

FIGURE 1 : Relationship Between Drug Pressure and Amount of Drug-Resistant HIV

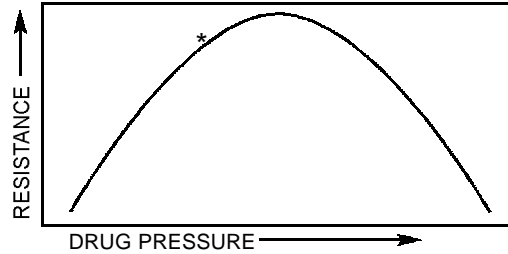


Figure 1 represents the relationship between the amount of drug pressure applied to HIV versus the viral drug-resistance that develops. At the extreme left of the curve, there is absolutely no drug pressure applied to the virus, and thus the amount of viral mutation that occurs and results in drug-resistant virus is very low. As drug pressure increases, however, the virus must mutate and become drug-resistant if it is to continue to "survive," or replicate. Drug-resistant virus is most likely to occur when there is enough drug pressure to select for drug-resistant virus, but not enough to significantly suppress viral replication (the star on the left side of the graph illustrates such a situation, for example, when patients are not adherent to their medications). At the far end of the graph, there is again little drug-resistant virus present because there is enough drug pressure to significantly inhibit viral replication. This makes the likelihood of a drug-resistant mutation small, as there are so few copies of the virus being made at any given time (this often occurs when a patient is on successful ARV treatment).

TABLE 1 : Advantages and Disadvantages of Genotypic and Phenotypic Testing¹⁷

ADVANTAGES	DISADVANTAGES
Genotypic Assays	
<ul style="list-style-type: none"> ♦ Less expensive (\$300 to \$480/test) ♦ Short turn-around (1-2 weeks) ♦ May detect presence of resistance mutations before they have affected phenotypic resistance 	<ul style="list-style-type: none"> ♦ Detect resistance only in dominant species of virus (>20% of patient's isolates) ♦ Interpretation requires understanding and knowledge of mutational changes (i.e. expertise) ♦ Technician experience may influence results ♦ May show discrepancy with phenotype ♦ Require viral load > 1000 copies/mL
Phenotypic Assays	
<ul style="list-style-type: none"> ♦ Interpretation more analogous to resistance testing of bacteria ♦ Assesses 3-dimensional molecule, including mutations and mutational interactions ♦ Reproducibility is good ♦ Advantage over genotype when multiple mutations exist 	<ul style="list-style-type: none"> ♦ More expensive (\$800-\$1000) ♦ Longer delay in reporting (2-3 weeks) ♦ Thresholds to define susceptibility to drug are arbitrary and non-standardized; do not always reflect achievable drug concentrations ♦ Detect resistance only in dominant species (>20% of patient's isolates) ♦ Require viral load >500-1000 copies/mL