Lung Disease:
Genes and the Environment

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Part 1: Abby's Story

Abby was experiencing a persistent cough, sinus problems, shortness of breath, and fatigue even after mild exercise. Her family doctor suggested that she see a pulmonologist (a doctor who specializes in treating respiratory problems). The pulmonologist discussed Abby's symptoms and he then conducted lung function tests. He told Abby that her lung function tests clearly showed that she had **COPD** (Chronic Obstructive Pulmonary disease).

COPD includes two breathing problems – emphysema and chronic bronchitis. Most cases of COPD are caused by exposure to inhaling pollutants such as smoke, fumes, chemicals, and dust. Genetics can also play a role in an individual's development of COPD.

Use the **What is COPD?** information sheet in your lab kit to answer questions 1 and 2.

1. How does emphysema lead to reduced ability to absorb oxygen and release carbon dioxide?

   _____

   _____

2. How does chronic bronchitis make it difficult to breathe?

   _____

   _____

The pulmonologist was concerned because Abby was only 40 years old, and symptoms of COPD usually do not show up until people are in their 60s or 70s. When he asked Abby questions about ways that she could have been exposed to inhaled pollutants, she revealed that she smoked about one pack of cigarettes per day. Abby also said that she worked for a house remodeling company and she was exposed to fumes, chemicals and dust at her workplace.

3. List at least 4 things in Abby's environment that could have increased her risk of developing COPD.

   _____

   _____

Part 2: Genes and COPD

The pulmonologist suspected that Abby may also have an inherited susceptibility for COPD. The most commonly known inherited risk factor for COPD are defective genes that cause **Alpha-1 Antitrypsin Deficiency** (also called **Alpha-1 deficiency** or **Alpha-1**).

Alpha-1 Antitrypsin (AAT) is a protective protein that prevents enzymes released by white blood cells from damaging lung tissue.

- People who do not have Alpha-1 deficiency have two normal genes (**MM**) that produce the protective AAT protein.
- People with Alpha-1 deficiency have two defective genes (**ZZ**) that do not produce protective AAT protein. These people are more likely to develop COPD because they do not make the AAT protein needed to prevent their lungs from being damaged by enzymes released by white blood cells.

> **Normal:**
>
> MM genes → AAT protein → prevents enzymes from breaking down lung tissue
>
> **Alpha-1 deficiency:**
>
> ZZ genes → no AAT protein → enzymes break down lung tissue

4. What does the protective protein AAT (Alpha-1 Antitrypsin) do?

   _____

   _____

5. How is the AAT level in a person with Alpha-1 deficiency different from a normal person who does not have Alpha-1 deficiency?

   _____

   _____

6. Why would people with Alpha-1 be more likely to develop COPD?

   _____

   _____

7. The pulmonologist ordered a simple blood test to determine if Abby had Alpha-1 Antitrypsin deficiency. Use the test sheet for **Abby's** serum to determine if she has Alpha-1 Antitrypsin deficiency.

   a) The circles on **Abby's** Alpha-1 Test Sheet in your kit have been spotted with antibodies that turn pink when they attach to the protective AAT protein.

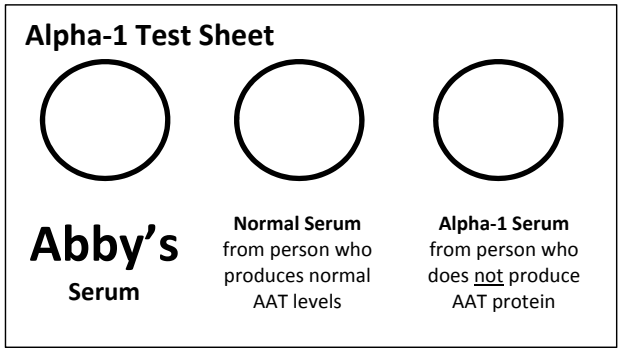
   b) Add one drop of Abby's blood serum to the first circle.

   c) Add one drop of normal serum (from a person who has normal AAT levels) to the second circle.

   d) Add one drop of Alpha-1 serum (from an Alpha-1 person who does not make the protective AAT protein) to the third circle.

   e) When antibodies on the test paper attach to the protective AAT protein, a pink color results. No color indicates that no AAT is produced.

   f) Record the results of the Alpha-1 tests on the diagram below.



8. Does Abby have Alpha-1 deficiency? Explain how you can tell.

   _____

   _____

9. COPD is a progressive disease. That means that Abby's lung function will gradually get worse with time—particularly if she continues to be exposed to environmental factors that cause COPD. List at least 4 actions Abby should take to reduce the rate at which her COPD progresses.

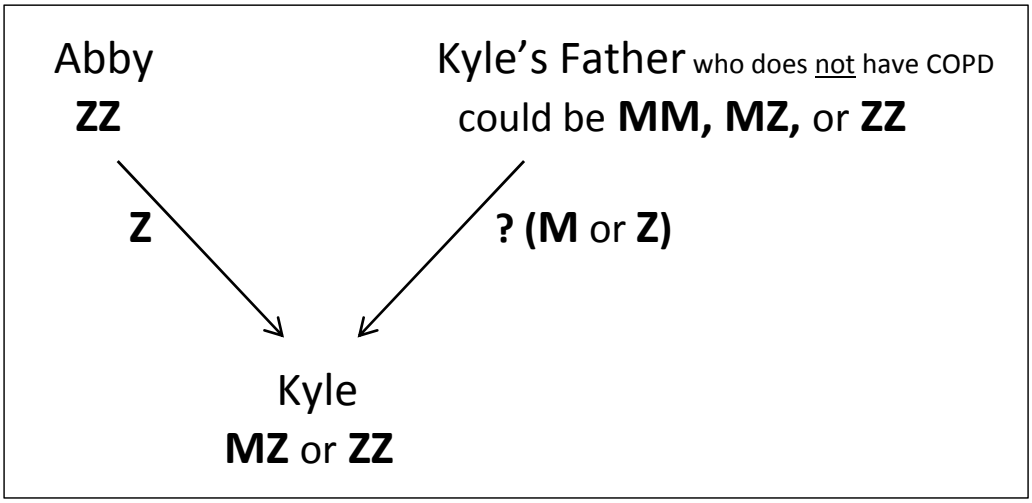
   _____

   _____

Part 3: Testing Kyle

The doctor explained that Abby had two **ZZ** genes that caused her Alpha-1 Antitrypsin deficiency. That meant that Abby's son Kyle would inherit one defective **Z** gene from her. The doctor also explained that a normal M gene produces protective AAT protein.

The diagram below shows the gene combinations that Kyle could have inherited from his mother and his father (who does not have COPD).



Use the information and diagram above to answer questions 1 and 2.

1. Circle the gene combination that would result in:

   - normal AAT levels. **ZZ** **MZ** **MM**
   - no AAT production. **ZZ** **MZ** **MM**
   - low level of AAT production. **ZZ** **MZ** **MM**

2. Circle the gene combinations that Kyle could have. **ZZ** **MZ** **MM**

The doctor strongly recommended that Abby's son Kyle be tested to see if he has Alpha-1 Antitrypsin deficiency.

3. Use the test sheet with **Kyle's** serum to determine if he has Alpha-1 deficiency.

    a) The circles on **Kyle's** Alpha-1 Test Sheet have been spotted with antibodies that turn pink when they attach to the protective AAT protein.

    b) Add one drop of Kyle's blood serum to the first circle.

    c) Add one drop of normal serum (from a person who has normal AAT levels) to the second circle.

    d) Add one drop of Alpha-1 serum (from an Alpha-1 person who does not make the protective AAT protein) to the third circle.

    e) When antibodies on the test paper attach to the protective AAT protein, a pink color results. A dark pink color indicates normal AAT protein levels. A lighter pink color indicates low AAT levels. No color indicates that no AAT is produced.

4. Which does Kyle's test result show? (circle one answer)

    - Dark pink indicating normal AAT level
    - Light pink indicating a lower than normal AAT level
    - No color indicating no AAT

5. How might you explain why Kyle produces higher amounts of AAT protein than his mother but lower amount of AAT protein than a normal person? *Hints: What gene (an **M** gene or a **Z** gene) did he inherit from his father? What is his genotype (**MM**, **MZ**, or **ZZ**)?*

_____

_____

The doctor explained that Kyle is an Alpha-1 carrier. He has one normal gene (**M**) for making the AAT protein and one mutant gene (**Z**) that does not make AAT protein.

6. How is an Alpha-1 carrier different from a normal person?

_____

_____

7. How is an Alpha-1 carrier different from a person with Alpha-1 deficiency?

_____

_____

8. Why do people like Kyle who are Alpha-1 carriers (the **MZ** genotype) have an increased risk for developing respiratory problems such as COPD?

_____

_____

Once Kyle discovered that being an Alpha-1 carrier makes people more susceptible to COPD, he wanted to take action to protect his lungs. Kyle's pulmonologist gave him an information sheet to help him understand the actions he could take to reduce his risks for COPD and other respiratory problems.

Kyle's doctor also explained that people who do not have Alpha-1 deficiency or are not Alpha-1 carriers may still develop COPD damage if they are exposed to environmental risk factors. That means all people should take actions to prevent COPD. These same preventative actions can also help to reduce asthma attacks and other respiratory problems.

Base your answers to questions 9 through 11 on the information in the ***Staying Healthy: Reducing Environmental Risk Factors for COPD*** in your lab kit.

9. Make a list of at least five actions that Kyle and other people could take AT HOME to prevent exposure to lung damaging environmental factors.

   - _____
   - _____
   - _____
   - _____
   - _____

10. Make a list of at least three actions that Kyle and other people could take AT WORK to prevent exposure to lung damaging environmental factors.

    - _____
    - _____
    - _____

11. Make a list of at least five actions that Kyle and other people could take WHEN OUTDOORS to prevent exposure to lung damaging environmental factors.

    - _____
    - _____
    - _____
    - _____
    - _____

Part 4: Not a Rare Disease, but Rarely Diagnosed

When Alpha-1 Antitrypsin (AAT) deficiency was first discovered in 1963, it was thought that it was a very rare disease only found in people with Northern European ancestry. However, research has now shown that Alpha-1 deficiency affects individuals in all racial subgroups worldwide.

In addition, research has shown that Alpha-1 deficiency is not a rare condition when compared to many other genetic disorders. In fact, it may be ranked in the top five most common single gene hereditary disorders in the world. Alpha-1 deficiency is underdiagnosed because its effects usually appear later in life and it is often misdiagnosed as an infectious disease, asthma, or allergies.

- Sickle Cell Anemia: affects **1 in 2,000** people
- Cystic Fibrosis: affects **1 in 2,500** people
- Alpha-1 Antitrypsin deficiency: affects **1 in 5,000** people
- PKU (phenylketonuria): affects **1 in 10,000** people

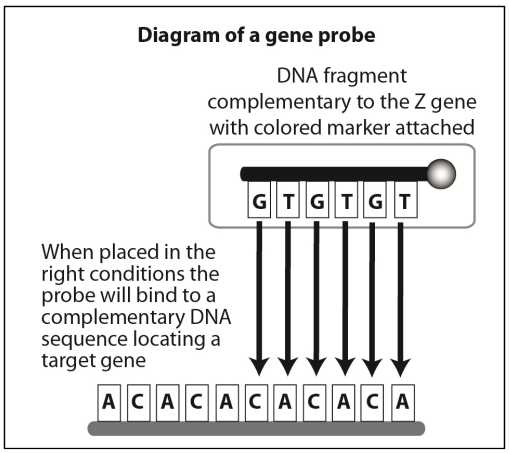
The effects of sickle cell anemia, cystic fibrosis and PKU usually appear in childhood.

1. List two reasons why Alpha-1 Antitrypsin deficiency is <u>rarely</u> diagnosed even though it is a relatively common genetic disease.
   - _____
   - _____

On the following page, you will simulate an experiment with 200 people to determine how many of them have one or two **Z** genes that put them at increased risk for developing COPD.

Researchers conducted gene probe tests to determine which of the 200 people had at least one **Z** gene. A gene probe is a DNA fragment with a colored marker attached to it. If a person has a **Z** gene, the gene probe will attach to it and produce a red spot.

You will simulate the research that used a gene probe to determine which of the 200 people have <u>one or two</u> **Z** genes that put them at increased risk for developing COPD.



2. Your lab kit contains a sheet of paper with 200 O's and X's on it. Each O or X has been dotted with blood serum from a different person.

    - The green X's represent 60 year-old adults with COPD.
    - The black O's represent 60 year-old adults who do <u>not</u> have COPD.

3. Place the clear plastic sheet with red spots labelled "Gene Probes for the Z Gene" on top of the sheet of X's and O's. <u>Be sure to line up the rectangle around the X's and O's with the rectangle around the red spots.</u>

    Red spots indicate that the gene probe has combined with **Z** genes. People who have one or two **Z** genes will be covered with a red spot.

4. Complete the following data table for the 200 people in the experiment.

Number of the 200 people who…	Count the…	Number
Have COPD	Green X's	
Do not have COPD	O's	
Have the **Z** gene	Red spots	
Do not have the **Z** gene	No red spots	
Have COPD but do <u>not</u> have the **Z** gene	Green X's with no red spot	
Have the **Z** gene and do <u>not</u> have COPD	O's with red spots	
Have the **Z** gene and have COPD	X's with red spots	

Base your answers to questions 5 through 10 on the information in the data table on the previous page.

5. Is it possible to have COPD and not have a **Z** gene? Support your answer with information from the gene probe tests.

_____

_____

6. What might cause COPD in people who do not have a **Z** gene?

_____

_____

7. Calculate the probability that a person who does not have the **Z** gene will develop COPD.

$$\frac{\text{\# who have COPD but do not have } \mathbf{Z} \text{ gene}}{\text{\# who do not have } \mathbf{Z} \text{ gene}} = \quad =$$

8. Is it possible to have a **Z** gene and not have COPD? Support your answer with information from the data table.

_____

_____

9. Calculate the probability that a person who has the **Z** gene will develop COPD.

$$\frac{\text{\# who have COPD and who have } \mathbf{Z} \text{ gene}}{\text{\# who have } \mathbf{Z} \text{ gene}} = \quad =$$

10. Based on the data collected from the 200 people in the experiment, are people who have the **Z** gene more susceptible to developing COPD? Support your answer with information from the data table on the previous page or your calculations.

_____

_____

_____

All newborns have screening tests designed to identify babies who may be at an increased risk of certain conditions such as PKU (phenylketonuria) and cystic fibrosis. This testing is expensive but worthwhile because it allows a condition to be identified and treated before problems occur. Currently no states in the US include testing for Alpha-1 in their newborn screening programs. Some people support newborn testing for Alpha-1 because it might enable people to avoid exposure to environmental factors for COPD. Other people are concerned about the cost of testing for Alpha-1 and about the invasion of their privacy that may result in prejudices or interfere with future employment.

11. Explain one reason why some people support testing newborns for Alpha-1.

_____

_____

12. Explain one reason why some people do not support testing newborns for Alpha-1.

_____

_____