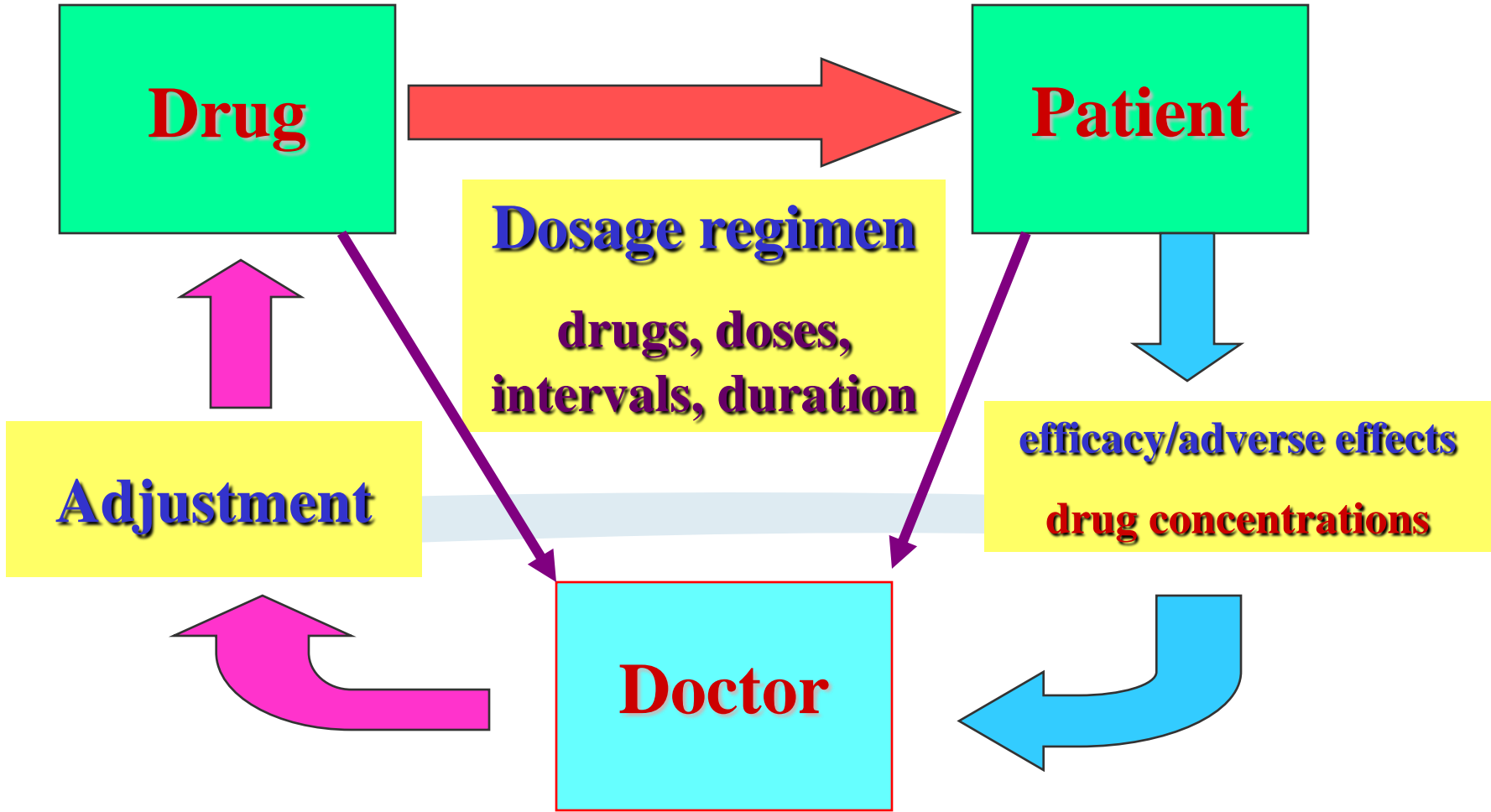


Chapter 3

Factors Influencing Drug Effects and Rational Therapeutics

影响药物效应的因素及合理用药

- **Drug Factors**
- **Patient Factors**
- **Rational therapeutics**



PRESCRIBED
DOSE



ADMINISTERED
DOSE



CONCENTRATION
AT LOCUS
OF ACTION



INTENSITY
OF EFFECT

药剂学过程

- patient compliance
- medication errors

药动学过程

- rate and extent of absorption
- body size and composition
- distribution in body fluids
- binding in plasma and tissues
- rate of elimination

药效学过程

- physiological variables
 - pathological factors
 - genetic factors
 - interaction with other drugs
 - development of tolerance
-
- drug-receptor interaction
 - functional state
 - placebo effects

Part A *Drug Factors*

- 1. *Physic-chemical properties of drugs*
- 2. *Dose forms*
- 3. *Administration*
- 4. *Multiple-drug therapy*
- 5. *Long-term drug therapy*

Part A *Drug Factors*

- *1. Physic-chemical properties of drugs*
- **Stability**
- **Molecular size**
- **Lipid- and water-soluble**
- **.....**

Part A *Drug Factors*

- *2. Dose forms*
- **slow release formulation**
- **controlled release formulation**
- **transdermal patch**
- **inhalation**

Part A *Drug Factors*

■ *3. Administration*

■ **Doses**

■ **Routes** oral

■ intramuscular injection

■ subcutaneous injection

■ intravenous injection or infusion

■ **Administration time**

■ **Dosing intervals**

■ **Dosing duration**

Part A *Drug Factors*

- *4. Multiple-drug therapy (drug combination)*
- **Drug-drug interactions**
 - pharmacy
 - pharmacokinetics
 - pharmacodynamics
- **Drug effects in combination**
 - **synergism:** potentiation / addition
 - **antagonism**

A

Mechanisms of Chemical Interactions

PHARMACO-KINETIC

biotransformation

distribution

absorption

excretion

PHARMACO-DYNAMIC

non-receptor

receptor

B

Classification of Chemical Interactions

ADDITIVE

SYNERGISTIC

POTENTIATION

ANTAGONISM

functional

chemical

dispositional

receptor

Efficacy: ↓, ↑

Toxicity: ↓, ↑

Part A *Drug Factors*

■ 药物在ADME上的相互作用

- (1) 影响胃肠道药物吸收的相互作用 药物在胃肠道内吸收时相互影响表现在：影响药物解离度、影响胃排空速度、影响肠蠕动、改变胃肠道环境、在胃肠道内相互结合等。
- (2) 影响药物血浆蛋白结合率的相互作用 当两种药物合用时，它们对血浆蛋白结合部位产生竞争，结合力强的药物将结合力弱的药物置换出来，后者血浆游离型浓度增加，药理活性也相应增强，增加的程度还受分布容积(Vd)的影响。

Part A *Drug Factors*

- (3) 肝药酶诱导 (酶促) 和抑制 (酶抑) 以及影响肝药酶的药物 一些药物反复应用可诱导肝微粒体酶活性增加, 这称为**肝药酶诱导作用** (酶促作用), 如苯巴比妥、利福平、苯妥英等; 也有些药物可抑制肝微粒体酶的活性, 称为**肝药酶抑制作用** (酶抑作用), 如西米替丁、氯霉素、异烟肼等。
- (4) 影响药物排泄的相互作用
 - ① 肾小球滤过, 改变肾血流量的药物可改变滤过率;
 - ② 肾小管主动分泌, 可在弱酸性或弱碱性药物载体 (转运体) 上相互干扰;
 - ③ 肾小管重吸收, 药物改变尿液pH值可改变其他弱酸或弱碱类药物的重吸收。

Part A *Drug Factors*

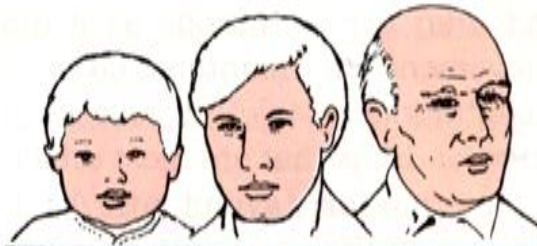
■ 药物在药效学上的相互作用

- (1) 生理性拮抗或协同 中枢抑制/兴奋; 凝血/抗凝血
- (2) 受体水平的协同或拮抗 激动剂/拮抗剂
- (3) 作用机制上的协同或拮抗 磺胺类/TMP;
■ 抑菌/繁殖期杀菌
- (4) 干扰神经递质转运或代谢 TCA/MAOI

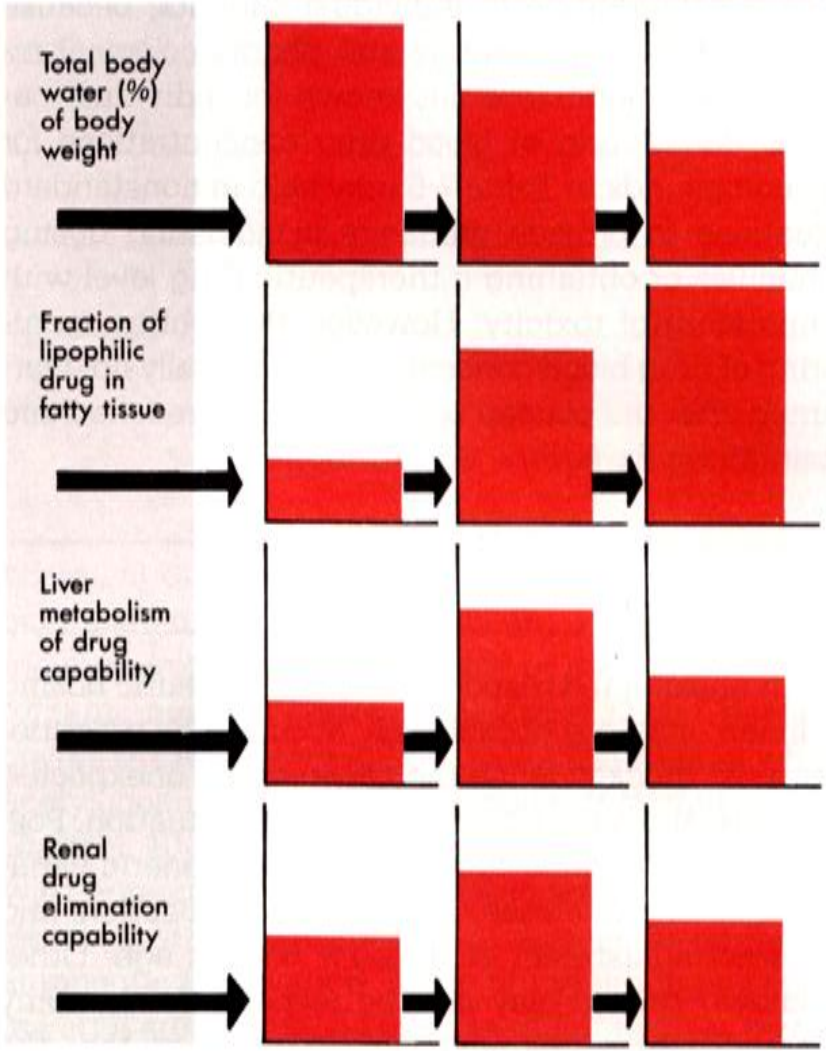
Part B *Patient Factors*

- **1. *Physiological Factors***
- **1.1 Age**
- **Children**
 - Sensitivity to drugs
 - Pharmacokinetic properties
- **Elderly**
 - Sensitivity to drugs
 - Pharmacokinetic properties





Infants Young adults Elderly



Age-related factors influencing pharmacokinetic processes



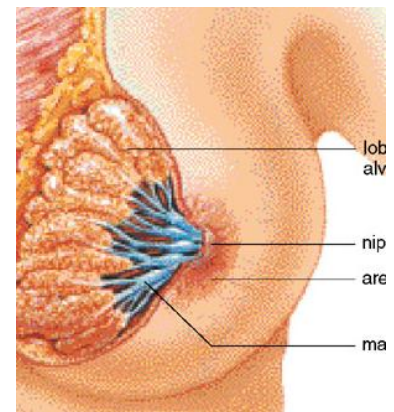
Part B *Patient Factors*

- **1.2 Body Weight**
- **Volume of distribution**
- **Fat / skeletal muscles**
- **lipid-soluble / water-soluble drugs**



Part B *Patient Factors*

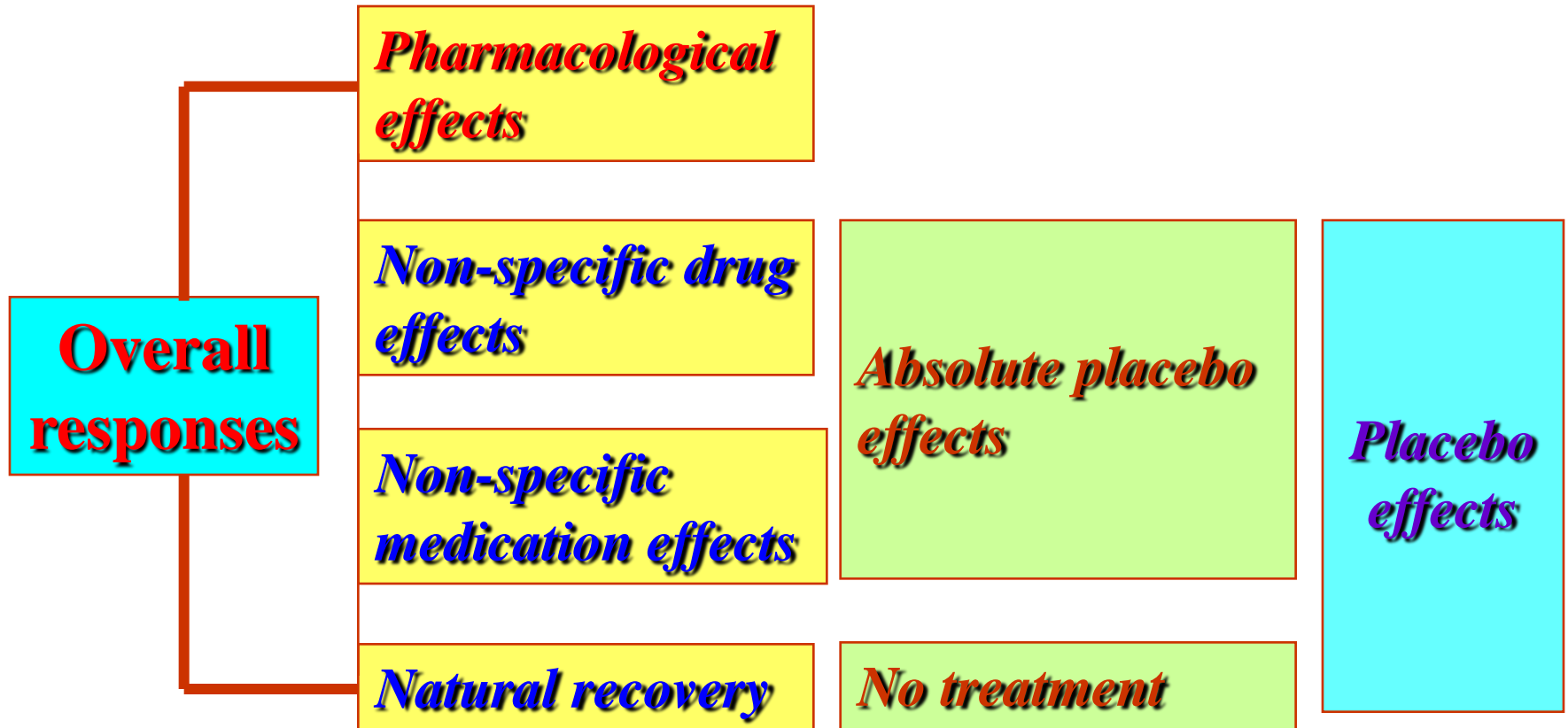
- **1.3 Sex**
- **Women**
- **Pregnancy**
- - malformation and dysfunction of the fetuses
- **Lactation**
- - milk: effects on infants



Part B *Patient Factors*

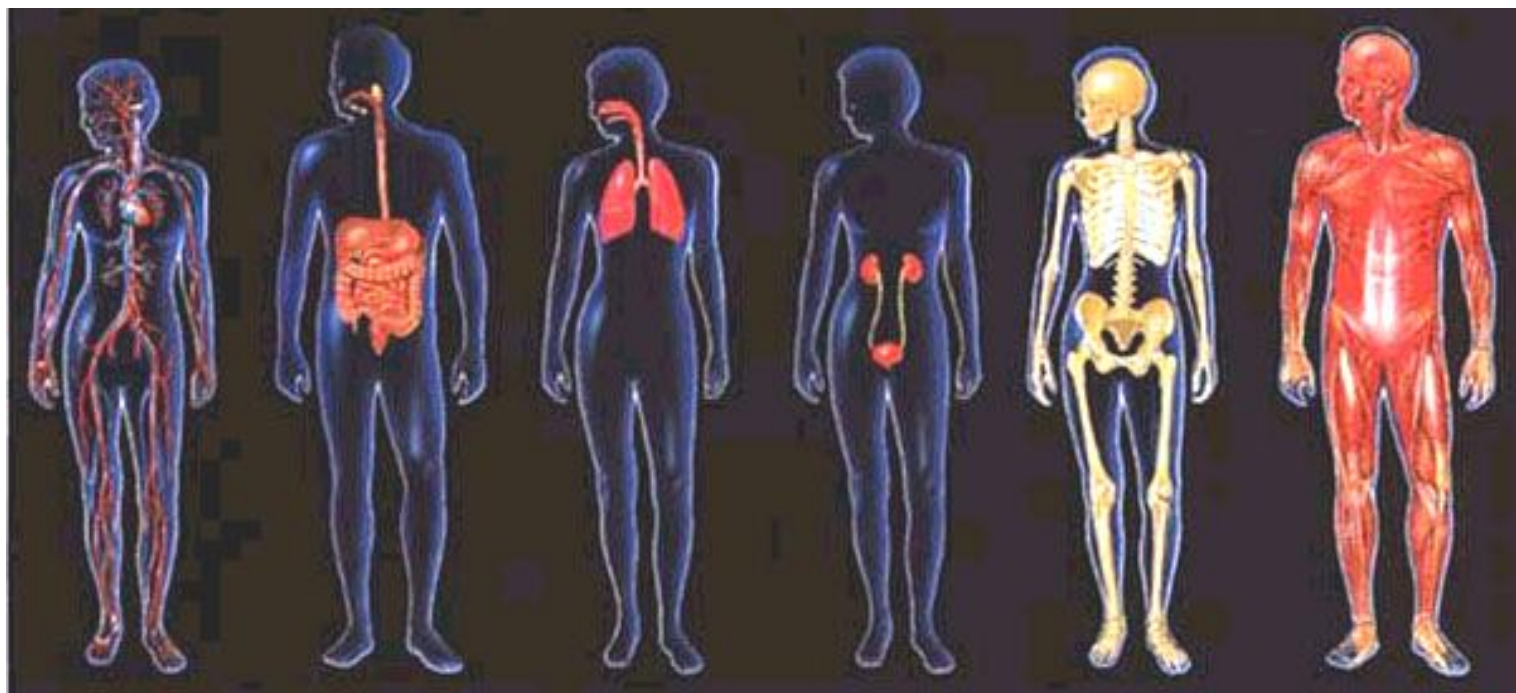
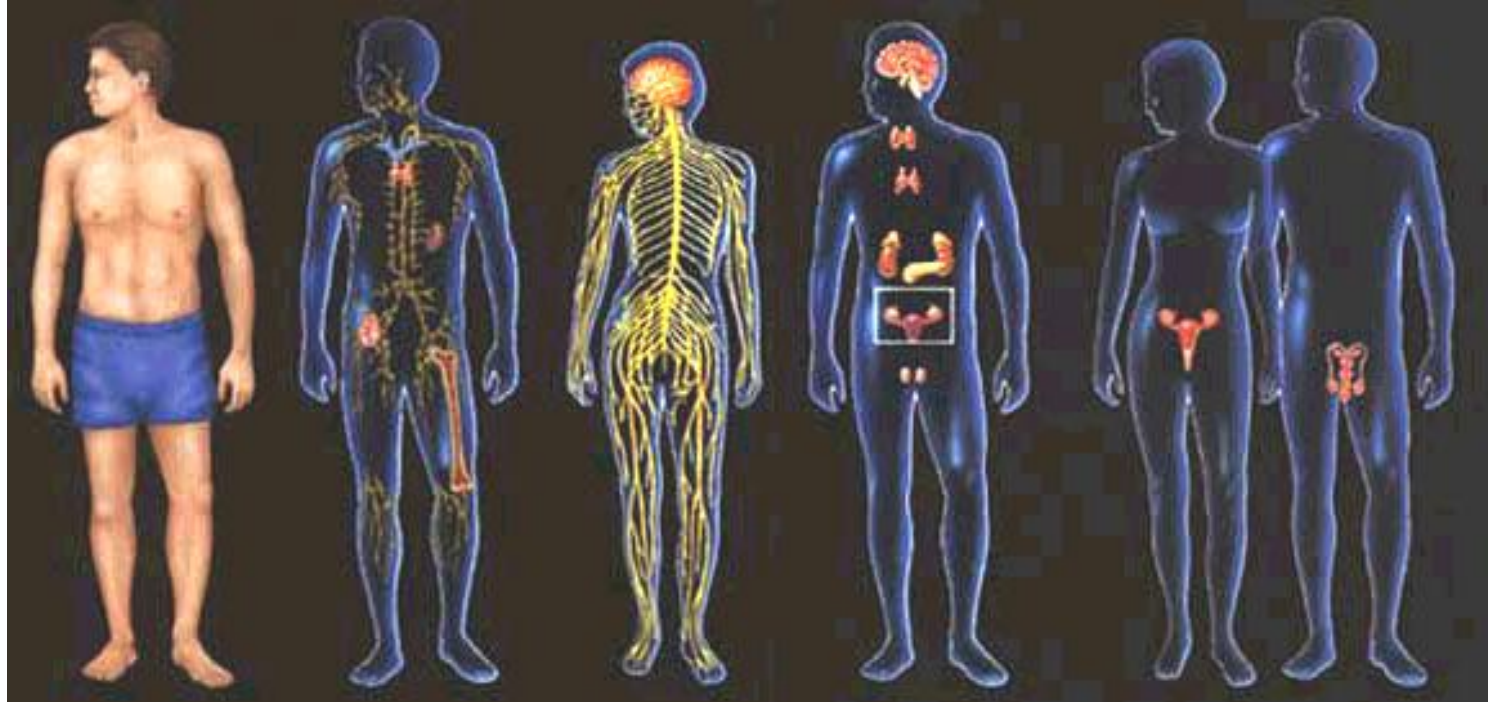
- *2. Psychological Factors*
- **Placebo effects**
- **Placebo effects commonly are manifested as alteration of mood, other subjective effects, and objective effects that are under autonomic or voluntary control.**

Part B *Patient Factors*



Part B *Patient Factors*

- **3. *Pathological Factors***
- **Heart diseases**
- **Hepatic diseases**
- **Renal diseases**
- **Gastrointestinal diseases**
- **Malnutrition**
- **Imbalances of acid-base or electrolytes**

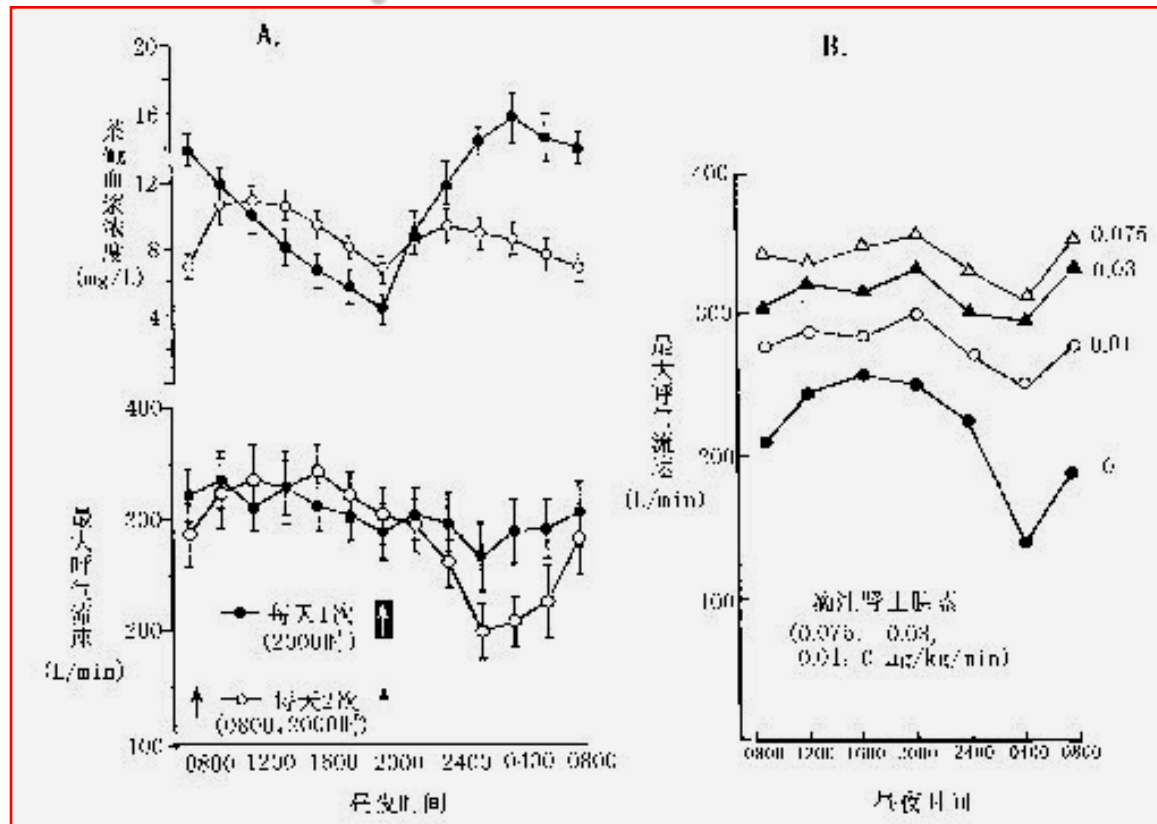


Part B *Patient Factors*

- **4. *Genetic Factors***
- **Pharmacogenetics**
- **abnormality of drug responses**
- ***example: tolerance of warfarin***
- **abnormality of pharmacokinetic properties**
- ***example: fast or slow acetylation***

Part B *Patient Factors*

- *5. Chronobiological Factors*
- **Circadian rhythms**



Part B *Patient Factors*

■ *6. Life Styles and Environment Factors*

■ **Nutrition**

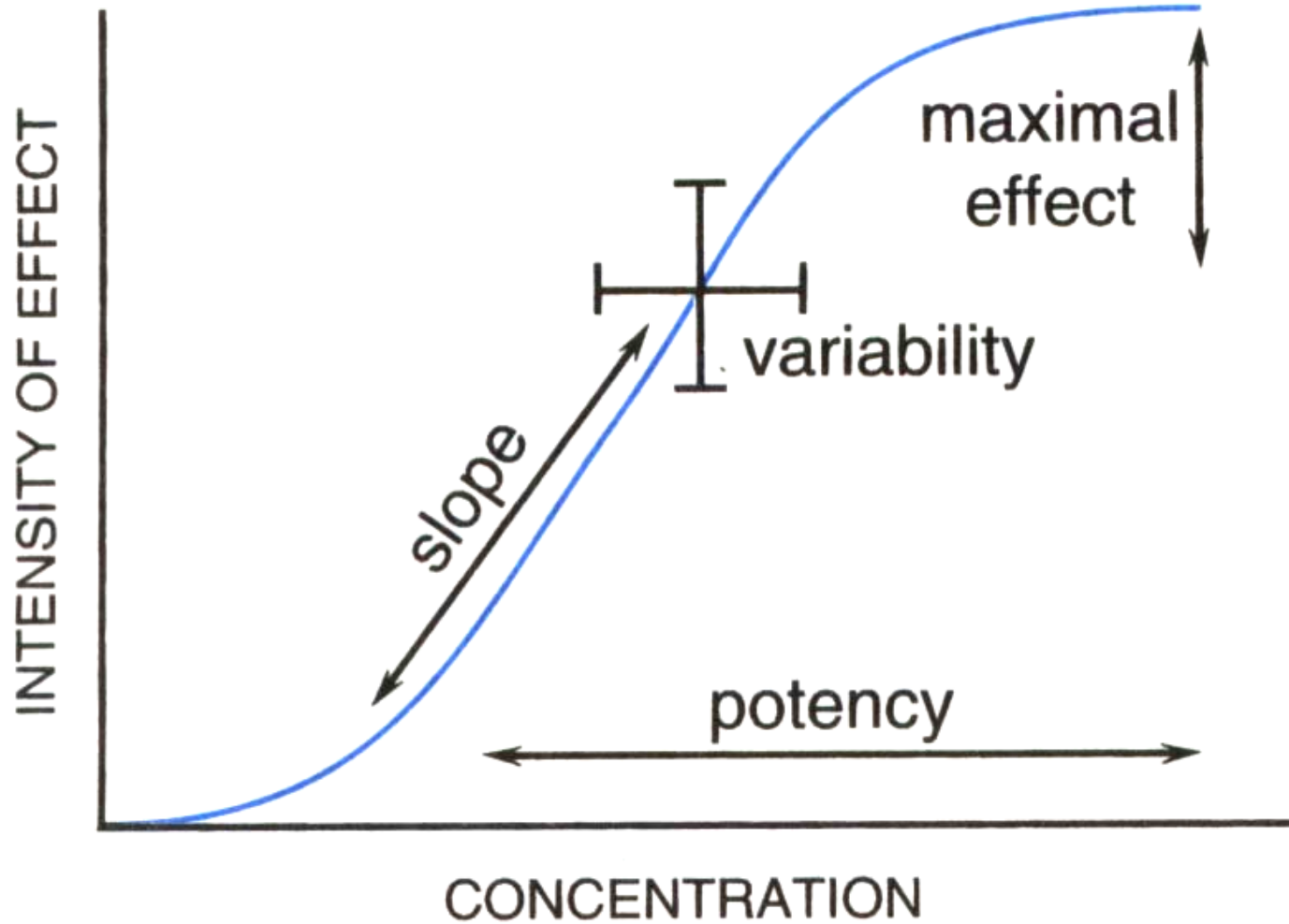
■ **Drinking & smoking**

■ **Environmental poisons**

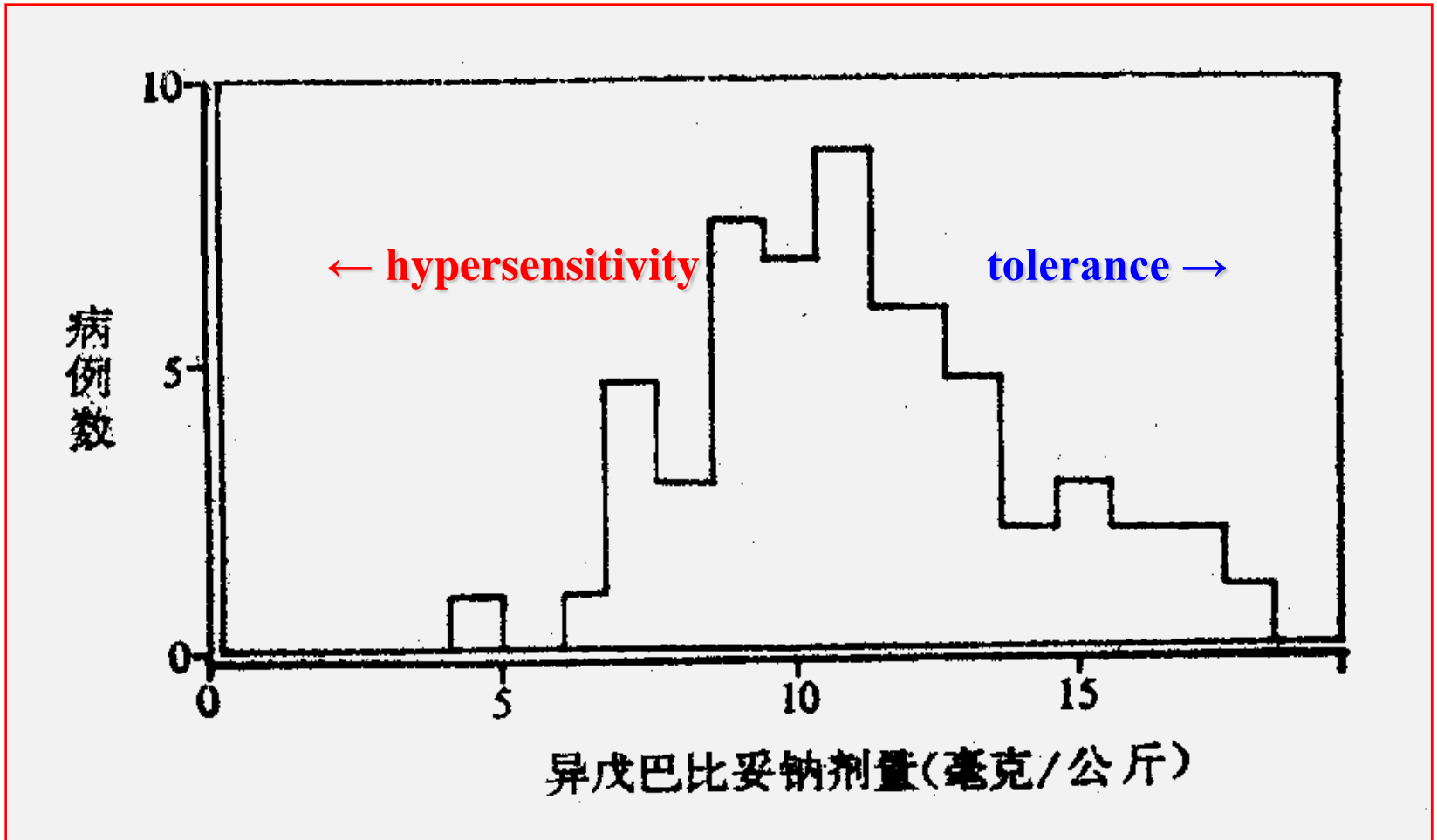


Part B *Patient Factors*

- **7. *Individual variation*** (个体差异)
 - **(1) Sensitivity to drugs**
 - Hypersensitivity
 - Hyposensitivity (tolerance)
 - **(2) Abnormal responses to drugs**
 - Idiosyncrasy (genetic abnormality)
 - Allergy (immunological abnormality)



The log concentration–effect relationship.



Individual variation of effective doses of amytal

Part B *Patient Factors*

- **8. *Changed responses after long-term drug use*** (长期用药后机体对药物反应的变化)
 - **(1) Tolerance and tachyphylaxis**
 - **(2) Resistance to chemotherapy**
 - **(3) Drug dependence**

Part B *Patient Factors*

- *Dependence*
- An adaptive state that develops in response to repeated drug administration.
- *Psychologic dependence* is manifested by compulsive drug-seeking behavior.
- *Physiologic dependence* is present when withdrawal of drug produces symptoms and signs.
- *Drug addiction* is defined as the compulsive, out-of-control drug use, despite negative consequences.
- *Drug abuse*: any use of a drug for non-medical purposes.
- *(a maladaptive pattern of drug use leading to clinically significant impairment or distress)*

Part C *Rational therapeutics*

- 1. Making an accurate diagnosis (正确诊断)
- 2. Understanding the pathophysiology of disease (了解疾病的病理生理特点)
- 3. Reviewing the menu of pharmacotherapeutic options (评估有关的治疗药物)
- 4. Selecting patient-specific drug and dose (选择适合的药物及剂量)
- 5. Selecting endpoints to follow (选择随访的观察指标)
- 6. Maintaining a therapeutic alliance with patient (与病人保持治疗上的联系)