Hardy-Weinberg law

The Hardy-Weinberg law states that both allele and genotype frequencies will remain constant from generation to generation in an infinitely large, interbreeding population in which mating is at random and there is no selection, migration or mutation (Hardy, 1908). Under conditions of Hardy-Weinberg equilibrium, expected genotype frequencies may be derived from population allele frequencies. Consider a polymorphism with three alleles A, B and C having frequencies p, q and r, respectively (Table 1).

Table 1. Derivation of expected genotype frequencies under conditions of Hardy-Weinberg equilibrium for a three allele system

Female parental gamete frequencies		Male parental gamete frequencies: **A** **p**	**B** **q**	**C** **r**
	A p	AA p^2	AB pq	AC pr
	B q	AB pq	BB q^2	BC qr
	C r	AC pr	BC qr	CC r^2

The sum of the allele frequencies $= p + q + r = 1$.

The sum of the genotype frequencies $= p^2 + 2pq + q^2 + 2pr + 2rq + r^2 = 1$

$= (p + q + r)^2$

Problem 1. Extend HWE to trisomy 21

Parental Hardy-Weinberg allele frequencies and genotype distributions

The chromosome 21genotype frequencies for individuals with trisomy 21 do not conform to Hardy-Weinberg expectations as this equilibrium was derived to apply to diploid populations. However, if the parents of individuals with Down syndrome were a random sample drawn from population in Hardy-Weinberg equilibrium, the chromosome 21 genotype distribution in individuals with trisomy 21 might be expected to be predicted by their parental genotypes.

Consider a two allele polymorphism with alleles A and B, with frequencies of p and q. Assume that nondisjunction has occurred at meiosis I, and that no crossing-over has taken place. Assume also that the nondisjoining parent may contribute gametes AA, AB or BB, with frequencies p^2, 2pq and q^2 respectively (expected genotype frequencies are derived as above; Table 2a).

Table 2a **Derivation of expected genotype frequencies for the inheritance of three alleles (A and B) in trisomy 21; meiosis I nondisjunction**

		Disjoining parental gamete frequencies		
		A	**B**	
		p	**q**	
Nondisjoining parental gamete frequencies	**AA**	AAA	AAB	
	p^2	p^3	p^2q	
	AB	AAB	ABB	Children's genotypes and their expected frequencies
	2pq	$2p^2q$	$2q^2p$	
	BB	ABB	BBB	
	q^2	pq^2	q^3	

The sum of the allele frequencies $= p + q = 1.$

The sum of the genotype frequencies $= p^3 + 3p^2q + 3q^2p + q^3 = 1$

$$= p^3 + 3pq(p + q) + q^3 = 1$$

$$= p^3 + 3pq + q^3$$

Table 2b Derivation of expected genotype frequencies for the inheritance of three alleles (A and B) in trisomy 21; meiosis II nondisjunction

Disjoining parental gamete frequencies

Nondisjoining parental gamete frequencies		A	B	
		p	**q**	
	AA	AAA	AAB	Children's genotypes and
	p	p^2	pq	their expected frequencies
	BB	ABB	BBB	
	q	pq	q^2	

The sum of the allele frequencies = $p + q = 1$.

The sum of the genotype frequencies = $p^2 + 2pq + q^2$

Homozygotes AAA and BBB are represented by the frequencies p^3 and q^3 respectively, while heterozygotes AAB and ABB are represented by the frequencies $3p^2q$ and $3pq^2$, respectively.

This derivation is an oversimplification, not accounting for chromosome 21 nondisjunction having occurred at the second meiotic division or for recombination.

The possible genotypes of the nondisjoining parent are AA, AB and BB with expected frequencies p^2, 2pq and q^2. If nondisjunction occurs at the second meiotic division the only possible gametes are AA and BB. A heterozygous individual would produce gametes AA or BB, each with a frequency of pq. Homozygous individuals would produce the gametes AA or BB with frequencies of p^2 and q^2, respectively. The nondisjoining parent would thus produce the gametes AA with the frequency $p^2 + pq = p(p + q) = p$ and BB with the frequency $q^2 + pq = q(p +q) = q$ (Table 2b).

Homozygotes AAA and BBB are represented by the frequencies p^2 and q^2 respectively, while heterozygotes AAB and ABB are each represented by the frequency pq.