NIH Curriculum: Glycogen Storage Disease – Using a Rare Disease to Learn about Molecular Biology

Glycogen Storage Disease Curriculum

Lesson 1:

PowerPoint Presentations
- What is GSD?
- What is GSD?

KWL Chart
"What is GSD?" Article
GSD Activity Slip (Entrance)
GSD Articles by GSD Type
GSD Case Studies
Directions for GSD Poster
Vocab Puzzle
Student Worksheet for Treatment Research PPT
GSD Activity Slip (Exit)
Quiz 1

Lesson 2:

*Review revised wording in plan RE: "Pipetting by Design"
"Using a Micropipette"
- Student Worksheet
- Answer Key

Pipetting A Rainbow Lab Activity
- Set-up
- Student Directions

Pipetting Competency Lab
How to Use a Centrifuge H.O.
Micropipet & Centrifuge
- Student Worksheet
- Answer Key

Virtual "Gel Electrophoresis" Lab
- Student Worksheet
- Answer Key ?

Lab Protocol Example

Lesson 3:

Entrance Slips
The Virtual DNA Extraction Lab: Questions for Review
Exit Slips

Lesson 4:

Bio Rad PCR Song Lyrics
Exit Slips (Provided by not included – no Entrance Slips provided)
PowerPoint Presentation – PCR
Virtual PCR Lab Study Guide

Purification of PCR Product
Dog DNA Chromographs

Lesson 5:
*No Lesson Plan
PowerPoint Presentation – Gene Therapy

Lesson 6:
PowerPoint Presentation - "The Importance of Nutrition in Treating GSD"
4 GSD Case Studies
Nutritional Guidelines Sheets for Case Studies
    Type 1 (only, none of the others provided)
PowerPoint Presentation – Nutritional Guidelines GSD I (Type I)
PowerPoint Presentation – Nutritional Guidelines GSD II (Types 0, IX, VI)
A Day in the Life Project:
    Type 0
    Type I
    Type IX
    Type VI
    Scenarios
    Parent Letter
    Teacher Letter

Supplemental
    Fun with Cornstarch Lab
    Extraordinary Measures Movie Guide & Key
    Extraordinary Measures Essay Topic

Also provided:
    Compare-Contrast Rubric – Not included in curriculum.

Lesson 1: Glycogen Storage Disease and the Nature of Science

Focus

Students will be introduced to Glycogen Storage Disease (GSD) and how it manifests itself genetically and physiologically. The disease will be the overlying theme as many biological concepts are presented throughout this unit. Students will be introduced to the disease through an introductory presentation, video and a comprehensive reading assignment.

Major Concepts

Glycogen storage disease is a genetically inherited disease characterized by deficiency in enzyme production along the pathway of glycogen storage and breakdown in the liver. There are five types of this disease that affect the liver and four of them will be discussed in this lesson. They are Types 0, I, IX, and VI . The different types of GSD are derived from exactly where the mutation occurs on the glycogen-gluconeogenesis pathway. In preparation for understanding this disease, we will introduce basic biological concepts such as how genetics plays a role in this disease by producing a mutation that affects the glycogen-gluconeogenesis pathway in the liver.

Objectives

After completing this activity, students will be able to:

- Figure out how the genetic inheritance of Glycogen Storage Disease works
- Classify the six types of GSD according to specific enzyme deficiency
- Recognize symptoms exhibited by GSD patients
- Be familiar with terminology related to GSD
- Be familiar with how patients manage the disease.

Prerequisite Knowledge

Students should have a working knowledge of basic genetics and the role of enzymes in metabolic pathways. If they do not, there is a brief summary of how these biological concepts work in the lesson. They should be able to use critical thinking skills to solve problems and answer questions. They should be able to examine books and other sources of information to see what has already been researched and discovered about a topic.

Overall Time Estimate

5 50-minute class periods

Vocabulary

metabolism, glycogen, enzyme deficiency, biopsy, autosomal recessive inheritance, sex-linked inheritance, hypoglycemia, hepatomegaly, lactic acid, ketones, lipids, hepatic adenoma

(It would be helpful to put these words up in your classroom in the form of a word wall and continue to review these words during this lesson)

National Science Education standards

Standard A All students should develop abilities necessary to do scientific inquiry and understandings about scientific inquiry.

Standard C All students should develop understanding of the molecular basis of heredity.

Standard E All students should develop abilities of technological design and understandings about science and technology.

Standard F All students should develop understanding of personal and community health. All students should develop understanding of science and technology in local, national, and global challenges.

Standard G All students should develop understanding science as a human endeavor; nature of scientific knowledge and historical perspectives.

Next Generation Florida Science Standards

SC.912.N.1.1 Define a problem based on a specific body of knowledge. 1. Pose questions about the natural world. 2. Conduct systematic observations. 3. Examine books and other sources of information to see what is already known. 4. Review what is known in light of empirical evidence. 8. Generate explanations tat explicate or describe natural phenomena (inferences).

SC.912.N.1.3 Recognize that the strength or usefulness of a scientific claim is evaluated through scientific argumentation, which depends on critical and logical thinking, and the active consideration of alternative scientific explanations to explain the data presented.

SC.912.N.1.4 Identify sources of information and assess their reliability according to the strict standards of scientific investigation.

SC.912.N.1.6 Describe how scientific inferences are drawn from scientific observations and provide examples from the content being studied.

SC.912.L.15.15 Describe how mutation and genetic recombination increase genetic variation

SC.912.L.16.2 Discuss observed inheritance patterns caused by various modes of inheritance, including dominant, recessive, codominant, sex-linked, polygenic, and multiple alleles.

SC.912.L.16.4 Explain how mutations in the DNA sequence may or may not result in phenotypic change. Explain how mutations in gametes may result in phenotypic changes in offspring.

SC.912.L.16.9 Explain how and why the genetic code is universal and is common to almost all organisms.

SC.912.L.16.10 Evaluate the impact of biotechnology on the individual, society and the environment, including medical and ethical issues.

SC.912.L.18.1 Describe the basic molecular structures and primary functions of the four major categories of biological macromolecules.

SC.912.L.18.11 Explain the role of enzymes as catalysts that lower the activation energy of biochemical reaction.

HE.912.C.1.4 Analyze how heredity and family history can impact personal health.

HE.912.C.1.8 Analyze strategies for prevention, detection, and treatment of communicable and chronic disease.

LA.910.2.2.3 The student will organize information to show understanding or relationships among facts, ideas, and events.

MA.912.S.1.2 Determine appropriate and consistent standards of measurement for the data to be collected in a survey or experiment.

Basic Science-Health Connection

This lesson allows students to understand how genetic inheritance influences basic biochemical mechanisms to cause the symptoms of GSD and, in turn, provide important clues for management and treatment of this disease.

Introduction

Students will utilize the KWL model, journal articles, a video documentary, and a PowerPoint presentation to be introduced to the causes, types, and management of GSD. This lesson is intended to serve as an introductory overview of exactly what GSD is and how it directly affects GSD patients.

Materials and Preparation

You will need to prepare the following:

- Copy of “Life By the Clock” (Video)
- KWL handout, 1 copy per student
- Reading articles:
    - *What is Glycogen Storage Disease?*, 1 copy per student
    - Articles on each GSD type (I,0, III, and VI), 1 copy of one type per group
    - Case studies specific to each GSD type studied (I,0, III, and VI), 1 copy of one type per group
    - Teacher Popcorn Reading Guide for “What is Glycogen Storage Disease? Article, 1 copy for the teacher
- What is GSD Article Entrance slip, 1 copy per student
- Highlighters

- Directions for GSD Poster Presentation/Rubric for grading poster, 1 copy per student
- PowerPoint "What is Glycogen Storage Disease?"
- Poster paper or flip chart paper, 1 per group
- Vocabulary Crossword Puzzle, 1 copy per student
- Student Worksheet for Treatment and Research portion of Power Point, 1 copy per student
- 10 Facts About GSD Exit slip, 1 copy per student
- Lesson 1 Quiz, 1 copy per student

Procedure

DAY ONE:

1. Introduce the KWL activity by writing the term "Glycogen Storage Disease" -1 in 100,000 people on the board and ask students to write in the "K" column everything they know about GSD. Many students will know nothing about GSD, which is fine, but have them brainstorm, based on the name, what it might mean based on prior knowledge.
2. Show the video "Life By the Clock"- Consider the following questions to use to prompt student discussion after the video:
    - Why do you think the video is entitled "Life By the Clock?"
    - What type of disease is Glycogen Storage Disease?
    - What symptoms do patients with GSD exhibit?
    - What treatments and or management for the disease were discussed?
3. Have students fill in the "W" column on the KWL to indicate what they WANT to know about GSD.
4. Hand out a copy of "What is Glycogen Storage Disesase?" to each student. Go around the room in a popcorn reading format and have each student read two sentences. Use the attached teacher guide to direct students on important aspects of the article and pause for discussion and reinforcement of the concepts in the article. You may even want to have students use highlighters to emphasize important parts of the article.
5. Homework-Complete Entrance slip for next class that lists 5 facts about GSD that they learned in class today and use the article to define 5 words that they were not familiar with prior to reading the article.

DAY TWO:

6. Have students turn in their homework entrance slips as they enter class.
7. Have students take out notebook paper to take notes on the PowerPoint. In addition to taking notes, tell them to write the metabolic pathway 3 times (for each Type of GSD that is going to be reviewed) as you are reviewing it-indicating where in the pathway the enzyme deficiency is occurring. Use the "What is Glycogen Storage Disease? PowerPoint until Slide 15. Go around the room while you are lecturing to make sure students are writing down the pathway and answer any questions that they may have. Encourage discussion!!

8. Divide class into 4 groups. Give each member of the group an article about a specific type of GSD (0, I, VI, or IX) a corresponding case study, and directions for the creation of a GSD poster for their specific type. Tell students to begin reviewing the information with their group and finish reading the article and case study for homework. They should come to class prepared to design the poster in about 20-30 minutes.

   DAY THREE:

9. Give each student group a piece of poster paper and markers and have them design their poster according to the directions given to them last class. After students are done creating their posters, have them read their case study to the class and present their poster. Have them make a connection between their case study and their poster as to why that Type of disease exhibits the symptoms that it does. (Tie in the defect with the metabolic pathway) As the presentations are being made the students can complete the "L" column of the KWL to indicate what they have LEARNED about GSD.
10. HOMEWORK: Crossword puzzle on GSD vocabulary.

    DAY FOUR:

11. Have students turn in their crossword puzzles that they did for homework.
12. Discuss treatment and research (gene therapy) for GSD using "What is Glycogen Storage Disease?" PowerPoint from slide 16 until the end of the presentation. Have students fill out the student worksheet as they are listening to the lecture.
13. Before leaving class for the day, have students fill out an Exit Slip in which they will write ten (10) facts that they have learned about GSD.
14. HOMEWORK: Study the pathways and where enzyme deficiencies may occur and what that causes.

    DAY FIVE:

    15. Quiz on pathways and enzymes and vocabulary.
    16. Begin Lesson 2.

Assessment

The following items can be used as assessments for this module:

- KWL Hand-out
- GSD Article Entrance Slip
- GSD Poster and Presentation
- Vocabulary Crossword Puzzle
- 10 Facts about GSD Exit Slip
- Lesson 1 Quiz

Resources

Association for Glycogen Storage Disease. (2006, October). *Type I Glycogen Storage Disease.* Retrieved 22 July, 2011, from Association for Glycogen Storage Disease: http://www.agsdus.org/

Association for Glycogen Storage Disease. (2006, October). *Type IX Glycogen Storage Disease.* Retrieved July 22, 2011, from Association for Glycogen Storage Disease: http://www.agsdus.org/

Association for Glycogen Storage Disease. (2006, October). *Type VI Glycogen Storage Disease.* Retrieved July 22, 2011, from Association for Glycogen Storage Disese: http://www.agsdus.org/

Association for Glycogen Storage Disease. (2006, October). *What is Glycogen Storage Disease?* Retrieved July 22, 2011, from Association for Glycogen Storage Disease: http://www.agsdus.org/

Association of Glycogen Storage Disease. (2006, October). *Type 0 Glycogen Storage Disease.* Retrieved July 22, 2011, from Association of Glycogen Storage Disease: http://www.agsdus.org/

Bonelli, H. B. (Director). (2003). *Life By the Clock* [Documentary].

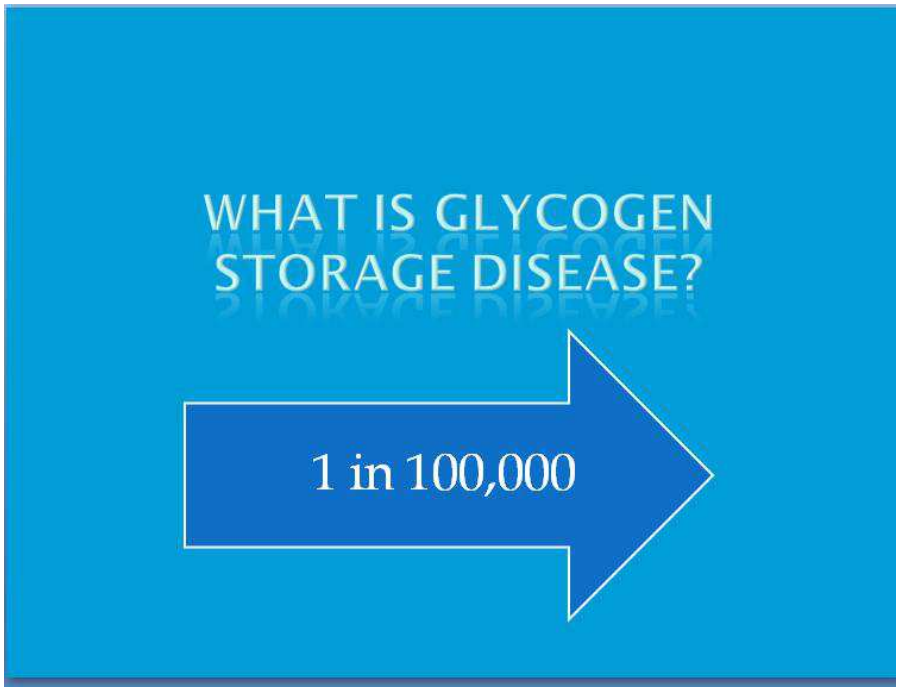
Weinstein, D. D. (2010, November 20). Gene Therapy for Glycogen Storage Disease. University of Florida College of Medicine.

Weinstein, D. D. (2011, June 2). The Glycogen Storage Diseases: A Clinical Update. Lugo, Spain: University of Florida College of Medicine.

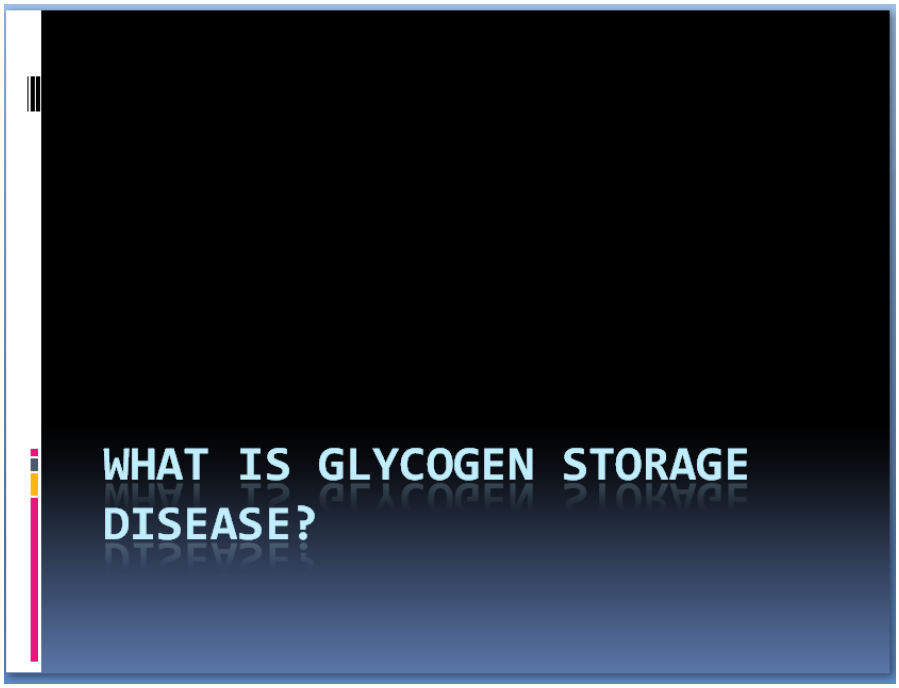
Student Pages

- KWL Hand-out
- "What is Glycogen Storage Disease?" article
- GSD Article Entrance Slip
- GSD Articles by GSD type
- GSD Case Studies
- Directions for GSD Poster Presentation/Rubric for grading poster
- Vocabulary Crossword Puzzle
- Student Worksheet for Treatment and Research portion of Power Point
- 10 Facts About GSD Exit slip
- Lesson 1 Quiz, 1 copy per student

See PowerPoint Presentation:



See PowerPoint Presentation:



GLYCOGEN STORAGE DISEASE

What You Know	What You Want to Learn	What You Learned

What is Glycogen Storage Disease? (Teacher Guide for Popcorn Reading)

All of the Glycogen Storage Diseases are considered **inherited** metabolic disorders. A metabolic disorder is a disease that disrupts metabolism. Metabolism is the process by which our body breaks down the food we eat and converts it to energy. Therefore, a person who has a metabolic disorder has a difficult time breaking down certain foods and creating energy. A metabolic disease is most frequently caused by an absence or deficiency in an enzyme (or protein). An enzyme can act to help the body break down food into energy. There are many enzymes in the body and each act like a machine on an assembly line. When one of the enzymes is not working properly, the process of breaking down of specific foods can go more slowly or shut down completely.

The underlying problem in all of the glycogen storage diseases is the use and storage of glycogen. Glycogen is the storage form of glucose (sugar). To briefly review metabolism, a simple form of sugar (glucose) is our bodies' main source of energy. After we eat, we have too much glucose in our blood, so our bodies store the extra glucose in the form of glycogen (much like we deposit our extra money in a bank). When our bodies need more energy, certain enzymes convert the glycogen back to glucose and withdraw it from the liver and the muscles (just like we withdraw spending money from the bank). Glycogen is a complex material made of individual glucoses linked together in long chains with many branches off the chains (just like a tree). Sometimes GSDs are also referred to as glycogenoses because they are caused by difficulty in glycogen metabolism.

Glycogen is mainly stored in the liver and muscle cells, but the kidneys and intestines also store some limited amounts of glycogen.

A person with a Glycogen Storage Disease (GSD) has an absence or deficiency of one of the enzymes responsible for making or breaking down glycogen in the body. This is called an enzyme deficiency. The enzyme deficiency causes either abnormal tissue concentrations of glycogen (too much or too little) or incorrectly or abnormally formed glycogen (shaped wrong). Depending on the type of GSD a person has, their enzyme deficiency may be important in all parts of the body, or only in some parts of the body, like the liver or muscle. Typically, the forms of GSD are described by the part of the body that has trouble because of the enzyme deficiency. The categories most often are: the liver only, the muscles only, or both the liver and the muscles. Other systems that may be involved include blood cells (red blood cells, white blood cells, and platelets), heart, and kidneys amongst others.

All types of GSD cause the body to either not be able to make enough glucose, or not be able to use glucose as a form of energy. Determining what type of GSD a person has (diagnosis) depends on an individual's symptoms. Typically a doctor will do a physical examination and some blood and urine testing. Occasionally, a muscle and/or

liver biopsy will be needed to measure the amount of a certain enzyme in that part of the body.

There are about eleven known types of GSD, which are classified by a number, by the name of the defective enzyme, or by the name of the doctor who first described the condition. For example, Glycogen Storage Disease type Ia, caused by a defect in the enzyme glucose-6-phosphatase, was originally known as “von Gierke's Disease” but is also referred to as “Glucose-6-Phosphatase Deficiency Glycogen Storage Disease”.

GSDs are genetic disorders. This means that they are caused by a change in a part of an individual’s genetic information. Our genetic information is stored on genes. Genes serve as the instruction manual for our bodies. They tell our bodies how to grow and function. They also determine our physical features, such as hair color and eye color. We have around 30,000 genes in every cell of our body. We get two sets of every gene, one set from our mother and one set from our father. This is why we appear to be a combination of our parents. Our parents have no control over which genes they pass on to us. The genes we inherit from our parents happen purely by chance.

If there is a change in the genetic information contained on one of these genes, our bodies are unable to read its instructions. Therefore, it may cause a difference in the way our body functions. This is similar to having a page missing out of an instruction manual for putting an appliance together. Without that page, we would be unable to properly assemble the appliance and it would not be able to work. Almost all forms of GSD occur when a child inherits an incorrect genetic instruction from both their mother and their father (autosomal recessive inheritance). Some forms of GSD are caused by a genetic change that is passed from mother to son (sex or X-linked inheritance).

Activity 1 Entrance Slip

List 5 things that you learned about GSD in general:

1.

2.

3.

4.

5.

List and define 5 words that you learned today:

1.

2.

3.

4.

5.

Activity 1 Entrance Slip

List 5 things that you learned about GSD in general:

1.

2.

3.

4.

5.

List and define 5 words that you learned today:

1.

2.

3.

4.

5.

Type 0 Glycogen Storage Disease – GSD Type III

Synonyms: Hepatic Glycogen Synthase Deficiency

Type 0 Glycogen Storage Disease (GSD 0) is caused by a deficiency in the enzyme named glycogen synthase. This enzyme is needed for the body to make glycogen. When a person has glycogen synthase deficiency, the amount of glycogen that the body can store in the liver is very low. Low amounts of glycogen in the liver mean that when a person is not eating (fasting) their blood sugar levels can get very low (hypoglycemia).

In patients with Type 0 Glycogen Storage Disease, the symptom of fasting hypoglycemia typically develops when a baby no longer gets fed during the night (late infancy). Early in infancy, children usually have no symptoms, but weaning from overnight feeds is often difficult. Children may have early-morning (before eating breakfast) drowsiness, appearance of looking pale, vomiting and fatigue, and sometimes convulsions associated with low blood glucose. During gastrointestinal illnesses ("stomach bugs") or periods of poor eating, children may appear to be very tired and lazy. Usually low blood sugar (hypoglycemia) is found as part of the labwork that the doctor or hospital does in order to figure out why a child is not acting energetic.

Children with GSD 0 may grow a bit slower than expected (have a mild growth delay). In general, people with Type 0 Glycogen Storage Disease do not have learning problems (they are developmentally normal). When exercising, people with GSD 0 may become tired more quickly than other individuals. Furthermore a person with Type 0 GSD may have muscle cramps because the body is trying to make energy from accumulated lactic acid. A person with Type 0 Glycogen Storage Disease will typically look no different from a person who does not have GSD 0. The liver will not be larger than normal. A doctor examining the first morning urine of someone with Type 0 GSD may see some signs (increased glucose and ketones in urine) that might make the diagnosis of diabetes as the first thing mentioned to a family.

Any child with a history of needing frequent meals or snacks and with hypoglycemia (where a doctor sees ketones in the urine) may have Type 0 Glycogen Storage Disease. Detailed blood and urine tests performed by a doctor may show patterns that are unique to GSD 0. If a doctor looks at a piece of liver from a person with GSD 0, they will see very little glycogen. Genetic DNA testing that is performed on a blood sample is now available.

The goal of treatment for Type 0 Glycogen Storage Disease is to prevent low blood sugar (hypoglycemia) by avoiding fasting. Frequent meals and snacks can be given every 3-4 hours during the day. Uncooked cornstarch can act as a "slow release" form of glucose for the body. Given in the proper amounts, it will prevent hypoglycemia overnight. A diet high in protein may help with the cramping, tiredness, and fatigue that many people with GSD 0 experience
At this time, Type 0 Glycogen Storage Disease is considered very rare. However, because testing for GSD 0 just recently became available, doctors think that GSD 0 is more common than previously thought. Type 0 GSD affects both males and females. People with Type 0 Glycogen

Storage Disease have been described from Eastern Europe, Western Europe, North America, and South America.

Genes are instructions for the body. Glycogen synthase deficiency is caused by a change in the glycogen synthase-2 (GYS2) gene. GSD 0 is inherited within families in an autosomal recessive fashion.

Links:
Type 0 GSD info from Online Mendelian Inheritance in Man searchable database (www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=240600)
Type 0 GSD info from e-medicine (www.emedicine.com/ped/topic873.htm)
"Liver Glycogen Synthase Deficiency" article from *Pediatrics* (http://pediatrics.aappublications.org/cgi/content/full/108/2/495)
GSD 0 from Madisons Foundation (www.madisonsfoundation.org/content/3/1/display.asp?did=627)

Type I Glycogen Storage Disease – GSD Type I

Synonyms: von Gierkes disease; Hepatorenal Glycogenosis; Type I Glycogenosis; Glucose-6-Phosphatase Deficiency Glycogen Storage Disease

Type I Glycogen Storage Disease accounts for about 25% of all cases of GSD diagnosed in the USA and in Europe and has an estimated incidence of about 1 in 100,000 live births.

In Type I Glycogen Storage Disease (GSD I), the most frequent first symptoms include an enlarged liver and low blood sugar (hypoglycemia). After we eat, excess glucose is stored as glycogen mostly in the liver to be used later when we are fasting (not eating for 3-4 hours) to maintain normal glucose levels in our body. In GSD I, the metabolic problem is centered in the liver because the enzyme needed to release glucose from glycogen is missing.

There are two different subtypes of Type I Glycogen Storage Disease – called type Ia and type Ib. GSD Ia is caused by a deficiency of the glucose-6-phosphatase (G6Pase) enzyme in liver, kidney and other organs of the body. GSD Ib is caused by a deficiency in glucose-6-phosphate translocase, or transporter (G6PT) enzyme, that helps in transporting G-6-Pase enzyme from one point to another. These two enzymes work together to help the body break down the storage form of sugar (glycogen) in to free glucose (sugar) for use when we are not eating. When a person does not have enough of either of these two enzymes, they usually have many of the same signs and symptoms early on in life.

Individuals with Type I Glycogen Storage Disease are unable to release glucose from glycogen mainly in the liver (see What is a Glycogen Storage Disease?). They cannot maintain their blood glucose (sugar) levels and within a few hours after eating they will develop hypoglycemia (low blood sugar). The low levels of glucose in the blood of these individuals often result in chronic hunger, fatigue, and irritability. These symptoms are especially noticeable in infants. Symptoms of hypoglycemia often appear when the time between feedings increases and the infant sleeps through the night. In infants, children and adults, symptoms may also be present when an illness prevents normal feeding routine and time. If the blood sugar is very low, some individuals may have seizures (hypoglycemic seizures).

Since people with Type I GSD are able to store glucose as glycogen but not able to release it normally, with time the stores of glycogen build up in the liver causing the liver to swell (hepatomegaly). This is much like being able to place groceries from the store into your kitchen cabinets, but not being able to get the food out of the cabinets when needed. Levels of hormones, lactic acid, triglycerides, lipids (fats), uric acid and other by-products of metabolism increase in the blood as the body tries to raise blood sugar. Fats get stored in the liver along with the glycogen, which leads to the enlargement of the liver. The liver does its many other functions normally, and there is not usually any evidence of liver failure. The kidneys are also enlarged due to increased glycogen storage.

The continued presence of low blood sugar can eventually leads to delayed growth and

development as well as abnormal levels of some metabolites (substances) in the blood and urine. High blood pressure has also been seen in a number of individuals and when this occurs, appropriate treatment is needed.

In addition to the problems described above, individuals with Glycogen Storage Disease Type Ib can develop frequent bacterial and fungal infections, due to abnormal functioning of the white blood cells called neurophils. These are the fighter cells of the body. Therefore, people with GSD Ib can have low levels of neutrophils in their blood (a finding called neutropenia). Many people with GSD Ib use a medicine called GCSF to increase the number of neutrophils in the body. People with Glycogen Storage Disease Type Ib may also develop chronic pancreatitis, chronic inflammatory bowel disease, and Crohn's disease.

The diagnosis of Type I GSD will always include blood studies such as blood glucose, cholesterol, triglycerides, lactate, and uric acid, measurements of growth, and ultrasound or other imaging studies to measure the size of the liver and kidneys. By looking for changes in the genes associated with GSD I, genetic (DNA) testing can be used to diagnose the majority of individuals with GSD Type Ia and Ib. Sometimes liver biopsy analysis will be needed to examine the enzyme levels of someone suspected to have Type I Glycogen Storage Disease, especially in situations when DNA testing is negative and the clinical suspicion of GSD I is high.

The treatments of Type I Glycogen Storage Disease are aimed at correcting the metabolic changes in the body and promoting growth and development. Current treatments consist of providing small, frequent feedings during the day. Most agree that fructose and galactose should be restricted, but the degree of restriction is still debated. The restriction of these sugars translates to no fruit, juice, table sugar, cake, pie, syrup, jelly, honey, and candy; and limited amounts of dairy foods including milk, yogurt and cheese. The majority of medical centers recommend the use of uncooked cornstarch, mixed in water, soy formula or soy milk (sucrose, fructose and lactose free). Cornstarch should not be mixed in drinks that contain high amounts of ascorbic or citric acid and the cornstarch drink should not be heated as this may alter its structure rendering it less effective. Cornstarch is digested slowly so it provides a steady release of glucose in between feedings. In some cases, an overnight tube feeding is required to provide a continuous delivery of glucose. Formulas should be sucrose, fructose and lactose free. The rate of the tube feeding is based on the liver’s normal glucose delivery rate and the age and weight of the child. Due to the many restrictions for the GSD I diet, it is necessary to supplement the diet with a multivitamin. Additional calcium supplementation may also be required. Because the diet for Type I Glycogen Storage Disease is complex, the ideal team should include a dietitian and a physician familiar with the long-term care and maintenance related to GSD I.

Patients with Type I Glycogen Storage Disease may develop benign tumors in the liver called hepatic adenomas. Adenomas are usually first noted around the time of puberty. They typically do not cause symptoms and are identified by routine imaging studies of the liver. In rare instances these can develop into liver cancer.

Renal (kidney) disease is another complication in GSD I patients, and most patients with type I glycogen storage disease older than age 20 yr have proteinuria (proteins excreted in urine). Many also have hypertension (high blood pressure), and kidney stones, among other changes in kidney functions. More severe kidney injury may occur with large amounts of protein in the urine, high blood pressure, and decreased ability of the kidneys to filter waste products due to damage to the filtering units of the kidney (glomeruli). In some patients with the advancement of renal/kidney disease, kidney failure can happen which can require dialysis and eventually kidney transplantation.

Other complications can include pulmonary hypertension, radiographic (X-ray) evidence of osteopenia (weak bones), and fractures.

In the past, many patients with Type I Glycogen Storage Disease did not survive infancy and childhood. Today, maintenance of normal or near normal blood sugar/glucose levels with effective therapy improves the metabolic abnormalities and reverses the severe growth failure characteristic of the untreated patients. It is still unclear whether long-term complications can all be prevented by dietary therapy. However, with earlier diagnosis, appropriate diet, and better metabolic control, many individuals with GSD I are doing very well and many adults are living longer and healthier lives.

Type III Glycogen Storage Disease - GSD Type III

Synonyms: Debrancher Deficiency; Cori Disease; Forbes Disease; Limit Dextrinosis

GSD type III is caused by a deficiency of glycogen debrancher enzyme (GDE) activity. Glycogen debranching enzyme along with another enzyme, phosphorylase, helps break down the branches of glycogen to release free glucose. Deficiency of GDE results in glycogen with short outer chains in liver, muscle, and heart tissues. The abnormal glycogen is not soluble and causes damage to tissues where it collects (liver and/or muscle). This can be compared having a piece of sand in your shoe that, although small, irritates the foot. This partial breakdown of glycogen into glucose also causes hypoglycemia (low blood sugar) because glucose sugar can not be released. The body is unable to properly metabolize glycogen (a complex form of sugar). Because of improper processing, glycogen is stored in the organs of the body.

Glucose, a simple form of sugar, is our bodies' main source of energy. After a person eats, there is too much glucose in the blood, so the body stores the extra glucose in the form of glycogen in the liver and muscles (much like one might deposit extra money in a bank). When the body needs more energy, certain enzymes convert the glycogen back to glucose and withdraw it from the liver and the muscles (just like one can withdraw spending money from the bank). One of the enzymes that helps break glycogen down into glucose in the muscles is called debranching enzyme. Individuals with GSD III either have a defective enzyme or lack a sufficient amount of this important enzyme. As a result, glycogen is not broken down completely and accumulates in the liver and/or muscle tissue. Accumulation of abnormal glycogen in the liver tissue causes it to become enlarged and not function properly.

GSD III is a genetic disorder and it is inherited as an autosomal recessive disease. This means it is caused by a change in a part of an individual's genetic information. Genetic information is stored on genes. Genes serve as the instruction manual for our bodies. They tell the body how to grow and function. They also determine physical features, such as hair color and eye color. A person has around a 30,000 genes in every cell of their body. Two sets of every gene are inherited, one set from the mother and one set from the father.

If there is a change in the genetic information contained on one of these genes, the body is unable to read the instructions. Therefore, it may cause a difference in the way the body functions. This is similar to having a page missing out of an instruction manual for putting an appliance together. Without that page, one would be unable to properly assemble the appliance and it would not be able to work. The gene responsible for making debranching enzyme (GDE) is called the amylo-1,6-glucosidase, 4-alpha-glucoanotransferase gene (AGL) gene. If one copy of the AGL gene is altered but the second copy is not, then the body can follow the instructions on the second copy in order to produce enough debranching enzyme. This is like having a second instruction manual to refer to. When both copies of an individual's AGL gene are altered, the body is unable to read any instructions on how to make the proper amount of debranching enzyme. As a result, the individual has GSD III.

There are two types of GSD III known as type IIIa and type IIIb. Most patients with Type III GSD have enzyme deficiency in liver and skeletal muscle. Patients that have enzyme deficiency in liver and muscle (including sometimes the heart muscle) have what is know as type GSD IIIa. Some patients (<15%) have debranching enzyme deficiency only in the liver whis is type GSD IIIb. During early years of infancy and childhood, the disease may present clinically just like GSD I: small stature, large liver, poor muscle tone (hypotonia) and hypoglycemia. Some liver symptoms (enlarged liver) often improve with age and may disappear after puberty. However, in some patients liver cirrhosis (damage to liver cells) can occur due to accumulation of abnormal glycogen..

Children with GSD III are often first diagnosed because they have swollen (distended) abdomens (belly) due to a very large liver. Some children have problems with low blood sugars when fasting (not eating for 4 hours) but this is not as common or as severe as in GSD I. Growth may be delayed or slow during childhood but most individuals reach a normal adult height. Muscle weakness (GSD IIIa) is commonly present in childhood and can, at times, become severe in adult age (requiring use of a wheel chair for mobility by 50-60 years). Although the enzyme defect does not go away, the liver often returns to a smaller size at puberty.

Elevated glycogen content is present in liver and muscle cells. A definite diagnosis and sub-typing (determining IIIa versus IIIb type) requires either liver biopsies or DNA based genetic testing. Biopsy of the liver shows inflammatory changes (swollen liver cells) with great elevations of abnormal-structured glycogen content and a deficiency of the debrancher enzyme (GDE). In GSD IIIa, biopsy of muscle and liver shows an accumulation of abnormal-structured glycogen and deficiency of debrancher enzyme. However, if only the liver is examined, the type of GSD cannot be determined. If genetic testing is performed and the person has a gene change in the area associated with GSD IIIb, a doctor may be able to use the mutation information and clinical information to determine GSD III type (type a versus type b).

Other complications associated with GSD III can include radiographic (X-ray) evidence of osteopenia (weak bones) and fractures. Often, a DEXA bone scan will be required to measure bone density. Also, chemical analysis of the blood usually shows low blood sugar and elevated levels of fat (cholesterol/lipids). However, uric acid and lactic acid levels, which are usually elevated in GSD I patients, are usually normal.

Currently, there is no effective treatment for this disease. Hypoglycemia (low blood sugar) can be controlled by frequent meals high in carbohydrates. Researchers have proven the storage of glycogen leads to liver cirrhosis progressing to liver failure. Patients with myopathy (weak muscles) have been tried on a diet high in protein, with some improvement; however, no long-term data is currently available.

GSD III is considered a muscular dystrophy because of the weakness of the muscle. As a result, people with GSD III may qualify for services offered by the Muscular Dystrophy Association (MDA).

People with debrancher deficiency have lived well into late adulthood. Muscle disorders seem to be an increasing problem with age in those persons with Type IIIa. Muscle weakness, though minimal during childhood, may become more evident in adults with onset in the third or fourth decade. These patients have slowly progressive weakness and distal muscle deterioration, and some patients eventually may require the use of a wheelchair for mobility. The heart may be mildly enlarged, but its function is typically normal. In rare instances, the heart muscle can thicken and result in heart failure and heart rhythm disturbances.

Links:

GSD info from Online Mendelian Inheritance in Man searchable database (www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=232400)

Type III GSD info from e-medicine (www.emedicine.com/ped/topic479.htm)

Muscular Dystrophy Association info on Type III GSD (www.mdausa.org/disease/dbd.aspx)

Glycogenosis Type III (http://moon.ouhsc.edu/kfung/JTY1/NeuroHelp/ZNN0IE24.htm)

GSD Type III (www.madisonsfoundation.org/content/3/1/display.asp?did=345)

 back to AGSD website

Type IX Glycogen Storage Disease – GSD Type IX

Synonyms: Phosphorylase Kinase Deficiency

GSD type IX is a disorder in which the body cannot break down (metabolize) glycogen (a complex form of sugar). When someone has GSD IX, glycogen is stored in the organs of the body (liver, muscle and rarely heart) instead of being used. To briefly review metabolism, a simple form of sugar (glucose) is the bodies' main source of energy. After a person eats, there is too much glucose in the blood, so the body stores the extra glucose in the form of glycogen in the liver and muscles (much like storing extra food from the grocery store in the pantry to be used later, when needed). When the body needs more energy, specific proteins (enzymes) change the glycogen back to glucose and take it out of the liver and the muscles (just like taking food out of the pantry).

There are many different steps involved in breaking down glycogen into glucose. Many different enzymes help each step of breakdown happen in a sequential manner. Patients with type of GSD IX glycogen storage disease have a deficiency of the enzyme called phosphorylase kinase. Phosphorylase Kinase Deficiency, PHK, constitutes the largest subgroup (1:100,000 births) of liver glycogenosis. When phosphorylase kinase is low or deficient, glycogen cannot be broken down completely. The phosphorylase kinase enzyme is a regulatory enzyme in the breakdown of glycogen; thus, the deficiency of this enzyme results in glycogen accumulation. When there is a defect in phosphorylase kinase, the body may not be able to make enough sugar (glucose) to use, and also the incompletely digested glycogen builds up (accumulates) in the body, primarily in the liver and muscles. Although some glucose (energy) is created from the successful earlier steps in the breakdown of glycogen, not enough glucose is made for the proper function of the body.

The clinical picture of Type IX glycogen storage disease is similar to that seen in Type VI GSD, liver phosphorlyase deficiency. GSD IX can cause low levels of glucose in the blood (hypoglycemia or low blood sugar), which has the potential to lead to seizures. This is more likely to happen after long periods of not eating (fasting), and can be prevented by maintaining a high carbohydrate (starchy foods) diet, adequate amounts of protein in the diet, and avoiding long periods of not eating. A deficiency in PHK causes glycogen accumulation in various tissues and organs including liver, muscle, blood cells but rarely in the heart. The liver can become irritated or inflamed from storing increased amounts of glycogen, which can cause some blood tests to be abnormal with elevated enzymes (ALT and AST) on liver function blood tests. The most common symptoms are enlarged liver, growth retardation, mild delay in motor development, and elevated blood lipids (fats). The symptoms usually improve as a child ages, and children usually reach their full potential height and weight by adulthood.

Phosphorylase kinase enzyme is made up of four different pieces (subunits), which we can compare to puzzle pieces. When putting together a puzzle, the picture is not complete unless all of the pieces are placed together correctly. In the same way, all the pieces (subunits) of this enzyme must come together correctly in order for the enzyme to work properly. If a puzzle

piece is missing or has the wrong shape, the puzzle cannot be completed. Likewise, if there is a change in one of the subunits, the enzyme cannot be assembled and formed properly and will not be able to perform its job in the breakdown of glycogen. The inheritance of Type IX glycogen storage disease can be either autosomal recessive or X-linked recessive.

There are multiple genes that provide the instructions to make the four pieces/subunits (i.e. alpha, beta, gamma, and delta) that make up the phosphorylase kinase enzyme. A change in a subunit is caused by a change in the gene that gives the instructions for that subunit. A definitive diagnosis of PHK deficiency requires demonstration of the enzymatic loss in certain tissues (blood (erythrocytes), muscle, heart and liver tissues). DNA testing is currently available for the subunits alpha1, alpha2, and gamma2. Not many patients have had genetic changes found in beta, delta1, and delta2.

The most common form of Type IX GSD is the X-linked form, which accounts for nearly 75% of all cases. X-linked recessive conditions mainly affect boys. The X-linked type involves genetic changes affecting the alpha-subunit of PHK genes (PHKA1 and PHKA2 genes). The main organs affected include the blood cells, muscle and liver. The clinical picture associated with these genetic changes is hepatomegaly (large liver), growth retardation, and mild to moderately elevated cholesterol and fat in blood and liver enzymes.

The most common autosomal recessive sub-types of GSD IX are caused by mutations in the PHKG2 gene or the PHKB gene. This form of GSD IX is inherited in an autosomal recessive manner. Although mutations in the PHKB gene can cause both liver and muscle glycogen accumulation, patients usually have liver complications. PHKB mutations tend to cause the mildest form of PHK deficiency. In contrast, individuals with mutations in the PHKG2 subunit of the PHK enzyme usually have more severe symptoms; PHKG2 gene changes are particularly associated with recurrent hypoglycemia, hepatomegaly and rarely liver fibrosis.

Currently, the only treatment for GSD IX is based on the symptoms of the condition. Hypoglycemia (low blood sugar) can be controlled by frequent meals high in carbohydrates with cornstarch supplements or night time stomach drip feedings if needed. As it is understood now, patients with mutations in the PHKA2 or PHKB genes typically have lessening of their symptoms by puberty. However, patients with more severe types and symptoms may need to remain on treatment regimens to avoid hypoglycemia.

As our understanding increases with GSD IX through long term research studies done on GSD IX patients, like other GSDs, the long term complications will be better understood. Research is still progressing and presenting more information about this disease. Prognosis (prediction of future health) is generally considered good for the liver forms of the disease; however, prognosis for the muscle forms is still unknown.

Summary of genes involved in Phosphorylast Kinase Deficiency

Gene Name	Inheritance	Subunit	Chromosomal Location	Tissue Affected
PHKA1	X-chromosomal	Alpha1	Xq12-13	Muscle
PHKA2	X-chromosomal	Alpha2	Xp22.2-p22.1	Liver
PHKB	Autosomal	Beta	16q12-13	Muscle and Liver
PHKG1	Autosomal	Gamma1	p11.2	Unknown
PHKG2	Autosomal	Gamma2	16p11.2-12.1	Liver
CALM1	Autosomal	Delta1	14q24-q31	Unknown
CALM2	Autosomal	Delta2	2p21	Unknown
CALM3	Autosomal	Delta3	19q13.2-q13.3	Unknown

Type VI Glycogen Storage Disease – GSD Type VI

Synonyms: Liver Phosphorylase Deficiency, Hers Disease

In Type VI Glycogen Storage Disease (GSD VI), the most frequent first symptoms include an enlarged liver and low blood sugar (hypoglycemia). After we eat, excess glucose is stored as glycogen mostly in the liver to be used later when we are fasting (not eating for 3-4 hours) to maintain normal glucose levels in our body. The phosphorylase enzyme plays a vital role in the breakdown of glycogen into glucose.

Clinical Features:
Clinically, this form of glycogen storage disease appears to be similar to, but is usually considerably milder than glucose-6-phosphatase deficiency GSD (type I GSD) since glucose can be made from protein. These patients present with hepatomegaly (liver enlargement) and growth retardation early in childhood. Since people with Type VI GSD are able to store glucose as glycogen but not able to release it normally, with time the stores of glycogen build up in the liver causing the liver to swell (hepatomegaly). This is much like being able to place groceries from the store into your kitchen cabinets, but not being able to get the food out of the cabinets when needed. Hypoglycemia (low blood sugars) and elevated ketone concentrations in the blood and urine after a period of fasting are the hallmarks of these disorders. Hyperlipidemia (elevated cholesterol and fats in the blood) and abnormalities in the liver function tests are usually mild if present. Lactic acid and uric acid are normal. The heart and skeletal muscles are not involved. The hepatomegaly improves with good metabolic control. Hepatic adenomas are rare in well treated individuals with GSD VI, and liver failure does not occur.

Diagnosis:
The diagnosis of this disease can be made by genetic testing from DNA extracted from blood or saliva. Liver biopsies to measure phosphorylase activity, which is reduced in this disease, are not necessary in most cases and not recommended if type VI GSD is suspected.

Treatment:
Treatment with cornstarch and a high protein diet is recommended in an effort to achieve normal labs and normal growth. Treatment improves growth velocity and bone density in this condition, and reduces the frequency of hypoglycemia and ketosis. Treatment is individualized in an attempt to maintain glucose concentrations above 70 mg/dL and normalize ketones after an overnight fast.

GSD Type Poster Presentation Directions

1. Read the article and case study on your specific type of Glycogen Storage Disease. (GSD)
2. Design a poster to be used to teach the rest of the class about your type of GSD.
3. Make sure to include the following with your poster:
    1) Type of GSD (i.e Type I)
    2) Names for Disease (i.e Hepatic Glycogen Synthase Deficiency)
    3) The deficient enzyme and what specific problems it causes for the patient (You may want to draw the glycogen/glucose pathway to help explain this to the class
    4) Symptoms
    5) How is the patient tested for GSD?
    6) Treatment
    7) How it is inherited-which gene?
4. Compare the case study to the article:
    1) What symptoms did the case study patient have compared to the symptoms listed in the article?
    2) Which gene was found to be affected in the case study patient compared to the one listed in the article?
    3) How does the treatment for the case study patient compare to the treatment described in the article?
5. You will be responsible for presenting your poster to the class and sharing the above information. Your poster will be graded using the rubric on the back of this sheet.

Glycogen Storage Disease Poster Presentation Rubric

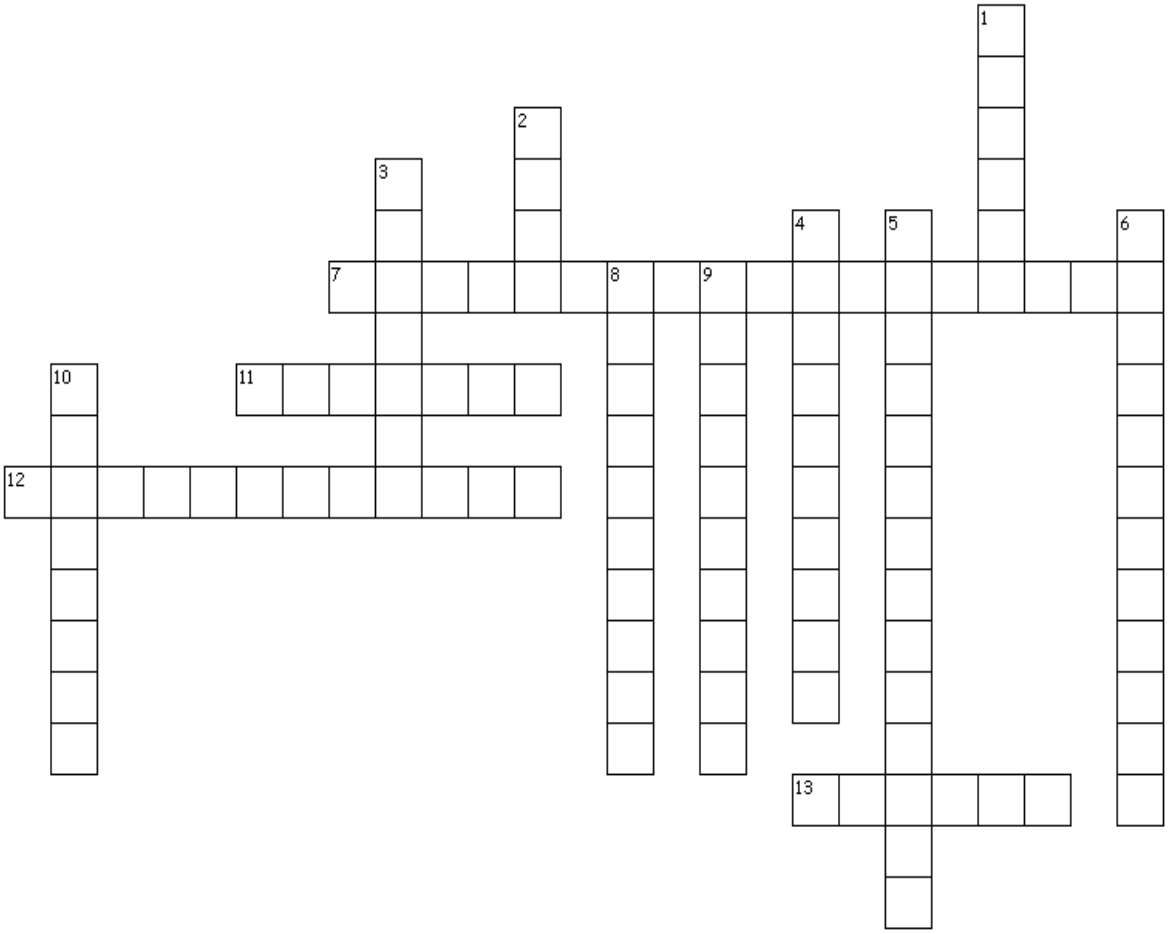
Name_____

Type of GSD listed	Yes (2)		No (0)	
Name of GSD listed	Yes (2)		No (0)	
Enzyme deficiency and problems caused	Yes (5)		No (0)	
Symptoms listed	Yes (5)		No (0)	
How patient is tested for GSD	Yes (2)		No (0)	
Treatment	Yes (5)		No (0)	
Gene Mutation	Yes (3)		No (0)	
Symptoms compared between case study patient and article	5	3	1	0
Gene mutation compared between case study patient and article	5	3	1	0
Treatment compared between case study patient and article	5	3	1	0
Poster is neat and easy to read	3	2	1	0
Poster is creative	3	2	1	0

TOTAL POINTS _____ (45 pts possible)

Glycogen Storage Disease- Vocabulary

Name: _____ Date: _____



Across

7. This type of inheritance is characterized by receiving a recessive gene from each parent. These genes are not sex-linked. In this type of inheritance there is a 25% chance of passing the recessive gene to the offspring.
11. products that result from the breakdown of triglycerides and fats - may be fuel for the brain
12. low blood sugar; can be the result of inability to break glycogen down into glucose
13. clinical removal of tissue to help diagnose disease

Down

1. one of the major macromolecules in living things; made of glycerol and fatty acid chains
2. Type VI GSD is also know by this name
3. ____-6-phosphate, cannot be produced in a person with Type Ia GSD. This prevents the glycogen that is in the liver from being converted back into glucose

4. lack of necessary catalysts in the liver to break glycogen into glucose: known as enzyme ____
5. these are lesions that may be found in the liver. Usually indicate a diseased state of the liver
6. enlarged and distended liver
8. all the chemical reactions that take place in a living thing; building up and breaking down chemical compounds
9. produced as a result of glucose being broken down without enough oxygen or enzymatic activity
10. large, complex carbohydrate stored in the liver, made of glucose; broken down by enzymes when the body needs energy.

Guide to Power Point (Slides 16-32): Treatment and Therapy of GSD

Name: _____Date: _____Score: _____

As we cover the information in the power point on treatment and therapy of GSD please provide the answers to the following questions.

1. What product was shown to be an acceptable treatment for Glycogen Storage Disease in 1982? What feature of this substance allowed it to be a successful treatment?

2. What was the goal of the treatment developed in 1982? What were the two components of the treatment that allowed the goal to be accomplished?

3. Explain how dosing differs among age groups.

4. How is the progress of a GSD patient monitored?

5. The study of GSD over the last decade has led to new practices and techniques in the field of medicine. List five of these.

6. What is the ULTIMATE goal of the GSD research? What are three ways this may happen?

7. What are the Maltese dogs being used for in the study of GSD?

8. List some reasons the Maltese makes a good research subject for this disease.

9. Describe some of the test subjects and list their names.

10. List two ways an “affected” dog (one that expresses the disease) can be diagnosed at birth.

11. When was gene therapy first done on dogs with GSD type Ia?

12. The graph on slide #25 shows a comparison to the affected dog without treatment to the dog two weeks after receiving the gene therapy. Blood glucose was taken periodically for 3 hours after eating. (Untreated, GSDIa dog was not allowed to fast more than 1 hr).

Explain what is happening with the dog that received the gene therapy treatment.

13. How does this compare with the control dog?

14. On the graph in slide 26 there is information about the dog's glucose levels after eight weeks. Explain what is happening. Why do you think this may have occurred?

15. After the second gene therapy what were the researchers able to do with the dogs after 6 months of age? What do you think this may signify about the function of the liver? Was the gene therapy successful??

16. If white, seemingly empty circles indicate storage of glycogen, compare the GSDIa, AAV2/8, AAV2/8+2/1 and the WT (wild type) tissue samples from slide 30. What do you think may be happening in the liver of this dog? Give reasons for your answer.

17. Take the information in slide 31 and organize it into a flow chart and will tell the story of the gene therapy research in the dogs with GSD. Use good linking words and descriptors to make this information tell a story.

18. Look at the last statement of the power point, slide 32. What do you think this means? Do you agree? If you were involved in this research what would be your next step?

Activity 1 Exit Slip

List 10 things that you learned about GSD from this lesson:

1.
2.
3.
4.
5.
6.
7.
8.
9.
10.

Activity 1 Exit Slip

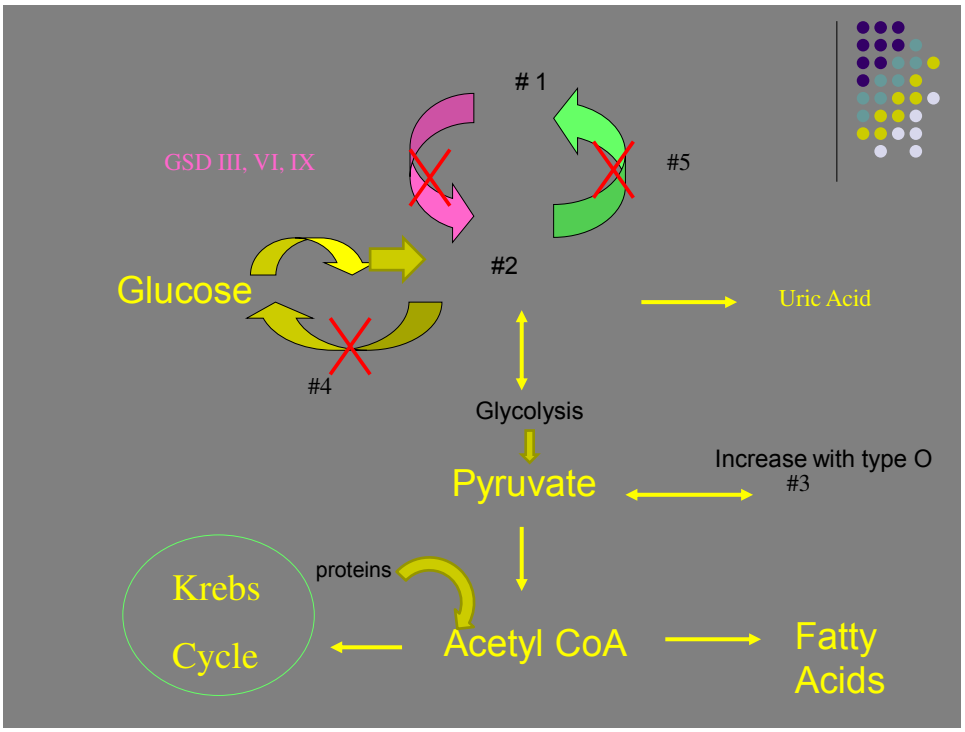
List 10 things that you learned about GSD from this lesson:

1.
2.
3.
4.
5.
6.
7.
8.
9.
10.

Quiz: Glycogen Storage Disease

Name: _____Date: _____Score: _____

Look at the diagram below, in the blanks below the diagram, fill in the information that is missing and is indicated by the corresponding numbers. (1 pt each)



1._____

2._____

3._____

4._____

5._____

II. Vocabulary Matching (1 pt. each):

_____6. hypoglycemia

_____7. autosomal recessive

_____8. biopsy

_____9. hepatic adenoma

_____10. metabolism

_____11. lipids

_____12. lactic acid

_____13. Her's Disease

_____14. Von Gierke's Disease

_____15. glycogen

_____16. deficiency

_____17. glucose

_____18. hepatomegaly

a. Type I GSD
b. Produced as a result of glucose being broken down without enough oxygen or enzymatic activity
c. One of the major macromolecules in living things; made of glycerol and fatty acid chains
d. Low blood sugar; can be the result of the inability to break glycogen down to glucose
e. Lack of necessary catalysts in the liver to break glycogen into glucose; known as enzyme _____
f. Enlarged and distended liver
g. Type VI GSD
h. All the chemical reactions that take place in a living thing; building up and breaking down chemical compounds
i. Large complex carbohydrate stored in the liver, made of glucose; broken down by enzymes when the body needs energy
j. These are lesions that may be found in the liver. They usually indicate a diseased state of the liver
k. Clinical removal of tissue to help diagnose disease
l. This type of inheritance is characterized by receiving a recessive gene from each parent. These genes are not sex-linked. In this type of inheritance there is a 25% chance of passing the recessive gene to the offspring
m. Glycogen can't be converted to this in Type I Glycogen Storage Disease

III. Match the Type of GSD with its deficient enzyme (1 pt each):

_____19. Type VI

_____20. Type I

_____21. Type IX

_____22. Type III

_____23. Type 0

a. Glucose Debranching Enzyme

b. Glycogen Synthase

c. Glucose-6-Phosphotase

d. Glycogen Phosphorylase

e. Liver Phosphorylase Kinase

IV. Extended Response:

24. A person that has a metabolic disorder had a difficult time breaking down certain foods and creating energy. Explain how this is the case using Type I Glycogen Storage Disease as an example. (3 pts)

25. List 3 symptoms that occur as a result of Glycogen Storage Disease and explain why they occur. (6 pts)

26. How is GSD currently being treated? Explain the process of how this treatment works. (3 pts)

27. List 3 positive aspects and 3 negative aspects involved with the treatment of GSD. (6 pts)

28. Which of the types of liver GSD is the only one that doesn't result in hepatomegaly? Explain why. (3 pts)

29. Which breed of dogs is currently being used in a gene therapy research project aimed at curing GSD? Why is this breed a good choice for this research? (3 pts)

30. What is gene therapy and how does it work? (5 pts)

31. Which Type of GSD is typically misdiagnosed as diabetes? Explain how this mistake can be made. (3 pts)

Extra Credit:

How old is the dog that received the first gene therapy treatment for GSD Ia and what is her name? (2 pts)

Lesson 2: Skills Needed to Work in a GSD Research Lab

Focus

Students will be introduced to three basic skills; pipetting, operation of a centrifuge, and electrophoresis that are helpful to have to be able to work in a GSD research lab. Students will use both hands-on and virtual labs to practice and become competent in these three important skills.

Major Concepts

DNA testing is a large portion of the work that is performed in GSD research labs. Students will gain basic knowledge of correct pipetting techniques and proper operation of a centrifuge. In addition, students will acquire a basic working knowledge of both how electrophoresis works and the steps to perform it. These basic skills are necessary in order to perform higher level skills such as DNA extraction, PCR, and DNA purification.

Objectives

After completing this activity, students will be able to:

- Precisely pipet volumes of liquid using pipets used in a research lab.
- Correctly balance and operate a centrifuge
- Understand how and why electrophoresis works.
- Be able to virtually perform an electrophoresis experiment utilizing an agarose gel.

Prerequisite Knowledge

Students should have a working knowledge of basic laboratory safety. They should be able to use critical thinking skills to solve problems and answer questions.

Overall Time Estimate

4-5 class periods- 50 minute classes

Vocabulary:

electrophoresis, gel, band, micropipette, centrifuge, buffer

National Science Education standards

Standard A All students should develop abilities necessary to do scientific inquiry and understandings about scientific inquiry.

Standard E All students should develop abilities of technological design and understandings about science and technology.

Next Generation Florida Science Standards

SC.912.N11-Define a problem based on a specific body of knowledge.

SC.912L16.12-Describe how basic DNA technology (restriction digestion by endonucleases, gel electrophoresis, polymerase chain reaction, ligation, and transformation) is used to construct recombinant DNA molecules (DNA cloning)

SC.912.N.1.2-Describe and explain what characterizes science and its methods.

SC.912.N.1.4-Identify sources of information and assess their reliability according to the strict standards of scientific investigation.

SC.912.N.1.6-Describe how scientific inferences are drawn from scientific observations and provide examples from the content being studied.

SC.912.N.1.7-Recognize the role of creativity in constructing scientific questions, methods, and explanations.

Basic Science-Health Connection

This lesson allows students to understand how basic laboratory skills are necessary to accurately perform DNA testing. DNA testing is used to diagnose GSD in patients and can be used instead of a more invasive procedure, such as a liver biopsy.

Introduction
Students will utilize short videos and hands-on and virtual labs to learn both the concepts behind and the performance of certain essential skills in the GSD research laboratory. These basic skills are necessary in order to perform more complex skills such as DNA extraction, PCR, and DNA purification.

Materials and Preparation:

You will need to prepare the following:

- Internet link video on "Using a Micropipette" http://www2.le.ac.uk/departments/genetics/vgec/education/post18/topics/recombinanttechniques/micropipette-4
- "Using a Micropipette" student worksheet-enough for each student

- Micropipette by Coordinates Lab: Make up stock of 6 colored solutions of water and food dye (red, blue, green, brown, orange, & purple). Aliquot in smaller containers for each student workstation. Copy student protocols for each student pair.
- "Pipetting a Rainbow" Activity: Make up colored stock solutions according to included directions. Aliquot to smaller containers for each student workstation. Copy student lab protocol for each student.
- Pipetting Competency Student Rubric
- Make standards using pipetting competency volumes to use to grade pipetting competency lab. (See included teacher directions)
- Microtubes
- 96 well ELISA plates
- Microtube holders
- Micropipettes
- Pipet tips
- "Using a Centrifuge" video at http://www.youtube.com/watch?v=IvA5fanKWXU
- "How to Use a Centrifuge" Hand-out
- "Micropipet and Centrifuge" Worksheet
- If the virtual pipetting lab is going to be used-use this site: http://www.udel.edu/present/Becky/lehman/pipette6.swf It may be helpful to print a copy of the directions on how to use the pipette and the lab protocol for each student.
- Here is a virtual agarose electrophoresis experiment to try with your students: http://learn.genetics.utah.edu/content/labs/gel/ Make a copy of the "Gel Electrophoresis" worksheet for every pair of students to go with the virtual experiment.
- Sample of lab protocol
- Computer with internet access

Procedure

DAY ONE:
(Prior to class, make sure you have the "Using a Micropipette" video bookmarked on your computer, enough "Using a Micropipette" student worksheets for every student, and the materials for the" Pipetting By Design" lab set up (See www.cpet.ufl.edu for lesson plan & protocol). For the lab, you will need for each pair of students, 1-96 well ELISA plate, 1 set of micropipettes P20 and P200, 1 Pipetting Protocol A-H, and the appropriate aliquots of colored water for each protocol.)
Ask students if any of them are familiar with using micropipettes or pipetting. Have them explain their experiences with using micropipettes or with pipetting.

1. Show the internet video on "Using a Micropipette" and have students fill out the worksheet while they are watching the video. Review the worksheet after the video and have students switch papers with each other and grade each other's papers. Have students turn in worksheets after the discussion.
2. If you have micropipettes in your classroom, give them out to students and review how to properly use them. You may want to play the video again and have students follow

along with it with the actual pipets. If time permits, you can start the "Pipetting By Design" lab activity. Have students work in groups of two to complete this activity.

3. If you do not have micropipettes in your laboratory, have students begin the virtual pipetting lab on the computer. (If you do not have computers available at school, this may be assigned for homework.)

DAY TWO

(Prior to class, make sure that you have the materials for the "Pipetting By Design" lab and the "Pipetting a Rainbow" lab set up.

4. Complete "Pipetting by Design" lab activity. If you are doing the virtual pipetting lab in class, you can have students continue to work on this activity during this class period.

EXTENSION-You can involve your art teacher in a cross-curricular activity of developing new designs for the "Pipetting By Design" lab activity. Give the art teacher a 96 well ELISA plate as a reference and have the art students create new designs. The science students can then develop a lab pipetting protocol to make the new designs.

5. Have students continue to work in pairs to complete the "Pipetting a Rainbow" activity.
6. Tell students that next class they will have a pipetting competency to complete to ensure that they know how to accurately pipet.

DAY THREE

(Prior to class, make sure that you have made a colored water solution for the pipetting competency. You can aliquot this stock solution into smaller containers for each student to use. It will also be helpful for you to make up the standards in which to compare the student's pipetting to in order to grade the competency. To do this, take 10 microtubes and label them 1-10 with a Sharpie. Pipet the correct volume of colored water that matches the volume on the rubric. You will also need to make a copy of the "How to Use a Centrifuge" and Micropipet and Centrifuge hand-out for each student in the class)

7. Give each student a copy of the "Pipetting Competency" rubric. Have each student label their microtubes from 1-10 with a Sharpie and place them into a microtube rack in order. Have student perform the competency by using the correct pipet and accurately pipetting the correct volume of colored water into their microtubes. After each student has completed the competency, use your standards to judge whether they pipetted each volume correctly or not. If they pipette the volume correctly, circle correct on rubric. If the pipette the volume incorrectly, circle incorrect on the rubric and have the student repeat that volume until they get it correct. (You can subtract points from the final score total for each volume that is pipette incorrectly.)
8. Play the "How to Use a Centrifuge" video. After the video, review the "How to Use a Centrifuge" hand-out with students. If you have an actual centrifuge in your lab, demonstrate the correct operation of it to your students. You also may want to have student practice balancing the centrifuge.
9. Give each student a copy of the "Micropipet and Centrifuge" Worksheet for homework. Have them complete it for the next class period.

DAYS FOUR & FIVE
(*Prior to these class periods, make a copy of the student version of the Virtual "Gel Electrophoresis" Worksheet for each pair of students in your class)*

10. Divide students into groups of two. Give each pair of students a copy of the Virtual "Gel Electrophoresis" Lab Worksheet. Have each pair of students sit at a computer, go to the website, and complete the worksheet.
11. ***EXTENSION for Day 5:*** In addition, have each pair of students write a lab protocol for gel electrophoresis using the virtual gel electrophoresis lab as a reference. An example of a lab protocol is included with this lesson. Show this to students so that they have a model to work from.

Assessment

The following can be used for assessment for this module:

- Pipetting Competency
- Centrifuge/Micropipetting Worksheet
- Virtual Gel Electrophoresis Worksheet
- Gel Electrophoresis Autosomal Recessive GSD Lab
- Sample Protocol write-up

References

http://www2.le.ac.uk/departments/genetics/vgec/education/post18/topics/recombinanttechniques/micropipette-4

http://www.youtube.com/watch?v=IvA5fanKWXU

http://www.udel.edu/present/Becky/lehman/pipette6.swf

http://learn.genetics.utah.edu/content/labs/gel/

University of Florida CPET-Pipetting by Design and Pipetting a Rainbow

Carolina Gel Electrophoresis Lab

"Using a Micropipette" Student Worksheet
Name_____

1. What are micropipettes used to measure?

2. How do you determine what volume a micropette measures?

3. What volume does a P2 micropipette pipet?

4. What volume does a P20 micropipette pipet?

5. What volume does a P200 micropipette pipet?

6. What volume does a P1000 micropipette pipet?

7. What happens if you use a micropipette outside of its range?

8. How do you set the volume on a pipet?

9. What volume would 152 be on a P2 micropipette?

10. What volume would 152 be on a P20 micropipette?

11. What volume would 152 be on a P200 micropipette?

12. What volume would 052 be on a P1000 micropipette?

13. What does the filter do in a pipette tip?

14. How is liquid drawn up and expelled with the micropipette?

15. List the steps in order to correctly use the micropipette:
    a) Put on a pipet tip.
    b)
    c)
    d)
    e)

f)
g)
h)
i)

16. What is the proper procedure to use if you have a very small volume to pipet?

17. How do you take off the pipet tip from the micropipette?

18. When should a new pipet tip be used?

19. Do not use a pipet without a _____ _____.

20. Do not use a pipet past its _____ limits.

21. If tip doesn't stay on end of the pipet, _____ _____with a new _____.

22. When taking up a liquid, don't push past the _____ stop. If you push past the first stop, the volume would be too _____.

23. When you are taking a _____ volume from a _____container, make sure the tip is _____the surface of the liquid.

24. Whenever you have liquid in the pipet, _____ lay the pipet _____. This can cause _____ _____, _____ _____, and _____ _____.

“Using a Micropipette” Student Worksheet (Answer Key)

Name_____

1. What are micropipettes used to measure?
   They are used to measure or transfer small amounts of liquids from .2 ul to 1000ul

2. How do you determine what volume a micropette measures?
   They are labeled with a capital P and a number (2, 20. 200, & 1000)

3. What volume does a P2 micropipette pipet?
   .02-2 ul

4. What volume does a P20 micropipette pipet?
   2-20 ul

5. What volume does a P200 micropipette pipet?
   20-200 ul

6. What volume does a P1000 micropipette pipet?
   100-100ul

7. What happens if you use a micropipette outside of its range?
   You may get inaccurate results or damage the internal mechanism

8. How do you set the volume on a pipet?
   Use the black thumb wheel or the push button on newer models

9. What volume would 152 be on a P2 micropipette?
   1.52 ul

10. What volume would 152 be on a P20 micropipette?
   15.2 ul

11. What volume would 152 be on a P200 micropipette?
   152 ul

12. What volume would 052 be on a P1000 micropipette?
   520ul

13. What does the filter do in a pipette tip?
It helps prevent contamination.

14. How is liquid drawn up and expelled with the micropipette?
With the push button

15. List the steps in order to correctly use the micropipette:
   a) *Put on a pipet tip*
   b) *Push the button down to the first stop*
   c) *Place the pipet tip about 2ml into the solution you wish to draw up*
   d) *Release the push button slowly and allow it to return to original position*
   e) *Pause to allow liquid to go up into tip*
   f) *Withdraw tip and place it into the recipient container*
   g) *Slowly push down on the push button-liquid will be released*
   h) *Push beyond the first stop*
   i) *Fully withdraw tip before release button*

16. What is the proper procedure to use if you have a very small volume to pipet?
You should touch the tip to the wall of the container while expelling the liquid

17. How do you take off the pipet tip from the micropipette?
Use the tip ejector-white button at top of micropipette

18. When should a new pipet tip be used?
with each new liquid, if tip touches any surface, or whenever in doubt

19. Do not use a pipet without a *tip attached*.

20. Do not use a pipet past its *volume* limits.

21. If tip doesn't stay on end of the pipet, *repeat procedure* with a new *tip*.

22. When taking up a liquid, don't push past the *first* stop. If you push past the first stop, the volume would be too *large.*

23. When you are taking a *large* volume from a *small* container, make sure the tip is *below* the surface of the liquid.

24. Whenever you have liquid in the pipet, *don't* lie the pipet *down*. This can cause *cross contamination, pipet damage, and inaccurate pipetting.*

Pipetting A Rainbow Lab Activity:
Set-up & Student Directions

Pipetting a rainbow solutions:

Mix in separate 50 ml conical tubes

- Blue: 14 ml corn syrup, 16 ml water, blue food dye
- Green: 10 ml corn syrup, 20 ml water, green dye
- Yellow: 6 ml corn syrup, 24 ml water, yellow dye
- Orange: 2 ml corn syrup, 28 ml water, orange dye
- Red: 30 ml water, red dye

Mix colored solutions up, until corn syrup is fully dissolved. Aliquot into 1.5 ml tubes.

Use the 200 µl and the 20 µl pipettes

1. Pipette 219 µl of the blue solution into a blank 1.5 ml tube.
2. Carefully and slowly add 210 µl of the green solution on top of the blue solution, making sure to not mix the blue with the green.
3. Add 435 µl of the yellow solution on top of the green solution – don't mix with the blue and green.
4. Pipette 300 µl of the orange solution on top of the yellow – don't mix.
5. Add 336 µl of the red solution on top of the orange – don't mix.

Did you reach the top line of the tube?

Use the 200 µl and the 20 µl pipettes

1. Pipette 219 µl of the blue solution into a blank 1.5 ml tube.
2. Carefully and slowly add 210 µl of the green solution on top of the blue solution, making sure to not mix the blue with the green.
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4. Pipette 300 µl of the orange solution on top of the yellow – don't mix.
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Did you reach the top line of the tube?

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5. Add 336 µl of the red solution on top of the orange – don't mix.

Did you reach the top line of the tube?

Pipetting Competency Lab

Name_____

1. Label 10 Eppendorf tubes 1-10 with a Sharpie.

2. Pipet the following volumes using colored water and the 2-20 microliter pipet:
    1. 3.5 µl Correct Incorrect
    2. 5 µl Correct Incorrect
    3. 10.2 µl Correct Incorrect
    4. 13.9 µl Correct Incorrect
    5. 18.3 µl Correct Incorrect

3. Pipet the following volumes using colored water and the 20-200 microliter pipet:
    6. 33 µl Correct Incorrect
    7. 57 µl Correct Incorrect
    8. 94 µl Correct Incorrect
    9. 148 µl Correct Incorrect
    10. 197 µl Correct Incorrect

Pipetting Competency Lab

Name_____

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2. Pipet the following volumes using colored water and the 2-20 microliter pipet:
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    4. 13.9 µl Correct Incorrect
    5. 18.3 µl Correct Incorrect

3. Pipet the following volumes using colored water and the 20-200 microliter pipet:
    6. 33 µl Correct Incorrect
    7. 57 µl Correct Incorrect
    8. 94 µl Correct Incorrect
    9. 148 µl Correct Incorrect
    10. 197 µl Correct Incorrect

How to Use a Centrifuge

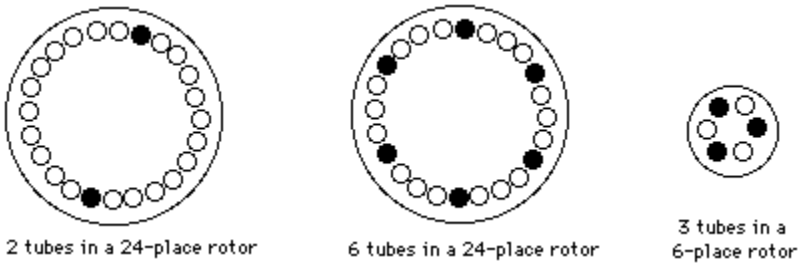
1. When you are adding several reagents to one tube, release each drop of reagent on the inside wall of the tube near the bottom.

2. Tightly close the caps on all the tubes to be placed in the microcentrifuge (also called microfuge).

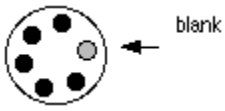
3. The microfuge rotor must always be balanced - you cannot, for example, insert *one* tube into a microfuge. Spinning in an unbalanced arrangement like this would damage the motor of the instrument.

4. The amount of liquid in the tubes should be similar, otherwise the rotor will spin unevenly (like wet towels spinning out of balance in a washing machine). You can always prepare a "blank" tube with the appropriate volume of liquid with which to balance a single tube.

   *Samples of **balanced** rotor configurations:*



   Question: What do you do if you only have 5 tubes?
   You must put in one extra (a blank) tube blank with equal volume.



5. After you have replaced the metal top (if your type of microfuge has a rotor top) and secured the lid of the microfuge, give the tubes a 1-2 second pulse. This will mix and pool all the reagents into a droplet in the bottom of each tube.

Adapted from: http://www.accessexcellence.org/AE/AEPC/geneconn/smallvol/worksheet.php

Micropipet and Centrifuge Worksheet
Name_____

Explain the reason for each of the following rules:

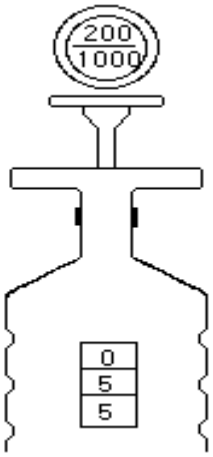
a. Always set the micropipet within its designated range.

b. Always use a micropipet with a tip.

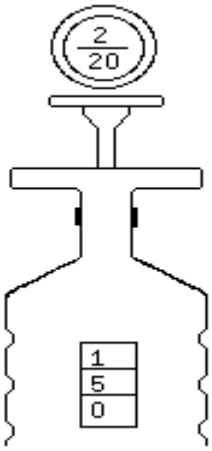
c. Always hold a loaded micropipet in a vertical position.

d. Always release the micropipet plunger slowly.

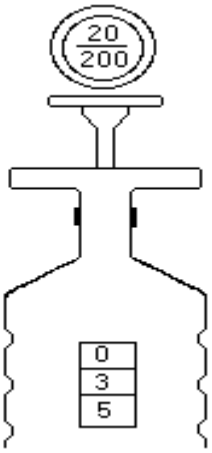
e. Observe the volume of liquid that is measured by micropipets a, b, and c.



a. 550 µL



b. 15 µL

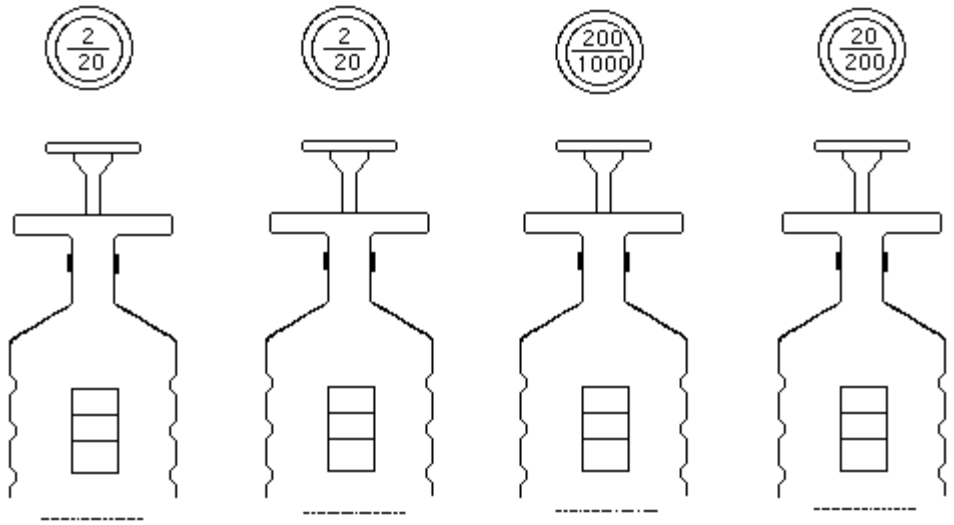


c. 35 µL

- Which micropipet (a, b, or c) is the P-20? _____
  What is its range? _____
- Which micropipet (a, b, or c) is the P-200? _____
  What is its range? _____
- Which micropipet (a, b, or c) is the P-1000? _____
  What is its range? _____

Select the appropriate micropipet and show what the dial should read to measure each of the following amounts of liquid. Write the amount on the line beneath the correct drawing.

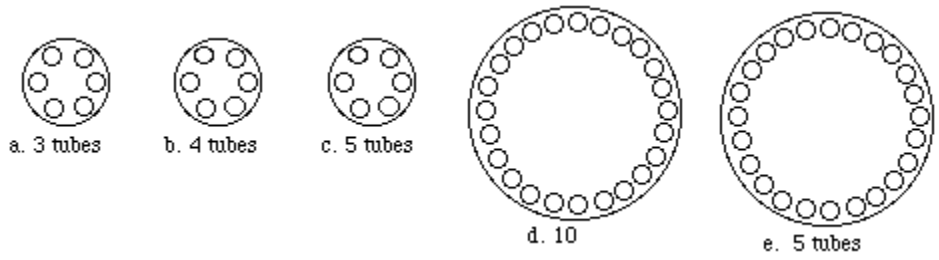
a. 150 µL b. 2.5 µL c. 300 µL d. 7 µL



025 *070* *030* *150*

Why is it important to balance a centrifuge before turning it on?

Show how you would arrange the given number of tubes in each centrifuge to balance the load. If you decide that you must add or remove tubes, explain.



Micropipet and Centrifuge Worksheet (Answer Key)
Name_____

Explain the reason for each of the following rules:

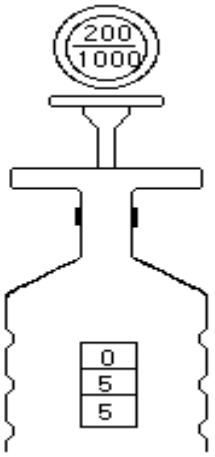
a. Always set the micropipet within its designated range.
You may get inaccurate results or damage the pipet mechanism

b. Always use a micropipet with a tip.
You will contaminate the pipet.

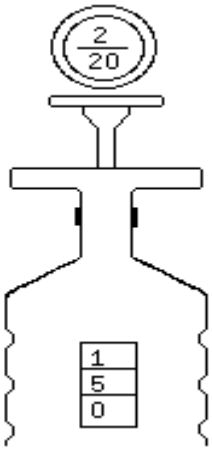
c. Always hold a loaded micropipet in a vertical position.
You could cause cross contamination, pipet damage, or inaccurate pipeting

d. Always release the micropipet plunger slowly.
You can get bubbles in tip or inaccurate volume or splashing

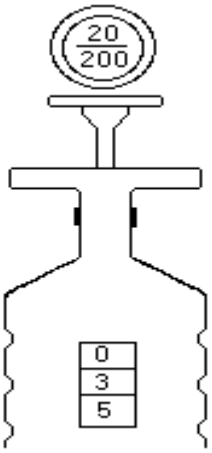
e. Observe the volume of liquid that is measured by micropipets a, b, and c.



a. 550 µL



b. 15 µL

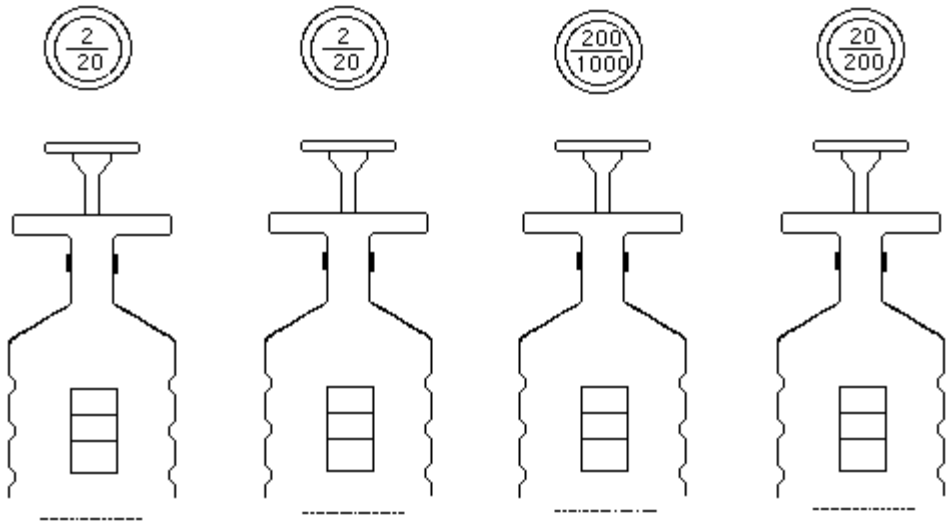


c. 35 µL

- Which micropipet (a, b, or c) is the P-20? _____b___
  What is its range? _____2ul-20ul____
- Which micropipet (a, b, or c) is the P-200? ___c_____
  What is its range? _____20ul to 200ul____
- Which micropipet (a, b, or c) is the P-1000? ____a____
  What is its range? _____200 ul to 1000 ul_____

Select the appropriate micropipet and show what the dial should read to measure each of the following amounts of liquid. Write the amount on the line beneath the correct drawing.

a. 150 µL b. 2.5 µL c. 300 µL d. 7 µL

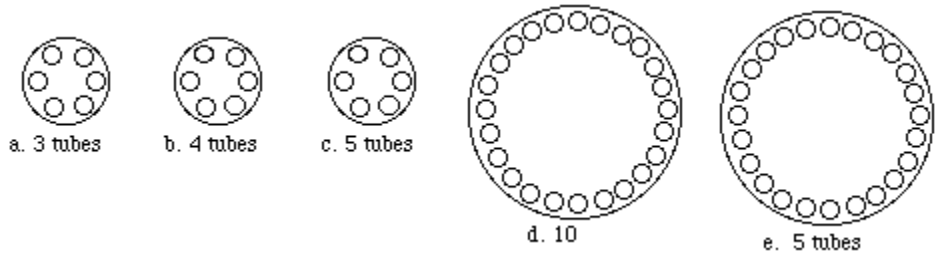


025 *070* *030* *150*

Why is it important to balance a centrifuge before turning it on?

It can cause the rotor to be unbalanced and the centrifuge will make a loud noise and hop off the counter.

Show how you would arrange the given number of tubes in each centrifuge to balance the load. If you decide that you must add or remove tubes, explain.



For a: Put a tube in every other space
For b: Put two tubes together with a space and then two more tubes
For c: You will need to add a blank for the 6th space and put a tube in each slot
For d: Put 5 tubes on 1 side and 5 on the other with 7 spaces in between each set of 5
For e: You need to add a blank of equal volume and have 3 on each side with 9 spaces in between each group of 3

Virtual "Gel Electrophoresis" Lab Worksheet

Name_____

In order to complete this lab, go to the following website:
http://learn.genetics.utah.edu/content/labs/gel/

1. What is gel electrophoresis used for?

2. What is a gel and what is it made of?

3. What is electrophoresis? Which way does the DNA move across the gel?

4. How do the DNA strands separate themselves on a gel?

5. What makes the DNA strands visible to the naked eye? What is a DNA band?

6. What are the 5 steps in performing electrophoresis?

1)
2)
3)
4)
5)

7. What materials do you need to make a gel?

8. What is the buffer?

9. What do you think the purpose of the gel comb is?

10. What materials do you need to load the DNA sample into the gel?

11. Why do add a loading buffer to your DNA sample?

12. Why do use a DNA standard?

13. When you turn on your power what charge will the black end generate and what charge will the red end generate? Which end needs to be closest to the wells and why?

14. What do the bubbles coming out of the electrodes mean?

15. What type of stain is used to stain your gel? How does this stain work?

16. What were the size estimates of your three DNA strands in your sample?

LAB PROTOCOL EXAMPLE

To make 2% gel

In a 250 ml Erlenmeyer flask:

1) Add 2 g agarose
2) Add 100 ml TBE buffer (1X)
3) Microwave until liquid gelatins into (Jell-O) consistency
4) Using Ethidium Bromide pipet 0.4 ul
5) Swirl to mix

To prepare PCR product for gel

1) Pipet 5 ul PCR product into a clean tube
2) Add 1 ul gel loading dye
3) Mix gently with the pipet tip

To Load the Gel

1) Fill the gel box with 1X TBE-fill up to half way up the electrode
2) Load gel in chamber with TBE
3) Remove comb (while under solution so you don't get bubbles in your well)
4) Load 1st well with DNA ladder
5) Load PCR Products-5ul each

Lesson 3: DNA Extraction

The Focus

Students will continue to focus on the biotechnology aspect of genetic investigation as they investigate how DNA is collected and separated from the tissue that is collected. This lesson continues to focus on the genetics of Glycogen Storage Disease. The main emphasis is how it is detected. [This could be a stand-alone lesson on DNA Extraction if the emphasis is not on GSD]

Major Concepts

The extraction of DNA from tissue samples is a major practice in genetic investigation. Crime scenes, law suits as well as medical diagnoses are a few of the applications of this process. Collection of the DNA will be stressed in addition to the actual process of removing the DNA from the cell. Cellular structure will be discussed and there will be a detailed look at the structure of DNA.

Objectives

After completing this lesson, students will be able to ..

- Visualize the structure of DNA
- Understand how tissue that contains DNA can be collected
- Explain how the DNA is separated from its tissue
- Recognize the equipment involved in DNA extraction
- Describe the functions of the various tools necessary for extracting DNA from tissue
- Explain why DNA extraction is important.

Prerequisite Knowledge

Students should have a working knowledge of the cell and the relationship of DNA to the cell. They should also be able to follow a lab protocol and adhere to lab safety rules. Understanding the use of micropipettes in the lab and being able to manipulate their use is important to this lab, also. A basic understanding of math and being able to calculate yield as a result of the extraction process would be important, especially for follow-up activities.

Overall Time Estimate

Three days (approximately), depends on lab times and follow-up. (50 minute classes)

Vocabulary

chromosomes, Eppendorf tube, centrifuge, micropipette, water bath, buccal, lysis, DNA, ethanol, extraction,

National Science Education Standards

Standard A All students should develop abilities necessary to do scientific inquiry and understandings about scientific inquiry.

Standard C All students should develop understanding of the molecular basis of heredity.

Standard E All students should develop abilities of technological design and understandings about science and technology.

Standard F All students should develop understanding of personal and community health. All students should develop understanding of science and technology in local, national, and global challenges.

Standard G All students should develop understanding science as a human endeavor; nature of scientific knowledge and historical perspectives.

Next Generation Florida Science Standards

SC.912.N.1.1 Define a problem based on a specific body of knowledge.

SC.912.N.1.3 Recognize that the strength or usefulness of a scientific claim is evaluated through scientific argumentation, which depends on critical and logical thinking, and the active consideration of alternative scientific explanations to explain the data presented.

SC.912.N.1.4 Identify sources of information and assess their reliability according to the strict standards of scientific investigation.

SC.912.N.1.6 Describe how scientific inferences are drawn from scientific observations and provide examples from the content being studied.

SC.912.N.14.6 Explain the significance of genetic factors, environmental factors, and pathogenic agents to health from the perspectives of both individual and public health.

SC.912.L.16.3 Describe the basic process of DNA replication and how it relates to the transmission and conservation of the genetic information.

SC.912.L.16.9 Explain how and why the genetic code is universal and is common to almost all organisms.

SC.912.L.16.10 Evaluate the impact of biotechnology on the individual, society and the environment, including medical and ethical issues.

SC.912.L.18.11 Explain the role of enzymes as catalysts that lower the activation energy of biochemical reaction.

HE.912.C.1.4 Analyze how heredity and family history can impact personal health.

HE.912.C.1.8 Analyze strategies for prevention, detection, and treatment of communicable and chronic disease.

LA.910.2.2.3 The student will organize information to show understanding or relationships among facts, ideas, and events.

MA.912.S.1.2 Determine appropriate and consistent standards of measurement for the data to be collected in a survey or experiment.

Introduction

This lesson is the lab reinforcement component that allows the students to experience the actual way in which genetic testing is done. This is a continuation of the introductory lab in Lesson 2 and provides the students with an in depth understanding of this basic biotechnology technique and allows them to actually carry out the protocol. The lesson is designed to be a two-part lab, where the initial process is done virtually as a class activity and then continues on the following day with an actual wet lab. *[Of course, these can each be done as stand-alone labs depending on time.]*

Materials and Preparation: You will need to prepare the following

- Entrance Slips
- http://learn.genetics.utah.edu/content/labs/extraction/
  Use this web site and go to the virtual lab on DNA Extraction
  This can be done in the computer lab or together as a class and go through each step.
- Make copies of the worksheet "The Virtual DNA Extraction Lab: Questions for Review" for your students
- Look at the lab protocol for the Strawberry DNA Extraction lab and gather the materials listed there.
- Set up Strawberry DNA Lab
- Lab Write Up
- Exit Slips

Procedure

DAY ONE

1. Have students do the Entrance Slips. This will help to "hook" them into the activities they are about to do and assess their prior knowledge.

2. Review material from Lesson 2.
3. There are two possibilities at this point:
    a. Link to the web site listed in *materials and preparation* and walk through this process together as a class. Students could take notes while taking turns to carry out the prescribed procedures.
    b. This could be a computer lab lesson where students individually link to the website and perform the virtual lab themselves.
4. After the virtual lab, students could be given the "Questions for Review" to work on. This could be an individual assignment or they could do it as a "paired review". Evaluate the review questions - assessment
5. Give out the introduction and protocol for the Strawberry lab. Read for homework.
    a. See www.cpet.ufl.edu for Strawberry Lab Protocol.

DAY TWO

6. Review the steps in the process of DNA Extraction.
7. Review lab safety.
8. DNA Extraction lab using Strawberries.
9. Exit slip.

DAY THREE

10. Write up the DNA Extraction Lab. Assessment.

DAY FOUR

11. Optional if time permits: variations on Strawberry DNA Extraction Lab

Entrance Slip

Please complete the following questions in preparation for today's lesson.

1. What is a micropipette? Why is this piece of equipment necessary when studying DNA?

2. Explain the function of a centrifuge and in your description include the proper way to use one.

3. What is DNA? Where is it found in living tissue?

Entrance Slip

Please complete the following questions in preparation for today's lesson.

1. What is a micropipette? Why is this piece of equipment necessary when studying DNA?

2. Explain the function of a centrifuge and in your description include the proper way to use one.

3. What is DNA? Where is it found in living tissue?

Entrance Slip

Please complete the following questions in preparation for today's lesson.

1. What is a micropipette? Why is this piece of equipment necessary when studying DNA?

2. Explain the function of a centrifuge and in your description include the proper way to use one.

3. What is DNA? Where is it found in living tissue?

The Virtual DNA Extraction Lab: Questions for Review

Name_____

Use this web site and go to the virtual lab on DNA Extraction:
http://learn.genetics.utah.edu/content/labs/extraction/

1. Why would you need to test human DNA?

2. What is the first step in the long laboratory process of analyzing DNA? Why does this step need to be done?

3. Why do we collect cells for DNA extraction? Why would red blood cells not be a good source for DNA extraction?

4. What are chromosomes?

5. What are the four steps in extracting DNA from Cheek cells?

6. There are at least ten items needed for DNA extraction. Name them.

7. What do you think the word buccal means? Why?

8. Describe how cheek cells are extracted.

9. You place a buccal swab in the Eppendorf tube. Where is the DNA at this point?

10. What does the word lysis mean? Why would you add lysis solution to the swab? How do you add the lysis solution?

11. What does lysis solution contain? How do these ingredients interact with the cheek cells?

12. What did the warm water bath provide?

13. What do you add when you remove the tube from the water bath?

14. What does the salt solution do?

15. What is the function of the centrifuge? Why do you have a second tube in the centrifuge?

16. What is in the bottom of the tube when you take it out of the centrifuge? Why? Where is the DNA?

17. How do you separate the solution with DNA from the cellular debris?

18. What do you add next? How do you add it?

19. How do you mix this solution?

20. Why are you able to see the DNA now? (Remember we are seeing it with our naked eyes!)

21. When you put the tube in the centrifuge this time what happens to the DNA?

22. List some options of what you can now do with the DNA you have extracted.

Exit Slip:

As you leave lab today, please complete the following questions about DNA Extraction.

1. Why did you pulverize the strawberries?

2. What did the salt and soap solution do to the strawberry's cells?

3. What was happening when you added the ethanol?

Exit Slip:

As you leave lab today, please complete the following questions about DNA Extraction.

1. Why did you pulverize the strawberries?

2. What did the salt and soap solution do to the strawberry's cells?

3. What was happening when you added the ethanol?

Exit Slip:

As you leave lab today, please complete the following questions about DNA Extraction.

1. Why did you pulverize the strawberries?

2. What did the salt and soap solution do to the strawberry's cells?

3. What was happening when you added the ethanol?

Lesson 4: PCR, Purification, and Chromographs – What Does It All Mean?

The Focus

Students continue to focus on the biotechnology aspect of genetic investigation. This lesson will allow students to follow through on what happens to the DNA that was extracted in lesson 3 and how it is used to predict genetic mutations.

Major Concepts

Polymerase chain reactions will be discussed. The purification of the PCR product will be demonstrated and the resulting chromographs will be examined and analyzed. These are higher level lab procedures. Opportunities for virtual, as well as, actual labs will be presented.

Objectives

After completing this lesson, students will be able to

- Explain the process of polymerase chain reaction (PCR).
- Understand how PCR is done in the laboratory setting.
- Explain how PCR can be used to detect genetic mutations.
- Understand how chromographs depict genetic mutations.

Prerequisite Knowledge

Students should have a working knowledge of the cell and the relationship of DNA to the cell. They should also be able to follow a lab protocol and adhere to lab safety rules. An understanding of genetic inheritance and the concept of autosomal recessive traits is important.

Overall Time Estimate

4-5 days (approximately), depends on lab times and follow-up. (50 minute classes)
Vocabulary: chromosomes, Eppendorf tube, centrifuge, micropipette, DNA, DNA polymerase, nucleotides (G,T,C,A), thermocycler, annealing, denaturing, elongation, primers, gel electrophoresis, carrier, mutation, wild type, chromograph

National Science Education Standards

Standard A All students should develop abilities necessary to do scientific inquiry and understandings about scientific inquiry.

Standard C All students should develop understanding of the molecular basis of heredity.

Standard E All students should develop abilities of technological design and understandings about science and technology.

Standard F All students should develop understanding of personal and community health. All students should develop understanding of science and technology in local, national, and global challenges.

Standard G All students should develop understanding science as a human endeavor; nature of scientific knowledge and historical perspectives.

Next Generation Florida Science Standards

SC.912.N.1.1 Define a problem based on a specific body of knowledge.

SC.912.N.1.3 Recognize that the strength or usefulness of a scientific claim is evaluated through scientific argumentation, which depends on critical and logical thinking, and the active consideration of alternative scientific explanations to explain the data presented.

SC.912.N.1.4 Identify sources of information and assess their reliability according to the strict standards of scientific investigation.

SC.912.N.1.6 Describe how scientific inferences are drawn from scientific observations and provide examples from the content being studied.

SC.912.N.14.6 Explain the significance of genetic factors, environmental factors, and pathogenic agents to health from the perspectives of both individual and public health.

SC.912.L.16.3 Describe the basic process of DNA replication and how it relates to the transmission and conservation of the genetic information.

SC.912.L.16.9 Explain how and why the genetic code is universal and is common to almost all organisms.

SC.912.L.16.10 Evaluate the impact of biotechnology on the individual, society and the environment, including medical and ethical issues.

SC.912.L.18.1 Describe the basic molecular structures and primary functions of the four major categories of biological macromolecules.

SC.912.L.18.11 Explain the role of enzymes as catalysts that lower the activation energy of biochemical reaction.

SC.912.L.16.12 Describe the basic DNA technology (restriction digestion, gel electrophoresis, polymerase chain reaction, ligation and transformation) is used to construct recombinant DNA molecules.

HE.912.C.1.4 Analyze how heredity and family history can impact personal health.

HE.912.C.1.8 Analyze strategies for prevention, detection, and treatment of communicable and chronic disease.

LA.910.2.2.3 The student will organize information to show understanding or relationships among facts, ideas, and events.

MA.912.S.1.2 Determine appropriate and consistent standards of measurement for the data to be collected in a survey or experiment.

Basic Science-Health Connection

The emphasis of this lesson is to understand current biotechnology techniques that are used in the laboratory setting to answer questions about genetics. Many disorders are the result of genetic mutation. An understanding of how these mutations may be detected will help students make the connection between basic science and health concerns.

Introduction

This lesson is the continuation of the lab reinforcement component that allows the students to experience the actual way in which genetic testing is done. This is a continuation of the introductory labs in Lessons 2 and 3. It provides the students with an in- depth understanding of these basic biotechnology techniques and allows them to actually carry out these protocols. The lesson is designed to be carried out sequentially if time permits, or to be used as *"stand alones*", where emphasis is needed and materials are available.

The major component of this lesson is PCR. Few high school labs have thermal cyclers, so this will be presented as a virtual lab and as a paper and pencil/role play game. (Follow-up can be done with gel electrophoresis but that will not be addressed in this lesson.) Analysis of chromographs will be discussed and students will have a chance to evaluate these as diagnostic tools for detection of mutation.

Materials and Preparation

You will need to prepare the following

- Link: http://www.youtube.com/watch?v=x5PkxCLads (PCR Song)
- Copy lyrics of the PCR Song
- Copy of the power point on PCR
- http://learn.genetics.utah.edu/content/labs/pcr

    - Use this web site and go to the virtual lab on PCR
    - There is background material here also, to complement the information in the power point.
    - The virtual lab can be done in the computer lab with students working individually or it can be discussed together as a class.
- Make copies of the worksheet "The Virtual PCR Lab: Questions for Review" for your students
- WEB SITES for the PCR DASH GAME
    - http://www.bush2base.vt.edu/readit/DNA/DNA files/Page799.htm
    - http://agsci.oregonstate.edu/aquatic-bt/sites/default/files/PDFs/FSIIID13.pdf
    - http://research.nmsu.edu/molbio/bioinfo/k-12/pcr_dash/pcrtemplate.html (site for templates)
- Make copies of Exit Slips
- Make copies of Information about Purification and Sample Chromograph

Procedure

DAY ONE

1. Quick review of material from Lesson 2 and 3. This is a continuation of the lab component in this unit. If you are using this lesson as a stand-alone check for understanding of micropipetting and gel electrophoresis.
2. Play the video from the YouTube link with the song about PCR.
    a. Discussion could follow to see what they remember about the song and its lyrics.
    b. Give out the copies of the lyrics and replay the video.
    c. Assess what they have learned by asking questions like:
        i. What is PCR? What are the steps of PCR? What do you need to carry out PCR? What is PCR used for? Who developed PCR?
        ii. Students should be taking notes.
    d. As you direct the discussion or monitor the small group talk lead students to a correct understanding of the phrases from the song (ie. "who's your daddy", "need to recombine", "solve a crime" and "heating and cooling and heating")
        i. Paternity testing, genetic engineering, forensics, thermal cycler process
3. Play the song again
4. Exit slip.

DAY TWO

5. Begin powerpoint on PCR – reinforces and builds on the information from DAY ONE
6. Practice the ideas of denaturing, annealing and extending.
    a. This may be a good time for a review of DNA.

DAY THREE

7. Virtual PCR Lab: Link on the website given.
    a. This can be done together as a class or in the computer lab in pairs or individually.

b. This lab mirrors the information presented in the powerpoint but allows actual manipulation of some of the equipment.
c. Use the Virtual PCR Lab Study Guide to allow students to reflect on the process.

8. Complete Study Guide for homework.

DAY FOUR

9. Look at the notes on Purification of the PCR Product. Project or give as handouts.
10. Walk through the process with the students or allow them to engage in a group discussion of the process.
    a. Try to direct their thinking to the actual PCR product that was removed from the thermal cycler. Some questions may be:
        i. What was added to the DNA as it was prepared for the thermal cycler? Where did this product go? Why is centrifugation necessary? Why would purification be important here?
11. Look at the chromograph (color is important with this handout since the C's, T's, G's, and A's are color coded).
    a. Remind students that a 3 base sequence (codon) indicates an amino acid. Change in one amino acid can change the protein that is produced and this can be the reason for the mutation. (Remember an enzyme is a protein and the mutation of the enzymes in the metabolic pathway of the liver is the cause of GSD.)
12. A follow-up activity could be the PCR Dash game. Link to the web site listed above. This is an excellent review for this unit.
    a. PLANNING AHEAD is crucial for a good experience.

DAY FIVE

13. Assessment: Ask students to sketch a flow chart or other graphic organizer to illustrate the process of PCR, Purification and Chromograph analysis.

Assessment

PCR Virtual Lab Questions

References

Mission Biotech-PCR PowerPoint
Dr. Weinstein's lab-Dog Chromographs
PCR Purification?
http://learn.genetics.utah.edu/content/labs/pcr
http://www.youtube.com/watch?v=x5PkxCLads

Bio Rad PCR Song Lyrics

There was a time when to amplify DNA,
You had to grow tons and tons of tiny cells.
(OOOH) Then along came a guy named Dr. Kary Mullis,
Said you can amplify in vitro just as well.
Just mix your template with a buffer and some primers,
Nucleotides and polymerases too.
Denaturing, annealing, and extending,
Well it's amazing what heating and cooling and heating will do.

[Chorus]
PCR when you need to detect mutation (detect mutation)
PCR when you need to recombine (recombine)
PCR when you need to find out who the Daddy is (who's your daddy?)
PCR when you need to solve a crime (solve a crime)

[X2]

Bio Rad PCR Song Lyrics

There was a time when to amplify DNA,
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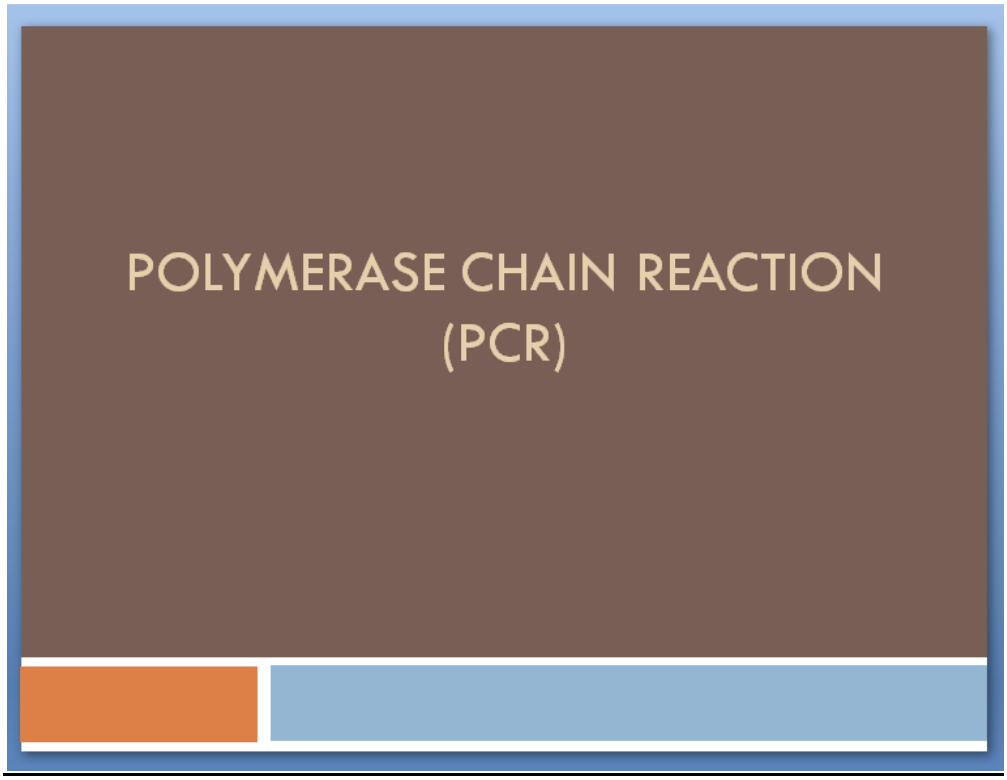
PCR when you need to solve a crime (solve a crime)

[X2]

See PowerPoint Presentation:



Virtual PCR – Study Guide

Name: _____Date: _____Score: _____

Go to the following website: http://learn.genetics.utah.edu/content/labs/pcr

As you work your way through the virtual PCR lab answer the questions that follow. Give complete answers and consider not only the process that is occurring but also the use of this valuable biotechnology tool.

1. For what does PCR stand?

2. PCR is a common tool used in labs. What is it used for, what does it actually do? How can this be applied in the world of science?

3. Briefly describe the human genome. What is it made of?

4. Where is most of the DNA in a cell located?

5. What can be accomplished by PCR in just a matter of hours?

6. What lab procedure (you accomplished in lesson 3) needs to be performed before PCR can take place?

7. What might you use as a tissue sample for DNA?

8. Why is it necessary to have specially designed tubes for PCR?

9. After you put the extracted DNA in the PCR tube what do you need to add? What is its function? Why do you have to do this twice? (Think about the structure of DNA.)

10. What are nucleotides? Why do you need to add them to the PCR mix?

11. What is DNA polymerase? What do they do during the process of PCR? Why does a specially selected polymerase have to be used during PCR?

12. Explain how the thermal cycler works. What is actually happening in the machine during the time period the DNA mixture is in the machine?

13. Why is the fact that nucleotide bases only pair with their complements so important during this process?

14. Remember the terms denaturing, annealing and extending from the PCR song? Explain those terms in relation to what is happening in the thermal cycler.

15. What is the significance of cycle 3 in the thermal cycler? What is beginning to be formed? Why did this process take until cycle 3 to begin to produce the desired results?

16. What is the result after 30 cycles?

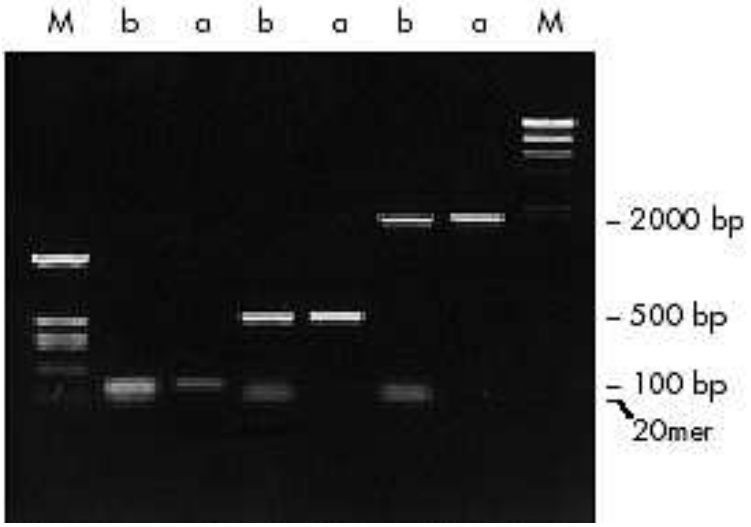
17. What is in the PCR tube with the pure DNA segments?

PURIFICATION OF PCR PRODUCT

After the process of PCR the DNA has been amplified and the product is millions of segments of the DNA that was targeted by the primers that were used. This is usually a gene or a specific exon. When analyzing the DNA with a chromograph to detect genetic mutations the DNA needs to be as pure as possible. The sample that comes from the thermal cycler is not as pure as it can be. It still has the original DNA strand and all the "cut" ends. There is also, the left-over nucleotides, polymerases, buffers and primers and salts in the tube. All this material needs to be washed away and only the pure DNA needs to be analyzed to produce the chromographs.

Extra material will cause lines and distortion in the chromographs.

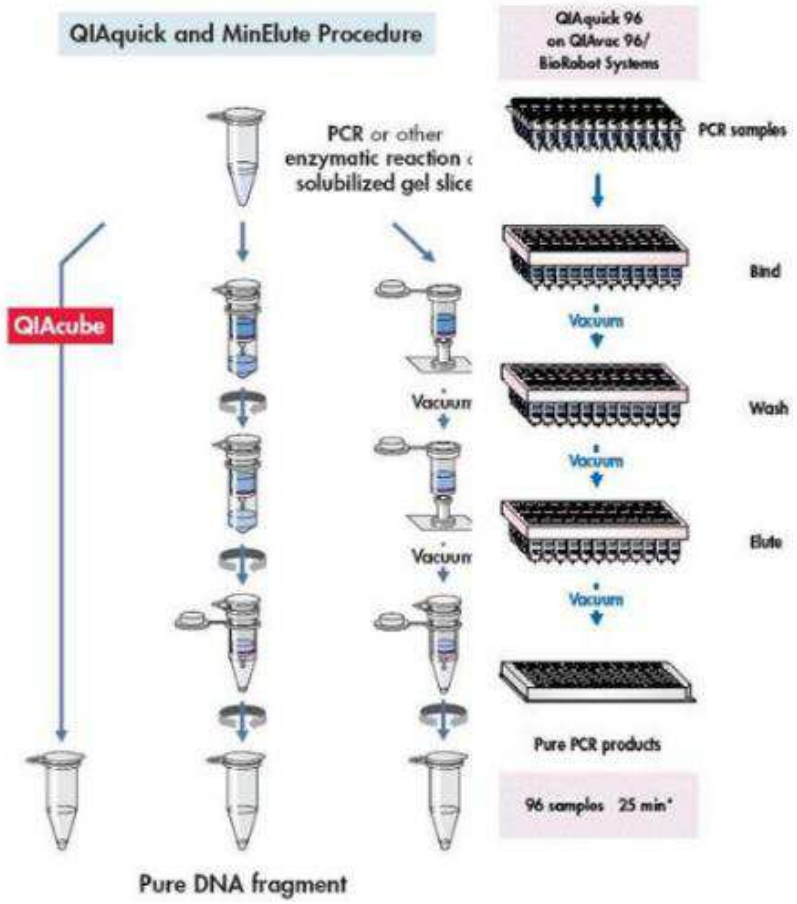
This can be accomplished by a process called **Purification.** The diagram below shows a photo of a gel from an electrophoresis. The columns on either end, marked "M", are the comparison markers. The columns marked "b" shows DNA run without purification and the columns marked "a" show DNA run after the purification process. You can note the shadows and blurring in the "b" columns. This is a result of impurities in the sample. The columns labeled "a" are crisper and more precise. This is a result of purification. When samples of DNA that have been purified are analyzed and chromographs are run the lines on the chromographs will be more precise.



How does purification take place?

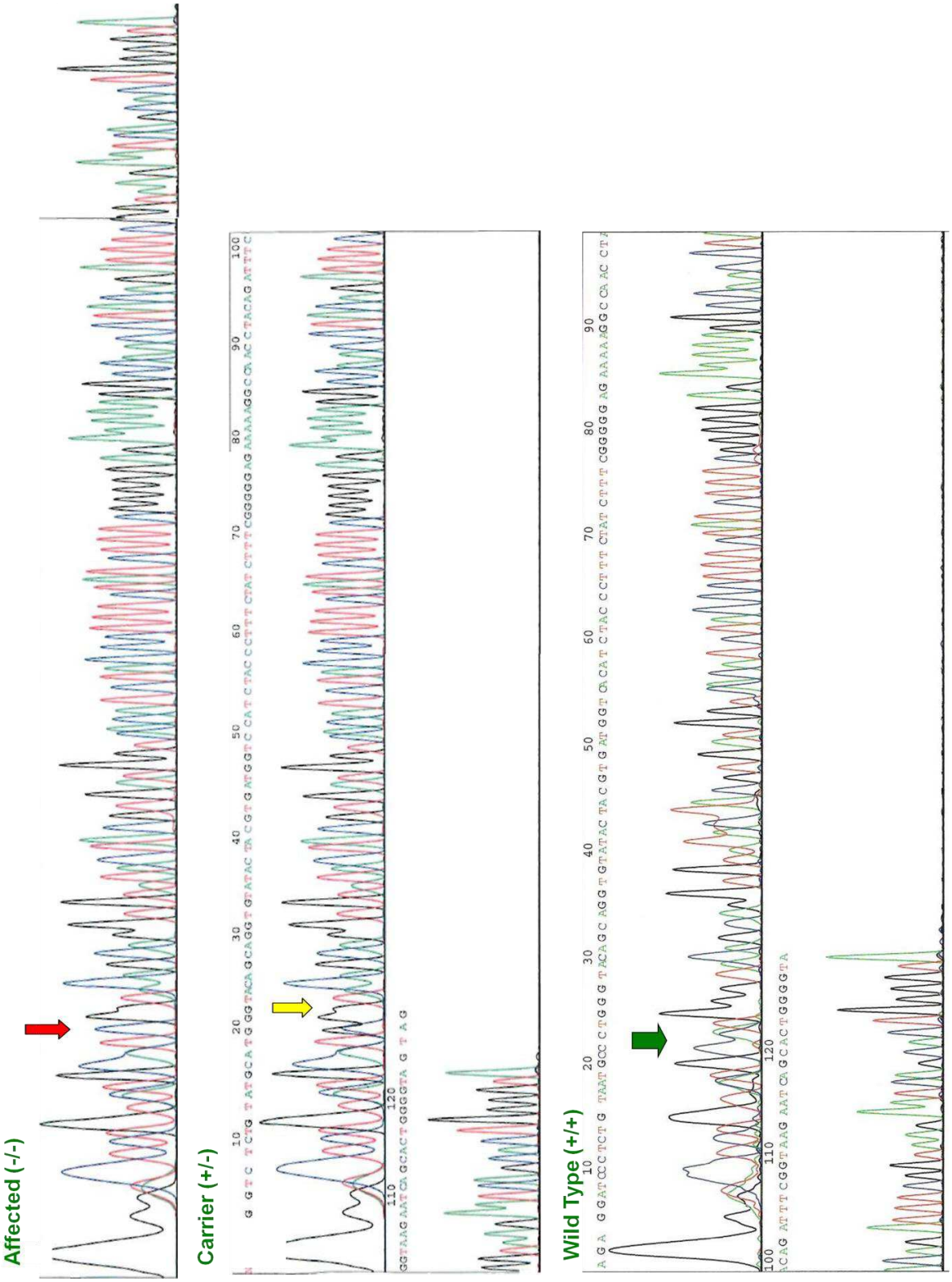
It is a three step process that involves buffers with varying degrees of salinity and attention to pH. Frequently a system of bind-wash-elute is used.

This process involves the use of a spin column with a silica-membrane, like the one below. This special tube is designed with a silica-membrane in it. This membrane will trap the DNA when it is run through the column and centrifuged. The product from the PCR has buffer added to it in the spin column. The spin column is placed in an Eppi tube for centrifugation. The buffer has a high salt content that causes the DNA to adsorb (stick to the surface) or bind to the surface of the membrane and the other material is spun through the membrane. These are the impurities that can now be discarded. The DNA is still attached to the membrane and the next step is to cause it to be released or eluted. The spin column is placed in a new Eppi tube and another buffer is added and the column is centrifuged. This buffer is referred to as an elution buffer and is less salty than the first buffer. This causes the DNA to release from the membrane and flow into the Eppi tube when it is centrifuged. The spin column can now be discarded. The DNA is in the Eppi tube and ready for analysis. This is analyzed in a special lab and the various nucleotide sequences are displayed as waves on a graph. They are color-coded to represent the four different nucleotides – hence the name, chromograph.



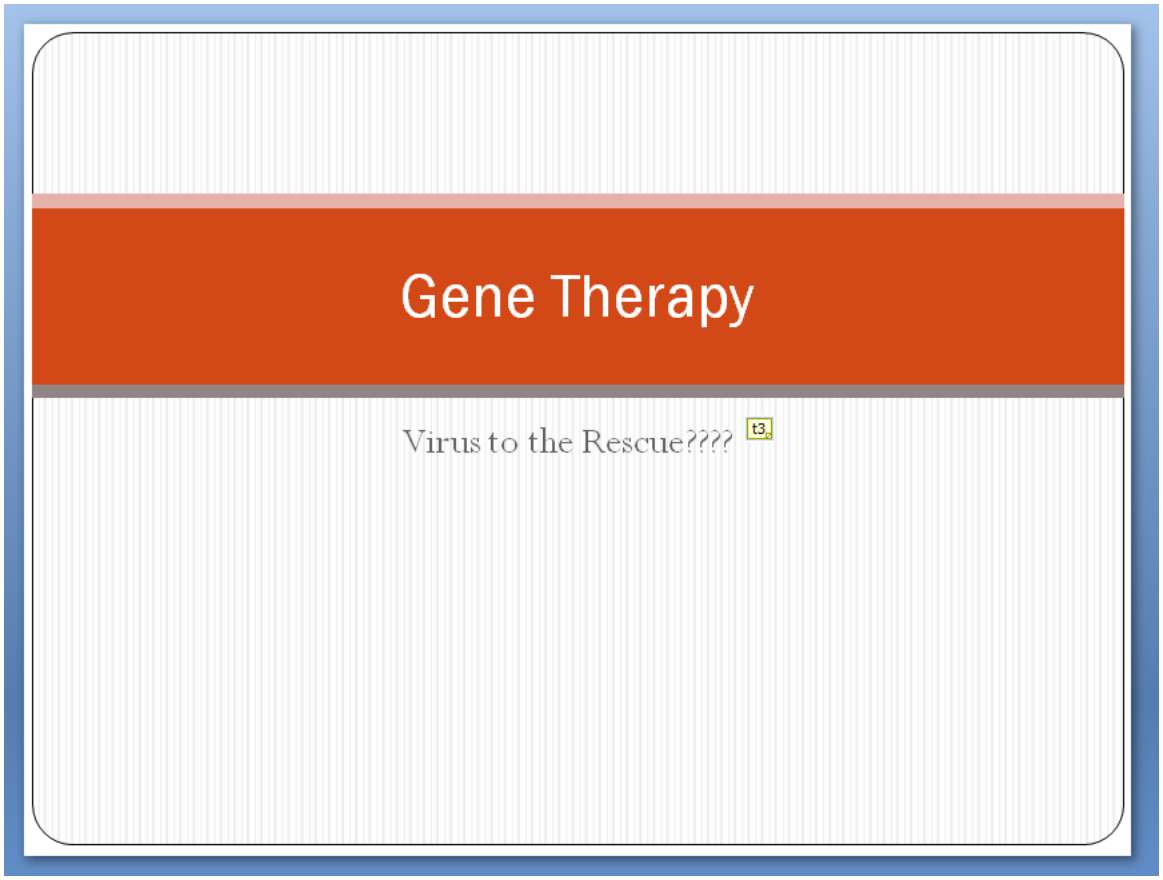
Visualization of the steps in PCR purification.

Dog DNA Chromographs



<u>Lesson 5:</u> Gene Therapy (*UNDER CONSTRUCTION)

See PowerPoint Presentation:



Lesson 6: A Day in the Life of a Patient with Glycogen Storage Disease

Focus

Four different case studies on Glycogen Storage Disease (GSD) will be presented. Students will be introduced to the nutritional management/treatment of a patient with four different types of GSD. In addition, students will be made aware of the daily struggles of a patient with GSD. Utilizing this information, students will be responsible for taking care of a simulated patient that has GSD.

Major Concepts

Glycogen storage disease is a genetically inherited disease characterized by deficiency in enzyme production along the pathway of glycogen storage and breakdown in the liver. There are four types of this disease that will be discussed in this lesson. They are Types I, III, V, VI and IX. Patients with different types of GSD have specific nutritional requirements in order to appropriately manage their disease.

Objectives

After completing this activity, students will be able to:

- Understand the daily nutritional requirements to manage Types I,
- Review four case studies about GSD.
- Manage a simulated patient with GSD for the period of 1 week.
- Create a daily meal plan for the simulated GSD patient.
- Document treatments given to the simulated patient for 1 week.
- Design an educational product to promote GSD awareness.

Prerequisite Knowledge

Students should have a working knowledge of basic genetics and the role of enzymes in metabolic pathways. They should be able to use critical thinking skills to solve problems and answer questions. They should be able to examine books and other sources of information to see what is already known.

Overall Time Estimate

Three or Four class periods. (50 minute classes). Two to two and a half weeks to work on project out of class.

Vocabulary

metabolism, glycogen, enzyme deficiency, biopsy, autosomal recessive inheritance, sex-linked inheritance, hypoglycemia, hepatomegaly, lactic acid, ketones, lipids, hepatic adenoma

National Science Education Standards

Next Generation Florida Science Standards

Basic Science-Health Connection

This lesson allows students to understand how rigorously following the researched nutritional and treatment regimens are critical for a patient with GSD.

Introduction

This activity introduces students to the daily struggles that a GSD patient experiences through case study presentation, a patient simulation exercise, nutritional specific planning, and creating an original educational component to make people aware of GSD.

Materials and Preparation

You will need to prepare the following:

- Copy of each of the 4 GSD Case Presentations for each student
- "The Importance of Nutrition in Treating GSD" PowerPoint
- "A Day in the Life of a GSD Patient" Assignment Directions Hand-out-copy for each student
- Nutritional Guidelines Specific to Type of GSD assigned to each student-1 for each student assigned to that type

Procedure

DAY ONE:

1. Use "The Importance of Nutrition in Treating GSD" PowerPoint to educate students on the importance of a strict diet in managing GSD.
2. Give a copy of each of the 4 GSD Case Studies to each student to read for homework. Have the student write down what Type of GSD that they think each case represents and nutritional implications for each case.

DAY TWO:

3. Discuss each case study and reveal which type of GSD each one is. Review Nutritional Guidelines sheets for each case study.

4. Give each student a copy of the “A Day in the Life of a GSD Patient” assignment sheet and the nutritional guidelines that go along with the GSD type that they are assigned. Explain to students that they will be pretending that they are caring for a patient with GSD for a period of a week. They will be responsible for giving and documenting cornstarch doses to the patient and writing a one day comprehensive meal plan that is specific for the management of their type of GSD.

Nutritional Guidelines for GSD Type I Notes

Name_____

1. What does GSD Type I cause?

2. What are the two types of carbohydrates? List examples of each.

3. What 2 simple sugars can't be used by a GSD Type I patient? Why?

4. How should fructose/galactose be limited in GSD Type I patients?

5. List the sugars that are allowed by GSD Type I patients:

6. List the sugars that are not allowed by GSD Type I patients:

7. What is the recommendation for eating the following types of foods for GSD Type I patients?

Fruits	Vegetables	Milk/Dairy	Meats
Fats	Beverages		

8. Give some examples of snack ideas for GSD Type I patients:

9. Why are multivitamins/calcium supplements recommended for GSD Type I patients? List some helpful tips when using these supplements.

10. What is cornstarch and how does it work?

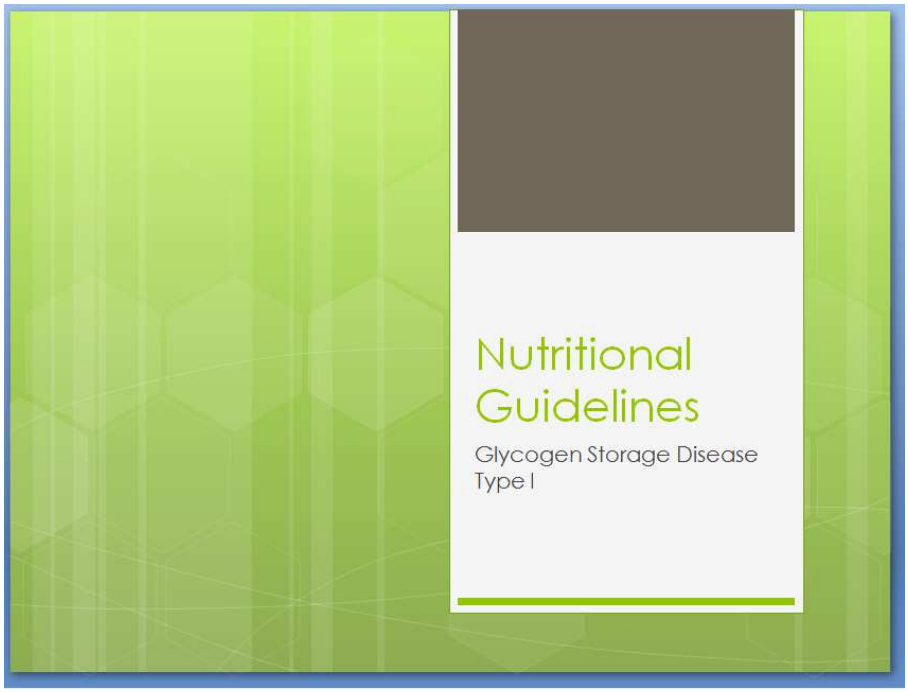
11. How many calories does cornstarch provide a day for a GSD Type I patient?

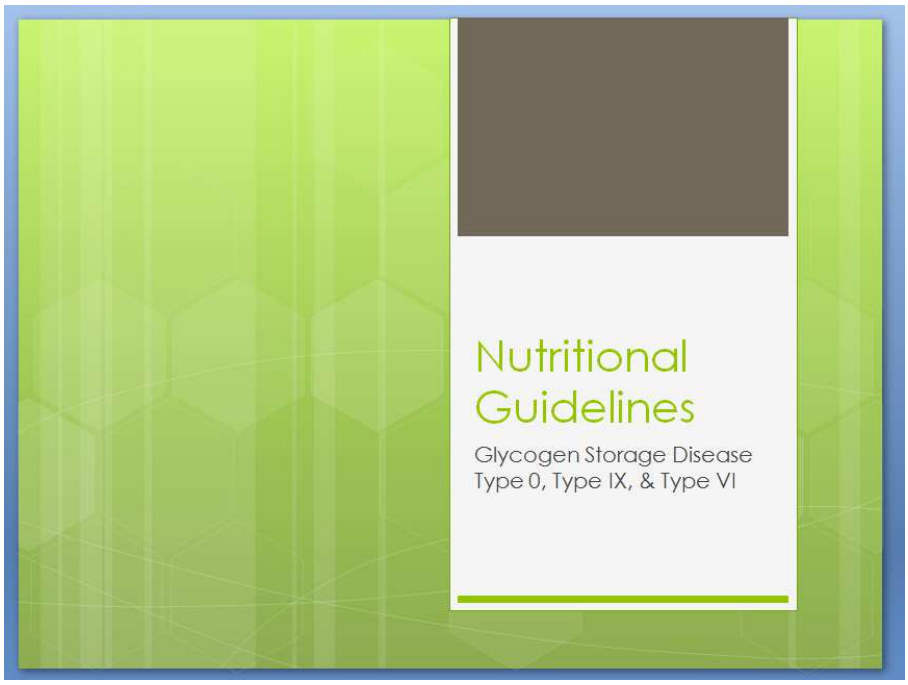
12. List the guidelines for mixing cornstarch:

13. List the important notes regarding cornstarch:

14. How did the cornstarch taste to you?

See PowerPoint Presentations:





Type 0

Your child is a 14 ½ year old with Type 0 Glycogen Storage Disease. He/she is currently in 8th grade and does well in school. He/she remains active outside the classroom and participates in basketball, soccer, and baseball/softball. He/she currently has soccer practice on Tuesday and Thursday nights and basketball practice on Monday and Wednesday nights. Basketball games are on Saturday morning and soccer games are on Sunday afternoon. In addition, your child has P.E. at school on Monday and Wednesday. It is important to your child that he/she not be different from his/her peers and most of his/her friends do not know that he/she has GSD.

Your child takes 30 grams of cornstarch at bedtime (10 p.m.) and 15 grams of cornstarch before exercise. Your child must monitor their blood glucose and ketones with a glucose meter and ketone meter prior to breakfast, lunch, and at bedtime.

Your child consumes a diet of around 3250 calories a day. He/she is allergic to seafood, fresh tuna, peanuts, and nuts. It is recommended that your child follow a diet high in complex carbohydrates and protein.

If your child is ill and can't tolerate their cornstarch, please go to the nearest hospital and have 10% dextrose run at 110 ml/hr.

You will be responsible for caring for your child for an entire week. During this week, you will be required to have your child with you at all times at school and at home. You will only be allowed to have 4 hours a day that you can have someone watch your child for you. The time that someone babysits for you must be documented on your log and the person babysitting must sign the log. You must keep a log of when you give your cornstarch dosages or when you check blood glucose or ketone levels. These logs must be signed by a teacher or a parent. If you are required to give a cornstarch dosage in the middle of the night (between 11pm and 6 am), you must text or call and leave a message with teacher. In addition, you will be required to keep a daily one page journal for every day of the project that addresses the question of the day and any other problems/situations that you may encounter during that day. Finally, you will be required to make a one-day food diary of what you would feed your child. (Please include any vitamin or mineral supplements also!) You must follow the dietary recommendations followed in class. You must check food labels to check that they are consuming simple sugars in the amounts that they are allowed to.

Cornstarch Log-Type O

Date	Time	Dosage	Parent/Teacher Signature

Glucose/Ketone Log-Type O

Date	Time	Glucose/Ketone Level	Parent/Teacher Signature

Babysitting Log-Type 0

Date	Times	Reason for Babysitting	Babysitter Signature

Journal Questions

DAY 1: Discuss how it feels how to a parent of a child that has Glycogen Storage Disease. Summarize your day with your child and discuss any challenges that you may have had.

DAY 2: Your child does not want his/her friends to know that he/she has Glycogen Storage Disease. How do approach this situation with your child? Summarize your day with your child and discuss any challenges that you may have had.

DAY 3: Your child comes down with a stomach virus and he/she can't tolerate his/her cornstarch? How would handle this situation? Summarize your day with your child and discuss any challenges that you may have had.

DAY 4: Your child has been hospitalized overnight as a result of his/her stomach virus. How do you handle this with your child? Summarize your day with your child and discuss any challenges that you may have had.

DAY 5: Your child wants to spend the night with his/her friend tonight. You know that this friend and this friend's parents do not know that your child has GSD. How do you handle this situation knowing that your child has to have a cornstarch dosage before bedtime? Summarize your day with your child and discuss any challenges that you may have had.

DAY 6: Your child sleeps in today until 11a.m. and hasn't eaten anything since his/her evening snack. What should you do to adjust for this? Summarize your day with your child and discuss any challenges that you may have had.

DAY 7: Summarize the impact of having a child with GSD had on your life during the course of the week. Include challenges that you have encountered, how you felt, and how this impacted your daily activities.

Food Diary-Type 0-(3250 Calories)

Breakfast

Snack

Lunch

Snack

Dinner

Snack

Cornstarch Dosages-(8 g Argo Cornstarch=30 calories)

A Day in the Life of a GSD Child Rubric

Cover Page for Journal (Includes Title of Project, Your Name, Your child's name, dates of project)	5 pts
Page that summarizes your child's information (Name, GSD Type, Picture, Age, Description of necessary information)	10 pts
Journal Entries-7 total	70 pts
Cornstarch Log-Signed	50 pts
Glucose/Ketone Log-Signed	35 pts
One-Day Food Diary	30 pts
Babysitting Log-Signed	25 pts
Care of Child (Rock Checks-3)	25 pts

_____
(250 pts total)

Type I

Your child is a 10 year old with Type Ia Glycogen Storage Disease. He/she is currently in 5th grade and is doing well in school. He/she has had a history of an enlarged liver, low energy level, and a slow growth rate prior to starting cornstarch therapy. He/she has recurrent morning nausea that may be due to increased lactate levels. He/she does not have any limitations from GSD and currently plays golf on Monday, Wednesday, and Friday. He/she is comfortable dealing with GSD in front of his/her peers.

Your child takes 56 grams of cornstarch at 8:00 a.m., 56 grams of cornstarch at 12:00 p.m., 56 grams at 3:30 p.m., 56 grams of cornstarch at 7:00 p.m., 60 grams of cornstarch at 10:00 p.m. and 70 grams of cornstarch at 2:30 a.m. In addition, an additional cornstarch dosage of 10 grams of cornstarch should be given per 1-2 hours of outside activity. Your child must monitor their blood glucose with a glucose meter and lactate levels with a lactate meter when they wake up, prior to lunch, and at 9:00 p.m.

Your child consumes a diet of around 2000 calories a day. He/she has no food allergies and no medication allergies. It is recommended that your child follow a diet with limited fructose, sucrose, and galactose.

If your child is ill and can't tolerate their cornstarch or is vomiting, please go to the nearest hospital and have 10% dextrose run at 85 ml/hr.

You will be responsible for caring for your child for an entire week. During this week, you will be required to have your child with you at all times at school and at home. You will only be allowed to have 4 hours a day that you can have someone watch your child for you. The time that someone babysits for you must be documented on your log and the person babysitting must sign the log. You must keep a log of when you give your cornstarch dosages or when you check blood glucose or lactate levels. These logs must be signed by a teacher or a parent. If you are required to give a cornstarch dosage in the middle of the night (between 11pm and 6 am), you must text or call and leave a message with the teacher. In addition, you will be required to keep a daily one page journal for every day of the project that addresses the question of the day and any other problems/situations that you may encounter during that day. Finally, you will be required to make a one-day food diary of what you would feed your child. (Please include any vitamin or mineral supplements also!) You must follow the dietary recommendations followed in class. You must check food labels to check that they are consuming simple sugars in the amounts that they are allowed to.

Cornstarch Log-Type I

Date	Time	Dosage	Parent/Teacher Signature

Glucose/Lactate Log-Type I

Date	Time	Glucose/Lactate Level	Parent/Teacher Signature

Babysitting Log-Type I

Date	Times	Reason for Babysitting	Babysitter Signature

Journal Questions

DAY 1: Discuss how it feels how to a parent of a child that has Glycogen Storage Disease. . Summarize your day with your child and discuss any challenges that you may have had.

DAY 2: Your child wants to go swimming today with his/her friends for approximately 2 hours. What special precautions do you take for your child in this instance? Summarize your day with your child and discuss any challenges that you may have had.

DAY 3: In school today, they are having a birthday party with cupcakes. How do you handle this situation with your child? Summarize your day with your child and discuss any challenges that you may have had.

DAY 4: How would handle going out to dinner with your GSD Type I child? Summarize your day with your child and discuss any challenges that you may have had.

DAY 5: You are stuck in traffic on the Turnpike on the way home from an after school activity. You don't have any cornstarch in the car and it is time for the 3:30 p.m. cornstarch dosage. What should you do? Summarize your day with your child and discuss any challenges that you may have had.

DAY 6: Your child wakes up vomiting and can't keep anything down. How do you handle this situation? Summarize your day with your child and discuss any challenges that you may have had.

DAY 7: Summarize the impact of having a child with GSD had on your life during the course of the week. Include challenges that you have encountered, how you felt, and how this impacted your daily activities.

Food Diary-Type I-(2000 Calories)

Breakfast

Snack

Lunch

Snack

Dinner

Snack

Cornstarch Dosages-(8 g Argo Cornstarch=30 calories)

A Day in the Life of a GSD Child Rubric

Cover Page for Journal (Includes Title of Project, Your Name, Your child's name, dates of project)	5 pts
Page that summarizes your child's information (Name, GSD Type, Picture, Age, Description of necessary information)	10 pts
Journal Entries - 7 total	70 pts
Cornstarch Log-Signed	50 pts
Glucose/Lactate Log-Signed	35 pts
One-Day Food Diary	30 pts
Babysitting Log-Signed	25 pts
Care of Child (Rock Checks-3)	25 pts

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(250 pts total)

Type IX

Your child is a 4 year old with Type IX Glycogen Storage Disease. He/she has reached all of his/her milestones appropriately, but appears to be weaker than his/her peers. In addition your child did not sleep entirely through the night for the first 4 years of life. He/she is a picky eater and it is a struggle to get him/her to eat protein at times. He/she craves carbohydrates but intake of fruit juice and fat has been associated with worsening of his/her diarrhea.

Your child takes 25 grams of cornstarch + 10 grams of Unjury after breakfast at 8:00 am, 25 grams of cornstarch + 10 grams of Unjury at 2:00 p.m., 10 grams of cornstarch + 5 grams of Unjury at 7:00 p.m., and 40 grams of cornstarch + 15 grams of Unjury at 11:00 p.m. Your child will require and additional 10 grams of cornstarch for every 1-2 hours of outside activity. In addition, your child's glucose and ketones need to be monitored in the morning, afternoon, and prior to bed.

Your child consumes a diet of around 1500 calories a day. He/she does not have any food allergies but does have an allergy to Fentanyl and Augmentin (medications). It is recommended that your child follow a diet high in complex carbohydrates and protein. In addition, a calcium and multivitamin supplement are recommended.

If your child is ill and can't tolerate their cornstarch, is vomiting, or ketone values are over 1.5 mmol/L, please go to the nearest hospital and have 10% dextrose be commended at 70 ml per hour.

You will be responsible for caring for your child for an entire week. During this week, you will be required to have your child with you at all times at school and at home. You will only be allowed to have 4 hours a day that you can have someone watch your child for you. The time that someone babysits for you must be documented on your log and the person babysitting must sign the log. You must keep a log of when you give your cornstarch dosages or when you check blood glucose or ketone levels. These logs must be signed by a teacher or a parent. If you are required to give a cornstarch dosage in the middle of the night (between 11pm and 6 am), you must text or call and leave a message with your teacher. In addition, you will be required to keep a daily one page journal for every day of the project that addresses the question of the day and any other problems/situations that you may encounter during that day. Finally, you will be required to make a one-day food diary of what you would feed your child. (Please include any vitamin or mineral supplements also!) You must follow the dietary recommendations followed in class. You must check food labels to check that they are consuming simple sugars in the amounts that they are allowed to.

Cornstarch Log-Type IX

Date	Time	Dosage	Parent/Teacher Signature

Glucose/Ketone Log-Type IX

Date	Time	Glucose/Ketone Level	Parent/Teacher Signature

Babysitting Log-Type IX

Date	Times	Reason for Babysitting	Babysitter Signature

Journal Questions-Type IX

DAY 1: Discuss how it feels how to a parent of a child that has Glycogen Storage Disease. Summarize your day with your child and discuss any challenges that you may have had.

DAY 2: You are stuck on I-95 in traffic and it is time for your child's 7 p.m. cornstarch dosage. You do not have any cornstarch in the car with you. What do you do? Summarize your day with your child and discuss any challenges that you may have had.

DAY 3: Your child has a play date at the park today at 11:00 a.m. What special precautions should you take for this? Summarize your day with your child and discuss any challenges that you may have had.

DAY 4: Your child wakes up in the morning with a ketone level of 2.5 mmol/L. What should you do? How would you handle this situation?

DAY 5: Your child's preschool class is having a Halloween party with cupcakes and candy. How would you handle this situation? Your child's preschool class is having a Halloween party with cupcakes and candy. How would you handle this situation?

DAY 6: How would you handle if your child refused to drink their cornstarch dosage?

DAY 7: Summarize the impact of having a child with GSD had on your life during the course of the week. Include challenges that you have encountered, how you felt, and how this impacted your daily activities.

Food Diary-Type IX-(1500 Calories)

Breakfast

Snack

Lunch

Snack

Dinner

Snack

Cornstarch Dosages-(8 g Argo Cornstarch=30 calories)

A Day in the Life of a GSD Child Rubric

Cover Page for Journal (Includes Title of Project, Your Name, Your child's name, dates of project)		5 pts
Page that summarizes your child's information (Name, GSD Type, Picture, Age, Description of necessary information)		10 pts
Journal Entries-7 total	70 pts	
Cornstarch Log-Signed		50 pts
Glucose/Ketone Log-Signed		35 pts
One-Day Food Diary		30 pts
Babysitting Log-Signed		25 pts
Care of Child (Rock Checks-3)	25 pts	

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(250 pts total)

Type VI

Your child is a 6 ½ year old with Type VI Glycogen Storage Disease. He/she is currently in 1st grade and is doing well in school. He/she has had a history of an enlarged liver and a slow growth rate prior to starting cornstarch therapy. He/she also has episodes of cramping in his/her legs in the afternoons approximately 1 time per month. He/she also suffers with frequent respiratory and sinus infections. He/she is able to participate in sports and physical education with no limitations.

Your child takes 36 grams of cornstarch in 4-6 ounces of fat free milk + 5 grams of Unjury at 6:30 a.m., 36 grams in 4-6 ounces of fat-free milk + 10 grams of Unjury, at 2:00 p.m., and 60 grams in 6 ounces of water + 10 grams of Unjury at 10:00 p.m. In addition, an additional cornstarch dosage of 10 grams of cornstarch should be given per 1-2 hours of outside activity. Your child must monitor their blood glucose and ketones with a glucose meter and ketone meter prior when they wake up, prior to lunch, and at 9:00 p.m.

Your child consumes a diet of around 1800 calories a day. He/she has no food allergies but is allergic to Clarithromycin and Clorahexadine/Chloroprep. It is recommended that your child follow a diet high in complex carbohydrates and protein.

If your child is ill and can't tolerate their cornstarch, is vomiting, or has a ketone level greater than 1.5 mmol/L, please go to the nearest hospital and have 10% dextrose run at 85 ml/hr.

You will be responsible for caring for your child for an entire week. During this week, you will be required to have your child with you at all times at school and at home. You will only be allowed to have 4 hours a day that you can have someone watch your child for you. The time that someone babysits for you must be documented on your log and the person babysitting must sign the log. You must keep a log of when you give your cornstarch dosages or when you check blood glucose or ketone levels. These logs must be signed by a teacher or a parent. If you are required to give a cornstarch dosage in the middle of the night (between 11pm and 6 am), you must text or call and leave a message with your teacher In addition, you will be required to keep a daily one page journal for every day of the project that addresses the question of the day and any other problems/situations that you may encounter during that day. Finally, you will be required to make a one-day food diary of what you would feed your child. (Please include any vitamin or mineral supplements also!) You must follow the dietary recommendations followed in class. You must check food labels to check that they are consuming simple sugars in the amounts that they are allowed to.

Cornstarch Log-Type VI

Date	Time	Dosage	Parent/Teacher Signature

Glucose/Ketone Log-Type VI

Date	Time	Glucose/Ketone Level	Parent/Teacher Signature

Babysitting Log-Type VI

Date	Times	Reason for Babysitting	Babysitter Signature

Journal Questions

DAY 1: Discuss how it feels how to a parent of a child that has Glycogen Storage Disease. . Summarize your day with your child and discuss any challenges that you may have had.

DAY 2: Your child wants to go swimming today with his/her friends for approximately 2 hours. What special precautions do you take for your child in this instance? Summarize your day with your child and discuss any challenges that you may have had.

DAY 3: In school today, they are having a birthday party with cupcakes. How do you handle this situation with your child? Summarize your day with your child and discuss any challenges that you may have had.

DAY 4: Your child has been put on the antibiotic, Omnicef for an upper respiratory infection. Since you have been giving the medicine to your child, you have noticed increased problems with hypoglycemia and increased ketone levels. What do you do? Summarize your day with your child and discuss any challenges that you may have had.

DAY 5: They change your child's lunchtime at school without informing you. How could this potentially be a problem and how would you handle it? Summarize your day with your child and discuss any challenges that you may have had.

DAY 6: Your child wakes up vomiting and can't keep anything down. How do you handle this situation? Summarize your day with your child and discuss any challenges that you may have had.

DAY 7: Summarize the impact of having a child with GSD had on your life during the course of the week. Include challenges that you have encountered, how you felt, and how this impacted your daily activities.

Food Diary-Type VI-(1800 Calories)

Breakfast

Snack

Lunch

Snack

Dinner

Snack

Cornstarch Dosages-(8 g Argo Cornstarch=30 calories)

A Day in the Life of a GSD Child Rubric

Cover Page for Journal (Includes Title of Project, Your Name, Your child's name, dates of project)	5 pts
Page that summarizes your child's information (Name, GSD Type, Picture, Age, Description of necessary information)	10 pts
Journal Entries-7 total	70 pts
Cornstarch Log-Signed	50 pts
Glucose/Ketone Log-Signed	35 pts
One-Day Food Diary	30 pts
Babysitting Log-Signed	25 pts
Care of Child (Rock Checks-3)	25 pts

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(250 pts total)

Supplemental “A Day in the Life” Materials

Scenarios:

Your child is acting irritable, appears shaky, and is complaining of dizziness and a headache. What should you do?

Your child skipped breakfast this morning. What should be your first course of action?

Your child’s blood glucose is 45 (normal is 60-100) and his/her ketone level is 1.4 mmol/L. What should you do?

Your child has a friend over today. The friend sees your child having a cornstarch treatment. The friend asks what it is for. How do you explain this to your child’s friend?

Your child doesn’t drink their entire cornstarch dosage. They have a seizure. What would you do?

Your child is acting irritable, appears shaky, and is complaining of dizziness and a headache. What should you do?

Your child skipped breakfast this morning. What should be your first course of action?

Your child’s blood glucose is 45 (normal is 60-100) and his/her ketone level is 1.4 mmol/L. What should you do?

Your child has a friend over today. The friend sees your child having a cornstarch treatment. The friend asks what it is for. How do you explain this to your child’s friend?

Your child doesn’t drink their entire cornstarch dosage. They have a seizure. What would you do?

10/24/11

Dear Parent/Guardian,

We have been currently studying a disease in class called Glycogen Storage Disease. It is a disease that is caused by the inability of the liver to convert glycogen to glucose, resulting in severely low blood sugars and an enlarged liver. Starting today 10/24 and continuing through Monday 10/31, I will be conducting a project with your child's 11th grade Medical Laboratory Assisting 3 class called "The Day in a Life of a Child with Glycogen Storage Disease" This project is similar to the egg project that is done in a psychology class, but the difference is that their child has a chronic illness. Your child will be carrying around a rock that will simulate their child with Glycogen Storage Disease. They must keep their rock child with them at all times during the course of this project. If they have to leave their rock child for any reason, they must have someone babysit their "child." They can only have a babysitter for a maximum of 4 hours on any day. Please make sure that your child documents any babysitting time that they used on their babysitting log.

Part of the treatment for this disease is that the patient has to be given cornstarch dosages at various times during the day and night to maintain his/her blood sugar levels. In addition, blood sugar, blood ketone, and blood lactate levels may have to be taken to regulate how the patient is doing. I am asking that you sign your child's log each day to prove that they remembered to administer their cornstarch dosages and take their blood levels at the correct times. It will be the student's responsibility to remind you to sign their log. If they have a cornstarch dosage from 11 pm until 6 am, your child will be responsible for sending me a text or leaving me a voice message that they administered their cornstarch dosage.

Please let me know if you have any concerns about your child participating in this project. You can reach me at school at 561.491.8493 or by email at allison.moyel@palmbeachschools.org. I feel that it is a great representation of what real parents of children with this disease go through on a daily basis. Please sign the bottom of this letter indicating that your child informed you about this project and that you give them permission to participate in it. Thank you!

Sincerely,

Allison Moyel
JFK Health Science Academy

Parent Signature

10/24/11

Dear Teachers,

Starting today 10/24 and continuing through Friday 10/28, I will be conducting a project with my 11th grade Medical Laboratory Assisting 3 students called "The Day in a Life of a Child with Glycogen Storage Disease" This project is similar to the egg project that is done in the psychology class, but the difference is that their child has a chronic illness. My students will be carrying around rocks that will simulate their child with Glycogen Storage Disease. Part of the treatment for this disease is that the patient has to be given a cornstarch dosage to maintain his/her blood sugar levels. If one of my student's has a cornstarch dosage due during the time of your class, could you please sign their cornstarch log indicating that they remembered to give the dosage to their child on time? It will be the student's responsibility to remind you to sign their log. Please also let me know if you see any mistreatment of any of the "Glycogen Storage Disease children" in the care of my students. I appreciate your help with this matter. If you have any questions or concerns, please email me. I would like to make this process the least disruptive as possible. Thank you!

Sincerely,

Allison Moyel
JFK Health Science Academy

Teachers-Please initial below to indicate that you have read this letter.

Period 1 _____

Period 2_____

Period 3_____

Period 4_____

Period 5_____

Period 6_____

Period 7_____

Supplemental Materials for Entire Curriculum:

Fun with Cornstarch Lab

What you need:

- 1 cup cornstarch
- bowl
- ABOUT 1/2 cup water
- spoon
- pie plate
- food coloring

Directions:

1. Empty 1 cup of cornstarch into a large bowl.

2. Stir while you add water SLOWLY -- don't add all of it if you don't need to.
    a. You need the consistency of thick pancake batter.
    b. It's better to add too little water than too much.
    c. Take your time!

3. Add a few drops of food coloring.

4. Stick your hands in the mixture.
    a. Record what it feels like.
    b. What happens when you try to roll some into a ball and then leave it alone?

5. Pour the water into a pie plate. (water is a liquid)
    a. smack it with your hand
    b. record what happens

6. Empty the pie plate. Pour the cornstarch mixture into a pie plate.
    a. smack it with your hand
    b. record what happens
    c. does it act differently than the water?

What Happened?

Extraordinary Measures Study Guide (Key)

Name_____

1. What unusual physical characteristics do you notice about the little girl (Meagan) and her brother (Patrick) at the beginning of the movie? List at least 3 of these characteristics.

2. What disease do these 2 children have? *Pompe Disease*

3. What do patients with this disease suffer from? (i.e. what symptoms do they have?) Is there currently a drug to treat this disease?

4. What happened to Meagan when she was hospitalized?

5. Where did John go after Megan had her first episode in the hospital?

6. According to Dr. Stonehill, what causes this disease? What is his theory for a cure?

.

7. It takes many years of research before a drug/therapy can be even sent to clinical trials. How long had Dr. Stonehill been working on his research?

8. How much are the medical costs for the Crowley's two kids per month?

9. What does Meagan give to Dr. Stonehill when he visits?

10. What does Mrs. Crowley mean by her statement, “Do we just accept our fate and do what the well meaning doctors say and wait for the worst to happen, or do we fight it?” What do you think you would do if you were in this position?

11. What difference did the Crowley’s notice with Patrick when he was feeding the ducks? How is this related to the progression of his disease?

12. Why did the investors want the drug therapy in clinical trials within a year? Do you think this a reasonable time frame? Why or why not?

13. Explain what Dr. Stonehill meant by the following comment: “I don’t care about the money, I am a scientist.”

14. What do you think the term “orphan drug” means?

15. Describe your feelings after the Temple family told/shared their story about their two girls at the fundraiser event.

16. How old was Lauren when she passed away?

17. Decisions have to made as to who can participate in clinical trials. Imagine that you had a child who could be potentially cured from a horrible disease by participating in a clinical trial. However, your child does not qualify for the clinical trial. What would you do? Explain your answer.

18. What is a sibling clinical trial?

19. Why was John Crowley's job in the biotech company a conflict of interest?

20. At the end of the movie, how did Dr. Stonehill know that the therapy worked on Meagan and Patrick?

Extraordinary Measures Study Guide (Key)
Name_____

21. What unusual physical characteristics do you notice about the little girl (Meagan) and her brother (Patrick) at the beginning of the movie? List at least 3 of these characteristics.

- *Both are in a wheelchair*
- *Both are on a ventilator*
- *Both have poor head control*

22. What disease do these 2 children have? *Pompe Disease*
What is the average lifespan for a person with this disease? *9 years*

23. What do patients with this disease suffer from? (i.e. what symptoms do they have?)
muscle deterioration in every part of the body-enlarged heart

Is there currently a drug to treat this disease? *No*

24. What happened to Meagan when she was hospitalized?
She went into cardiac arrest and almost died

25. Where did John go after Megan had her first episode in the hospital?
Nebraska

26. According to Dr. Stonehill, what causes this disease? What is his theory for a cure?
The enzyme glycogen builds up in the skeletal muscle and the body can't break it down. The glycogen builds up in the heart and skeletal muscle and the diaphragm fails to work properly. His theory is to make the enzyme nano-6-phosphate and get more of it into the cells so that the cells can break down the glycogen.

27. It takes many years of research before a drug/therapy can be even sent to clinical trials. How long had Dr. Stonehill been working on his research?
10 years

28. How much are the medical costs for the Crowley's two kids per month?
$40,000

29. What does Meagan give to Dr. Stonehill when he visits?
An orange goldfish

30. What does Mrs. Crowley mean by her statement, "Do we just accept our fate and do what the well meaning doctors say and wait for the worst to happen, or do we fight it?" What do you think you would do if you were in this position?
Answers will vary

31. What difference did the Crowley's notice with Patrick when he was feeding the ducks? How is this related to the progression of his disease?
He couldn't throw bread to the ducks; this shows that his disease is progressing

32. Why did the investors want the drug therapy in clinical trials within a year? Do you think this a reasonable time frame? Why or why not?
They wanted the drug therapy in clinical trials within a year because the sooner they could test it, the sooner it could potentially go to market and they could make an investment. Answers will vary for the second question.

33. Explain what Dr. Stonehill meant by the following comment: "I don't care about the money, I am a scientist."
He doesn't care about the money…he is more interested in seeing his research succeed.

34. What do you think the term "orphan drug" means?
An orphan drug is a drug used to treat a disease of low incidence.
35. Describe your feelings after the Temple family told/shared their story about their two girls at the fundraiser event.
Answers will vary.

36. How old was Lauren when she passed away?
9 years old

37. Decisions have to made as to who can participate in clinical trials. Imagine that you had a child who could be potentially cured from a horrible disease by participating in a clinical trial. However, your child does not qualify for the clinical trial. What would you do? Explain your answer.

Answers will vary

38. What is a sibling clinical trial?

Siblings with the same genetic disease participate in a clinical trial together

39. Why was John Crowley's job in the biotech company a conflict of interest?

He was working for the company that was developing a drug to treat a disease that his children had. If they were chosen for a clinical trial, it would be considered a conflict of interest or favoritism.

40. At the end of the movie, how did Dr. Stonehill know that the therapy worked on Meagan and Patrick?

They were laughing because they were on a sugar high. The glycogen could break down to sugar in their cells.

“Extraordinary Measures” Essay Assignment: Write a five paragraph essay comparing and contrasting Pompe Disease (GSD Type II) to GSD Type Ia that we studied in class. Make sure to include information about the causes of each disease, the symptoms of each disease, the treatment for each disease, and the research being conducted. In addition, give your opinion as to what you think about why clinical trials are currently being done on humans for GSD II and why they are only being done on animals for GSD Ia. Are clinical trials on children and babies ethical in this case? Why or why not? Make sure to include at least 5 sentences in each paragraph.

“Extraordinary Measures” Essay Assignment: Write a five paragraph essay comparing and contrasting Pompe Disease (GSD Type II) to GSD Type Ia that we studied in class. Make sure to include information about the causes of each disease, the symptoms of each disease, the treatment for each disease, and the research being conducted. In addition, give your opinion as to what you think about why clinical trials are currently being done on humans for GSD II and why they are only being done on animals for GSD Ia. Are clinical trials on children and babies ethical in this case? Why or why not? Make sure to include at least 5 sentences in each paragraph.

“Extraordinary Measures” Essay Assignment: Write a five paragraph essay comparing and contrasting Pompe Disease (GSD Type II) to GSD Type Ia that we studied in class. Make sure to include information about the causes of each disease, the symptoms of each disease, the treatment for each disease, and the research being conducted. In addition, give your opinion as to what you think about why clinical trials are currently being done on humans for GSD II and why they are only being done on animals for GSD Ia. Are clinical trials on children and babies

ethical in this case? Why or why not? Make sure to include at least 5 sentences in each paragraph.