

Deacon's Challenge

No. 36 Answer

The incidence of the Gilbert genotype is common in the US and Europe. If the incidence of the variant bilirubin-UGT (UGT1A1) promoter associated with Gilbert's in a population is 9%, what proportion of the population carry at least one copy of the variant promoter? (Assume Hardy-Weinberg equilibrium applies).

MRCPath, November 2003

Gilbert's follows an autosomal recessive mode of inheritance. If the normal promoter, A, has an incidence p and the variant promoter, a, has an incidence q , then according to the Hardy-Weinberg equilibrium, the distribution of the genotypes AA, Aa and aa will be p^2 , $2pq$ and q^2 respectively.

The incidence of the Gilbert genotype, aa, is q^2 which we are told is 9% (0.09).

Therefore, $q = \sqrt{0.09} = 0.3$

and since $p + q = 1$, it follows that $p = 1 - q$, i.e. $p = 1 - 0.3 = 0.7$

The genotype AA (incidence p^2) is the only one without at least one copy of the variant promoter

$$p^2 = 0.7^2 = 0.49$$

Therefore the proportion of the population with at least one copy of the variant promoter

$$\text{(i.e. } q^2 + 2pq) = 1.0 - 0.49 = \mathbf{0.51 \text{ (51%)}}$$

Question No. 37

The analytical imprecision (Cva) of serum iron in your laboratory is 10%. Iron was measured on several occasions in healthy volunteers, and the within-subject coefficient of variation of the measured iron results was found to be 15% (calculated using nested ANOVA).

Estimate the true biological coefficient of variation in serum iron.

Calculate the expected coefficient of variation of the results in these volunteers if the analytical procedure is performed in duplicate (on a single sample per patient with results expressed as the mean of the duplicate determinations) instead of singlicate.

MRCPath, November 2003