Case 7
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Tom is a 42-year-old male who enjoys walking his dog Loki in the woods behind his house. One evening in the woods, he notices ripe wild berries that he cannot identify. Tom decides to take a handful of them to snack on during the rest of his walk. That evening, Tom experiences stomach discomfort prior to bed.

The next day Tom hurries to his local hospital after contracting a fever (100 F) and discovering scaly patches on his hands and forearms. His blood test is positive for fungal cell wall components. Tom’s doctor diagnoses him with fusariosis, a fungal infection caused by *Fusarium*, from the wild berries that he consumed the previous day. Tom is in need of a strong antifungal drug.
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• The prescriber is treating Tom with:

  Voriconazole (Vfend)

• Question 1: How does this drug work to treat fungal infections?

  Hint: pharmacodynamics; use https://www.pharmgkb.org/annotatedDrugs
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- Metabolism of Voriconazole:

  Voriconazole $\xrightarrow{\text{Liver}} \text{CYP2C19} \xrightarrow{\text{Inactivation of Voriconazole}} \text{Removal from body}$

- Key pharmacogene for Voriconazole: $\text{CYP2C19}$
You recommend preemptive testing of Tom’s CYP2D6 genotype before initiating voriconazole therapy. In the meantime, you have the genotypes of Tom’s parents in the electronic medical records.

Dad: *1/*2  
Mom: *6/*17
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• Question 2: What genotypes and phenotypes are possible for Tom based on mom and dad’s genotype?

<table>
<thead>
<tr>
<th>Possible Genotypes (*X/*X)</th>
<th>Phenotype (Poor/Normal/Intermediate/Ultrarapid Metabolizer)</th>
<th>Drug Therapy Recommendation (Use/Don’t Use/Change Dose)</th>
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Use This Website To Look Up Genotype-Based Dosing: https://www.pharmgkb.org/guidelineAnnotation/PA166161537
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• Tom underwent genotyping and you have received the results from the laboratory.

\[ CYP2C19: \ast 1/\ast 17 \]

• Question 3: What is Tom’s phenotype?

• Question 4: What do you recommend for their treatment? Why (better or worse benefit/toxicity)?