Embryonic Development, Congenital Abnormalities,
And Their Effect On The Function Of Human Body Systems

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This curriculum unit is recommended for 7th grade Science but can be adapted for high school Biology

Keywords: Genetics, inheritance, pedigree chart, Punnett Square, human body systems, developmental biology

Teaching Standards: See Appendix 1 for teaching standards addressed in this unit.

Synopsis: This curriculum unit combines 7th grade North Carolina Science Standards on genetics, inheritance, and the human body to investigate how problems with the development of the human embryo can impair the functioning of the human body systems after birth. A variety of genetic disorders and environmental influences will be explored as means to discuss the proper structure and function of human body systems while simultaneously exploring issues of genetics and inheritance. Students will be able to practice the use of pedigree charts and Punnett squares while relating the disorders to how they affect the human body systems. Students will also explore how environmental factors can affect survival due to the influence they have on the developing human body systems and their functions. The disorders and environmental influences featured in this unit typically affect more than one human body system as to highlight the interdependence between the systems.

I plan to teach this unit during the coming year to 120 students in 7th grade science.

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Introduction

Rationale

Genetics and the human body are two science topics that middle school students can get very interested in and have many questions about as they relate what they are learning to their own families and experiences. Currently, these units are taught separately at my school. This unit is designed to take these topics in the 7th grade science standards and connect them in way that allows students to deepen their knowledge of these topics while keeping them interested and engaged in the subject.

When teaching pedigrees, a common activity in middle school science classes is to incorporate hemophilia and the lineage of Queen Victoria. Another interesting example are the Blue Fugates of Kentucky. They are high interest examples because they are real, rare, dramatic disorders, and interesting to contemplate. What would life be like if your blood did not clot properly? Or if your skin was blue? This unit takes the idea of using real life examples to review genetics while also learning about conditions affecting the human body systems. When a student understands the function of the cardiovascular system, for example, the danger of a disorder that affects blood clotting becomes more clear.

I wanted to use case studies in this unit because they can help make learning and applying scientific knowledge fun and interesting while allowing students to practice 21st century skills they will need in a variety of settings, such as critical thinking, communication, and working with others. The case studies also allow students to practice reading in the content area. I used real case studies when possible, adapting them as necessary to be age appropriate.

The seminar title was “How to build a human?” and sessions focused on developmental biology. This unit looks at examples where something in the building of a human goes differently than expected. This requires providing students with some understanding of the specializing that occurs as the single celled zygote undergoes cell division and specialization to form the finished human body. Disorders may be due to inherited conditions such as is the case with hemophilia but they can also be due to environmental conditions during development, as was the case with thalidomide. This unit is designed to connect development biology to examples of inherited disorders as well as environmental conditions during pregnancy that impact the finished human body systems. Examining specific disorders through cases studies provides students opportunity to work with each other to learn about interesting disorders while continuing to practice Punnett squares and pedigree analysis. Learning about the disorders also connects to studying the function of each body system and how a malfunction impacts other systems in the body.

School Demographics

The school this unit was designed for is a middle school that contains over 1600 students in grades 6-8. Eighteen percent of the students are economically disadvantaged. Seventy five percent of students identify as White, 13 percent Hispanic, 7 percent Black, and 3 percent Asian. In recent years, it has exceeded growth as measured by the state End of Grade math and reading exams. In 2013, 68% of students were at grade level. By 2019, 6 years of consistent growth had raised that number to 87% of students. As measured by the state, this school had the highest growth of all schools in the district. In addition, 7 of the 8 subgroups showed a growth index of 4.0 or better.

Science is taught daily in 65 minute blocks. Class size is approximately 30 students per class. I designed this unit for my 7th grade science classes. Within a single class there is often a wide range of student performance. Some students are taking high school level math, are in honors language arts, and scored 5s on their EOGs. In the same classroom there may be students receiving a variety of services due to 504 plans or IEP plans that maybe in place to help those students. Six percent of my students are current English Language learners or have exited the program. Sixteen percent of the students are students with disabilities. Twenty six percent of the students scored at level 1 or 2 on the reading EOG in 6th grade, indicating that they are not meeting on grade level proficiency. Thirty five percent earned a 5 (the highest score).

Unit Goals

The North Carolina Essential Standards for Grade 7 include a unit on the human body and a unit on genetics. Please see *Appendix 1: Teaching Standards* for the specific standards. The goal of this unit is to apply those standards in a series of case studies that examine how congenital abnormalities of various organs can affect function. Some of the abnormalities examined have a genetic origin while others are due to factors present during prenatal development.

Before beginning this unit, students will already have completed units on the human body and genetics. They should already be able to explain that the human body is made of cells that form tissues that form organs that work together in the systems of the human body. They should know the functions of these major human body systems and be able to infer patterns of heredity though the use of Punnett Squares and the interpretation of pedigrees showing inheritance of a genetic disease. This unit will expand on those skills beginning with a brief introduction to developmental biology to show, in a grade level appropriate manner, how an embryo develops from one cell to a multi-cellular organism with highly specialized functioning.

They will then examine a variety of case studies in this unit. They will use these case studies to analyze the patterns of genetic traits and make predictions by creating pedigrees based off the information. They will also be able to explain how various interactions with the prenatal environment influenced human characteristics, primarily in terms of the function of the human body system affected in each case study example.

Content Research

Human Development

Human DNA is organized into 23 pairs of chromosomes. One chromosome is inherited from each parent. It is the 23rd pair that typically determines the sex of the offspring. XX will result in female while XY will result in male. If there was an error during the DNA replication process that precedes the formation of the sex cells (sperm and egg), then it is possible for humans to have part of a chromosome deleted or a mutation of a gene on a chromosome.[1] Problems during cell division could result in offspring with an additional or missing chromosome. Any of these issues can result in serious problems during development. Specific examples will be included in this unit and explained later in this section.

A human embryo begins to develop once a sperm has entered an egg. As they fuse, fertilization occurs and a calcium signal is released that works to prohibit additional sperm from entering.[2] After fertilization, the zygote undergoes a period of rapid cell division (mitosis), which is called cleavage. Now resembling a ball of cells, this blastocyst is what implants in the uterine lining. In the gastrula stage, three germ layers form, each eventually different types of cells. The innermost layer, the endoderm, will give rise to lung and digestive cells. The mesoderm will lead to the skeletal and muscular system and various other organs, while the ectoderm ultimately results in skin, the neural crest, and neuron cells.[3] As the cells continue dividing, they also begin differentiating, meaning that it is beginning to specialize and will eventually result in a specific type of cell. This is determined by different chemical signals received by each cell. After approximately 2 weeks of development post fertilization, the blastocyst is considered to be an embryo. For approximately the next five weeks, the embryo develops and organs form. It is during this critical time of organ formation where many birth defects can occur. At the end of this stage, the approximately two inch long embryo is considered a fetus, which continues to grow and develop for an additional 28 weeks.[4]

Genetics and Inheritance

The genetic information inherited through the sperm and egg determines what traits the offspring has. A gene is a segment of DNA that codes for a particular protein that contributes to a function in the cell and body. The phenotype is the way an organism looks or behaves while the genotype is the actual combination of genes the organism has. Recessive traits can be masked by dominant traits but reappear in future generations as the genes continue to be passed down. Dominant traits will be expressed if the allele that makes them is present.

Two tools that are helpful when analyzing inheritance are pedigrees and Punnett squares. A pedigree chart is a diagram that shows a type of family tree that uses particular symbols to include genetic information. A Punnett square shows possible offspring combinations due to a particular cross of parent traits. For a 7th grade science classroom, Punnett square practice is limited to simple Mendelian inheritance patterns where a single gene or two are responsible for traits. More genetically complicated traits, such as human height, are beyond the scope of a Punnett square due to all the genetic and environmental factors involved in determining the phenotype of an individual.

Genetic Disorders

Hemophilia

One disorder studied in this unit is hemophilia. Hemophilia is a condition where the body does not properly form blood clots. As a result, any small cut or bruise can potentially be life threatening due to external or internal hemorrhaging. It is an X-linked recessive disorder, meaning that the gene responsible for the disorder is found on the X chromosome and if an individual has a copy of the normal, dominant, blood clotting gene, they will not express the condition. Only an individual lacking a version of the normal blood clotting gene will have hemophilia. As a result of the gene being on the X chromosome, males are affected much more commonly than females. This is because males only have one X chromosome. Females, however, have two copies of the X chromosome so they would need both to be lacking the normal version of the gene in order to express the trait. Instead, females may be carriers of the gene, in which case they have a 25% chance of having a normal son, 25% chance of having a normal daughter, 25% of having a son with hemophilia, and 25% chance of having a daughter who is also a carrier for the disease.

There are actually two main forms of hemophilia but since the genes involved are both on the X chromosome, both disorders display the same patterns of inheritance. Hemophilia A is due to a mutation on the F8 gene, which affects the structure of a protein known as coagulation factor VIII. Hemophilia B, which is rarer, is due to a mutation on the F9 gene, which affects coagulation factor IX. In both cases, the impacted protein is not able to fully participate in the blood clotting process.[5] Blood clots are what function to seal off damaged blood vessels after an injury. When this process is impaired, greater blood loss results.

Queen Victoria's offspring provide an obvious option for a potential case study that combines science and world history in an interesting way. Queen Victoria, likely through a spontaneous mutation that occurred in her DNA, was a carrier for the hemophilia B gene. She had one son with hemophilia and by studying her family pedigree, it becomes clear that two of her daughters were carriers as well, as they each had sons with hemophilia.[6] In perhaps the most famous case in her family, her great-grandson Alexis, heir to Russian throne and son of Tsar Nikolas II, had hemophilia, a fact that was concealed from the public. His parents, the Tsar and Tsarina, were very concerned with his health and his mother developed a close relationship with the monk Rasputin, whom she believed to be able to help Alexis and ease his suffering. Rasputin was not popular in the press or in the political realm and this was one of many contributing factors leading to the Russian Revolution of 1917 and the eventual execution of the Tsar's entire family, Alexis included.[7]

Cystic fibrosis

Cystic fibrosis is an inherited disease characterized by the body's production of a thick, sticky mucus instead of a runnier form. This thick mucus can block the airway, making it difficult to breath and more likely for infections to occur. In addition to affecting the respiratory system, the disorder impacts the digestive system as well. Thick mucus can impair the function of the pancreas, which is responsible for producing insulin. As the pancreas struggles to produce insulin, individuals with cystic fibrosis can develop cystic fibrosis-related diabetes. Cystic

fibrosis affects the reproductive system as well. In males, mucus often creates a blockage during development that keeps the vas deferens (the tubes that transport sperm out of the testes) from forming properly, rendering it necessary for them to undergo fertility treatment in order to successfully reproduce.[8] The mutation also impairs cilia and flagella movement, which also affects the sperm. For many years, individuals with cystic fibrosis did not survive childhood. Now that infants are screened for the disease at birth and a variety of treatment methods and medications are available, the average life expectancy has increased to almost 40 years of age.

Cystic fibrosis is due to a mutation of the CFTR gene on the seventh chromosome. This affects how chlorine ions are moved in and out of cells, which then affects water regulation. The result is the thicker, stickier mucus and high salt content in their sweat.[9] It is an autosomal recessive gene, meaning that someone must have 2 copies of the allele in order to have the condition. The parents must have both been carriers of the disorder and the individual inherited both recessive copies of the allele. Punnett squares and pedigree charts are useful tools to examine the familial inheritance patterns.

Huntington's Disease

Huntington's Disease is a disorder that is inherited as a dominant trait, meaning that an individual who has a parent with Huntington's Disease has a 50% chance of also having the disorder.[10] Huntington's Disease affects the nervous system and typically presents in adulthood through involuntary movements and emotional/cognitive decline. It is fatal and there is no cure.

Huntington's Disease is due to a mutation of a single gene on the fourth chromosome. This gene codes for a protein called huntingtin. Individuals with Huntington's Disease contain an allele that consists of a repetitive sequence that affects the formation of the protein. The malformed protein clumps in the brain and causes nerve cell death.

Because it is a dominant trait, the study of Huntington's Disease provides exposure to a different inheritance pattern. Ethical considerations can be discussed as well, as people who have a family history of the disease can undergo testing to determine if they will also have the disorder. It also provides an opportunity to discuss how dominance does not equate to high frequency. While it is an autosomal dominant disorder, it is thankfully rare.[11]

Androgen Insensitivity Syndrome

Androgen Insensitivity Syndrome is, like hemophilia, due to a gene located on the X chromosome. In this case, the protein made by this AR gene is an androgen receptor. These receptors are important because they are what helps cells respond to androgens, which are hormones that guide male sexual development. The most commonly known androgen is testosterone. If there is a mutation in the AR gene that affects androgen receptors, cells are less responsive to the signals communicated by the androgens, which affects sexual development.[12] Therefore, this syndrome connects to the endocrine and the reproductive system. Its effects are most noticeable during sexual development in utero and then again during puberty.

The default sexual development pattern in humans is female. Specific signals at specific times are necessary to form male reproductive structures. When the body cannot communicate with these signals, the external sex characteristics are female. Internally, however, the hormone

signals resulted in undescended testes and no internal female organs. The lack of uterus and therefore menstruation is typically not discovered until teenage years.

The vast majority of cases result because either the mother had inherited an altered copy of the AR gene on one of her two X chromosomes or the mutation occurred in the egg before or in the early stages of fetal development.[13] Pedigree charts can be included in this study to illustrate how mothers can act as carriers of the mutation, similar to hemophilia. Because genetic XY males with Androgen Insensitivity Syndrome are unable to reproduce and pass on this trait, it could also incorporate Punnett square practice to demonstrate how rare it would be for a XX individual to be homozygous recessive and express this AR gene mutation.

Prenatal environment- Teratogens

Thalidomide

One of the earliest well publicized examples of a drug interaction affecting embryo development was the case of thalidomide in 1950s and 60s. While thalidomide had not received FDA approval in the United States, it was being used in several other counties to combat morning sickness in early pregnancy.[14] At the time, physicians incorrectly believed the placenta was impervious to any drugs the mother ingested.[15] After thalidomide terribly indicated this was not the case, the way drugs are tested and approved was changed. Thalidomide affects embryonic development between days 20 and 36 after fertilization. A little as one single dose was determined to be enough to cause deformities.[16] One of the most distinctive defects resulting from thalidomide exposure is limb malformation, namely phocomelia, which is when the longer limbs such as the humerus or femur, are shortened. In severe cases, called amelia, the limbs may be missing altogether.[17] Research suggests this occurs due to thalidomide destroying blood vessels during development that leads to the loss of limb signaling pathways, although the exact mechanism is still unknown.[18] Today thalidomide has been shown to be effective against leprosy and multiple myeloma, so the drug and dangers to embryos still exist, although it is rare.[19]

Accutane (Isotretinoin) Exposure

Isotretinoin is another clear example of a drug that will impair embryo development (teratogen) and is potentially one that the students may encounter in the coming years as it is used to combat a form of severe acne. Like thalidomide, exposure during the stages of embryonic development that may be before a woman knows she is pregnant can lead to malformations. With isotretinoin, the main abnormalities affect the lips, ear, and eye as well as mental impairment.[20]

Another interesting avenue to explore regarding Accutane is the program that the FDA and Accutane manufacturer put in place to increase awareness of the damaging effects the medication has on embryos and the importance of preventing conception. Originally called the Pregnancy Prevention Program, it was later modified and renamed the SMART (System to Manage Accutane Related Teratogenicity) program. Requirements combine education, using measures such as informational brochures, with mandatory pregnancy tests and no automatic refills to hopefully minimize exposure. However, now that Accutane's patent has expired and many generics are available, the situation needs continuous monitoring.[21]

Prenatal environment- other

Dutch Hunger Winter

During World War 2, Nazi forces blocked food supplies to the Netherlands from October 1944 to May 1945. Known as the Dutch Hunger Winter, this time of nationwide food shortage made it possible for scientists to be able to examine the long-term effects of short-term food deprivation on human health. The country's population was typically well fed before and after the famine, thus creating a clear beginning and end timeline, and several studies have been conducted since to analyze this "natural experiment" that occurred, particularly in terms of how it affected humans who experienced it during the prenatal stages of development.[22]

In the various studies that have been conducted on children whose in utero development was marked by this famine, several key trends have emerged. As adults, this population experienced elevated rates of conditions such as diabetes, obesity, and schizophrenia. Their LDL cholesterol and triglyceride levels were elevated as well. As the cohort aged, further studies found that there was "a ten percent increase in mortality after 68 years," per Dr. Lumey, one of the researchers.[23] Further research has investigated the F2 generation (whose parents were in utero during the Hunger Winter) and found that some of the offspring has higher BMIs than would be statistically expected.[24]

This particular example provides an opportunity to include instruction on epigenetics, which is when there has been an alteration to gene activity without actually changing the DNA of an individual. Sometimes these changes can be passed on to the next generation. Currently the best understood epigenetic process is DNA methylation, where a methyl group (CH_3) is added to the DNA. It does not change the DNA sequence but can alter its function.[25] While some of the more well-known studies on epigenetics focus on mice and rats, current research on humans is investigating links between epigenetics and schizophrenia, aging, and cancer.[26]

Instructional Implementation

Teaching Strategies

Background knowledge/Previous instruction

This unit focuses on connecting student knowledge about genetics and the human body. Previously, students received direct instruction on genetics topics such as Punnett squares, pedigree charts, DNA, mitosis, and meiosis. They also know the main function and organs of the human body systems. This information was initially provided through direct instruction. After learning what Punnett squares and pedigree charts are, however, students need practice. We begin with providing them with examples of Punnett squares and pedigree charts and having students interpret them. After exhibiting mastery of that skill, they receive problems where they create the Punnett squares and pedigree charts themselves. Case studies are part of this practice.

Case Studies

Case studies provide students with an opportunity to apply that knowledge. Reading in the content area is also included as each activity begins with them reading the case. Students will then use process skills and critical thinking to expand on the case.

The criteria for selecting the topics in the case studies are to include a variety of disorders or environmental influences while ensuring that the cases can be modified to be appropriate for the middle school science class. In terms of variety, some cases indicate problems with development (such as with Androgen Insensitivity Syndrome) while others focus more on ongoing problems, such as in the case of cystic fibrosis. Many different body systems are included in the various categories. As students read about the cases, students may be asked to identify with the medical provider. They may be asked what they would do if they were the patient or parent of the patient. In the cases of Alexsei Romanov and the Dutch Hunger Winter, connections can be made to their social studies content as 7th grade social studies covers 20th Century world history.

The case studies are frequently broken down into segments so that students receive the new information in chunks. Students have the opportunity to answer comprehension questions on what they read and then use the information provided to practice Punnett squares, interpreting and making pedigrees, or apply their knowledge of the function of the various human body systems. For lower level readers, additional support in terms of modifying the text can be provided. Several case studies encourage students to work together and think, pair, share which can also help support a struggling reader.

Sensitivity/Considerations of family situations

When teaching about genetics and inheritance it is important to be sensitive to individual family situations and circumstances. Not all students live with, or even know, their biological parents. In many cases when a student was adopted, the student knows this, but not in all cases. In addition, it is possible that a child's biological father is not who the family believes him to be. A middle school science class is not where these family secrets should be discovered. While activities where students examine their own traits (widows peak vs smooth hairline, attached vs unattached earlobes, blood types) are fun, they needs to be approached with caution, especially if activities expand to include family characteristics. Students also need reminding that most human characteristics are not inherited in a single gene, complete dominance pattern. Multiple genes code for skin, hair, and eye color and trying to examine those patterns in their own family is beyond the scope of middle school genetics. For these reasons, most of my genetics lessons use examples not directly related to my students.

A second area of concern when discussing the human body and disorders is that it is always possible that a student has personal experience with whatever disorder is being discussed. Maybe they have the condition or a family member does. The teacher does not always know this information. Sometimes a student is willing to share their knowledge and it enriches instruction. For example, I have had students with diabetes share with the class how they monitor their blood sugar. Other times, however, specifics of the disorders need to be dealt with sensitively. This is particularly the case regarding matters of mortality rates and reproduction.

A final area of concern is how to discuss the impact of the prenatal environment on the developing fetus. For the purposes of this unit, I selected dramatic examples of exposure in utero impacting development while avoiding topics that may be connected to the home lives of the students. While a discussion of fetal alcohol syndrome, for example, would be interesting and educational, it could potentially result in a situation where a student experiences stress and concern if a pregnant family member choses to have an alcoholic beverage in the presence of the student.

Sequencing

Because the unit functions through the application of previously acquired content knowledge, there is a lot of flexibility in the order in which the specific genetic disorders or prenatal environmental factors are explored. I decided to group them, first doing the genetic disorders, then teratogens, then by reading an article on the Dutch Hunger Winter to show that other factors affect development as well.[27] Links to the case studies and articles are available in Appendix 3: Teacher Resources. Because the genetic conditions connect to the greatest number of 7th grade science standards, I have chosen them to explain in detail below.

Lessons/Activities

Huntington's Disease

The Huntington's Disease case study moves through a 5 part sequence, completed over 2 days, that investigates a family affected by the disorder. I am modifying the case study "Genetic Testing for Huntington's Disease" from the Life Sciences Learning Center at the University of Rochester.[28] While it appears well designed for a high school level class, it can be simplified and can work well in my 7th grade setting.

In part one, students are introduced to a patient whose grandmother died of Huntington's disease and now that the girl is an adult, she is deciding if she wishes to undergo the genetic testing to determine if she carries the gene. Because students are likely unfamiliar with the disorder, they read a brief description about the disease, how it is inherited, and what problems it causes, and how testing is done. Because the disorder primarily affects brain cells, it is an opportunity to show connections in how one improperly functioning system can affect another. This is different from cystic fibrosis, where one gene affects several systems directly.

Next, students will complete an activity where beads in bags represent the alleles that can be inherited. Students will simulate drawing genes from each parent to determine the genes the offspring receive. Because reading is such a major part of using case studies, students, particularly those with weaker reading skills, will appreciate this approach of mixing in activities.

After the activity, students receive the pedigree chart for the family as is known at this point in the study and they answer questions about it. There is then a script of a conversation between the patient, her father, and her brother. Students will act out the conversation and analyze the various reasons expressed in favor of and against getting genetic tests. If the lesson needed to be condensed, this could be cut without sacrificing the main objectives of the unit, but it does provide a nice opportunity to discuss the real emotions behind these cases.

The final activity in the case study introduces students to repeating mutation on the gene. Using zip lock bags and 2 different lengths of paper, the teacher demonstrates how the different alleles appear during the genetic testing. While explaining a PCR (polymerase chain reaction) machine and gel electrophoresis to middle schoolers may seem to be too much of an enrichment, the simple explanations with visuals keep the information at an accessible level. Instead of doing the simulated Electrophoresis Gel, however, I will color the appropriate sections on the graphic representing the electrophoresis gel so students can see the results. Using this data, students will be able to complete the laboratory reports for the family. This particular activity makes the study of genetics seem more applicable and real world than random worksheets on Punnett squares and pedigree charts.

Cystic Fibrosis

The case study on cystic fibrosis will allow students to incorporate genetics and human body systems. I am modifying the case study "Sometimes it *is* All in the Genes" from the National Center for Case Study Teaching in Science.[29] Because it was originally published in 2003, the final section on gene therapy/treatment options for cystic fibrosis is outdated. The lesson will be subdivided into four parts as they work through the case.

At the beginning, students will read an introduction about the patient, a pregnant woman who is considering finding out if she is a carrier of the gene for cystic fibrosis. In groups of 3, students will use academic conversations to discuss why the patient would or would not want to be tested and identify what they would chose in that situation and why. To research cystic fibrosis and investigate the impact on various human body systems, students will then complete a webquest based on information available from The University of Wisconsin Cystic Fibrosis Center.[30]

Students will then return to the case study, where we discover that the patient is a carrier. She decides to have the father tested as well. Questions the students will answer will allow them to make Punnett square charts showing the mother is a carrier. By comparing a Punnett square where the father is also a carrier to one where he is not, students will be able to discuss the odds of the baby being affected by the disorder.

In part 3 of the case study, we learn that the father is a carrier as well. Students will return to the Punnett squares and determine the likelihood of the child having cystic fibrosis and decide if they would chose to undergo a diagnostic amniocentesis if they were in that situation. In part 4, we find that the child was born with cystic fibrosis. Students will then be able to create a pedigree chart for the family. Part 4 will include updated dialogue about gene therapy that is better in line with current scientific knowledge.[31] We will only read page 1 of part 4 before switching instead to the updated article on gene therapy and cystic fibrosis. Students will then share their opinions in small groups about whether Joshua should be enrolled in a clinical trial or not.

Hemophilia

The hemophilia case study focuses on Queen Victoria's descendants and places a large emphasis on pedigree charts. The case study "Hemophilia: "The Royal Disease" from the National Center

for Case Study Teaching in Science provides the pedigree chart and as it weaves the narrative of the family, asks probability questions that require the use of Punnett Squares to answer.[32] I have modified the case so that my students will be turning in the family tree I provide them into a pedigree chart. The names and correct circle/square diagram has been provided for the main family members. The class will read the first page of the case study together, which sets the stage. Then students will work in small groups to fill out the family pedigree one piece of the family at a time, similar to the sequence in the original case study. First, students will look at the afflicted Leopold and his offspring. They will read the small passage to fill in the pedigree chart for his descendants and answer 3 questions where they create Punnett Squares. Next they will repeat the process for Beatrice and her descendants. Finally, they will look Alice and her descendants, which includes the Russian royal family. This is the larger piece of the family pedigree and the most interesting due to the historical events surrounding the family, much of which ties back to Alexis' hemophilia.

Assessment

Each case study provides its own assessment opportunity. I have sequenced them in this order intentionally. The Huntington's disease activity supports the content with hands on modeling and visuals (using the strips of paper to represent the gene length). The cystic fibrosis activity, by comparison, involves more in depth work with Punnett squares and human body systems and is better positioned later in the unit. The final activity on hemophilia also combines pedigree charts with Punnett squares while including questions on human body systems and could fall later in the unit.

Notes

[1] "Chromosome fact sheet"
[2] "Fertilization"
[3] Slonczewski, Chapter 14
[4] "Embryonic Development"
[5] "Hemophilia - Genetics Home Reference - NIH."
[6] Aronova-Tiuntseva, "Hemophilia," 1.
[7] Aronova-Tiuntseva, "Hemophilia," 4.
[8] "Cystic Fibrosis- Genetics Home Reference- NIH."
[9] "Cystic Fibrosis- Genetics Home Reference- NIH."
[10] "About Huntington's Disease"
[11] "Huntington Disease- Genetics Home Reference- NIH"
[12] "Cystic Fibrosis- Genetics Home Reference- NIH."
[13] "Androgen Insensitivity Syndrome- Genetics Home Reference- NIH"
[14] Vargesson, "Thalidomide-Induced Teratogenesis," 140.
[15] Lerner, "Essential Primary Sources," 291.
[16] Vargesson, "Thalidomide Induced Teratogenesis," 144.
[17] Vargesson, "Thalidomide Induced Teratogenesis," 145.
[18] Vargesson, "Thalidomide Induced Teratogenesis," 148.
[19] Vienna, "Thalidomide use in Brazil," 12.
[20] "The Embryo Project Encyclopedia," "Isotretinoin," 1.
[21] Koren, "Generic isotretinoin," 1567.
[22] Lumey, "Dutch Winter Hunger," 1196.
[23] Zimmer, "The Famine," 1.
[24] Veenendaal, "Transgenerational effects," 550
[25] Weinhold, "Epigenetics," A163.
[26] Weinhold, "Epigenetics," A164.
[27] Zimmer, "The Famine," 1-2.
[28] "Genetic Testing for Huntington's Disease" 1
[29] Galbraith, "Sometimes it is All in the Genes," 1.
[30] University of Wisconsin, "What is Cystic Fibrosis."
[31] "Gene Therapy for cystic fibrosis"
[32] Aronova-Tiuntseva, "Hemophilia," 1-5.

Appendix 1: Implementing Teaching Standards

North Carolina Grade 7 Essential Standards and Clarifying Objectives

7.L.1: Understand the processes, structures and functions of living organisms that enable them to survive, reproduce and carry out the basic functions of life.

7.L.1.3 Summarize the hierarchical organization of multi-cellular organisms from cells to tissues to organs to systems to organisms.

7.L.1.4: Summarize the general functions of the major systems of the human body (digestion, respiration, reproduction, circulation, and excretion) and ways that these systems interact with each other to sustain life.

In this unit, these standards are addressed as we discuss the effects the genetics conditions or prenatal environment on specific human body systems. For students to understand the impact of the conditions and environment, they need to understand general functions of the systems. Seeing how these conditions and environment affect multiple systems shows students that the systems interact. In addition, the topic of early embryo development connects to the progression in complexity from cell to the entire organism.

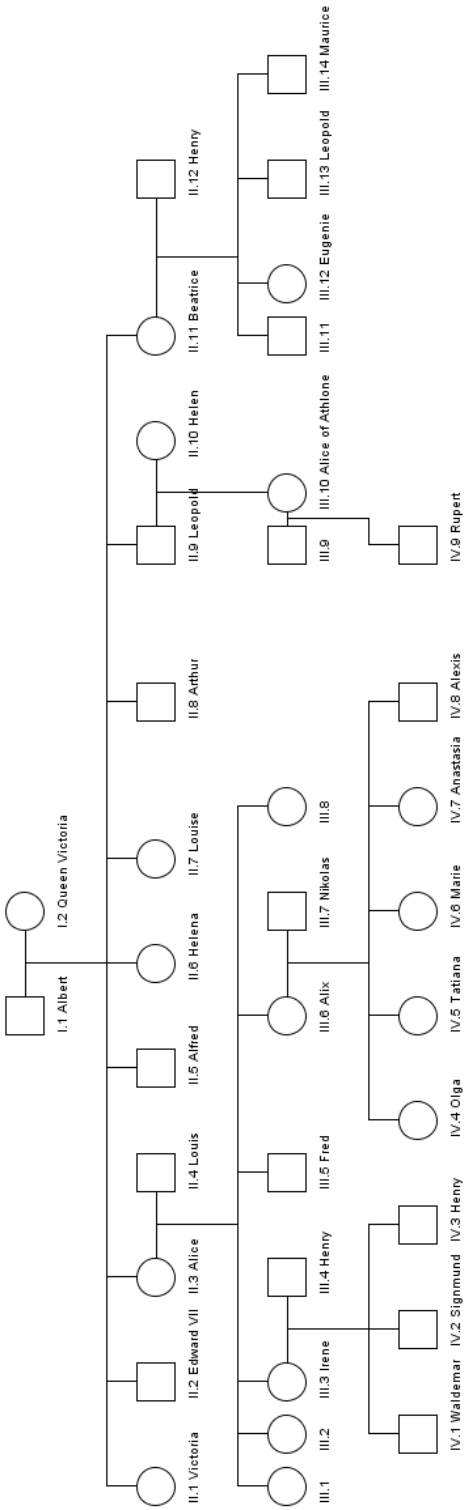
7.L.2: Understand the relationship of the mechanisms of cellular reproduction, patterns of inheritance and external factors to potential variation among offspring.

7.L.2.2: Infer patterns of heredity using information from Punnett squares and pedigree analysis.

7.L.2.3 Explain the impact of the environment and lifestyle choices on biological inheritance (to include common genetic diseases) and survival.

The case studies on prenatal environment connect to the environmental/lifestyle part of this last standard (L.2.3). The genetic conditions studied are inherited in pattern that connect with L 2.2.

Appendix 2: Student Resources



This is the blank pedigree chart I made for students to complete using the free pedigree chart maker at https://www.cegat.de/en/for-physicians/pedigree-chart-designer/

Resources to help students with content

"Course Playlist." Science with The Amoeba Sisters. Accessed October 14, 2019. https://www.amoebasisters.com/playlist.html.
The Amoeba sisters have short videos covering a variety of biology topics. Worksheets are also available for use in the classroom.

Crash Course - Biology. Accessed October 14, 2019. https://thecrashcourse.com/courses/biology.
This website contains all the Crash Course Biology videos. They are high interest and quick paced.

"Developmental Biology Facts for Kids." Developmental biology Facts for Kids. Accessed October 14, 2019. https://kids.kiddle.co/Developmental_biology.
A lot of information on developmental biology is too advanced for a middle school student. This information is more age appropriate. The diagram on Human Embryogenesis is a helpful visual.

Appendix 3: Teacher Resources

Cystic Fibrosis

Galbraith, Anne, and David Howard. "Sometimes It Is All in the Genes." Sometimes It Is All in the Genes - National Center for Case Study Teaching in Science, September 24, 2002. http://sciencecases.lib.buffalo.edu/cs/collection/detail.asp?case_id=235&id=235.
This is the case study I am modifying for the lesson on cystic fibrosis

"Gene Therapy for Cystic Fibrosis." CF Foundation. Accessed October 14, 2019. http:/www.cff.org/Research/Research-Into-the-Disease/Restore-CFTR-Function/Gene-Therapy-for-Cystic-Fibrosis
This is updated information on gene therapy and cystic fibrosis. I like how it compares the types of therapies to modifying a book. I think students will understand the analogy. This link works best when copied and pasted into a browser.

University of Wisconsin Hospitals and Clinics Authority. "What Is Cystic Fibrosis (CF)?" UWHealthkids.org. Accessed October 14, 2019. https://www.uwhealthkids.org/cf-center/what-is-cystic-fibrosis-cf/34311.
This is the website that contains general information on cystic fibrosis for the students. I particularly like how it breaks down the parts of the body affected as it helps make the connections to the human body systems clear.

Huntington's Disease

"Genetic Testing for Huntington's Disease." Genetic Testing for Huntington's Disease - Lessons - Resources - Life Sciences Learning Center - University of Rochester Medical Center. Accessed October 15, 2019. https://www.urmc.rochester.edu/life-sciences-learning-center/resources-lessons/lessons/genetic-testing-huntingtons-disease.aspx.
This is the original case study. There is a student version and a teacher's guide (including a list of all needed supplies).

Hemophilia

Aronova-Tiuntseva, Yelena, and Clyde Freeman Herreid. "Hemophilia: The Royal Disease." Hemophilia: "The Royal Disease". National Center for Case Study Teaching in Science, n.d. http://sciencecases.lib.buffalo.edu/cs/files/hemo.pdf.
This is the original case study. In the student appendix, I have a simpler pedigree chart that shows the family members but has the students determine the individual's carrier, afflicted, not afflicted status.

Article for Dutch Hunger Winter

Zimmer, Carl. "The Famine Ended 70 Years Ago, but Dutch Genes Still Bear Scars." The New York Times. The New York Times, January 31, 2018. https://www.nytimes.com/2018/01/31/science/dutch-famine-genes.html.
This will be read as a class and used in as the basis for a discussion

General Resources to find and adapt case studies

"Genetic Disorders." Genome.gov. Accessed October 14, 2019. https://www.genome.gov/For-Patients-and-Families/Genetic-Disorders.
This website contains information on a wide variety of inherited conditions. Links are also available to learn more about the various disorders. Information here could be used to create case studies, pedigree charts, or Punnett square practice.

"Genetics Home Reference - NIH." U.S. National Library of Medicine. National Institutes of Health. Accessed October 14, 2019. https://ghr.nlm.nih.gov/.
This website also contains a wide variety of information about various genetic disorders.

Herreid, Clyde F., Nancy A. Schiller, Carolyn Wright, and Ky Herreid. "ABOUT." National Center for Case Study Teaching in Science (NCCSTS). Accessed October 14, 2019. http://sciencecases.lib.buffalo.edu/cs/.
This website contains many cases studies that can be adapted for a variety of levels.

"Human Embryogenesis." Khan Academy. Khan Academy. Accessed October 14, 2019. https://www.khanacademy.org/test-prep/mcat/cells/embryology/a/human-embryogenesis.
This site consists of nice visuals and clear information explaining the development of the human embryo.

"Teacher Resources and Lessons." Lessons - Resources - Life Sciences Learning Center - University of Rochester Medical Center. Accessed October 14, 2019. https://www.urmc.rochester.edu/life-sciences-learning-center/resources-lessons/lessons.aspx.
This website consists of a wide variety of lessons related to life science. The Huntington's Disease lesson was adapted for use in this unit.

"Welcome to Teach.Genetics," Teach.Genetics, Accessed October 14, 2019. https://teach.genetics.utah.edu/.
This website contains several units relating to genetics that can be adapted for a variety of levels. Each unit consists of individual lessons that can be taught on their own or as part of the larger unit.

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"Androgen Insensitivity Syndrome - Genetics Home Reference - NIH." U.S. National Library of Medicine. National Institutes of Health. Accessed September 17, 2019. https://ghr.nlm.nih.gov/condition/androgen-insensitivity-syndrome.

Aronova-Tiuntseva, Yelena, and Clyde Freeman Herreid. "Hemophilia: The Royal Disease." Hemophilia: "The Royal Disease". National Center for Case Study Teaching in Science, n.d. http://sciencecases.lib.buffalo.edu/cs/files/hemo.pdf.

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