Testing for Genetic Disorders that Cause Brain Damage

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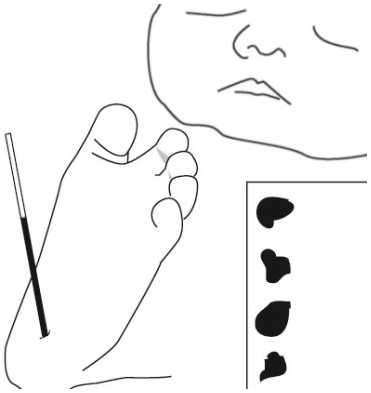
Part 1: Newborn Screening Tests



Matt is watching his twins, Anna and Cody, in the newborn nursery. The nurse pokes the babies' heels, collects drops of blood on a card, and then puts tiny Band-Aids® on their heels.

When Matt asks the nurse why she did that, she explains "State law requires that all babies get newborn screening tests for a variety of genetic (inherited) disorders. The blood spots from Anna and Cody will be sent to a laboratory to be tested to determine if they have any rare genetic disorders."
The nurse gives Matt a brochure, ***A Parent's Guide to Newborn Screening***.

Use the information in the *A Parent's Guide to Newborn Screening* brochure to answer questions 1 through 3.

1. Why is it important to test the blood of babies who appear to be healthy for disorders that could affect their brain development?

   _____

   _____

2. What might happen if a disorder that affects brain development is not detected and treated promptly and properly?

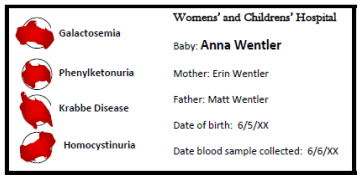
   _____

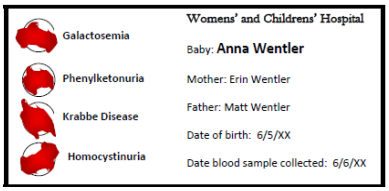
   _____

3. A genetic disorder is a disease caused by a change in a gene, called a mutation. Genetic brain disorders specifically affect the development and function of the brain. Based on the information in the brochure, list at least three types of genetic brain disorders that can be diagnosed by newborn screening tests.

   - _____
   - _____
   - _____

Your lab kit contains two newborn screening cards with dried drops of Anna's and Cody's blood and four test solutions to test for four different disorders—galactosemia, phenyketonuria, homocystinuria disease, and Krabbe's disease.





4. Follow these instructions to test Anna's and Cody's blood to determine if they have one of the four different disorders.

   - Add 2 drops of the appropriate test solution to each of the dried blood spots. *For example, add 2 drops of Galactosemia Test Solution to the circles labeled Galactosemia on each card.*
   - Use a toothpick to **gently** stir the test solutions around in each circle that contains the dried blood. *Use a different toothpick for each blood sample.*
   - If the test solution turns pink, the baby's blood contains a biochemical that indicates the baby may have the genetic disorder.

5. What can you conclude from the result of the twins' newborn screening tests? Support your answer with evidence from the blood tests.

   _____
   _____
   _____

Part 2: Follow-up Tests to Confirm the Diagnosis

A pediatrician meets with Matt and Erin in the hospital. He tells them that Anna's newborn screening test indicates that she may have a genetic (inherited) disease called phenylketonuria, or PKU. Children with PKU have dangerously high levels of an amino acid called phenylalanine in their blood. High levels of phenylalanine can poison brain cells, leading to mental retardation. He explains that it is very important to bring Anna back to the hospital in a week so that the hospital lab can test the level of phenylalanine in her blood.

1. Your lab kit contains a tube of Anna's blood plasma (the clear liquid part of blood) collected when her parents brought her in for follow-up testing. Use the phenylalanine test paper in your kit to determine the concentration of phenylalanine in the blood sample.
    - Dip one end of a strip of phenylalanine test paper into Anna's blood plasma.
    - Use the Phenylalanine Color Chart in your kit to determine the concentration of phenylalanine in Anna's blood plasma.

2. What can you conclude based on the results of Anna's phenylalanine test?

    _____

    _____

Part 3: What is PKU?

Matt and Erin (Anna's parents) are really worried about Anna. The doctor assures them that with immediate and proper treatment, PKU is not a life-threatening disease. He explains that babies with PKU are born with normal brains. Because brains continue to develop during childhood, high levels of phenylalanine in the blood can poison brain cells leading to mental retardation, small head size, behavioral problems, seizures, tremors, and jerking movements of arms and legs.

To prevent damage to Anna's developing brain, she will need to go on a special diet to reduce the phenylalanine in her blood. The doctor makes an appointment for Matt and Erin to meet with a team of specialists who will help them understand how to care for Anna and answer any questions that they have.

Read the *Parent Guide: Understanding PKU* fact sheet in your kit and use the information in the fact sheet to answer the following questions.

1. What causes PKU?

   _____

   _____

2. What is phenylalanine?

   _____

1. Circle the letter of the statement that best describes children with PKU.
   A. They lack a gene for the enzyme phenylalanine hydroxylase (PAH)
   B. They need extra phenylalanine added to their diet
   C. They produce an excess of phenylalanine hydroxylase (PAH)
   D. They do <u>not</u> need phenylalanine to make proteins

2. What is the function of the phenylalanine hydroxylase (PAH) enzyme?

   _____

   _____

3. A person who does not have the PAH (phenylalanine hydroxylase) enzyme will _____ (have/not have) PKU.

4. How does a missing phenylalanine hydroxylase (PAH) enzyme lead to high blood phenylalanine levels?

_____

_____

5. How will excess phenylalanine in Anna's blood affect her brain if she doesn't get prompt and appropriate treatment?

_____

_____

6. What must Anna's parents do to be certain that her brain develops normally?

_____

_____

7. List five foods which should be avoided in Anna's diet to prevent brain damage and mental retardation? Be specific.

- _____
- _____
- _____
- _____
- _____

Optional: To learn more about PKU, visit Your Genes Your Health at: www.ygyh.org/pku/whatisit.htm To see videos and animations, be sure to click on the words in the list on the left side of the screen.

Part 4: Inheritance and PKU

Matt and Erin don't understand how Anna can have PKU when she has healthy parents and a healthy twin brother. No other family members have PKU. They are worried that Cody or their future children may develop PKU. The doctor suggests they meet with a genetic counselor. Genetic counselors are trained specialists who help people understand the information about inherited diseases that run in their families.

The genetic counselor explains that the gene involved in PKU comes in two forms or alleles:

- One form of the PKU gene is a dominant allele (**P**) that makes a normal enzyme to break down phenylalanine.
- The other form of the PKU gene is a recessive allele (**p**) that makes an enzyme which does not work properly.

People with at least one dominant allele (P) do NOT have PKU. People, like Anna, who have two recessive alleles (pp) will have PKU.

The genetic counselor uses simple sticker models to illustrate how PKU is inherited. Here is a KEY to what the stickers represent.

Allele = alternate forms of a gene

Dominant = Dominant alleles show their effect even if there is only one copy of that allele in a pair. For example, **PP** or **Pp**

Recessive =Recessive alleles show their effect only if there are two copies of the alleles in a pair. For example, **pp**

P sticker (white) = dominant allele makes normal enzyme

p sticker (yellow) = recessive allele makes an enzyme that does not work properly

Homozygous = pair of identical alleles (**PP** or **pp**)

Heterozygous = pair of alleles not identical (**Pp**)

Phenotype = traits or characteristics that an individual shows (PKU or no PKU)

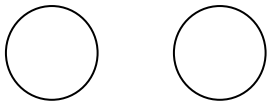
Genotype = alleles that an individual has inherited (**PP**, **Pp, or pp**)

1. Complete the "Phenotype" column in the table below by writing either "Has PKU" or "Does not have PKU.

Genotype	Phenotype
PP	
Pp	
pp	

Your kit contains sheets of stickers. Use these stickers and the information above to answer the following questions. ***Note: If you are working with other students, one student should use the stickers and other students should write letters in the circles. Be sure to clearly show the difference between a P and a p.***

2. What two stickers would you select to represent Anna who has PKU? Apply the appropriate stickers or write the letters in the circles below.



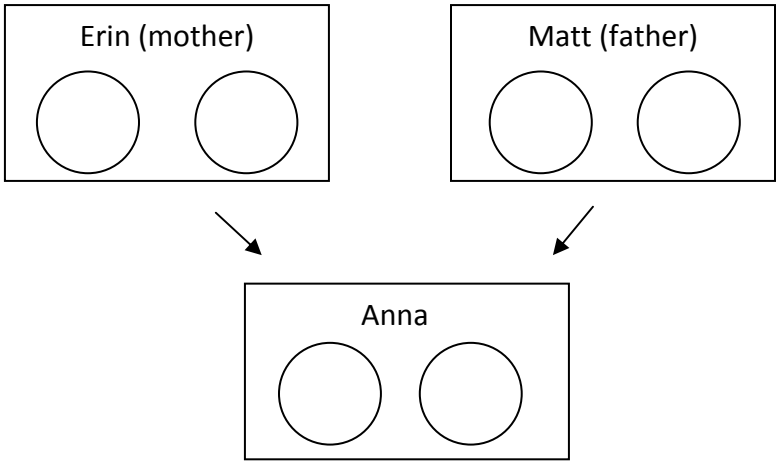
3. Circle Anna's genotype. **PP** **Pp** **pp**

4. Circle Anna's phenotype. **Has PKU** **Does not have PKU**

5. Is Anna heterozygous or homozygous for this trait? **Homozygous** **Heterozygous**

6. Anna has PKU. Both of her parents do NOT have PKU. Arrange the stickers (or write letters) to show how two healthy parents can have a child with PKU. *Remember that a child gets one allele for this trait from EACH parent.*

(or write letters)



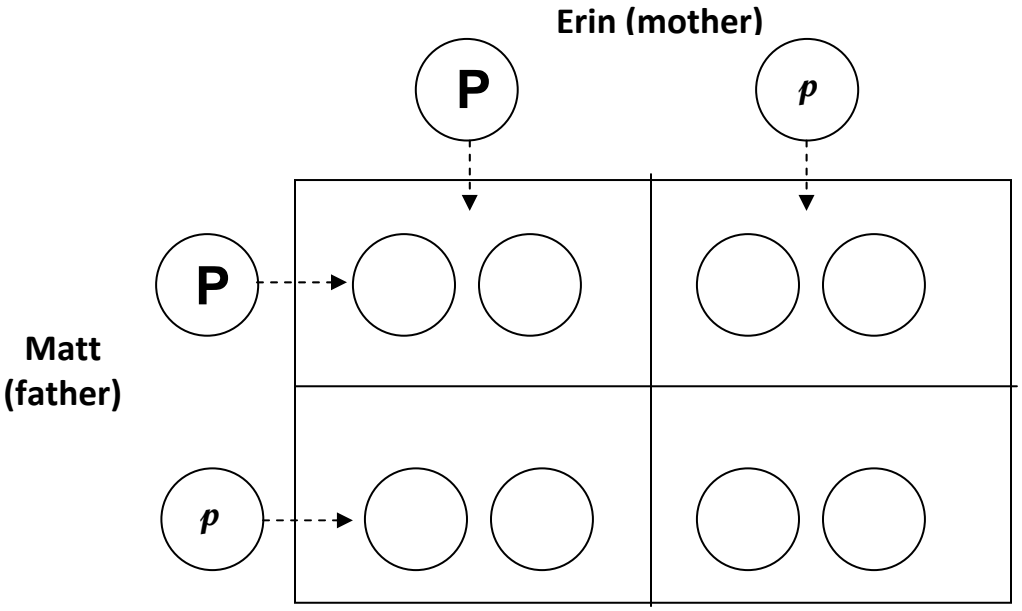
7. Circle Erin's (mother) genotype. **PP** **Pp** **pp**

8. Circle Erin's (mother) phenotype. **Has PKU** **Does not have PKU**

9. Circle Matt's (father) phenotype. **Has PKU** **Does not have PKU**

10. Are Anna's parents heterozygous or homozygous for this trait? **Homozygous** **Heterozygous**

11. Matt and Erin hope to have more children. They want to know what the chances are that future children could have PKU. The genetic counselor showed them how to set up a Punnett square. Complete the Punnett square by placing stickers (or writing letters) in the boxes.



12. If Matt and Erin have another child, what is the probability (chance) that the child will have PKU?

_____

13. If Matt and Erin have another child, what is the probability (chance) that the child will NOT have PKU?

_____

14. A carrier is a person who shows the dominant trait, but carries a recessive allele that can be passed to their offspring. What is the probability that Matt and Erin could have a child who is healthy but is a carrier for the PKU allele?

_____

15. Cody (twin brother) does not have PKU. Matt and Erin want to know if Cody is a carrier for the recessive **p** allele that causes PKU. Can you tell from this Punnett square whether Cody is a carrier for the PKU allele? Explain why or why not.

_____

_____

Part 5: Genetic Testing for the Gene that Causes PKU

The genetic counselor explains that, when Cody grows up, he should know whether he is a carrier for the recessive allele that causes PKU. She explains that it is possible to test Cody's DNA to determine if he carries the recessive "**p**" allele that causes PKU. This genetic testing could be done now or when Cody is older. Matt and Erin decide to have the testing done now.

1. Why is it important that Cody know whether he is homozygous or heterozygous for the PKU gene?

   _____

   _____

The DNA copies from each family member are treated with a restriction enzyme that cuts DNA at specific base sequences. This restriction enzyme:

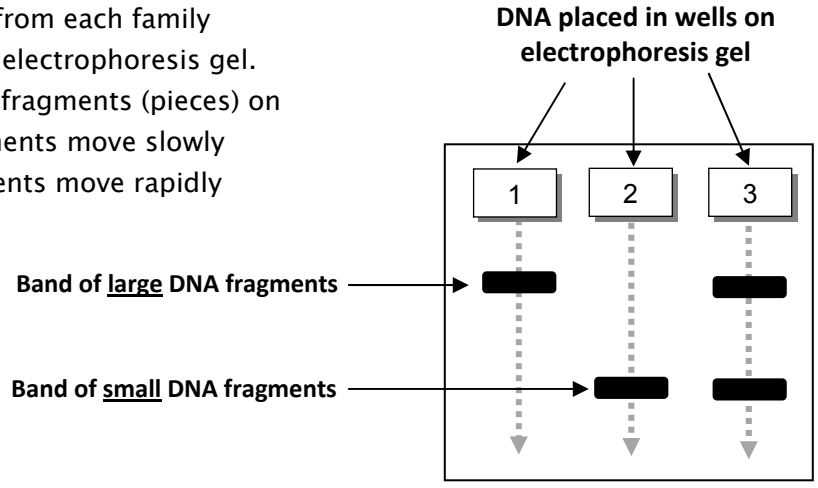
- Does NOT cut the DNA for the normal **P** allele.
- Cuts the DNA for the **p** allele to make two equal-sized, small fragments.

2. Circle the genotype that will result in all large pieces of DNA: **PP** **Pp** **pp**

3. Circle the genotype that will result in all small pieces of DNA: **PP** **Pp** **pp**

4. Circle the genotype that will result in both large and small pieces of DNA: **PP** **Pp** **pp**

To test the DNA samples for the family members, the lab technician placed samples of DNA from each family member into a different well on an electrophoresis gel. **Gel electrophoresis** separates DNA fragments (pieces) on the basis of size. Large DNA fragments move slowly through the gel. Small DNA fragments move rapidly through the gel.



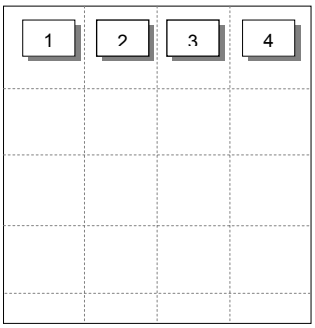
5. A person with the PKU who has the **pp** genotype would have only small DNA fragments. Which pattern of bands (1, 2 or 3) would represent a person with the **pp** genotype that causes PKU? _____

6. A healthy person with the **PP** genotype would have only large DNA fragments. Which pattern of bands (1, 2 or 3) would represent a person with the **PP** genotype? _____

7. A healthy person with the **Pp** genotype would have both large and small DNA fragments. Which pattern of bands (1, 2 or 3) would represent a person with the **Pp** genotype? _____

Your lab kit contains a simulated paper version of the electrophoresis gel that the lab technician made for the family.

You can't see the DNA pieces on this gel because DNA is colorless. To see the DNA, you will need to add a DNA stain to the gel. This stain will attach to the DNA fragments on the gel and turn them pink.



1. Place the simulated paper electrophoresis gel into the white plastic tray.

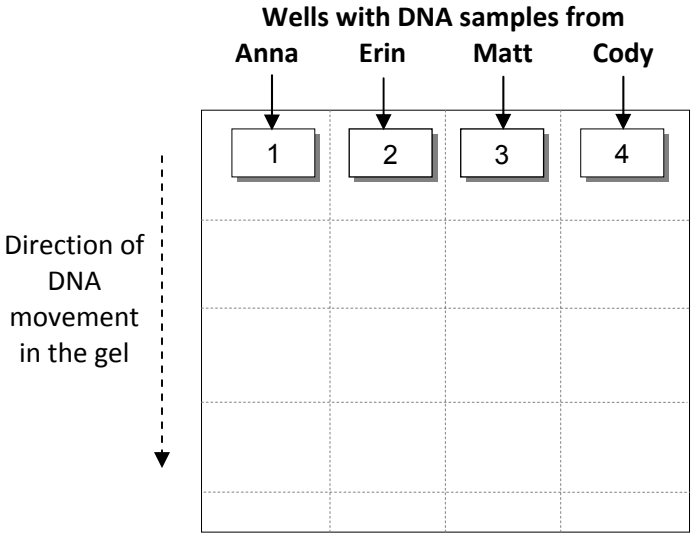
2. Add 10 ml of water to the small measuring cup.

3. Pour the entire contents of the tube of **DNA stain** into the water in the measuring cup.

4. Use the stirrer to mix the DNA stain until it dissolves.

5. Pour the DNA stain solution into the white plastic tray.

6. Observe the pink DNA bands on the gel. Record the banding pattern on the diagram of the electrophoresis gel below.



Answer the following questions based on your observation of the pattern of bands on the gel. (Circle the correct answers.)

7. The DNA sample from Anna was placed in **Well 1.**
   - What DNA fragments do you observe for Anna? **Large** **Small** **Both large and small**
   - What is Anna's genotype? **PP** **Pp** **pp**
   - Is Anna heterozygous or homozygous? **Heterozygous** **Homozygous**

8. The DNA sample from Erin (mother) was placed in **Well 2.**
   - What DNA fragments do you observe for Erin? **Large** **Small** **Both large and small**
   - What is Erin's genotype? **PP** **Pp** **pp**
   - Is Erin heterozygous or homozygous? **Heterozygous** **Homozygous**

9. The DNA sample from Matt (father) was placed in **Well 3.**

   - What DNA fragments do you observe for Matt? **Large** **Small** **Both large and small**
   - What is Matt's genotype? **PP** **Pp** **pp**
   - Is Matt heterozygous or homozygous? **Heterozygous** **Homozygous**

10. The DNA sample from Cody was placed in **Well 4.**

   - What DNA fragments do you observe for Cody? **Large** **Small** **Both large and small**
   - What is Cody's genotype? **PP** **Pp** **pp**
   - Is Cody heterozygous or homozygous? **Heterozygous** **Homozygous**

11. Will it be possible for Cody to have a child who has PKU? Explain why or why not.

_____

_____