

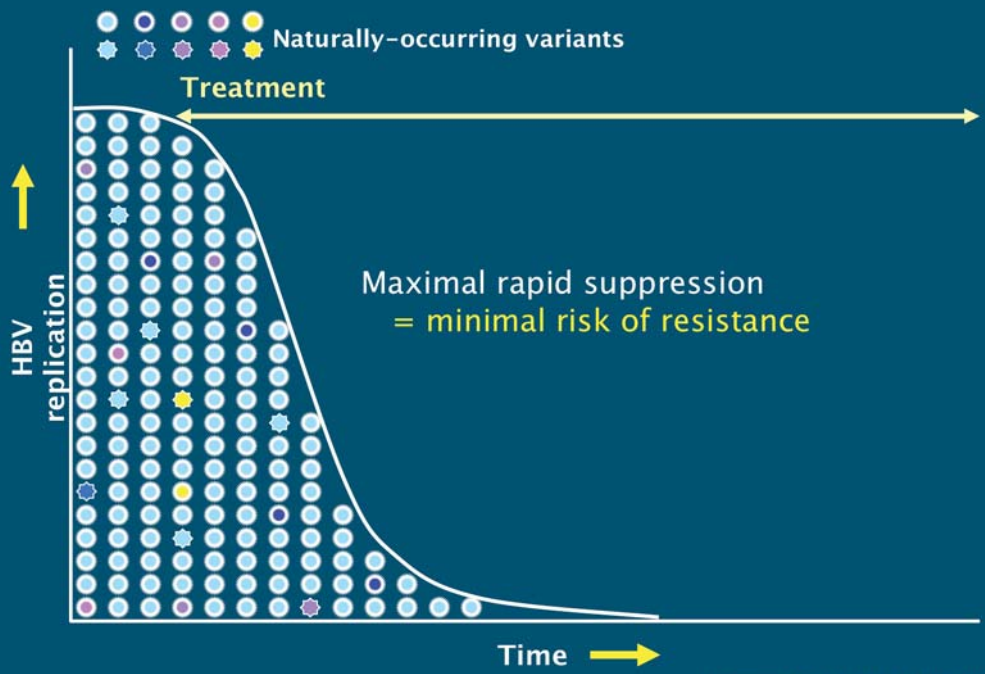
Hepatitis B Antiviral Drug Resistance: Navigating the Way Forward

Professor Stephen Locarnini

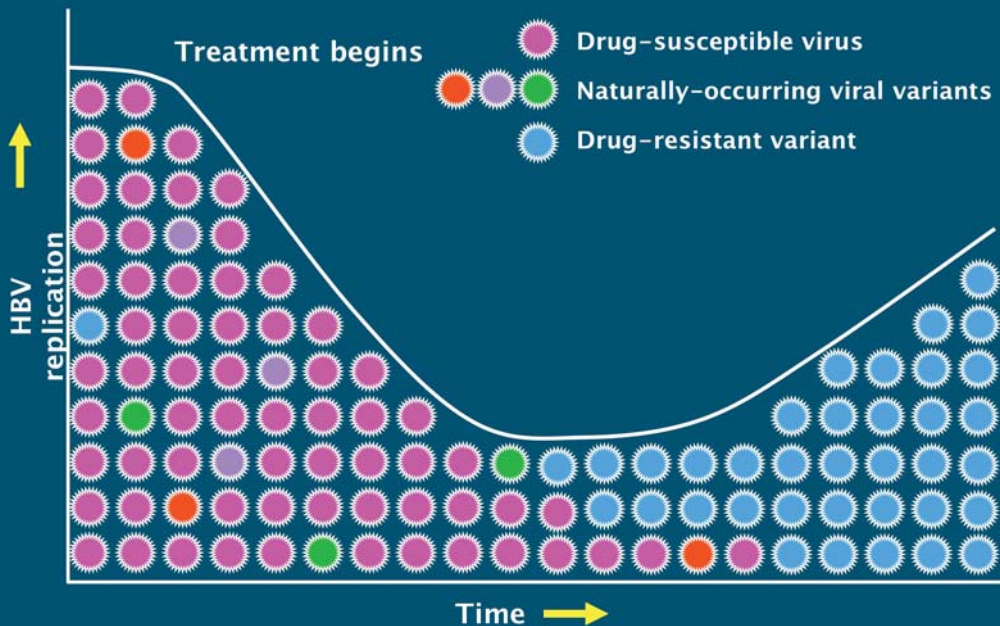
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How Does Antiviral Drug Resistance Occur?

Drug Potency and Maximal Suppression of Viral Replication



Incomplete Suppression of Viral Replication Allows the Selection of Resistant Virus



Viral Replication and Mutational Frequency

- High virion production: 10^{12-13} virions per day
- Wild-type HBV Pol lacks proof-reading function
- High mutational rate: 10^{-5} substitution/base/cycle
- 10^{10-11} point mutations produced per day
- All possible single base changes can be produced per day
- Single / double mutations pre-exist in HBV from patients prior to therapy:

WHY MOST MONOTHERAPIES FAIL

- Triple / quadruple mutations require replication in the presence of selection pressure and rarely pre-exist:

WHY COMBINATION TREATMENT WORKS