CHAPTER 8 : CALCULATION OF DOSES - PATIENTS PARAMETERS

Objectives

Upon successful completion of this chapter, the student will be able to:

- Describe factors to consider in determining doses for pediatric and elderly patients.
- Calculate doses based on factors of age, body weight, and body surface area.
- Utilize dosing tables and nomograms in calculations.
- Calculate doses for single and combination chemotherapy regimens.

Introduction

For certain drugs and for certain patients, drug dosage is determined on the basis of specific patient parameters.

1. The patient's age
2. Weight
3. Body surface area
4. Nutritional and functional status.

Among patients requiring individualized dosage are:

1. Neonates
2. Other pediatric patients
3. Elderly patients with diminished biologic functions
4. Individuals of all age groups with compromised liver and/or kidney function
5. Critically ill patients, and patients being treated with highly toxic chemotherapeutic agents

Pediatric Patients

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

- Because of the range in age and bodily development in this patient population, the inclusive groups are defined further as follows:

1. *Neonate (newborn), from birth to 1 month*
2. *Infant, 1 month to 1 year*
3. *Early childhood, 1 year through 5 years*
4. *Late childhood, 6 years through 12 years*
5. *Adolescence, 13 years through 17 years of age*

A neonate is considered *premature* if born at less than 37 weeks' gestation.

Proper drug dosing of the pediatric patient depends on a number of factors, including:

1. The patient's age and weight
2. Overall health status
3. The condition of such biologic functions as respiration and circulation
4. The stage of development of body systems for drug metabolism (e.g., liver enzymes) and drug elimination (e.g., renal system).

In the neonate, these biologic functions and systems are underdeveloped.

- ✓ **Renal function**, for example, develops over the span of the first 2 years of life.

Case (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:**

< 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?

Case (2)

- **A pediatric patient is being administered enalaprilat (VASOTEC IV) every 12 hours by intravenous injection to manage hypertension and possible heart failure.**
- **Based on a dose of 5 mcg/kg, the patient is receiving 55 mcg of enalaprilat per dose.**
- **The physician wishes to convert the patient to oral enalapril at a dosage of 100 mcg/kg as a single daily dose.**
- **The standard procedure is to crush a 2.5-mg tablet of enalapril, mix with sterile water to make 12.5 mL, and administer the appropriate dose using a calibrated oral dispenser.**

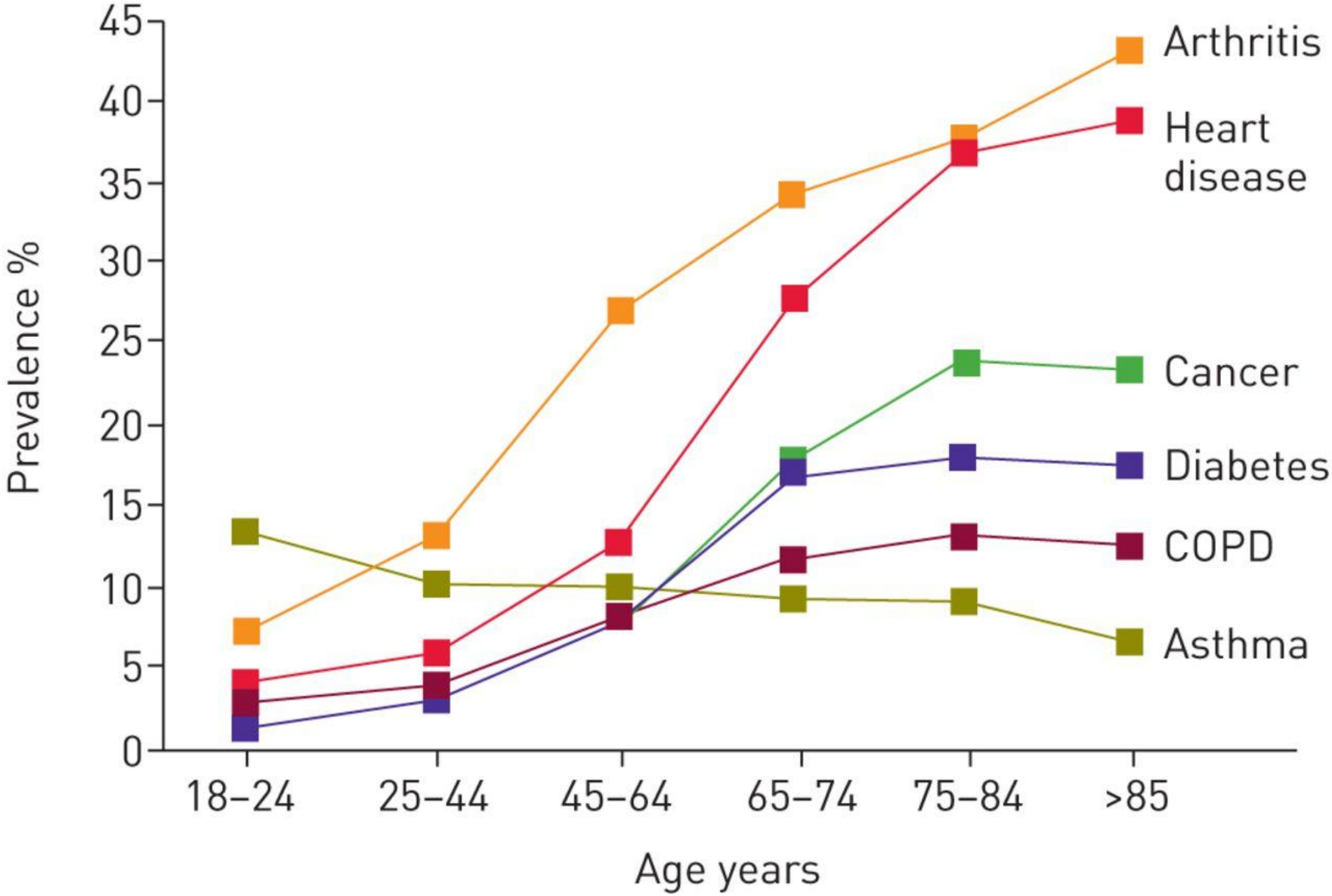
Calculate the dose, in milliliters, to be administered to this patient.

Geriatric Patients

- ***Geriatric medicine*** or ***geriatrics*** is the field that encompasses the management of illness in the elderly.

<u>Some conditions are particularly common in the elderly, including:</u>

1. Degenerative osteoarthritis
2. Congestive heart failure
3. Venous and arterial insufficiency
4. Stroke
5. Urinary incontinence
6. Prostatic carcinoma
7. Parkinsonism
8. Alzheimer disease.


Prevalence %
45
40
35
30
25
20
15
10
5
0
18–24
25–44
45–64
65–74
75–84
>85
Age years
Arthritis
Heart disease
Cancer
Diabetes
COPD
Asthma

There are a number of other common features of medication use in the elderly, including:

- ✓The long-term use of maintenance drugs
- ✓The need for multidrug therapy

Special Considerations in Dose Determinations for Elderly Patients

Dose determinations for elderly patients frequently require consideration of some or all of the following:

1. Therapy is often initiated with a lower-than-usual adult dose.
2. Dose adjustment may be required based on the therapeutic response.
3. The patient's physical condition may determine the drug dose and the route of administration employed.
4. The dose may be determined, in part, on the patient's weight, body surface area, health and disease status, and pharmacokinetic factors.
5. Concomitant drug therapy may affect drug/dose effectiveness.
6. A drug's dose may produce undesired adverse effects and may affect patient compliance.
7. Complex dosage regimens of multiple drug therapy may affect patient compliance.

Dosage Forms Applicable to Pediatric and Geriatric Patients

Oral Administration

- **Chewable tablets and solid gel forms** (medicated "gummy bears") that disintegrate or dissolve in the mouth are also often used for pediatric and geriatric patients.

- In addition, *tablet splitting* and *tablet crushing* are options for individuals unable or unwilling to swallow whole tablets.

Drug dosage based on **Age**

[a] *Young's rule*, based on age:

$$\frac{\text{Age}}{\text{Age} + 12} \times \text{Adult dose} = \text{Dose for child}$$

Cowling's rule:

$$\frac{\text{Age at next birthday (in years)} \times \text{Adult dose}}{24} = \text{Dose for child}$$

Fried's rule for infants:

$$\frac{\text{Age (in months)} \times \text{Adult dose}}{150} = \text{Dose for infant}$$

Clark's rule, based on weight:

$$\frac{\text{Weight (in lb)} \times \text{Adult dose}}{150\ \text{(average weight of adult in lb.)}} = \text{Dose for child}$$

Example

- *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?

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 these data, calculate the dosage range for digoxin for a 20-month-old infant weighing 6.8 kg.

Drug Dosage Based on Body Weight

- In some cases, the *usual dose* is expressed as a specific quantity of drug per unit of patient weight, such as *milligrams of drug per kilogram of body weight* (abbreviated *mg/kg)*.

- **The patient's weight is an important factor in dosing since the size of the body influences the drug's concentration in the body fluids and at its site of action**.

Examples:

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.?

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.?

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

Case (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?

Dosing Tables

- *Using the following table and a daily dose of 0.5 mg/kg, how many 20-mg capsules of the drug product should be dispensed to a patient weighing 176 lb. if the dosage regimen calls for 15 weeks of therapy?*

TABLE 8.2 DOSING BY BODY WEIGHT FOR A HYPOTHETICAL DRUG

BODY WEIGHT		TOTAL mg/DAY		
KILOGRAMS	POUNDS	0.5 mg/kg	1 mg/kg	2 mg/kg
40	88	20	40	80
50	110	25	50	100
60	132	30	60	120
70	154	35	70	140
80	176	40	80	160
90	198	45	90	180
100	220	50	100	200

Drug Dosage Based on Body Surface Area

The *body surface area (BSA)* method of calculating drug doses is widely used for two types of patient groups:

1. Cancer patients receiving chemotherapy
2. Pediatric patients

- The average adult is considered to have a BSA of 1.73 m^2.
- Thus, in reading Table 8.3, a person with a BSA of 1.30 (or about 75% of that of the average adult) would receive about 75% of the adult dose.

TABLE 8.3 APPROXIMATE RELATION OF SURFACE AREA AND WEIGHTS OF INDIVIDUALS OF AVERAGE BODY DIMENSION

KILOGRAMS	POUNDS	SURFACE AREA IN SQUARE METERS	PERCENTAGE OF ADULT DOSE*
2	4.4	0.15	9
3	6.6	0.20	11.5
4	8.8	0.25	14
5	11.0	0.29	16.5
6	13.2	0.33	19
7	15.4	0.37	21
8	17.6	0.40	23
9	19.8	0.43	25
10	22.0	0.46	27
15	33.0	0.63	36
20	44.0	0.83	48
25	55.0	0.95	55
30	66.0	1.08	62
35	77.0	1.20	69
40	88.0	1.30	75
45	99.0	1.40	81
50	110.0	1.51	87
55	121.0	1.58	91

* Based on average adult surface area of 1.73 square meters.
Adapted from Martin EW et al., *Techniques of Medication,* J. B. Lippincott, 1969:31, who adapted it from *Modell's Drugs of Choice* (Mosby).

Example

- *If the adult dose of a drug is 100 mg, calculate the approximate dose for a child with a BSA of 0.83 m^2, using*

(a) *The equation*

(b) *Pervious table*

$$\text{Patient's dose} = \frac{\text{Patient's BSA } (m^2)}{1.73\ m^2} \times \text{Drug dose (mg)}$$

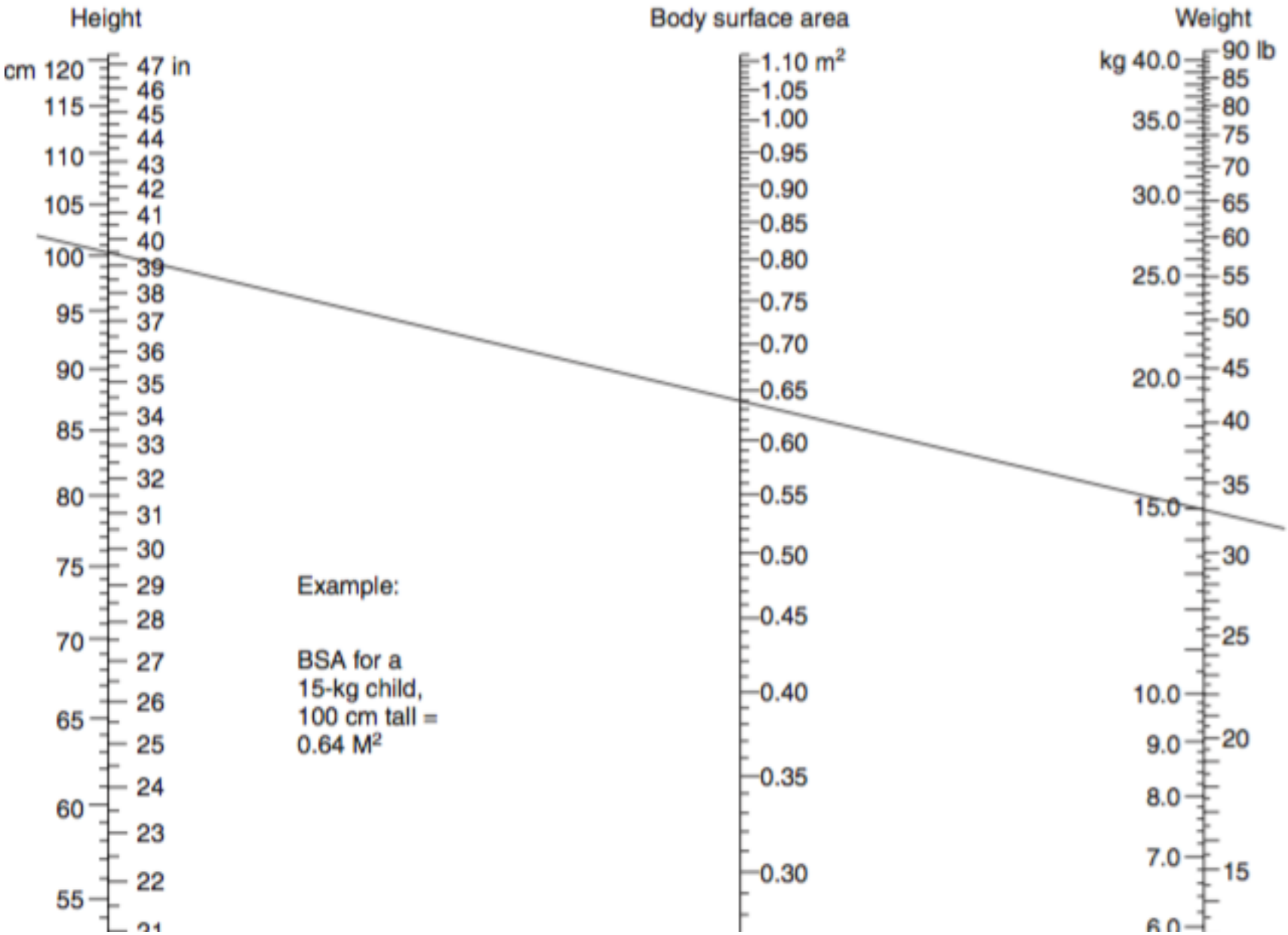
Nomograms

- Most BSA calculations use a standard *nomogram*, which includes both weight and height.

- The BSA of an individual is determined by drawing a straight line connecting the person's height and weight.

The point at which the line intersects the center column indicates the person's BSA in square meters. In the

Nomogram for Determination of Body Surface Area from Height and Weight



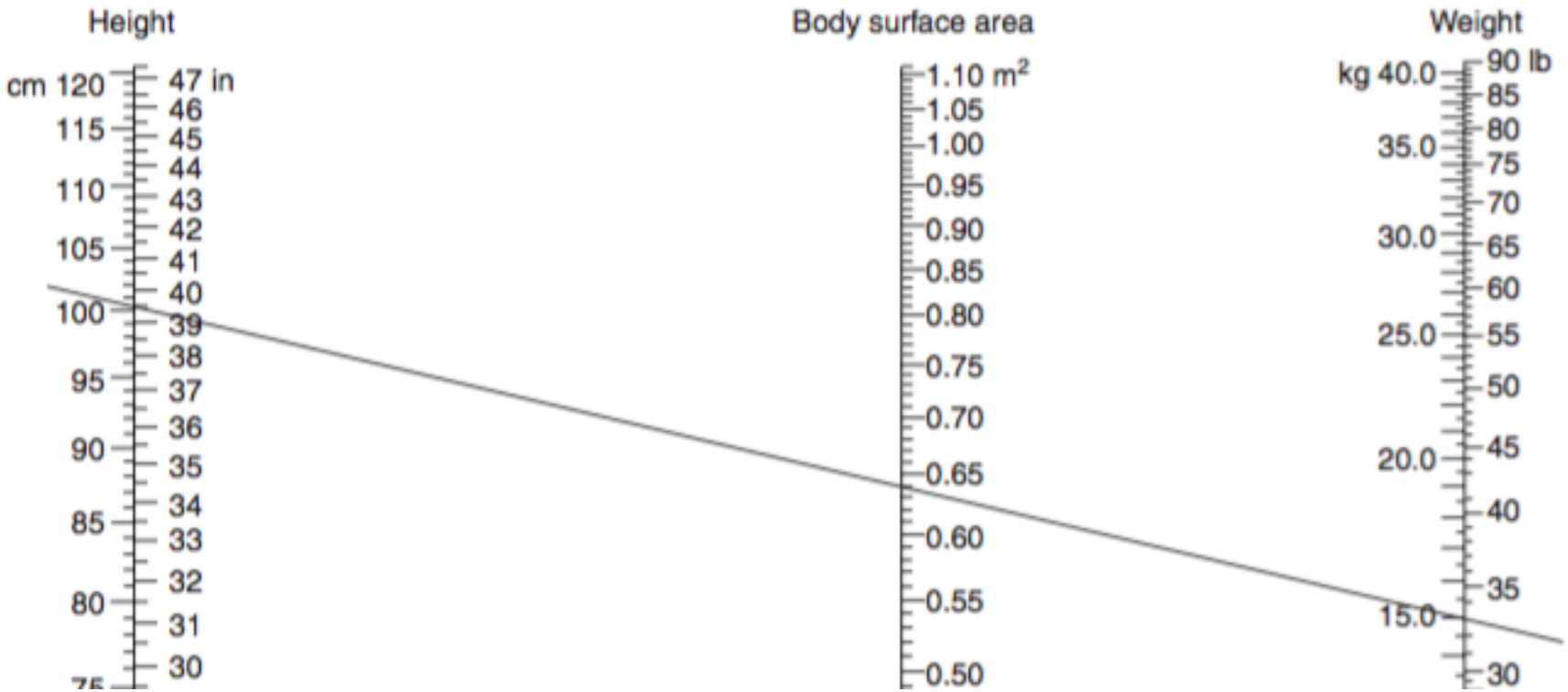
Dose Based on Body Surface Area

$$\text{Patient's dose} = \frac{\text{Patient's BSA } (m^2)}{1.73\ m^2} \times \text{Drug dose (mg)}$$

$$\text{Patient's BSA } (m^2) = \sqrt{\frac{\text{Patient's height (cm)} \times \text{Patient's weight (kg)}}{3600}}$$

- *If the adult dose of a drug is 75 mg,*

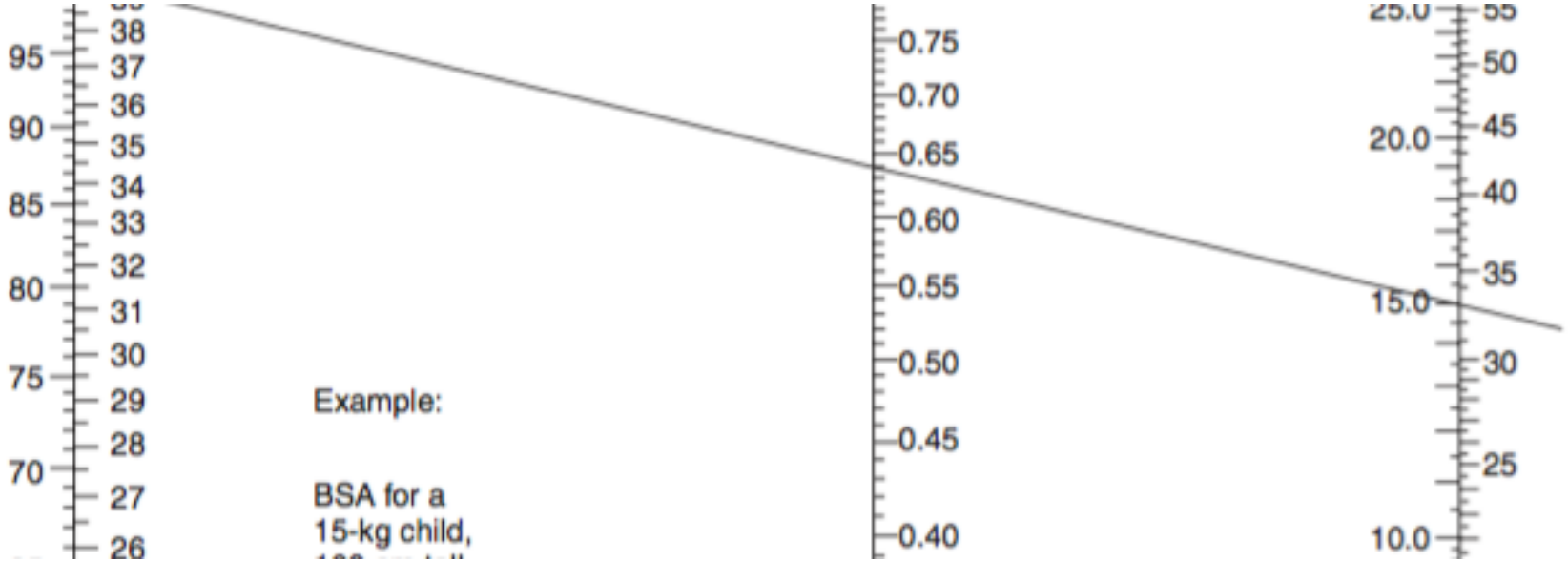
- *What would be the dose for a child weighing 40 lb. and measuring 32 in. in height using the BSA nomogram?*



Example (2)

- *The usual pediatric dose of a drug is stated as 25 mg/m^2.*

- *Using the nomogram, calculate the dose for a child weighing 18 kg and measuring 82 cm in height.*



Example (3)

- *If the dose of a drug is 5 mg/m^2, what would be the dose for a patient with a BSA of 1.9 m^2?*

BSA Equation

- In addition to the use of the nomogram, BSA may be determined through use of the following formula:

$$\text{BSA, m}^2 = \sqrt{\frac{\text{Ht (cm)} \times \text{Wt (kg)}}{3600}}$$

Example

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

Dosage Based on the Medical Condition to be Treated

By using this table, calculate the IV drug dose for a 3-pound 3-ounce neonate.

TABLE 8.5 PARENTERAL DOSAGE SCHEDULE FOR A HYPOTHETICAL DRUG BASED ON PATIENT AGE AND CONDITION BEING TREATED

	DOSE	ROUTE	FREQUENCY
Adults			
Urinary tract infection	250 mg	IV or IM	q12h
Bone and joint infections	2 g	IV	q12h
Pneumonia	500 mg–1 g	IV or IM	q8h
Mild skin infections	500 mg–1 g	IV or IM	q8h
Life-threatening infections	2 g	IV	q8h
Lung infections (normal kidney function)	30–50 mg/kg (NMT 6 g/day)	IV	q8h
Neonates (up to 1 month)	30 mg/kg	IV	q12h
Infants and Children (1 month to 12 years)	30–50 mg/kg (NMT 6g/day)	IV	q8h

Special Dosing Considerations in Cancer Chemotherapy

- The term ***chemotherapy*** applies to the treatment of disease with chemical drugs or ***chemotherapeutic agents***.

Types

The major categories of chemotherapeutic agents include

1. alkylating agents
2. antimetabolites
3. plant alkaloids
4. antitumor antibiotics
5. steroid hormones.

Administration

- Chemotherapeutic agents most often are administered:

1. Orally
2. By intravenous injection
3. By continuous intravenous infusion
4. Other routes of administration are used as required, including:

✓intraarterial (artery)

✓intrathecal (spinal column)

✓intramuscular injection

✓or administration to a specific site, such as:

- the lung (intrapleural)
- the abdomen (intraperitoneal)
- the skin (topical), or others.

Cancer chemotherapy is unique in the following ways:

1. It may involve single or multiple drugs of well-established drug therapy regimens or protocols, or it may involve the use of investigational drugs as a part of a clinical trial.

1. Combinations of drugs may be given by the same or different routes of administration, most often oral and/or intravenous.

3. The drugs may be administered concomitantly or alternately 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, with *D* for "day," followed by the day(s) of treatment during a cycle, with a dash (–) meaning "to" and a comma (,) meaning "and."

- Thus, *D 1–4* means "days 1 to 4," and *D1,4* means "days 1 and 4."

4. The drugs used in combination chemotherapy often fit into a standard drug/dosage regimen identified by abbreviations or *acronyms*.

- ✓ A treatment for bladder cancer referred to as MVAC consists of methotrexate vinblastine doxorubicin (or actinomycin) cisplatin
- ✓ A treatment for colorectal cancer called FU/LU consists of fluorouracil leucovorin
- ✓ A treatment for lung cancer called PC consists of paclitaxel carboplati
- ✓ A treatment for ovarian cancer called CHAD consists of cyclophosphamide hexamethylmelamine adriamycin diamminedichloroplatinum (cisplatin).

5. In addition to the use of abbreviations for the drug therapy regimens, the drugs themselves are commonly abbreviated in medication orders, such as:

- ✓ MTX for “methotrexate,”
- ✓ DOX, for “doxirubicin,”
- ✓ VLB, for “vinblastine,”
- ✓ CDDP for “cisplatin.”

6. For systemic action, chemotherapeutic agents are usually dosed based either on body weight or on body surface area.

- Often, the drug doses stated in standard regimens must be reduced, based on a particular patient's diminished kidney or liver function and, thus, his or her ability to metabolize and eliminate the drug(s) from the body.

6. For certain patients, high-dose chemotherapy is undertaken in an effort to kill tumor cells.

Example (1)

- *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 the nomogram for determining BSA

(a) find the patient's BSA and

(b) calculate the quantity of each drug in the regimen.

Example (2)

- *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 m^2*

Practice Questions

- In a clinical trial of ciprofloxacin (CIPRO), pediatric patients were initiated on 6 to 10 mg/kg intravenously every 8 hours and converted to oral therapy, 10 to 20 mg/kg, every 12 hours.

Calculate the ranges of the total daily amounts of ciprofloxacin that would have been administered intravenously and orally to a 40-lb. child.

- Erythromycin Ethylsuccinate 400 mg/5 mL

Disp. 100 mL
Sig. _____ tsp. q.i.d. until all medication is taken.

If the dose of erythromycin ethylsuccinate is given as 40 mg/kg per day

(a) What would be the proper dose of the medication in the Signa if the prescription is for a 44-lb. child?
(b) How many days will the medication last?

- A 142-lb. patient was receiving filgrastim (NEUPOGEN) in doses of 10 mcg/kg/day when, as a result of successful blood tests, the dose was lowered to 6 mcg/kg/day.
- Using an injection containing 0.3 mg filgrastim per 0.5 mL,

Calculate the previous and new dose to be administered.

(a) 17.7 mL and 64.6 mL

(b) 5.23 mL and 3.14 mL

(c) 1.08 mL and 0.65 mL

(d) 3.87 mL and 2.3 mL

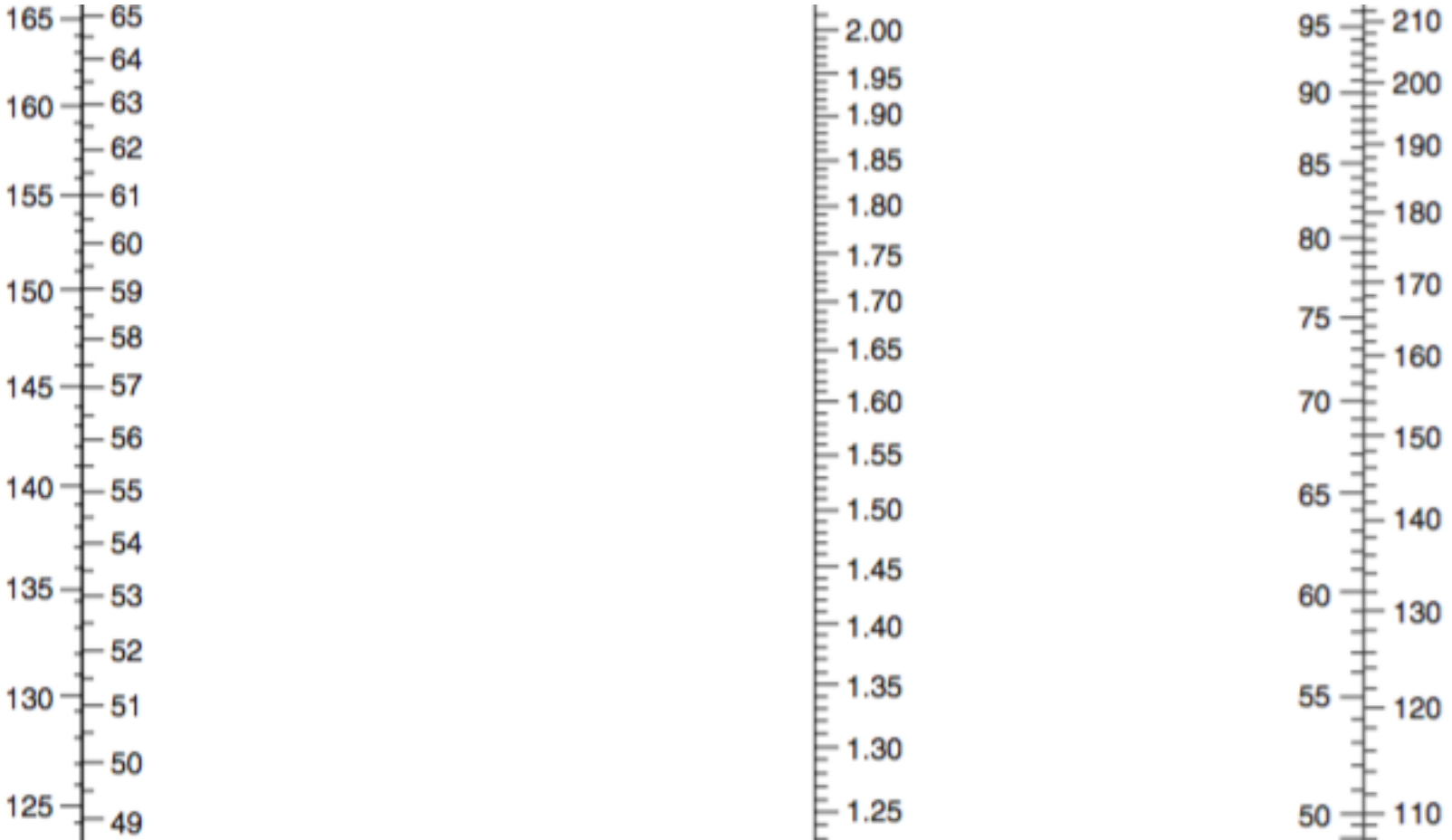
- If the administration of gentamicin at a dose of 1.75 mg/kg is determined to result in peak blood serum levels of 4 mcg/mL.
- Calculate the dose, in milligrams, for a 120-lb. patient that may be expected to result in a blood serum gentamicin level of 4.5 mcg/mL.

- The initial maintenance dose of vancomycin for infants less than 1 week old is 15 mg/kg every 18 hours.

(a) What would be the dose, in milligrams, for an infant weighing 2500 g?

(b) How many milliliters of an injection containing 500 mg per 25 mL should be administered to obtain this dose?

- If the dose of TAXOL (paclitaxel) in the treatment of metastatic ovarian cancer is 135 mg/m^2, what would be the dose for a patient 155 cm tall and weighing 53 kg?



- The pediatric starting dose of ritonavir (NORVIR) is 250 mg/m^2 by mouth twice daily.
- The available oral solution contains 600 mg of ritonavir in each 7.5 mL of solution.
- The correct volume and corresponding quantity of ritonavir to be administered to a child with a body surface area of 0.75 m^2 per dose is:

(a) 5.6 mL (450.4 mg)
(b) 2.8 mL (450.4 mg)
(c) 2.8 mL (225.2 mg)
(d) 2.3 mL (187.5 mg)

- A three-agent dosage regimen, termed VAD, for the treatment of multiple myeloma includes the following drugs taken over a 28-day cycle:
- Vincristine 0.4 mg/d, CIVI
- Doxorubicin, 9 mg/m^2/d CIVI, D 1–4
- Dexamethasone 40 mg/d, PO, D 1–4, 9–12, 17–20

Calculate the total quantity of each drug administered over the course of the treatment cycle for a patient with a BSA of 1.65 m2.

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