Lesson 1: Constructing a Pedigree

Engage
1) Present the following scenario to the class: Marge Simpson is disappointed that none of her children have the blue/purple hair that runs in her family. She asks you, a genetic counselor, to analyze her family history and tell her what the likelihood is that her children will have blue/purple haired-children.

2) Introduce students to the symbols used in a standard pedigree (Appendix I) and to the descriptions of the Simpson family members (Appendix II) that Marge has provided. Using input from students, construct a three-generation pedigree of the Simpson family on the board and infer as much about the blue/purple hair phenotype as possible. Discuss with the class, arriving at the conclusion that it probably is not a trait that is inherited in a simple Mendelian manner. Ask students “What information does a pedigree give you? Why might someone who has a medical concern be interested in creating a pedigree?”
   - Appendix I includes the symbol for a consanguineous marriage, which is generally considered a marriage of third cousins or closer.

Explore
1) Divide students into six groups and assign each group to the case history of a family (Appendix III) where chromosome analysis has been ordered either prenatally or soon after birth. Each student will act as a genetic counselor, constructing a pedigree for the family based on the information in the case history. Have students complete the pedigree individually, then work together as a team to build a consensus pedigree. Students should note any significant disease/trait patterns within the pedigree.

2) As homework, have students choose one trait to map by creating a three-generation pedigree of their own family.
   - Exercises that deal with students’ family histories always pose a challenge for those students that may not know much about their families. In these cases, students should create a pedigree for their adopted/foster family, a friend’s family, or a fictional TV/movie/book family.
Appendix I

For individuals, indicate known phenotypes underneath their symbol.

- **P P P** Current pregnancy (gestational age indicated underneath if known)
- **△** Miscarriage (gestational age and cause indicated underneath if known)
- **n n n** Children of unknown number
- **d.** Note age of death and cause (if known)
Appendix II

**ABRAHAM**
Father of Homer and Herb.

**MOTHER**
Mother of Homer.

**CLANCY**
Father of Marge, Patty, and Selma.

**MOHAN**
Mother of Marge.

**PATTY**
Daughter of Clancy and Jackie, sister of Marge, and Selma’s identical twin.

**SELMA**
Daughter of Clancy and Jackie, sister of Marge, and Patty’s identical twin.

**HOMER**
Son of Abraham and half-brother of Homer.

**MARGARET**
Mother of Bart, Lisa, and Maggie, daughter of Clancy and Jackie, sister of Patty and Selma.

**JING**
Selma’s adopted daughter.

**HERB**
Son of Mona and Abraham, half-brother of Herb.

**LISA**
Daughter of Homer and Marge, sister of Maggie and Bart.

**MAGGIE**
Daughter of Homer and Marge, sister of Lisa and Bart.
Appendix III

THE SINGH FAMILY

Neela and Samir Singh are a healthy, nonconsanguineous couple of Indian descent. Mrs. Singh is 30 years old, and this is her first pregnancy. She is currently 10 weeks pregnant.

Given the family history of recurrent first trimester miscarriages, as well as the presence of children with multiple abnormalities and severe developmental delay that died soon after birth, Mrs. Singh’s doctor has recommended that chorionic villus sampling be performed to rule out any structural chromosome abnormalities.

Mr. Singh is 28 years old and reportedly in good health. He has:
- three brothers, ages 26, 31, and 35.
  - The 26 year-old is healthy and has a healthy 3 year-old daughter.
  - The 31 year-old is healthy and has two sons ages 7 and 5.
  - The 35 year-old brother is in good health. His 11 year-old son has been diagnosed with mild intellectual disability, and he has a healthy 8 year-old daughter.

Mr. Singh’s mother is 54 years old, and she has been diagnosed with macular degeneration, which can lead to severe vision loss and even blindness. She has:
- Three sisters who are in their late 50s to early 60s. They are in good health for their age. Each has four healthy children—two boys and two girls each.

Mr. Singh’s father is 55 years old and in good health. He has:
- One brother—aged 60
  - The 60 year-old brother has a 30 year-old daughter who is healthy (she has a twin son & daughter who are 5 years old and in good health) and a 35 year-old son who has no children.

Mrs. Singh reports that a “genetic problem” exists in her family. She remembers being told that she was tested for this family “problem” when she was a little girl and even though she’s perfectly healthy, something is “wrong” with her genetic information. Mrs. Singh does not have any medical documentation of her test results and she explained that her family doesn’t discuss this matter at all. She reports that:
- Two sisters were born with severe birth defects and died shortly after birth.
- Her older 30 year-old brother is healthy and has one healthy 3 year-old son, but he and his wife have experienced three first-trimester miscarriages.
- Her two younger siblings (a brother & a sister) are not yet married and are in good health.

Mrs. Singh’s mother died last year from pneumonia. She was 55 years old. She has
- One living brother (57 years-old) who has three healthy children.
- One sister who died as a child from an accident.

Mrs. Singh’s father is 57 years old. He suffers from severe depression due to the loss of his wife.
- His sister and his brother produced several children that were born with severe birth defects and died shortly after birth.
Calvin and Cherise Jackson are a healthy nonconsanguineous couple of African American ancestry. Mrs. Jackson is 33 years old, and is currently 9 weeks pregnant. Given their previous pregnancy history, they are very concerned about the health of their fetus. They requested that chorionic villus sampling be performed to rule out any fetal chromosomal abnormalities.

Mrs. Jackson is 33 years old, and she suffers from asthma, for which she requires medication and an inhaler. Mrs. Jackson reports that she was adopted, and she has no history about her biological parents.

- This is the couple’s fourth pregnancy together—they have a 3 year-old daughter who was born with a cleft lip, which was surgically repaired. Mr. and Mrs. Jackson have also experienced two first-trimester miscarriages.

Mr. Jackson is a healthy, 35 year-old man, and he has a healthy 10 year-old daughter from a previous marriage. Mr. Jackson has identical twin brothers who are 32 years old.

- One brother has two children—a healthy 4 year-old son and a 2 year-old daughter who has been diagnosed with sickle cell anemia.
- The other brother and his wife are currently expecting their first child.

Mr. Jackson’s mother is 67 years-old and she suffers from diabetes.

- She has two brothers. Her two brothers (aged 70 and 72) also have diabetes.
  - The eldest brother has two healthy daughters in their 50s.
  - Her other brother had a son that had sickle cell anemia and died from complications of the disease when he was 14 years old. He also has a healthy daughter who is in her 40s and is reportedly in good health.

Mr. Jackson’s father is deceased—he passed away of complications from a massive stroke when he was 66 years old. He was an only child.
THE RAMIREZ FAMILY

Rosa and Juan Ramirez are a healthy nonconsanguineous couple from Ecuador. Mrs. Ramirez is 23 years old and is currently 20 weeks (5 months) pregnant.

A few weeks ago, when she was 15 weeks pregnant, Mrs. Ramirez opted to have a prenatal screening test performed on her blood. A screening test is not diagnostic—it can only suggest a statistical possibility that a problem may exist.

Mrs. Ramirez’ screening results indicated an increased chance that her fetus might have a chromosome abnormality.

An ultrasound was performed to take fetal measurements and to rule out any structural abnormalities. It revealed that the fetus has

- shortened femur (thigh) bones,
- an enlarged head,
- and a serious heart defect.

These abnormal ultrasound results, coupled with the abnormal blood screening test results prompted Mr. and Mrs. Ramirez to have the amniocentesis. Mr. and Mrs. Ramirez’ obstetrician hopes to obtain information about the fetal chromosomes and determine if the abnormal ultrasound findings are the result of a chromosome problem.

Mrs. Ramirez has one sister and four brothers:

- This is the couple’s third pregnancy together—they have one healthy 2 year-old daughter and have experienced one spontaneous miscarriage that occurred in the first trimester.
- Her 25 year-old sister was diagnosed with juvenile diabetes as a child. She has healthy 2 year-old non-identical twin girls.
- Her 21 year-old brother is healthy and is expecting his first child.
- Her remaining 3 brothers are still in Ecuador, and they’re all younger than 17 years old. (no children)

Mrs. Ramirez’s mother is 56 years old, and she had a hysterectomy last year (her uterus removed) because of uterine cancer.

- She has three older sisters who are all in their 60s. They all have children who are reportedly in good health. Mrs. Ramirez doesn’t have much information about her mother’s family history.

Mrs. Ramirez’ father was killed in an accident when he was 53 years old.

- He had several brothers and sisters, but Mrs. Ramirez has no information about them or their children. She is unaware of any birth defects or developmental delays in his family.

Mr. Ramirez is a healthy 25 year-old man who has been diagnosed with asthma. He has

- Two older sisters (ages 27 and 29) who have both experienced first-trimester miscarriages. His 27 year-old sister had two miscarriages and has no living children, and his 29 year-old sister had three miscarriages and has a 5 year-old son with Down syndrome.
- Mr. Ramirez reports that his father is an only child. His parents (Mr. Ramirez’s grandparents) experienced five first trimester miscarriages, and he had a sister who was born with multiple birth defects. She died when she was 2 years old.
- Mr. Ramirez’s mother is healthy and in her late 50s. Both of Mr. Ramirez’s parents live in Ecuador, and he does not have the opportunity to see them as often as he would like.
THE WOLF FAMILY

Jill and Mitchell Wolf are a healthy, nonconsanguineous couple of French Canadian and Eastern European Jewish ancestry. Mrs. Wolf is 31 years old, and this is her third pregnancy.

A routine 20-week ultrasound to observe the fetal anatomy revealed multiple abnormalities:

- a narrowing of the aorta—the main artery of the heart,
- a large single kidney spanning across the abdomen called a horseshoe kidney),
- and an accumulation of fluid at the base of the fetal neck was noted.

Mr. and Mrs. Wolf elected to pursue the amniocentesis procedure to determine whether the observed pattern of anomalies represents a chromosomal disorder.

Mrs. Wolf is originally from Montreal, Canada. She has:

- a healthy 9 year-old son from a previous marriage.
- a healthy 5 year-old daughter with Mr. Wolf.
- one older brother. He has a healthy 16 year-old daughter and a 13 year-old son who was born with a heart defect that was repaired after birth.

Mrs. Wolf’s mother is 53 years old and has been diagnosed with breast cancer. She’s currently receiving radiation therapy. She has:

- a 60 year-old sister who was diagnosed with skin cancer in her mid-50s. She has three healthy children in their 30s. All have healthy children.

Mrs. Wolf’s father is 66 years-old, and he has high blood pressure. He has:

- one younger, 52 year-old brother who has one daughter who was adopted from Korea when she was an infant.

Mr. Wolf is 40 years old. He has a healthy 11 year-old son from a prior marriage.

Mr. Wolf’s mother is in her 70s and she has been exhibiting early signs of Parkinson’s disease. She has:

- two brothers in their late 60s.
- One had a heart attack last year. He has two daughters, who each have a son and a daughter.

Mr. Wolf’s father is in his mid-70s. He suffered a mild stroke 3 years ago and has been in physical therapy since. He had:

- one sister who died in a car accident when she was 68 years old. She had three children—two daughters and one son. They are currently alive and well. Each has one son.
THE DOHERTY FAMILY

Sean and Karen Doherty are a healthy nonconsanguineous Caucasian couple. Mr. Doherty reports that his family originates from Ireland and Scotland, while Mrs. Doherty’s family is of completely Swedish descent. Mrs. Doherty is a healthy 42 year-old-woman who is currently 16 weeks (4 months) pregnant. This is the couple’s third pregnancy together—they have two healthy sons, aged 5 years and 8 years. Mrs. Doherty’s obstetrician recommended that she have an amniocentesis performed because she is AMA—of advanced maternal age.

Mrs. Doherty has:
- one 38 year-old sister in good health with two healthy daughters ages 4 and 3.
- Mrs. Doherty’s father is 79 years old, and he suffered a heart attack last year. He has
  - one healthy 80 year-old living sister, who has two sons (ages 58 and 53) that both are in good health for their age.
  - Mrs. Doherty’s mother is 75 years old and in good health.
- She had one brother who died when he was 76 from a stroke. This brother had a daughter who died when she was 13 years old from a “breathing problem.” Mrs. Doherty has no further information about this relative.

Mr. Doherty is a 45 year-old man in good health. He has an adopted 40 year-old sister, who has three daughters who are all healthy.
- Mr. Doherty’s mother is 75 years old, and she has diabetes. She is an only child.
- Mr. Doherty’s father is 76 years old, and he had two sisters.
  - One sister was born with Trisomy 21 and died from heart problems when she was 20 years old.
  - His other sister is 70 years old and in good health for her age. She never had any children.
THE GREENE FAMILY

Tina Greene is a 26 year-old woman of Scottish, German, and French ancestry who delivered her third child early yesterday morning. She and her husband Carl, who is 24 years old and of German and Irish descent have healthy 18 month-old fraternal twin sons.

The medical staff in the nursery observed that the newborn:

- is smaller than expected,
- has poor muscle tone (a “floppy” baby),
- and has a larger than normal space between the big and second toes on both feet.

The physician taking care of Mrs. Greene ordered that chromosome analysis be performed on the newborn’s blood to rule out any chromosome abnormalities.

Mrs. Greene has one brother and one sister.

- Her brother is 30 years old, and he does not have any children.
- Her sister is 35 years old, and she has a healthy 5 year-old son.

Mrs. Greene’s mother is 54 years old and has back problems. She has

- A 58 year-old brother who has prostate cancer
  - He has a 36 year-old daughter who is obese. She has
    - a 3 year-old son who has a hearing problem and
    - a 6 year-old daughter who is in good health.
- A brother who died when he was 25 years old in the Vietnam War
- A 66 year-old sister who is beginning to show signs of dementia. She has
  - a healthy 30 year-old daughter who is expecting her first child in June.

Mrs. Greene’s father is 58 years old and is an alcoholic. He is not involved with the family and left three years ago. He has

- a 62 year-old sister who is a nun in Ireland and
- a 55 year-old sister in good health who has three healthy sons.

Mr. Greene has

- a 28 year-old brother with developmental delay resulting from exposure to alcohol as a fetus (fetal alcohol syndrome, FAS).

Mr. Greene’s mother is 58 years old and has recently been diagnosed with lung cancer from smoking. She is not currently in good health. She has

- a 63 year-old sister who is healthy and has two healthy sons—they have healthy children as well.

Mr. Greene’s father is 60 years old, an only child, and he has insulin-dependent diabetes.