Calculation of Doses: Patient Parameters

By
Ass. Prof. Dr. Mohamed Akl

Introduction

- For certain drugs and for certain patients, drug dosage is determined based on specific patient parameters:
  - Age, Weight, and Body surface area,
  - Nutritional and functional status.
- Among patients requiring individualized dosage are:
  - Neonates and other pediatric patients,
  - Elderly patients with diminished biologic functions,
  - Individuals of all age groups with compromised liver and/or kidney function,
  - Critically ill patients, المرضى في حالة حرجة
  - Patients being treated with highly toxic chemotherapeutic agents.
  - Patients being treated with certain drugs with a narrow therapeutic window.

Pediatric Patients

- Pediatrics is the branch of medicine that deals with disease in children from birth through adolescence مرحلة المراهقة

The inclusive groups are defined further as follows:

- **Neonate (newborn):** from birth to 1 month.
- **Premature:** if born at less than 37 weeks' gestation.
- **Infant:** 1 month to 1 year;
- **Early childhood:** 1 year through 5 years;
- **Late childhood:** 6 years through 12 years;
- **Adolescence:** 13 years through 17 years of age.

Pediatric Patients

- Proper drug dosing of the pediatric patient depends on:
  - patient's age and weight,
  - Overall health status,
  - The condition of such biologic functions as respiration and circulation,
  - The stage of development of body systems for drug metabolism (e.g., liver enzymes) and drug elimination (e.g., renal system).

- In the neonate:
  - Biologic functions and systems are underdeveloped.
    - Renal function develops over the span of the first 2 years of life.
  - The most used drugs in neonates, infants, and young children are antimicrobial agents, which are eliminated primarily through the kidney.
  - If drug elimination rate isn't properly considered,→ drug accumulation in the body could occur, leading to drug overdosage and toxicity.

Pediatric Patients

Case in Point 8.1: A hospital pharmacist is asked to determine the dose of clindamycin for a 3-day-old neonate weighing 3 lb. 7 oz. In checking the literature, the pharmacist determines that the dose is listed as follows:[4]

<1200 g: 10 mg/kg/day divided q12h.
<2000 g and 0–7 days old: 10 mg/kg/day divided q12h
<2000 g and >7 days old: 15 mg/kg/day divided q8h
>2000 g and 0–7 days old: 15 mg/kg/day divided q8h
>2000 g and >7 days old: 20 mg/kg/day divided q6h

Each divided dose is to be added to an intravenous infusion at the scheduled hour and infused over a period of 20 minutes.

Clindamycin is available in an IV bag containing 600 mg/50 mL of injectable solution. How many milliliters of this solution should be given for each divided dose?

- Body weight =3 lb 7 oz = (3×454)+ (7× 28.35) =1560.45
- $10\ mg/kg \times 1560.45 / 1000 = 15.6\ mg$
- Each divided dose = $15.6\ mg / 2 = 7.8\ mg$
- Volume of the injectable solution: $\frac{600\ mg}{50\ mL} = \frac{7.8\ mg}{X}$ → So $X = 0.65$ mL

Geriatric Patients

- Regarding chronological age العمر الزمني, the term "elderly" has several accepted definitions.
- *Geriatric medicine* or geriatrics is the field that involves the management of illness disability in the **elderly**.
- The functional capacities of most organ systems decline throughout adulthood → important changes in drug response occur with advancing age.

Pharmacotherapy:

- the use of pharmacologically active substances in the treatment of disease and illness
- It is of disproportionate use استخدام غير متناسبin the elderly compared with other age groups.

Some conditions are particularly common in the elderly, including:

- degenerative osteoarthritis,
- venous and arterial insufficiency,
- urinary incontinence,
- congestive heart failure,
- parkinsonism
- prostatic carcinoma,
- stroke,
- Alzheimer disease.

Geriatric Patients

- Many elderly patients have coexisting pathologies that require multiple-drug therapies.
- Medications in the elderly are prescribed not only to relieve symptoms and manage diseases but also to improve bodily function, enhance the quality of life, and prolong survival.
- Most age-related physiologic functions peak before 30 and decline gradually.
- Physiological capacity and function decline with aging.
- Kidney function is an important factor in drug dosing for the elderly, as reduced function results in reduced drug elimination.
- About 1% of the blood flow to the kidneys is lost every year after age 30, which adds up to a 30% to 40% drop in most 60- to 70-year-olds.
- Start with low dose; monitor for need of dose adjustment.

Geriatric Patients

- Because of reduced kidney function, → increases the probability of toxic drug levels in the body and adverse drug effects, → initial drug dosing in elderly patients is often lower than the usual adult dose.
- Often, adverse effects or unsatisfactory therapeutic outcomes require dosage adjustments or medication changes.
- *Pharmacokinetic parameters* are important in the dosing of certain drugs in the elderly patient.

Other common features of medication use in the elderly, including:

- the long-term use of maintenance drugs;
- the need for multi-drug therapy,
- accompanied by an increased risk of medication interactions and adverse drug effects
- difficulties in patient compliance due to
  - impaired cognition ضعف الإدراك
  - depression or apathy اللامبالاة, and economic reasons
  - confusion over the various dosing schedules of multiple medications,

Geriatric Patients

Special Considerations in Dose Determinations for Elderly Patients

- Therapy is initiated with a lower-than-usual adult dose.
- Dose adjustment may be based on the therapeutic response.
- The patient's physical condition may determine drug dose and route of administration.
- The dose depends on the patient's weight, body surface area, health, disease status, and pharmacokinetic factors.
- Concurrent drug therapy may affect drug/dose efficacy.
- A drug's dose may produce undesired adverse effects and may affect patient compliance.
- Complex dosage regimens of multiple drug therapy may affect patient compliance.

Dosage forms applicable to pediatric and geriatric patients

- In the general population, solid dosage forms, such as tablets and capsules, are preferred for the oral administration of drugs. → because of
  - their convenience, ease of administration, lower cost per dose, etc...
  - However, solid dosage forms are often difficult or impossible for the pediatric, geriatric, or disabled patient to swallow.
- liquid forms are preferred, such as oral solutions, syrups, suspensions, and drops.
  - An **advantage** of liquid forms is that the dose can easily be adjusted by changing the volume of liquid administered
  - When necessary, liquid forms of medication may be administered by oral feeding tube.

Many options for individuals unable or unwilling to swallow whole tablets:

- When a liquid product isn't available, make an oral liquid from a solid.
- Chewable tablets and solid gel forms that disintegrate or dissolve in the mouth.
- Tablet splitting and tablet crushing.

- For systemic effects, injections may be used rather than the oral route in pediatric and geriatric patients.

Drug dosage based on age

- Age is a factor in the determination of drug dosage, especially for young or elderly patients.
- **newborns** are abnormally sensitive to certain drugs because of the **immature** state of their **hepatic and renal function**.
- **Elderly individuals** may also respond abnormally to the usual adult dose of a drug because of **impaired ability to metabolize or eliminate** the drug or because of other concurrent **pathologic conditions**.

Fried's rules:

- Which has been recommended for calculating doses for infants younger than 2 year of age,
- It is based on the assumption that an adult dose can be tolerated safely by a child when he reach 150 months (12.5 year).

Infant dose = (Age in months / 150) ×Adult dose

Drug dosage based on age

Young's rule:

- for children of 2 years and older

$$\text{Child's dose} = \frac{\text{Age in years}}{\text{age in years} + 12} \times \text{Adult dose}$$

- Today, these rules are not in general use because age alone is no longer considered a singularly valid criterion in the determination of an accurate dosage for a child.
- When age is used to determine the dosage of a potent therapeutic agent, it is usually combined with another factor, such as weight.

❑ An over-the-counter cough remedy contains 120 mg of dextromethorphan in a 60-ml bottle of product. The label states the dose as 1½ teaspoonfuls for a child 6 years of age. How many milligrams of dextromethorphan are contained in the child's dose? • From the data in table 8.1, calculate the dosage range for digoxin for a 20-month-old infant weighing 6.8 kg.

1½ teaspoonful = 7.5 ml

$$\frac{60\ ml}{120\ mg} = \frac{7.5\ ml}{X\ mg}$$ So x = 15 mg dextromethorphan

TABLE 8.1 CALCULATION OF PEDIATRIC DOSAGES OF DIGOXIN BASED ON AGE AND WEIGHT

AGE	DIGOXIN DOSE (μg/kg)
Premature	15 to 25
Full term	20 to 30
1 to 24 months	30 to 50
2 to 5 years	25 to 35
5 to 10 years	15 to 30
Over 10 years	8 to 12

From the data in Table 8.1, calculate the dosage range for digoxin for a 20-month-old infant weighing 6.8 kg.

From the data in Table 8.1, calculate the dosage range for digoxin for a 20-month-old infant weighing 6.8 kg.

$$\frac{30\ \mu g}{X} = \frac{1\ Kg}{6.8\ Kg} \rightarrow \text{So } X = 204\ \mu g$$

$$\frac{50\ \mu g}{Y} = \frac{1\ Kg}{6.8\ Kg} \rightarrow \text{So } Y = 340\ \mu g$$

Dose range, 204 to 340 μg

Drug dosage based on age

- Some **over-the-counter medications (**OTC) purchased for self-medication (i.e. non potent medications) include labeling instructions that provide guidelines for safe and effective dosing.
- For pediatric use, doses generally are based on **age groupings**,
  - e.g., 2 to 6 years old; → give X_1 mg
  - 6 to 12 years old; → give X_2 mg
  - over 12 years of age → give X_3 mg
- For children 2 years of age or younger, the label recommendation generally states "**consult your physician**.“

Drug dosage based on body weight

- Generally, heavy individuals can withstand larger dose, than a person with less weight.
- The usual doses for drugs are considered generally suitable for **70-kg (154-lb)** individuals.
- The **ratio** between the **amount of drug** administered and the **size of the body** influences the **drug concentration** at its site of action.
  - drug dosage may require adjustment from the usual adult dose for **abnormally lean or obese patients**.
- A useful equation for the calculation of dose based on body weight is

$$\text{Pediatric's dose (mg)} = \text{Patient's weight in kg} \times \frac{\text{drug dose } (mg)}{1\ kg}$$

Drug dosage based on body weight

- Generally, heavy individuals can withstand larger dose, than a person with less weight.
- The usual doses for drugs are considered generally suitable for **70-kg (154-lb)** individuals.
- The **ratio** between the **amount of drug** administered and the **size of the body** influences the **drug concentration** at its site of action.
  - drug dosage may require adjustment from the usual adult dose for **abnormally lean or obese patients**.
- A useful equation for the calculation of dose based on body weight is

$$\text{Pediatric's dose (mg)} = \text{Patient's weight in kg} \times \frac{\text{drug dose } (mg)}{1\ kg}$$

Drug dosage based on body weight

- The determination of drug dosage for young patients based on body weight is considered more dependable than that based strictly on age.

- **Case 1:** The usual initial dose of chlorambucil is 150 mcg/kg of body weight. How many milligrams should be administered to a person weighing 154 lb.?

Answer

- 150 mcg = 0.15 1kg = 2.2 ib
- $\frac{2.2\ (ib)}{154\ (ib)} = \frac{0.15\ (mg)}{X\ (mg)}$ so X = 10.5 mg

- **Case 2:** The usual dose of sulfisoxazole for infants over 2 months of age and children is 60 to 75 mg/kg of body weight. What would be the usual range for a child weighing 44 lb.?

Answer

- 20 kg = 44 ib
- 60 mg/kg × 20 kg = 1200 mg 75 mg/kg × 20 kg = 1500 mg

CASE IN POINT 8.3: A hospital pharmacist is called to a pediatric nursing station to calculate the quantity of an injection to administer to a pediatric patient. The daily dose of the injection for the child's weight is stated as 15 mg/kg/day, divided into three equal portions. The child weighs 10 kg. The injection contains 5 mg/mL of the prescribed drug.

How many milliliters of injection should be administered?

Answer

- 15 mg/kg × 10 kg = 150/3 = 50 mg
- 50 mg/5 mg/ml=10 ml

Drug dosage based on Body Surface Area (BSA)

- It is widely used in two types of patient groups:
  1. **cancer patients** receiving chemotherapy,
  2. **pediatric patients** of all **childhood ages**, • with the general exception of

→ premature and full-term newborns, whose immature renal and liver functions require additional assessment in dosing.

- The average body surface area for an adult has been given as 1.73 m^2; therefore, the child's dose can be calculated using the following formula:

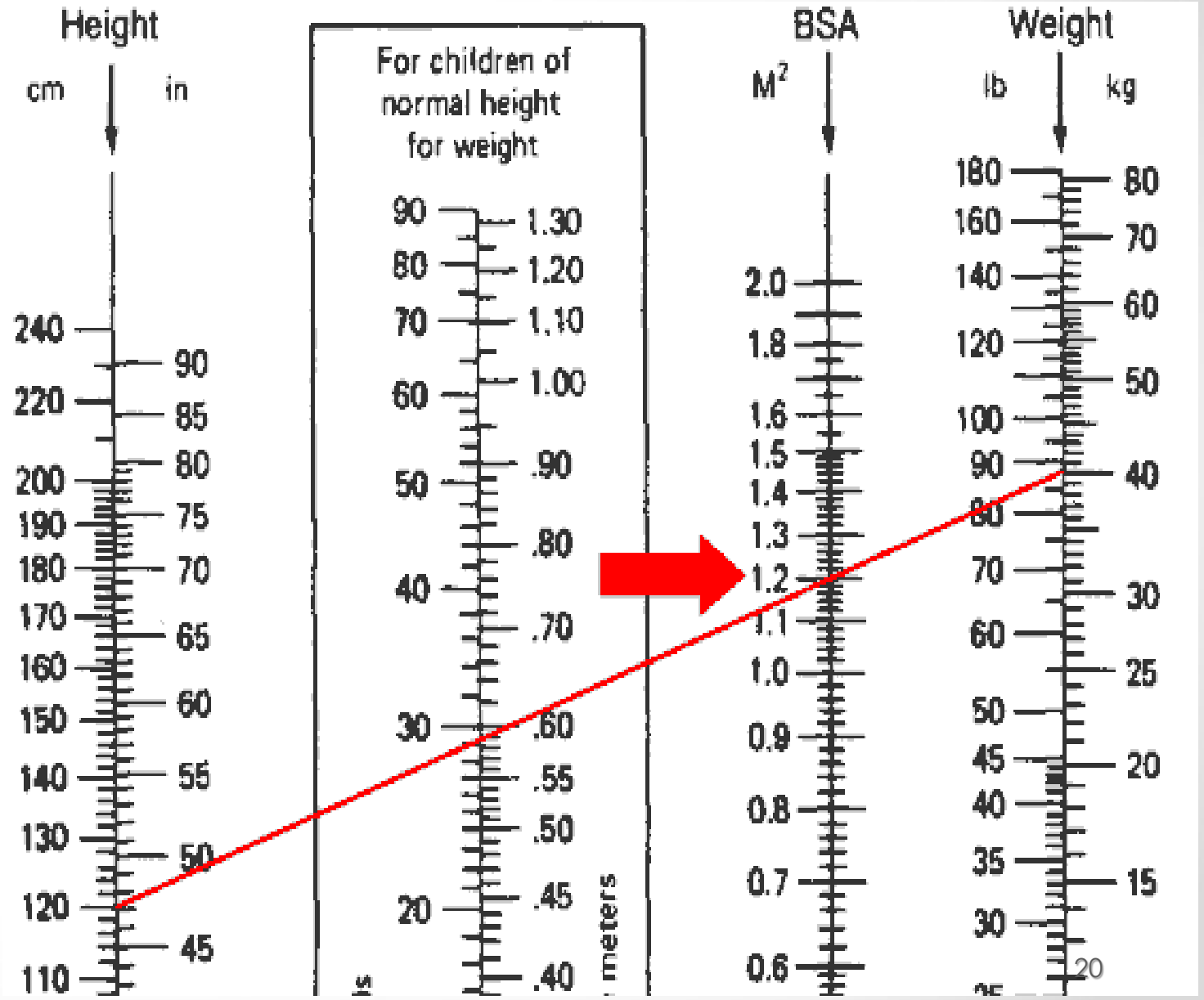
$$\text{Child's dose} = \frac{\text{BSA in } m^2 \text{ of child}}{1.73\ m^2} \times \text{Adult dose (mg)}$$

- If there is need to determine a patient's BSA, a monogram or the following equation $\sqrt{\frac{\text{patient's } \boldsymbol{height}\ (cm) \times \text{patient's } \boldsymbol{weight}\ (kg)}{3600}}$

Drug dosage based on Body Surface Area (BSA)

Nomograms: Body Surface Area Dosage with Relation to Weight and Height in Children or Adults

- For more precise calculation of doses based on BSA, one should refer to a **standard nomogram**, which includes both **weight and height** as factors influencing **BSA**.
- The nomograms may be used for determining BSA from weight and height.
- The BSA in square meters (m^2) is indicated where a straight line drawn to connect the height and weight of the child intersects the surface area column.
  - In the example shown in Figure 8.1, a child weighing 15 kg and measuring 100 cm in height has a BSA of 0.64 m^2.



Drug dosage based on Body Surface Area (BSA)

Example 1: The doctor has ordered an antibiotic whose average adult dose is 250 mg per day. What would the dosage for this medication be on a child who has a length of 120 cm and weight of 40 kg?

- From the nomogram BSA = 1.2 m^2

answer

$$\text{Child dose} = \frac{1.2\ m^2 \quad x\ 250}{1.73\ m^2} = 176\ \text{mg/day}$$

Example 2: If the adult dose of a drug is 75 mg, what would be the dose for a child weighing 40 lb and measuring 32 in. in height? (Use the body surface area method.)

- From the nomogram, the BSA = 0.60 m2

answer

- $\text{Child dose} = \frac{0.6\ m^2 \quad x\ 75}{1.73\ m^2} = 26\ \text{mg.}$

- Example: Calculate the BSA for a patient measuring 165 cm in height and weighing 65 kg.

Answer

$$BSA = \sqrt{\frac{165 \times 65}{3600}} = 1.73\ m^2$$

Special dosing considerations in cancer chemotherapy

Chemotherapy:

- It applies to the treatment of disease with chemicals drugs or chemotherapeutic agents.

In treating cancer:

- chemotherapy, o surgery, o radiation therapy,
- hormone therapy, o immunotherapy.
- alternative treatments o complementary therapy.

- Chemotherapy is primarily associated with the treatment of cancer patients, and is considered the mainstay of such treatment in that it is effective in widespread or metastatic cancer, whereas treatments such as surgery and radiation therapy are limited to specific body sites.
- Combination therapy is included in a patient's treatment plan (e.g., radiation and chemotherapy).

Special dosing considerations in cancer chemotherapy

- Chemotherapeutic agents most often are administered
  - orally or by intravenous
  - injection or infusion;
- other routes of administration may be used as required, including
  - Intramuscular injection or
  - intrathecal (around spinal column endings),
  - Intraarterial (artery),
  - subcutaneous injection.
- administration to a specific site, such as
  - the lung (intrapleural),
  - the skin (topical), or others.
  - the abdomen (intraperitoneal),
- Although a single anticancer drug may be used in a patient's treatment plan, combination chemotherapy perhaps is more usufal.
- By using combinations of drugs having different mechanisms of action against the target cancer cells:
  - the effectiveness of treatment may be enhanced,
  - lower doses used,
  - side effects reduced.
- The combination chemotherapy plans often include:
  - two-agent regimens, three-agent regimens, four-agent regimens.

Special dosing considerations in cancer chemotherapy

Cancer chemotherapy is unique in following ways

1. may involve **single or multiple drugs** of well-established drug therapy regimens or protocols,
2. may involve the use **of investigational drugs** as a part of a clinical trial.
3. Combinations of drugs may be given by the same or by different routes of administration.
4. The drugs may be administered concurrently متزامن or alternately بالتناوب on the **same or different days** during a prescribed treatment cycle (e.g., 28 days).

The days of treatment generally follow a prescribed format of written instructions

- "D" for day, followed by the day(s) of treatment during a cycle,
  - a dash (-) meaning "to“
  - a comma (,) meaning "and."
- Thus "D 1-4" means days 1 to 4, and "Dl,4" means days 1 and 4.

Special dosing considerations in cancer chemotherapy

- The drugs used in combination chemotherapy often fit into a standard drug/dosage regimen identified by abbreviations or acronyms. For example,
  - bladder cancer: "MVAC" consists of methotrexate + vinblasrine + doxorubicin (or acrinomycin) + cisplatin;
  - colorectal cancer : "FU/LU" is fluorouracil + leucovorin;
  - lung cancer: "PC" is paclitaxel + carboplatin;
  - ovarian cancer: "CHAD" for cyclophosphamide + hexamethylmelamine + adriamycin + diamminedichloroplatinum (cisplatin).

- The drugs themselves are commonly **abbreviated** in medication orders:
  - "MTX" for methotrexate,
  - "DOX" for doxirubicin,
  - "VLB" for vinblastine,
  - "CDDP" for cisplatin.

Special dosing considerations in cancer chemotherapy

- For systemic action, chemotherapeutic agents are usually dosed based either on body weight or on body surface area.
- The drug doses stated in standard regimens must be reduced, based on a particular patient's diminished kidney or liver function.
- Doses may also be reduced based on patient's CBC (platelets & WBC count).

- To help prevent chemotherapy errors, a pharmacist must be able to do the following for each patient:
  - correctly interpreting a medication order for chemotherapeutic agents,
  - following the individualized dosing regimen,
  - calculating each dose of medication prescribed,
  - dispensing the appropriate dosage forms and quantities/strengths required.

Example calculations of chemotherapy dosage regimens

Example1

- Regimen: VC Cycle: 28 d;
- repeat for 2–8 cycles
- Vinorelbine, 25 mg/m^2, IV, D 1,8,15,22
- Cisplatin, 100 mg/ m^2, IV, D 1.
- For each of vinorelbine and cisplatin, calculate the total intravenous dose per cycle for a patient measuring 5 ft. 11 in. in height and weighing 175 lb.
- From monogram for destemming BSA (a) find the "patient's" BSA and b) calculate the quantity of each drug in regemin.

Answer

a. BSA = 2 m^2
b. Vinorelbine: 25 mg × 2 (BSA) × 4 (days of treatment) = 200 mg
c. Cisplatin: 100 mg × 2 (BSA) × 1 (days of treatment) = 200 mg

Example calculations of chemotherapy dosage regimens

Example2: Regimen:

- CMF Cycle: 28 d
- Cyclophosphamide, 100 mg/m^2/d po, D 1–14.
- Methotrexate, 40 mg/ m^2, IV, D 2,8.
- Fluorouracil, 600 mg/ m^2, IV, D 1,8.
- Calculate the total cycle dose for cyclophosphamide, methotrexate, and fluorouracil for a patient having a BSA of 1.5 m2.

Answer

BSA = 1.5 m^2

a. Cyclophosphamide: 100 mg × 1.5 (BSA) × 14 (days of treatment) = 2100 mg
b. Methotrexate : 40 mg × 1.5 (BSA) × 2 (days of treatment) = 120 mg
c. Fluorouracil: 600 mg × 1.5 (BSA) × 2 (days of treatment) = 1800 mg

Case in Point 8.4[14]: In treating a 54-year-old female patient, an oncologist selects the drug temozolomide, an antitumor agent used in the treatment of refractory astrocytoma (brain tumor). The drug is used as part of a 28-day regimen, during which the first five days of treatment include temozolomide at a once-daily dose of 150 mg/m^2/day. The patient's medical chart indicates that she measures 5 ft. in height and weighs 117 lb. The physician asks the pharmacist to determine the proper combination of available capsules to use in dosing the patient. The drug is available in capsules containing 5, 20, 100, and 250 mg of temozolomide. What combination of capsules would provide the daily dose of this drug?

answer

$$\text{BSA} = \sqrt{\frac{152.4 \times 53.2}{3600}} = 1.5 \text{ m}^2$$

- Daily dose=150 mg/m^2 × 1.5 m^2 = 225 mg
- To obtain 225 mg, the patient may take two 100-mg capsules, one 20-mg capsule, and one 5-mg capsule daily.