CHAPTER 23

ADULT CRITICAL CARE

23.1.1 GENERAL PRINCIPLES OF PHARMACOLOGY IN CRITICAL ILLNESS

» Pharmacokinetic (PK, “what the body does to the drug”) and pharmacodynamic (PD, “what the drug does to the body”) variations in critical care patients occur secondary to underlying illness, rapidly changing multiorgan dysfunction, and the use of multiple supportive modalities.

» Therapeutic response and clinical outcomes are affected by altered drug absorption, plasma protein binding, volume of distribution, renal and hepatic clearance, and affinity of binding of drug molecules to target receptors. These PK and PD changes in critical illness can contribute to

suboptimal dosing, adverse outcomes, increased risk of medication errors, and adverse drug reactions.

» Loading doses may be required to achieve timeous therapeutic responses (e.g. phenytoin, beta-lactam, antimicrobials, vancomycin), especially for medicines with a long plasma half-life. Maintenance doses should be adjusted based on extent and trend of organ dysfunction, and clinical indication for the therapy.

» Careful dose titration based on clinical observation is required for medications with a rapid onset of action, or where vital parameters can be readily monitored.

» Therapeutic drug monitoring (TDM) is recommended, where possible, to assist in dose adjustment.

» Where renal replacement therapy is used, dosing should be tailored to account for changes in volume of distribution and clearance of medications.

» Polypharmacy may contribute to adverse outcomes secondary to drug interactions or toxicity.

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