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Parenteral Medications
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Edited by

Kenneth E. Avis
The University of Tennessee
Memphis, Tennessee

Herbert A. Lieberman
H.H. Lieberman Associates, Inc.
Consultant Services
Livingston, New Jersey

Leon Lachman
Lachman Consultant Services
Westbury, New York

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Parenteral Drug Administration: Routes, Precautions, Problems, Complications, and Drug Delivery Systems

Richard J. Duma

Medical College of Virginia, Virginia Commonwealth University, Richmond, Virginia

Michael J. Akers

Eli Lilly and Company, Indianapolis, Indiana

Salvatore J. Turco

Temple University, Philadelphia, Pennsylvania

Parenteral, from *para enteron* (Greek), meaning "to avoid the intestines," includes in its broadest sense, any drug (or fluid) whose delivery does not utilize the alimentary canal for entry into body tissues. Although drugs applied topically to the eye, ear, and skin, or even inhaled, may be broadly interpreted as parenterals, medical and pharmaceutical health care deliveries generally limit the definition to those drugs injected or infused *directly* into tissues, tissue spaces, vessels, or body compartments.

The development of techniques for administering parenterals, coupled with innovative designs of new devices to achieve and monitor their delivery, occur almost daily and are enabling therapeutics to approach an exact science. In addition, parenteral therapy is not restricted to hospitals or clinics but is being increasingly employed, even in its most invasive forms of delivery (e.g. intravenous), to manage patients at home and in the work place. Most patients readily accept or easily adapt to almost every form of parenteral therapy, and many self-administer their own drugs, even when the route of delivery is intravenous (e.g., home infusion programs).

Parenteral administration offers many advantages over therapy given by nonparenteral routes. Most notably, therapeutists can reliably predict with considerable accuracy the pharmacokinetics and pharmacology of the agents they prescribe; they can quickly interdict a rapidly progressive lethal process or disease; and, even though the physiology and pathology of patients may be complicated, they can "fine tune," stratify and quantitate results. However, despite these advantages, parenteral administration is not without

certain, measurable risks and limitations that the professional must intelligently weigh in terms of risks, benefits, and costs.

This chapter will attempt to review and update the usage of parenteral administration in today's practice of medicine. However, since the subject is dynamic and the technology is growing, the reader must appreciate that some of the material contained herein may become quickly outdated.

I. GENERAL INDICATIONS FOR PARENTERAL ADMINISTRATION OF DRUGS

The parenteral routes of drug administration are indicated for one or more of the following reasons:

1. To ensure delivery of adequate concentrations of the drug in question to diseased tissues or target areas of the body, especially when inadequate or marginal transport of that drug into the tissues or target areas is anticipated. *Example*: Direct intraventricular injection of drugs (e.g., antibiotics such as the aminoglycosides) which cross the "blood-brain-meninges barrier" poorly may be used in certain patients with bacterial or fungal meningitis and/or ventriculitis.
2. To permit the user to exert direct control over certain pharmacologic parameters, such as the time of drug onset, serum peak and trough levels, tissue concentrations, and rate of elimination of the drug from the body. *Example*: Intravenous or direct cardiointraventricular routes may be desirable to achieve immediate effects in emergencies such as might occur in the control of life-threatening hypotension, hypertension, or arrhythmias; or intramuscular routes may be desirable to obtain protracted or sustained effects, such as the use of benzathine penicillin G in the treatment of infections.
3. To allow the therapist, when outpatient management is desirable, to guarantee dosage and drug compliance, especially when the patient cannot be relied upon to self-medicate. *Example*: The use of long-acting (monthly) intramuscular penicillins may be used to manage children prophylactically for rheumatic heart disease in order to prevent Group A streptococcal pharyngitis.
4. To deliver a biologic effect that cannot be achieved through oral administration, perhaps because of nonabsorbance from the alimentary canal or degradation by gastric acidity. *Example*: Therapeutic peptides and proteins such as insulin, human growth hormone, other products from recombinant DNA technology, and polyene antibiotics (such as the antifungal agent amphotericin B).
5. To administer a drug when the desired route (e.g., oral) may not be available. *Example*: In patients who are aspirating or who have had the upper gastrointestinal tract stream diverted or removed (e.g., because of a carcinoma) a parenteral route may be necessary.
6. To provide a local effect when it is desirable to minimize or avoid systemic toxic effects or reactions. *Example*: Methotrexate may be given intrathecally to patients with leukemia and leukemic involvement of the meninges to avoid the systemic, toxic effects that would occur if an intravenous route was employed.

7. To administer drugs to the unconscious, uncooperative, or uncontrollable patient. *Example*: Patients with uncontrollable grand mal seizures often will not cooperate in the oral administration of drugs or will be at risk to aspirate if compelled to take medicines by mouth. Similarly, patients unconscious from narcotic abuse, anesthetic usage, or trauma, or uncooperative patients such as those suffering delerium tremens or a psychosis, may be satisfactorily managed by using parenteral routes.
8. To permit rapid correction of fluid and electrolyte imbalances and to supply short- or long-term nutritional needs (hyperalimentation or parenteral feeding). *Example*: Patients suffering severe dehydration or electrolyte depletion for a variety of reasons (e.g., heat stroke) can be rapidly corrected with intravenous electrolyte solutions; and patients whose intestinal tracts have been resected for one reason or another may be intravenously "fed" a complete diet of all the necessary amino acids, glucose, minerals, and vitamins for prolonged and indefinite periods of time.
9. To achieve a desired local effect. *Example*: Local anesthetics for tooth extractions or local anti-inflammatory agents for inflamed joints may be injected directly into the site in question to avoid systemic effects or "systemic" dosages.

II. PHARMACEUTICAL FACTORS AFFECTING PARENTERAL ADMINISTRATION

Certain pharmaceutical characteristics dictate the method or route of parenteral administration, and once the dosage form is injected or infused, influence the rate and extent of drug availability. These characteristics will be reviewed briefly in this section, but the reader is also referred to Chapter 3 for a more detailed treatment of the biopharmaceutical factors affecting parenteral drug availability.

A. Solubility of the Drug and Volume of the Injection

A drug must be completely solubilized, preferably in water, before it can be administered by intravenous injection. Both the extent of drug solubility in its intended vehicle and the dose required for the desired therapeutic effect will determine the volume of the injection. Parenteral routes other than the intravenous one have limitations regarding the maximum volume of medication administered (e.g., intradermal, intramuscular, intraocular, intraventricular, and intrathecal, to name a few).

B. Vehicle Characteristics

Drugs in aqueous vehicles may be administered by any parenteral route, whereas drugs in nonaqueous vehicles, which may or may not be water miscible, are administered most frequently by the intramuscular route. The intravenous route may be used for a few drugs in mixed solvent systems (e.g., diazepam, digoxin, and phenytoin), but precautions must be applied in adjusting the rate of drug infusion to avoid drug precipitation at the site of infusion.

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