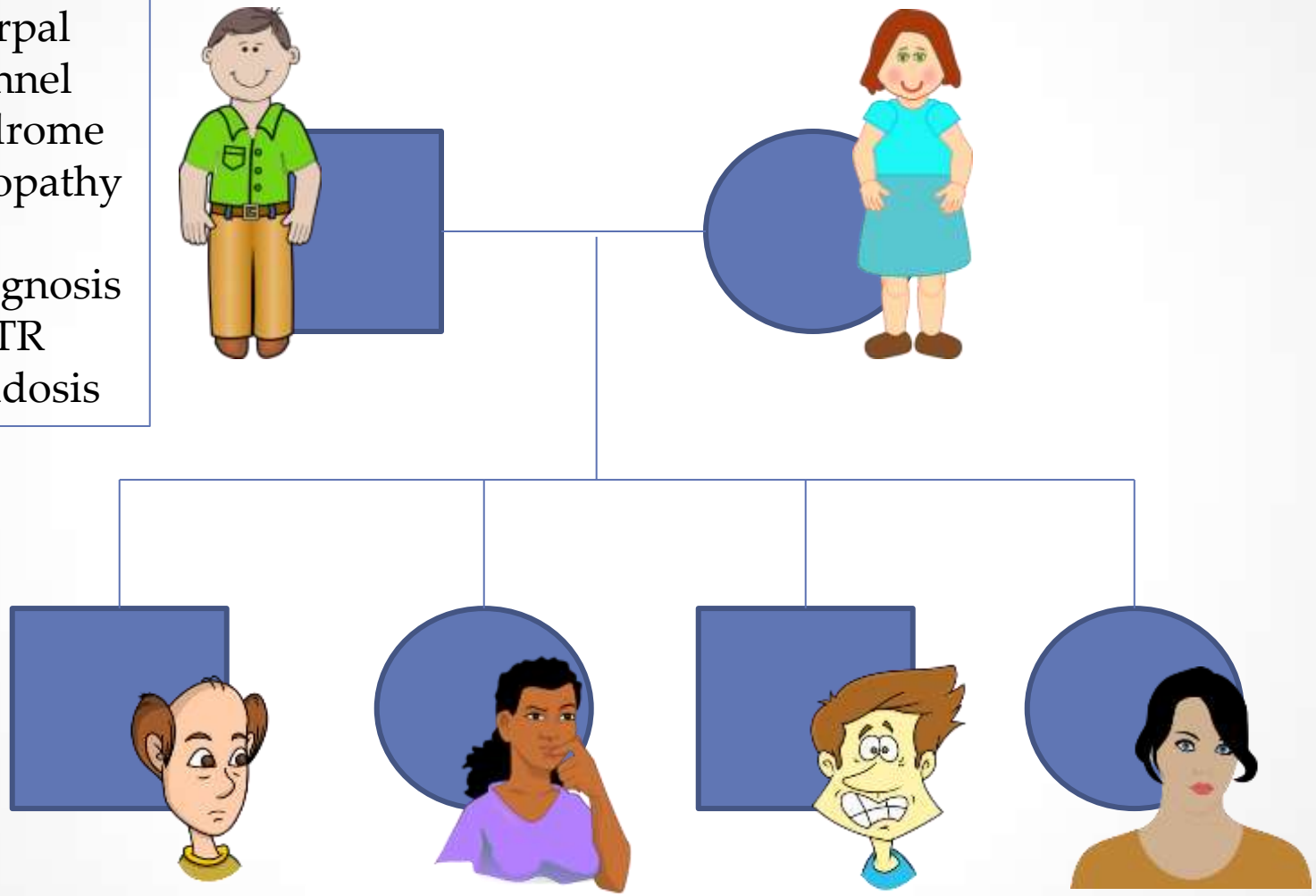


Rapezzi, Claudio, et al. *European heart journal* 34.7 (2012): 520-528.

So what does this mean for my family?

- Heart issues
  - Carpal Tunnel Syndrome
- Neuropathy

New diagnosis of TTR Amyloidosis

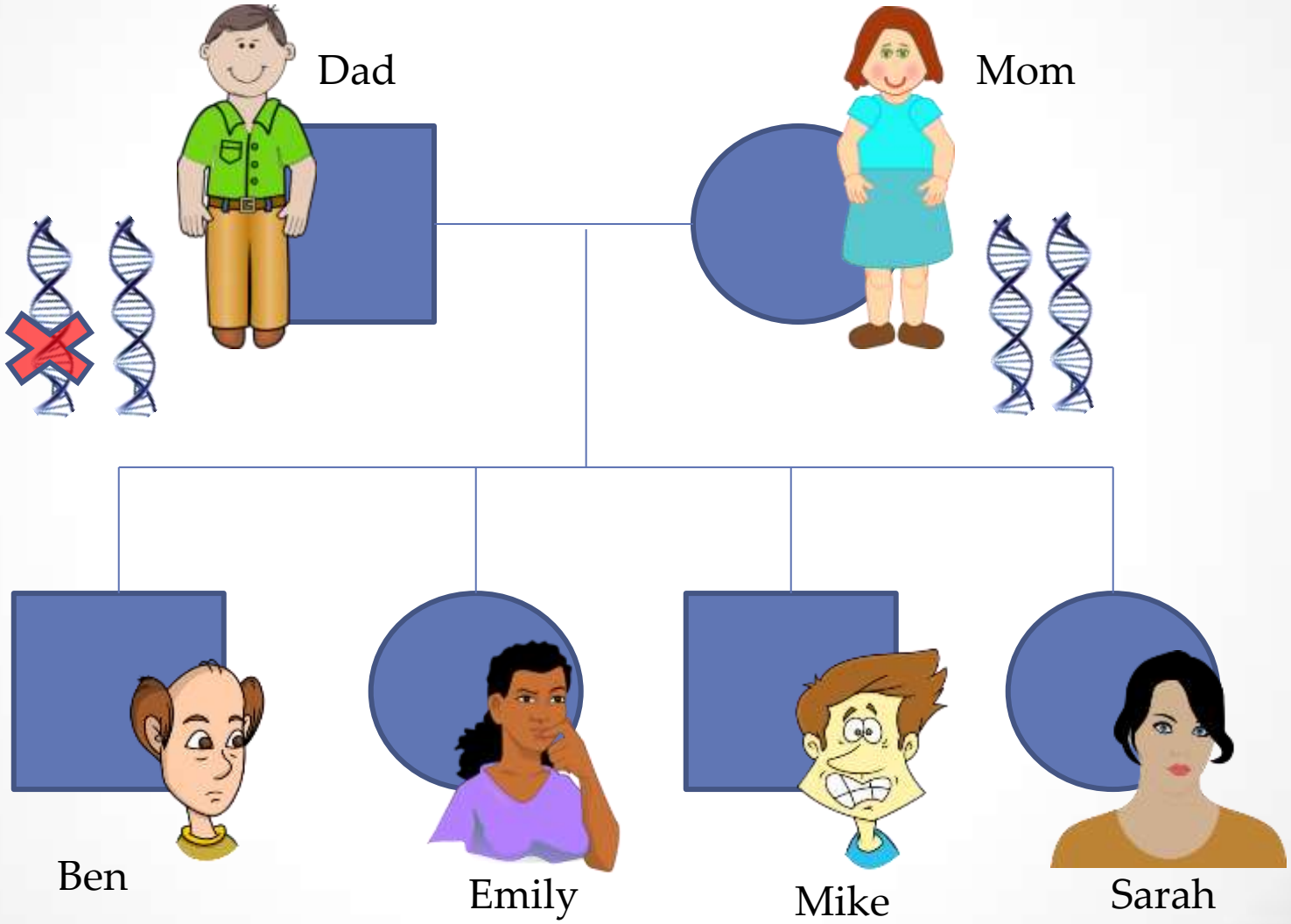


How Do I Share This Information with my Loved Ones?

- Open communication!
- Family letter
- Other resources
  - Amyloid Support Group website
- Identify the family communicator

- You know your family best!

So what does this mean for my family?



I don't have symptoms of TTR amyloidosis,
Should I be tested?

Ben

Sarah

Emily

No way! I do NOT want
to be tested
for TTR Amyloidosis!

Mike

Should I Get Tested?

- Genetic testing is a personal choice
- Help make life choices
  - Lifestyle choices
  - Reproductive decisions
- Relieve anxiety of uncertainty
- Know for the sake of children
- Allow for earlier diagnosis and clinical monitoring

- Genetic testing is not a crystal ball!

How will I feel if I am not at risk?

How will I react if I am positive?

Am I able to handle the impact of the positive result?

How will I use this information?

Is now the right time?

Sarah

What about my insurance?

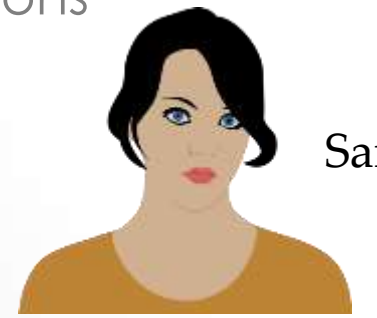
- Insurance often covers the cost of the testing
- Genetic Information Non-Discrimination Act
  - Protects most individuals from discrimination for:
    - Health Insurance
    - Employability
  - Does not apply to:
    - Life Insurance
    - Disability Insurance
    - Long-term Care Insurance

Testing Logistics

- Testing usually performed through blood draw or saliva collection
- Analysis of known familial mutation in TTR gene
  - Or other gene causative of amyloidosis in some cases!
- Two to Three weeks later…

Okay… results are in.

- **Positive Result**
  - Mutation identified
  - Did inherit mutation
  - Seek care with physician and medical team with experience in TTR Amyloidosis
  - Continue with regular evaluations

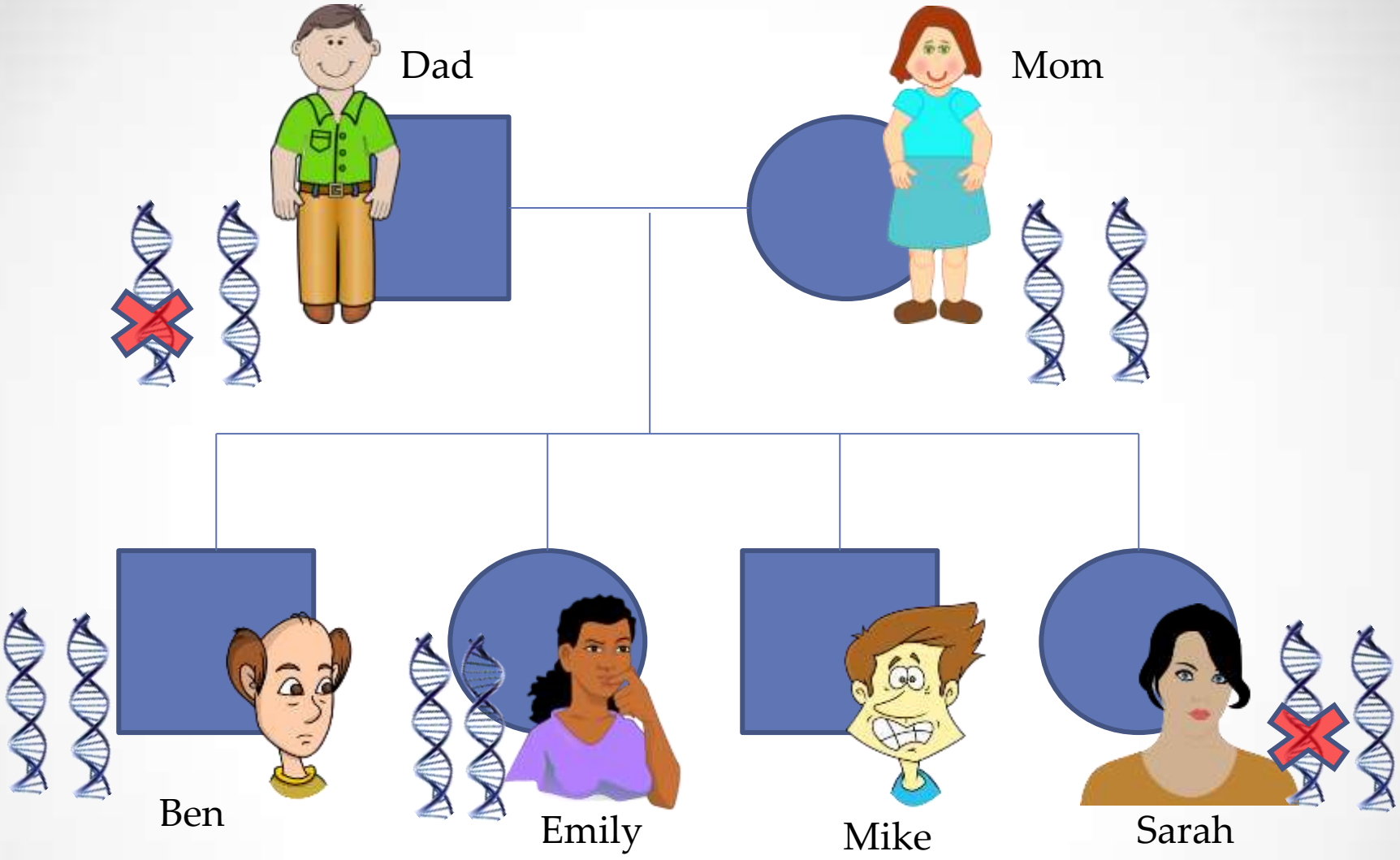


Sarah

- **Negative Result**
  - No mutation identified
  - Did not inherit mutation
  - No further evaluations needed

Ben

Emily


Dad
Mom
Ben
Emily
Mike
Sarah

Who else is at risk?

- All first degree relatives of an individual with familial amyloidosis have a 50% chance of also carrying the gene mutation
  - Children
  - Siblings
  - Parents

  - Other relatives are at risk too!
    - Aunts, uncles, cousins, grandparents, and more!

- Symptoms are variable! Even in the same family.
  - Different age of onset
  - Severity of symptoms
  - Types of symptoms

Sharing Information About Risk

August 17, 2018

Dear Family Member,

This letter is written to inform you that a member of your family, ***, has been found to have a condition called familial transthyretin (TTR) amyloidosis. Because familial TTR amyloidosis is a hereditary condition, you could also be at increased risk to have this condition.

Your family member had genetic testing that identified a specific mutation within the **TTR** gene called p.**Val50Met (c.148G>A) (legacy name Val30Met).** This was tested through ***/

Symptoms of Familial TTR Amyloidosis can appear during adulthood, but varies person to person. The condition results from a buildup of a substance in your body called amyloid. The build-up can occur in the heart, nerves, GI tract, and other organs. Symptoms may include shortness of breath, fluid build-up (congestive heart failure), peripheral neuropathy (tingling or numbness in hands and/or feet), autonomic neuropathy, and carpal tunnel syndrome. Some individuals may have other rare symptoms of TTR Amyloidosis.

Familial TTR amyloidosis is caused by a genetic alteration (or mutation) within a gene called Transthyretin necan develop amyloidosis, and any child born to a person with familial amyloidosis has a 50% chance of inheriting the gene mutation. Additionally, siblings of an individual with Familial TTR Amyloidosis also have a 50% chance of carrying the gene mutation. Some individuals may have more severe disease, or experience symptoms at earlier age than others. Some people who inherit the mutation will never develop symptoms. There are some treatment options available currently and others that are currently being researched. There is no cure for Familial TTR Amyloidosis.

Genetic testing is available to you to determine if you also carry this mutation and are, therefore, predisposed to Familial TTR Amyloidosis. However, if you are having any symptoms, further testing, like a biopsy, may be necessary. Your specific test results will then determine if other members of your family (like your children) may be at risk to inherit the mutation predisposing to Familial TTR Amyloidosis.

Genetic testing is a personal decision. Some individuals choose to have genetic testing for family planning, life planning, and other reasons. However, there are many things to think about before proceeding with genetic testing. Those wishing to pursue genetic testing should meet with a Genetic Counselor to inform them about the testing process including the benefits, limitations, psychosocial implications, and insurance concerns related to testing. We encourage those seeking genetic testing to work through a specialist familiar with familial amyloidosis to ensure appropriate interpretation and follow up of results.

Please bring a copy of your relative's test report and/or this letter with you to your appointment if you choose to pursue genetic testing.

So why genetic counseling?

- You cannot "unlearn" information
- Make sure you or your loved ones are informed about the risks, benefits, and logistics of genetic testing PRIOR to beginning the process
- Provide you tools to adapt and share information with family members

To find a genetic counselor in your area:

www.findageneticcounselor.com

Thank you!

Questions?

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