

What is the most Important Indicator of Risk ? Mean, AUC, Maximal Change, Central Tendency, Categorical Changes, and Potential PK/PD Modeling

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Considerations with Drug-Induced Hypertension

Dose-dependency

Inherent susceptibility

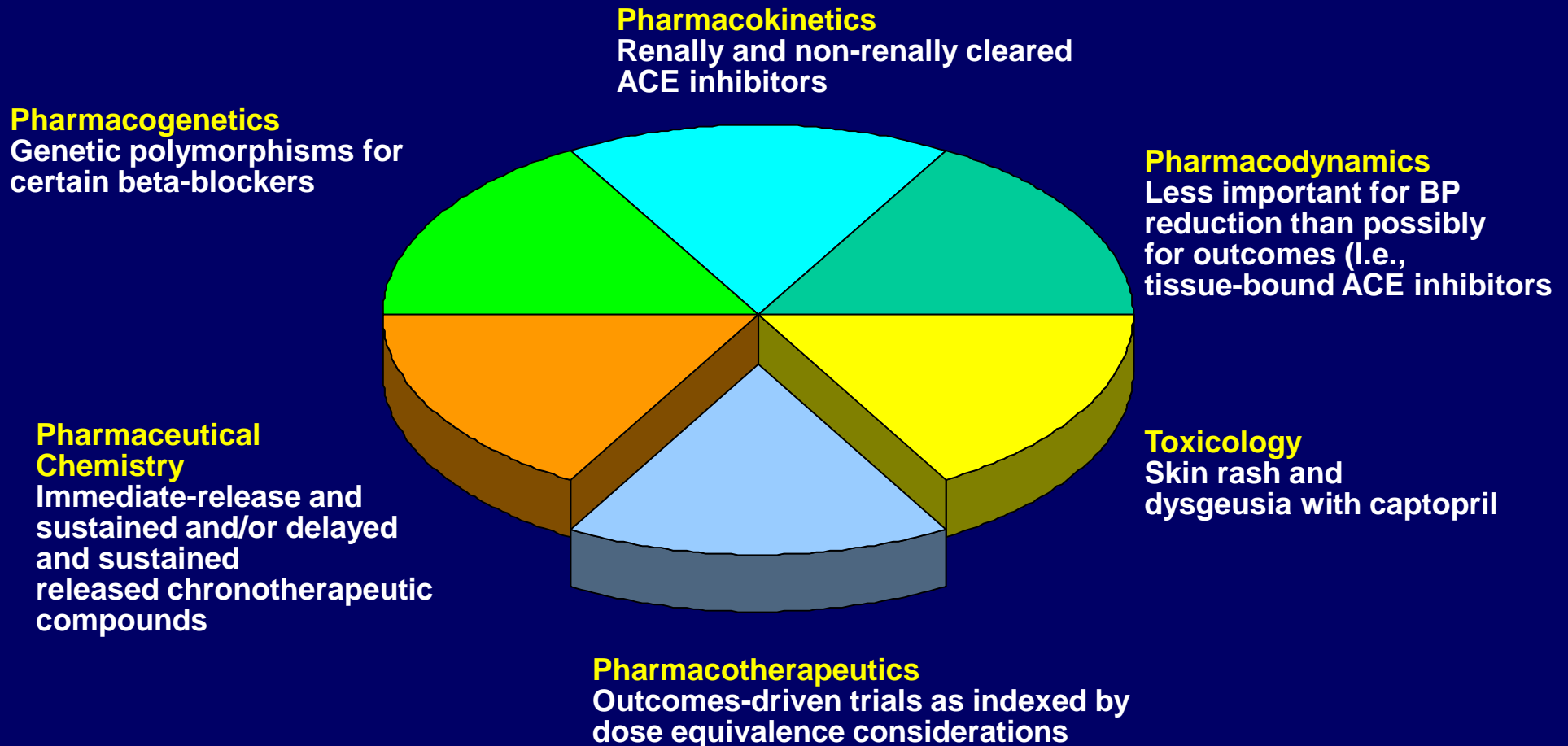
Relationship to frequency of dosing

Immediate or sustained release

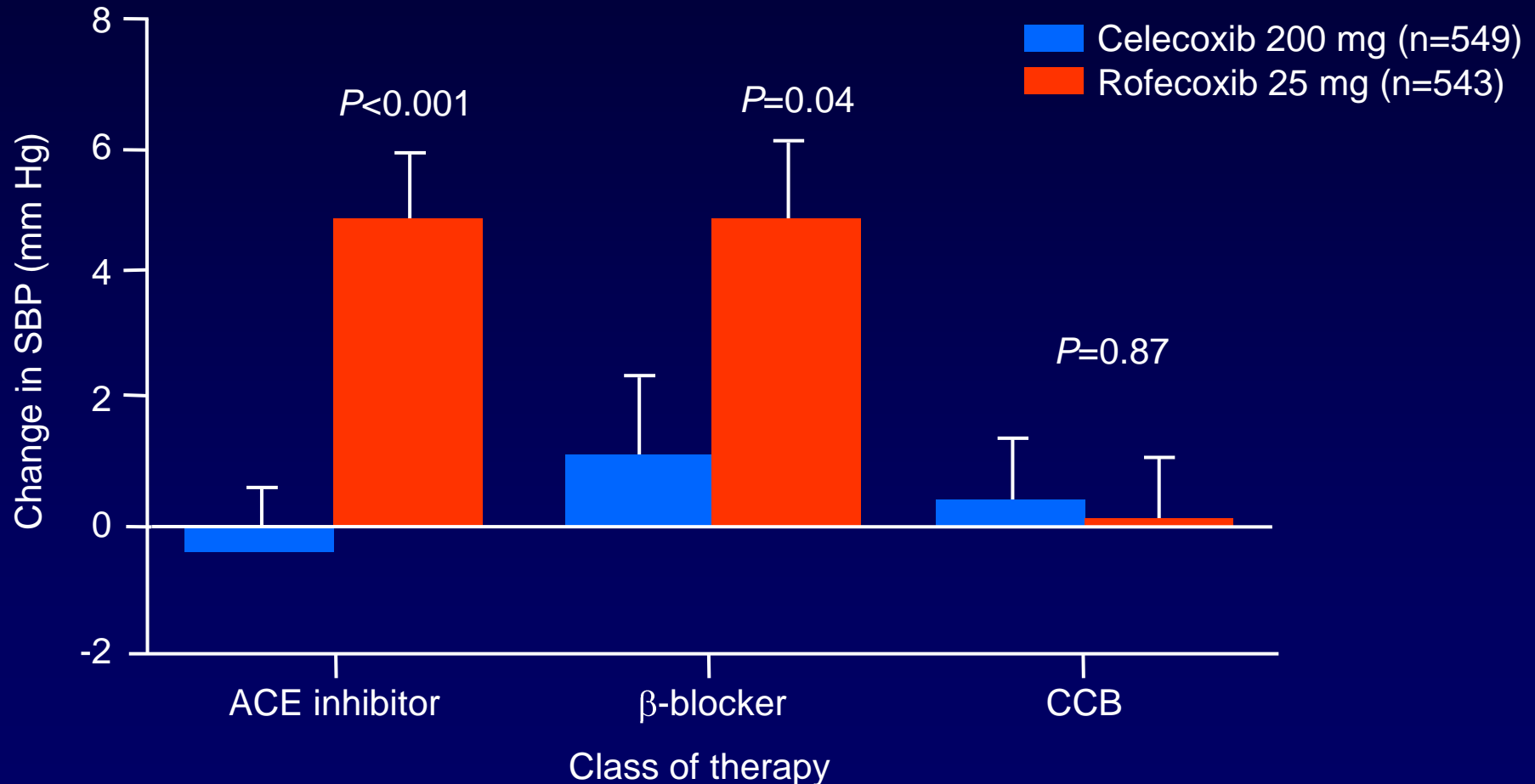
Class effect

Influence of concomitant antihypertensive medications

Multiple Points of Differentiation Amongst Drug Class Members

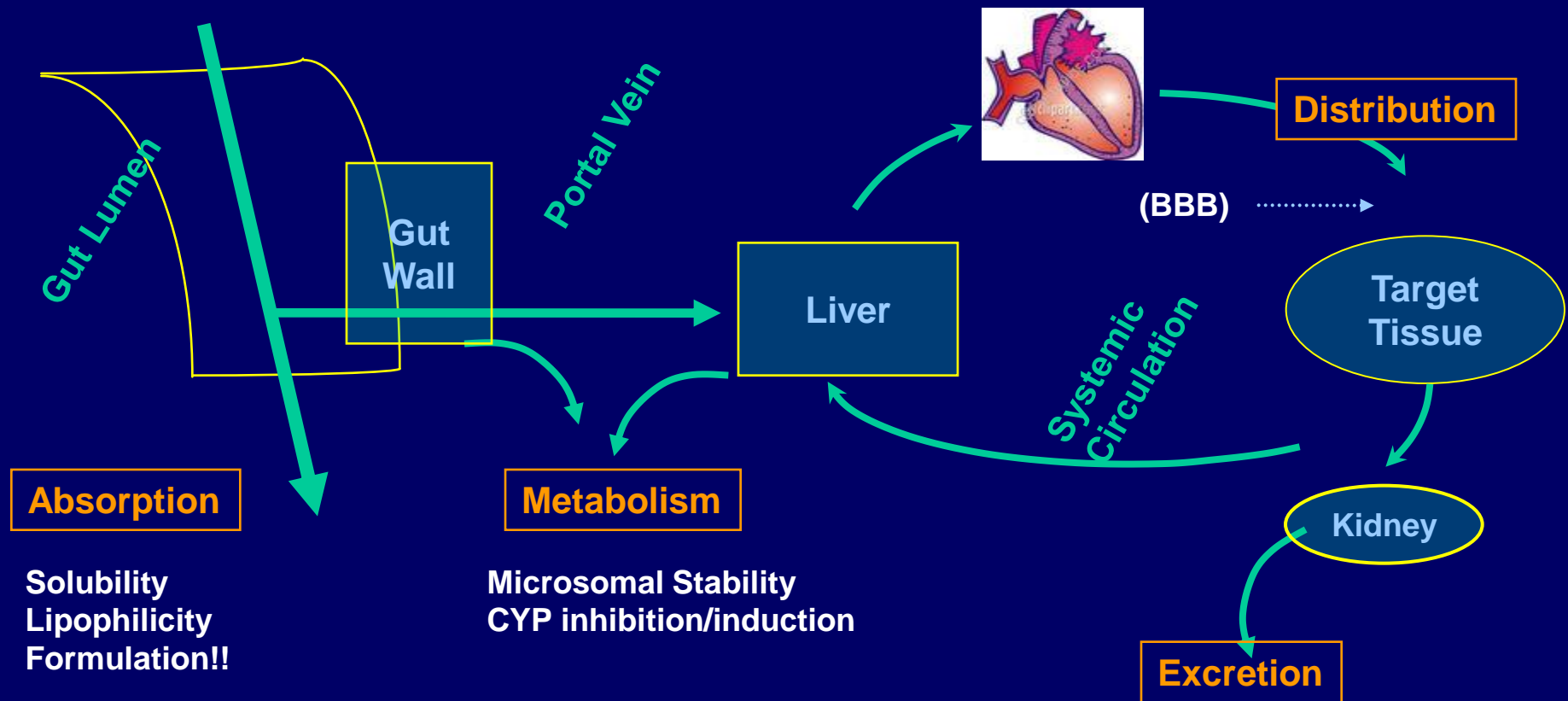


Effects of COX-2 Selective Inhibitors on Systolic BP in Treated Hypertensives

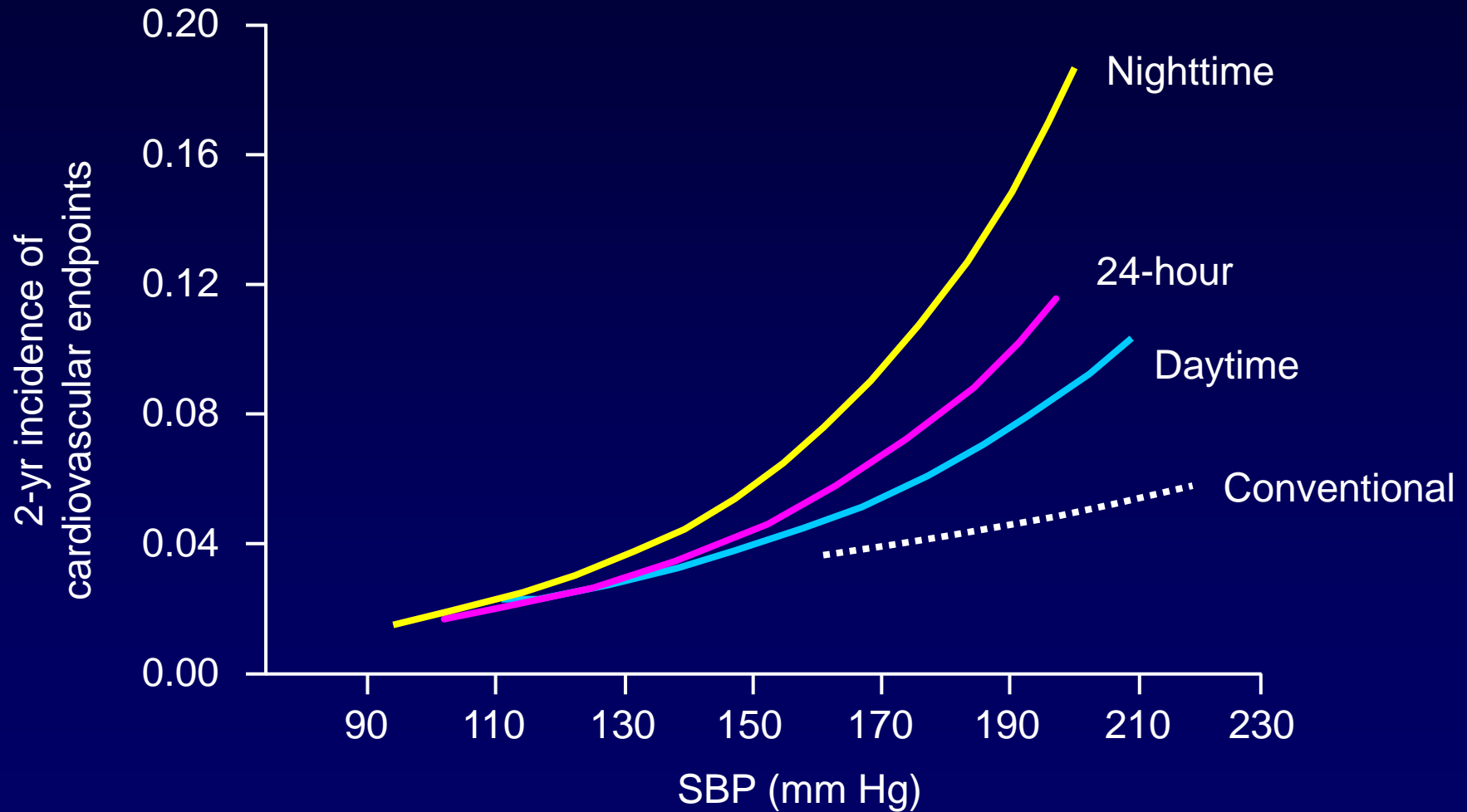


Pharmacokinetics ADME

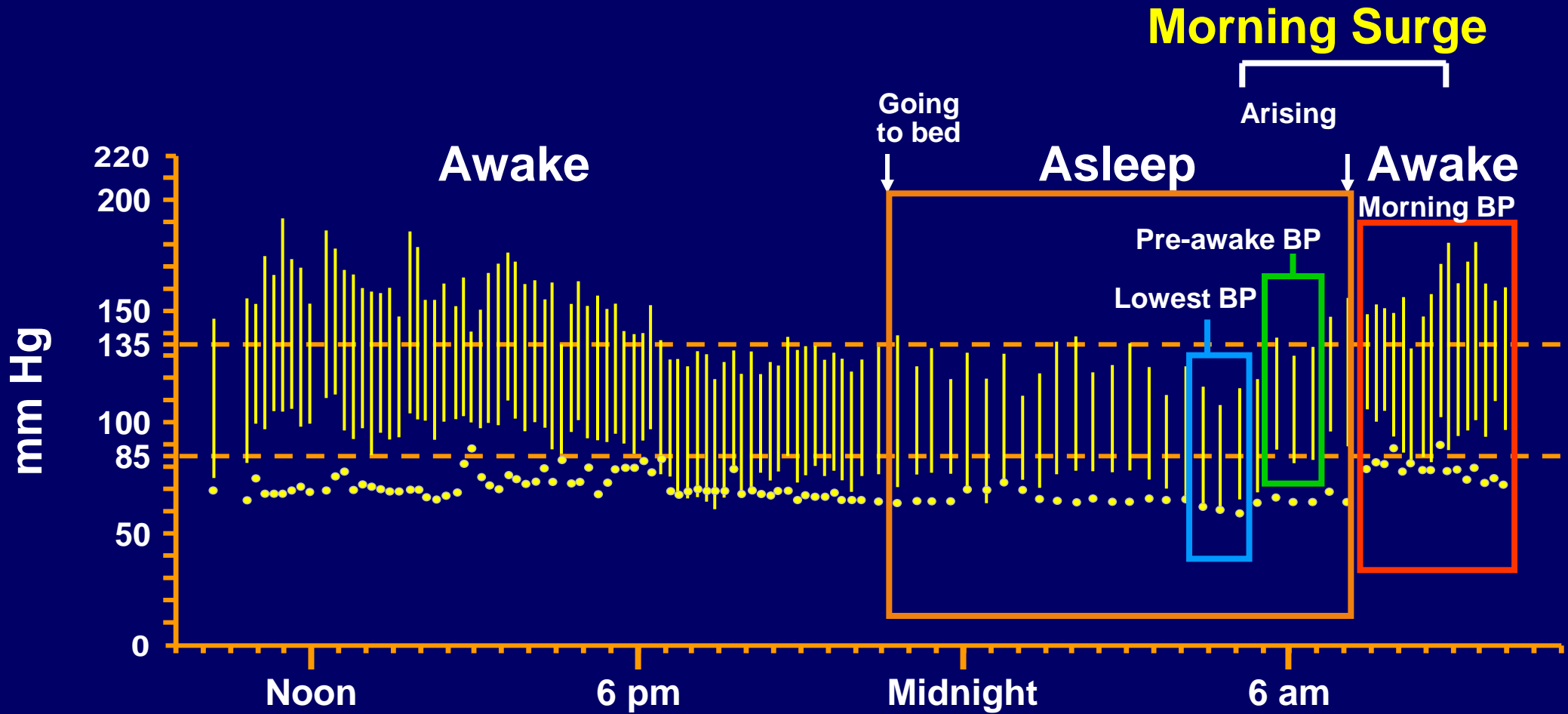
Ultimate goal is to have an adequate exposure and duration of the drug at the target tissue, as normally extrapolated from systemic (blood) concentration.



Conventional, 24-Hour, Daytime, and Nighttime SBP as Predictors of CV Endpoints: Syst-Eur

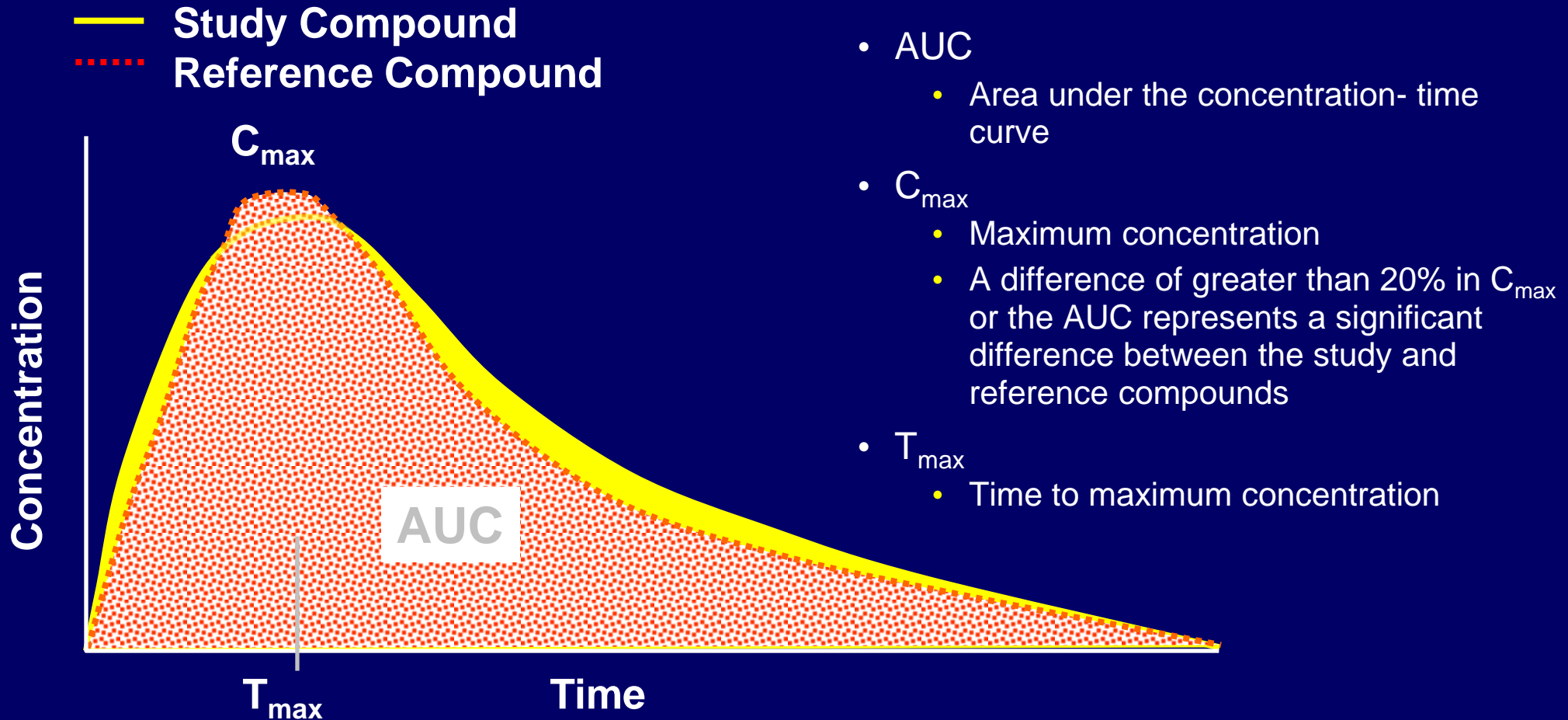


24-Hr Ambulatory Blood Pressure



Pharmacokinetic Studies

Key Measurements

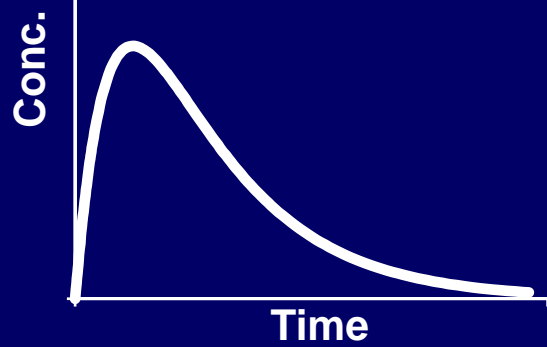


Approved Drug Products With Therapeutic Equivalence Evaluations. 23rd ed. 2003. FDA/CDER Web site. Available at: [http://www.fda.gov/cder/ob/docs/preface/ecpreface.htm#Therapeutic Equivalence-Related Terms](http://www.fda.gov/cder/ob/docs/preface/ecpreface.htm#Therapeutic%20Equivalence-Related%20Terms).

Accessed September 29, 2003.

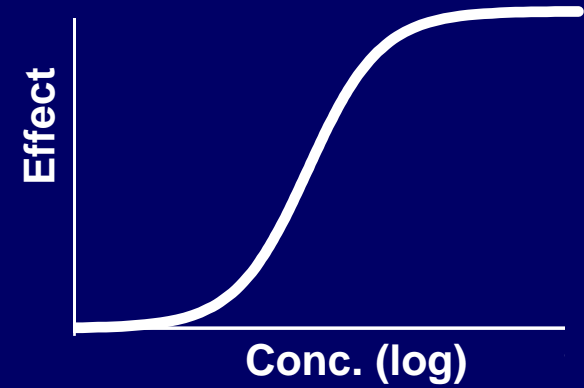
Pharmacokinetics

conc. vs time



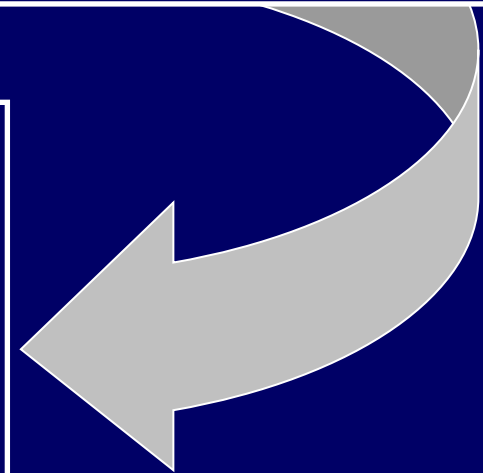
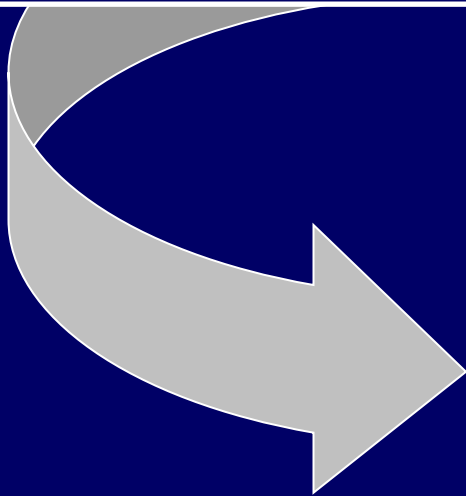
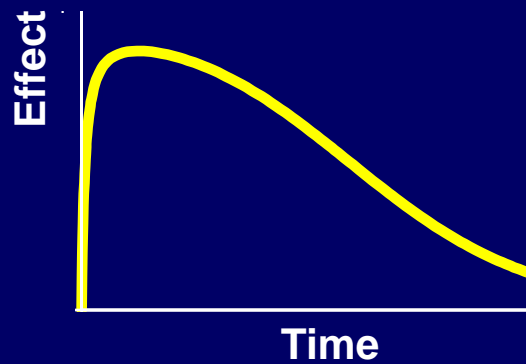
Pharmacodynamics

conc. vs effect

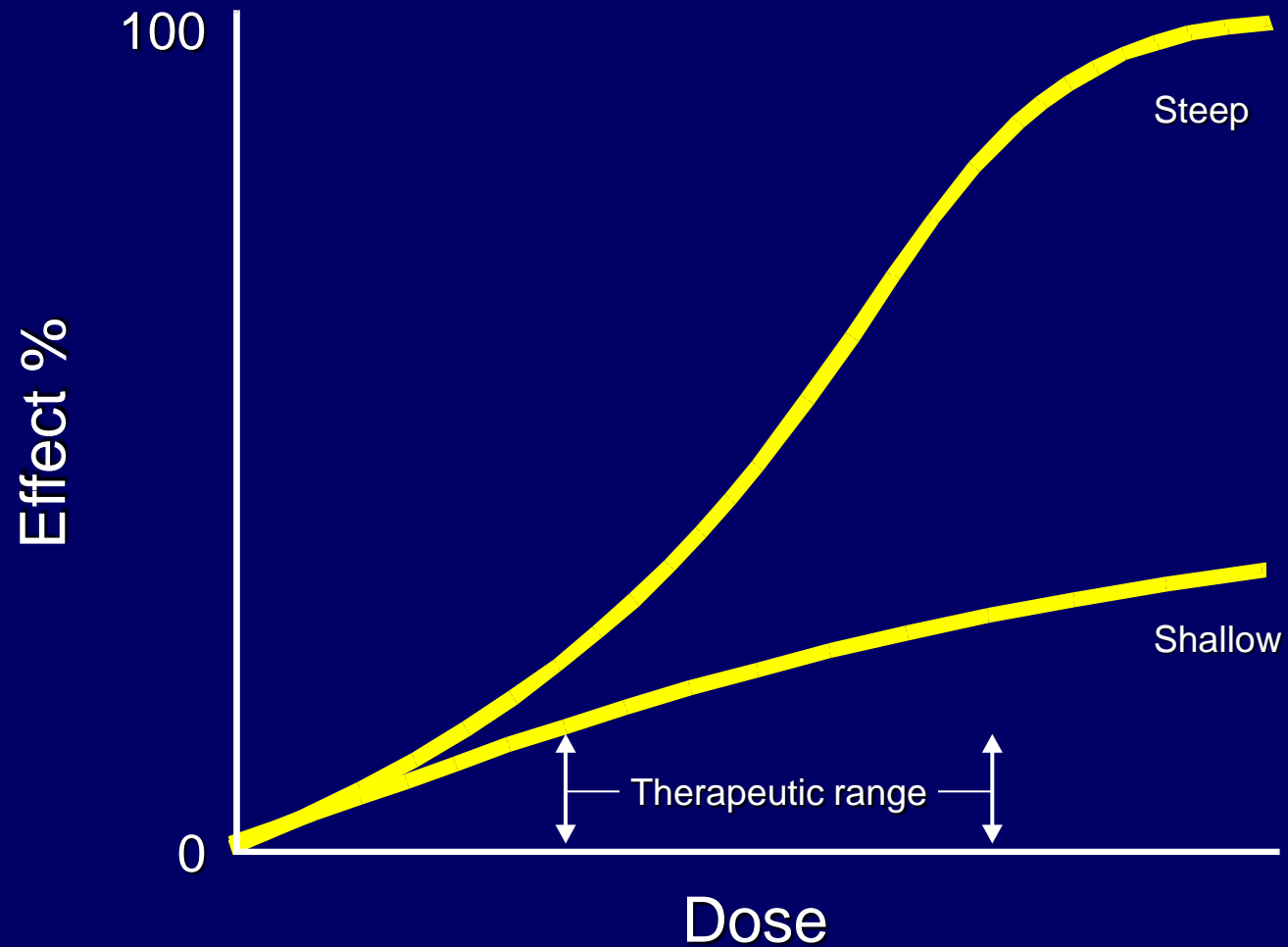


PK/PD

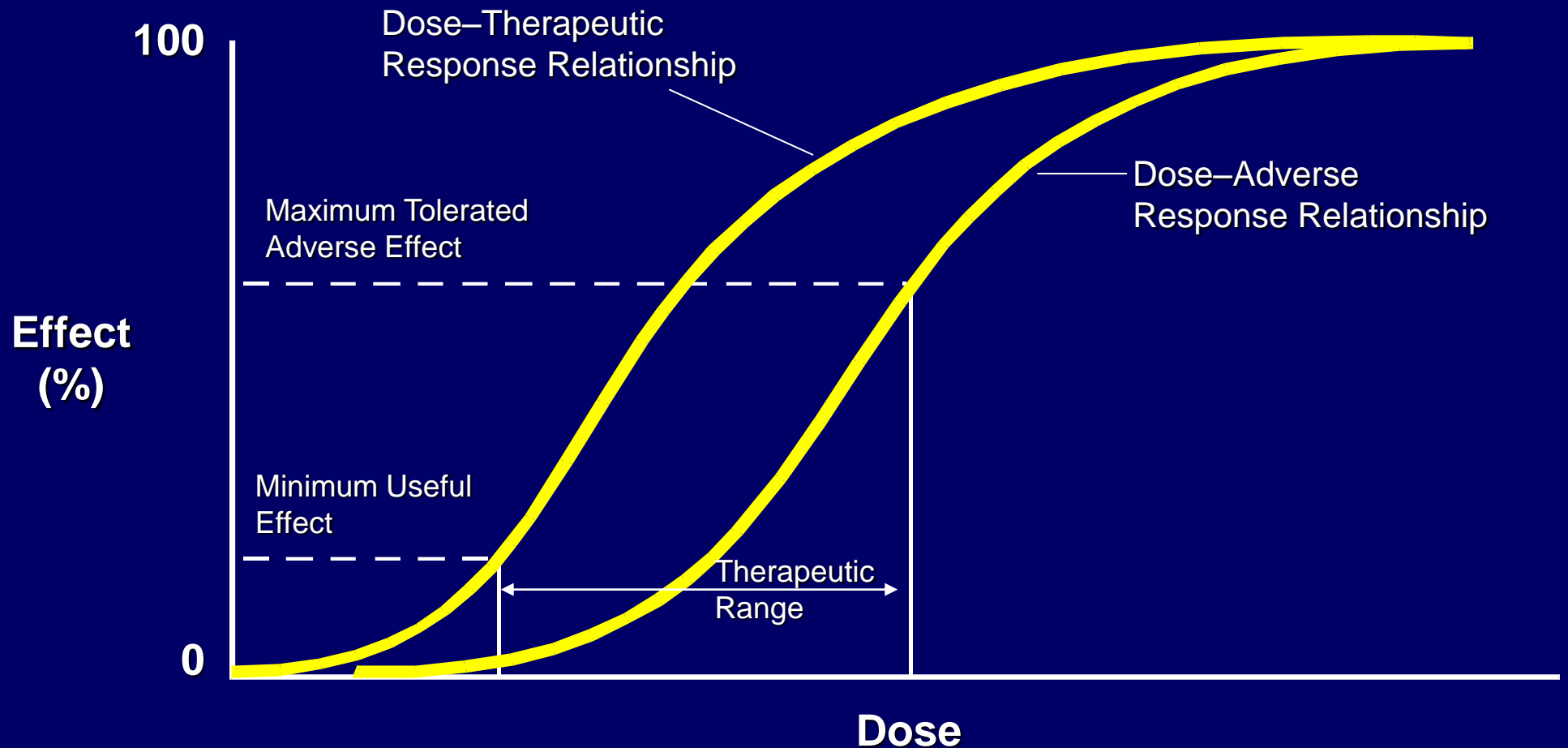
effect vs time



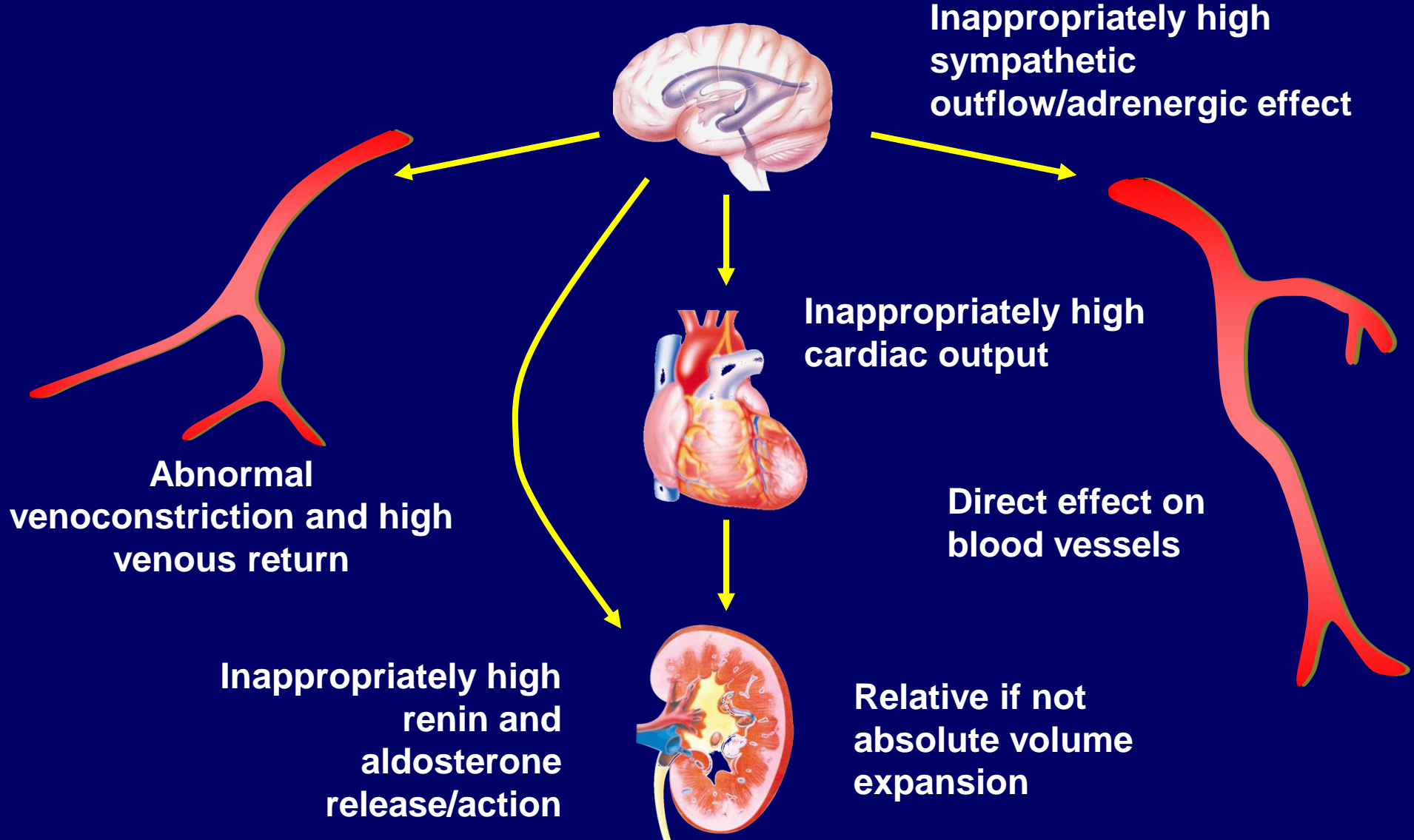
Therapeutic Considerations in the Dose-Response Relationship



Dose–Response and Dose–Adverse Event Relationship for an Antihypertensive



Pathophysiology of Drug-Induced Hypertension

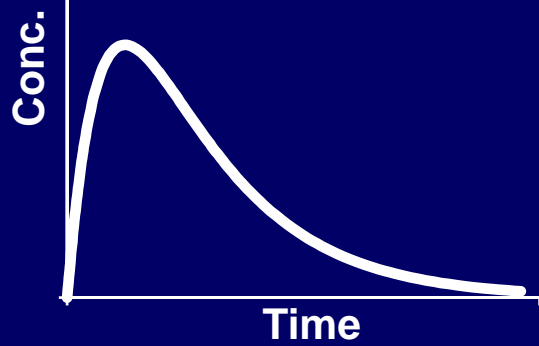


Issues Surrounding Impact of Drugs on 24-hour Ambulatory Blood Pressure

- Morning or evening dosing
- Nocturnal administration of specialized formulations
- Importance of pharmacodynamics and kinetics
- Influence of the circadian variation of physiologic factors

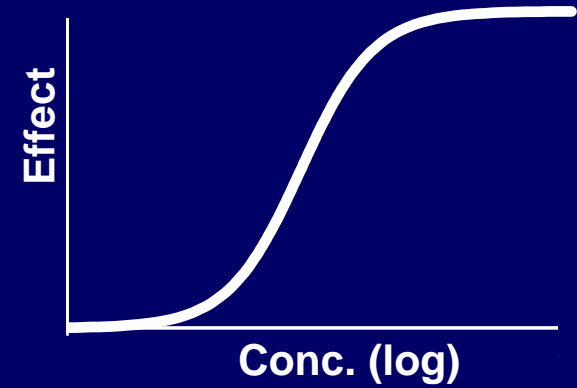
Pharmacokinetics

conc. vs time



Pharmacodynamics

conc. vs effect



PK/PD

effect vs time

