

## OPTIMIZATION OF DOSAGE REGIMEN

- ▶ Incorporating the patient's characteristics in the process of initiating a drug dosage regimen is an important step toward optimization of drug therapy, but it does not guarantee the success of the therapy.
- ▶ We still need to evaluate the outcome of the treatment and we still find in some cases that the therapeutic objective has not been achieved.

- ▶ Traditionally, the management of drug therapy has been accomplished by monitoring the incidence and intensity of both desired therapeutic effects and undesired adverse effects.

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## Clinical experience with individualization and optimization based on plasma drug levels

### A: ANTIARRHYTHMIC DRUGS

**1- Quinidine ( $t_{1/2}$  6-8 hrs ):** It is useful for treatment of atrial and ventricular arrhythmia. It is usually administered orally but may be given by IM or IV.

- ▶ When usual dosages of quinidine are given to patients on enzyme-inducing drugs, such as phenobarbital, phenytoin, or rifampin, low sub-therapeutic blood levels of quinidine are likely to result.
- ▶ Quinidine concentrations of about 3 to 8  $\mu\text{g/ml}$  are considered therapeutic when nonspecific assay methods are used.

- ▶ The frequency of gastrointestinal disturbances increases with quinidine levels above 5  $\mu\text{g/ml}$ ; cardiovascular disturbances are a concern at concentrations exceeding 8  $\mu\text{g/ml}$ .

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### 2- Lidocaine ( $t_{1/2}$ : 2 hrs)

- Lidocaine is the most frequently used intravenous antiarrhythmic agent for the short term management of ventricular arrhythmias.
- In some patients, the clearance of lidocaine decreases with continuous infusion: dosage reduction may be required during therapy.
- Co-administration of cimetidine or propranolol which decreases liver blood flow and inhibits hepatic metabolism, may also require dosage reduction of lidocaine.

- Plasma levels of lidocaine less than 1.5  $\mu\text{g/ml}$  are usually ineffective. The usual therapeutic lidocaine concentration ranges from 1.5 to 4.0  $\mu\text{g/ml}$ , but levels up to 8  $\mu\text{g/ml}$  may be needed in some patients.

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### B. ANTIBIOTICS

#### 1- Aminoglycoside Antibiotics

- ▶ The aminoglycoside antibiotics are effective in treating pneumonia, urinary tract, soft tissue, burn wound, and other systemic infections caused by gram-negative organisms.
- ▶ All aminoglycosides are ototoxic and nephrotoxic and have a relatively low therapeutic index.
- ▶ The major elimination route for the aminoglycosides is renal excretion, largely by way of glomerular filtration.
- ▶ The half-lives of gentamicin and tobramycin in patients with renal function are variable but avg about 2.5hr.

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