

Block 2: The Human Blueprint
Week 6: Genes Gone Wrong
Case 9: Greg and Michelle Johnson
STUDENT VERSION



GOAL

The students will explore cystic fibrosis as it relates to population risk calculations and its phenotypic effect on growth limitation.

LEARNING OBJECTIVES

To be released at the end of the IQ week.

CASE VIGNETTE

Greg and Michelle Johnson are a young Caucasian married couple, each 25 yrs. old. Michelle is 12 weeks pregnant and both are present for a prenatal appointment with Michelle's obstetrician, Dr. Judy Carver. During the visit, Dr. Carver discusses various screening tests, including the quad screen and cystic fibrosis genetic analysis. She explains to the couple that she is following the American College of Obstetrics and Gynecology (ACOG) guidelines for expecting couples.

Michelle is not interested in the quad screen, but is interested in screening for cystic fibrosis because one of her first cousins has this disorder.

Dr. Carver explains that, by using the Hardy Weinberg equilibrium, she can calculate the odds that Greg and Michelle have for their child to develop cystic fibrosis or CF. She tells them that they have an *a priori* risk of 1 in 2500 for having a child with CF based on their ethnic background alone. Dr. Carver then estimates that Michelle's risk for having a child with CF would increase to 1 in 400, given she has a first cousin with CF. Even though the couple is confused, Michelle has blood drawn for screening of mutations in the CF gene.

Michelle returns to Dr. Carver's office for a follow-up visit and to learn about her screening results. The CF testing demonstrates that she is a carrier of the $\Delta F508$ CFTR mutation.

The couple is nervous at first. Dr. Carver explains that the risk that their child has for developing CF depends initially on Greg's population risk of being a carrier of a CFTR mutation, but this risk is modified either up or down depending upon whether a mutation is also discovered in Greg. Their *a priori* risk is now 1 in 100 for having a child with cystic fibrosis. Greg decides to undergo the screening test, and they are much relieved when they learn that Greg's screening test is negative for CFTR mutations.

Greg and Michelle's son, Brian, was born at term without any difficulties. His birthweight, length, and head circumference was normal. His Ohio Newborn Screen is normal, but he born two months prior to the

implementation of immunoreactive trypsinogen test now required of all babies born in Ohio. At two months of age and on subsequent visits, however, Brian's weight begins to drop, which causes some concern by his pediatrician, Dr. Kidd. He reviews the information from Brian's grow chart and finds that Brian's weight has crossed from his original weight at the 75th percentile to less than the 3rd percentile. Based on his weight for length being below the third percentile, Dr. Kidd diagnoses Brian with "failure to thrive." Numerous formula changes and caloric supplementation are attempted without success.

At six months of age, Brian is admitted to the hospital with pneumonia. During the admission, an additional finding of copious foul smelling stools is discovered. The parents had not told Dr. Kidd about this before, as they thought it was the result of formula changes. Dr. Kidd asks for the gastroenterology and pulmonary specialists to review Brian's hospitalization and was surprised that both consultants think that cystic fibrosis could be a cause. He then orders a sweat chloride test which was positive for CF. Greg and Michelle want to know how this could happen, since they had prenatal CF screening and were told that Greg's screening test was negative for CF.