Handbook of Applied Therapeutics

NINTH EDITION

Burgunda Sweet

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Wolters Kluwer

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The authors, editors, and publisher have exerted every effort to ensure that drug selection and dosage set forth in this text are in accordance with the current recommendations and practice at the time of publication. However, in view of ongoing research, changes in government regulations, and the constant flow of information relating to drug therapy and drug reactions, the reader is urged to check the package insert for each drug for any change in indications and dosage and for added warnings and precautions. This is particularly important when the recommended agent is a new or infrequently employed drug.

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Preface

The text, *Applied Therapeutics: The Clinical Use of Drugs*,[1] provides a unique blend of factual information and practical application for both the beginning student and the mature practitioner. In the day-to-day management of patients, the clinician often needs quick access to "clinical pearls" to formulate rapid therapeutic decisions. It is for this purpose that the first edition of *The Handbook of Applied Therapeutics* was published. Now, several editions and many years later, this newest edition has been prepared to reflect the substantial increase in drug knowledge since the 2006 publication of the 8th edition.

In these times of national attention on medical errors, escalating costs, and shortages of nurses and pharmacists, we hope that the ready accessibility of clinically important drug information will make *The Handbook of Applied Therapeutics* a valuable tool for assisting in the safe and efficient use of drugs. The editor has abstracted hundreds of valuable tables and other information from the 10th edition of *Applied Therapeutics: The Clinical Use of Drugs*. To achieve portability of size, only the most essential data has been included. Therefore, the user is strongly encouraged to refer to the primary text for more detail and for literature documentation.

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[1]*Applied Therapeutics: The Clinical Use of Drugs*, 10th ed., 2012, edited by Brian K. Alldredge, Robin L. Corelli, Michael E. Ernst, B. Joseph Guglielmo, Pamala A. Jacobson, Wayne A. Kradjan, Bradley R. Williams (ISBN 9781609137137).

Notice to the Reader

Drug therapy information is constantly evolving. Our ever-changing knowledge and experience with drugs and the continual development of new drugs necessitates changes in treatment and drug therapy. The editor, authors, and publisher of this work have made every effort to ensure that the information provided herein was accurate at the time of publication. *It remains the responsibility of every practitioner to evaluate the appropriateness of a particular opinion or therapy in context of the actual clinical situation and with due consideration of any new developments in the field*. Although the editor has been careful to recommend dosages that are in agreement with current standards and responsible literature, the student or practitioner should consult several appropriate information sources when dealing with new and unfamiliar drugs.

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Table of Contents

CHAPTER 1

Assessment of Therapy and Medication Therapy Management*

Medication Therapy Management Services

- Medication Therapy Management Services (MTMS) include comprehensive medication therapy review, developing a personalized medication record, a medication action plan, intervention or referral, and documentation of the encounter. They can be applied to any patient in a variety of settings. Data needed to perform MTMS can be obtained from many sources including the patient, paper chart, pharmacy information system, and electronic health record.
- The general approach to an MTMS patient encounter is shown in Figure 1.1.
  - Data-rich environments (e.g., hospitals, long-term care facilities, outpatient medical clinics) are those settings where there is a wealth of information available to practitioners from the medical record, pharmacy profile, and medication administration record.
  - Data-poor environments (e.g., community pharmacies) are those settings where clinicians are often required to make assessments with limited information. Pharmacy information systems are generally considered to be data poor, requiring information requests from patients or other clinicians.
- Taking an accurate and complete medication history is crucial to a successful MTMS encounter. A proactive interview of the patient or caregiver by the clinician using effective communication principles is particularly important in the data-poor environment (Table 1.1).

Obtaining Patient History

- Use of a standardized form to complete MTMS facilitates quick retrieval of information, minimizes inadvertent omission of data, and enhances the ability of other practitioners to use shared records.
- A careful and complete patient interview should include a medical, medication, and social history and must be provided in a culturally sensitive manner.
- The goal of the medication history is to obtain and assess prescription and nonprescription medications, the intended purpose and appropriateness for each medication, how they are being taken, how long they have been used, and whether the patient believes they are providing therapeutic benefit.
- Medication reconciliation is the comprehensive evaluation of a patient's medication regimen any time there is a transition in care. The goal is to avoid medication errors such as omissions, duplications, dosing errors, or drug interactions and to assess compliance and adherence patterns.

*The reader is referred to Chapter 1, Assessment of Therapy and Medication Therapy Management, written by Marilyn R. Stebbins, PharmD, Timothy W. Cutler, PharmD, CGP, and Patricia L. Parker, PharmD, BCPS, in the 10th edition of *Applied Therapeutics: The Clinical Use of Drugs* for a more in-depth discussion. All notations to reference numbers are based on the reference list at the end of that chapter. The editor of this handbook expresses her thanks to Drs. Stebbins, Cutler, and Parker and acknowledges that this chapter is based on their work.

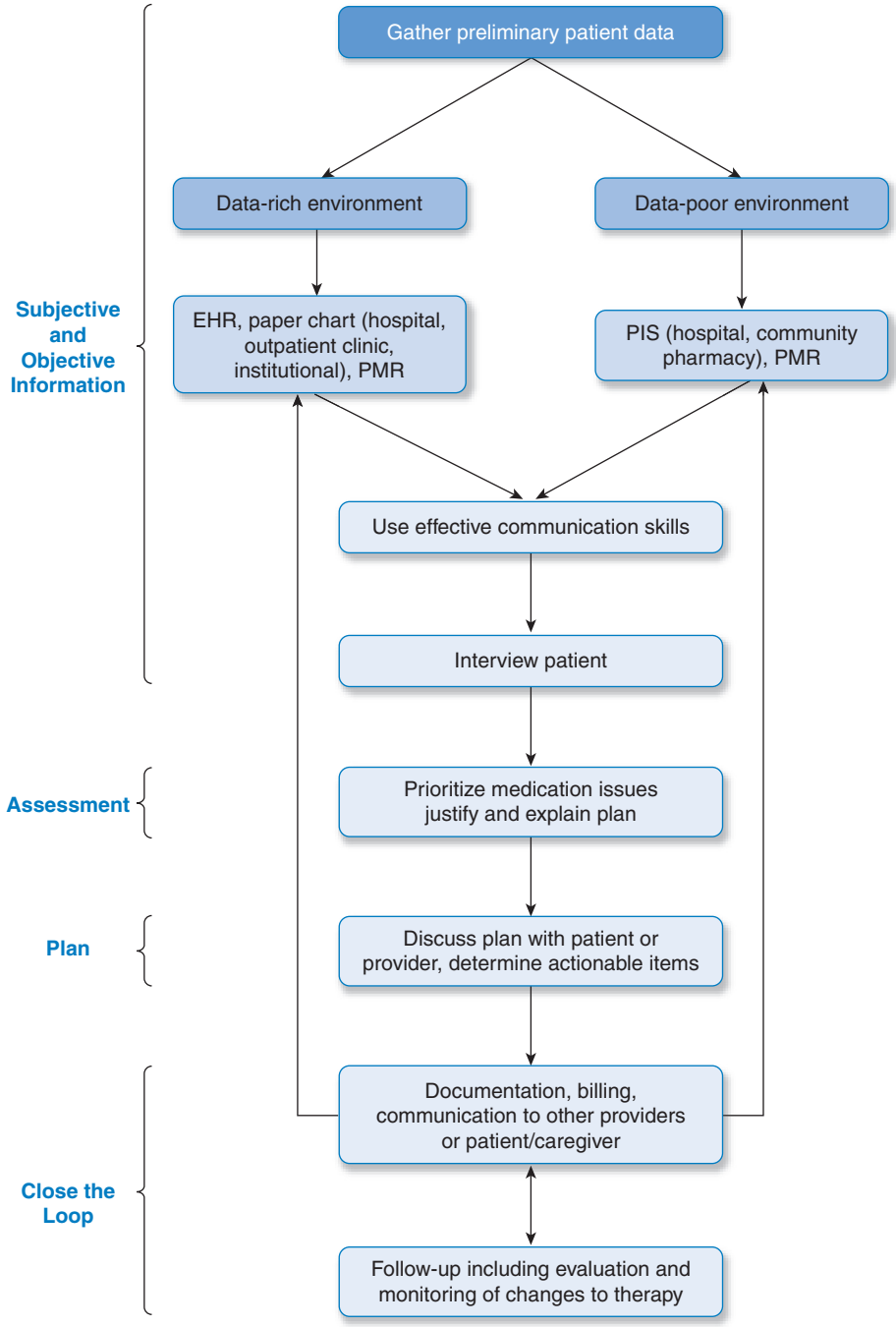

Figure 1.1 General approach to a patient encounter. EHR, electronic health record; PIS, pharmacy information system; PMR, personal medication record.

TABLE 1.1 **Interviewing the Patient**

Importance of Interviewing the Patient

Establishes professional relationship with the patient to:
- Obtain subjective data on medical problems
- Obtain patient-specific information on drug efficacy and toxicity
- Assess the patient's knowledge about, attitudes toward, and pattern of medication use
- Formulate a problem list
- Formulate plans for medication teaching and pharmaceutical care

How to Set the Stage for the Interview

- Have the patient complete a written health and medication questionnaire, if available
- Introduce yourself
- Make the setting as private as possible
- Do not allow friends or relatives without permission of the patient
- Do not appear rushed
- Be polite
- Be attentive
- Maintain eye contact
- Listen more than you talk
- Be nonjudgmental
- Encourage the patient to be descriptive
- Clarify by restatement or patient demonstration (e.g., of a technique)

General Interview Rules

- Read the chart or patient profile first
- Ask for the patient's permission to conduct an interview or make an appointment to do so
- Begin with open-ended questions
- Move to close-ended questions
- Document interaction clearly and succinctly

Information to Be Obtained

- History of allergies
- History of adverse drug reactions
- Weight and height
- Drugs: dose, route, frequency, and reason for use
- Perceived efficacy of each drug
- Perceived side effects
- Adherence to prescribed drug regimen
- Nonprescription medication use (including complementary and alternative medications)
- Possibility of pregnancy in women of childbearing age
- Family or other support systems

Source: Teresa O'Sullivan, PharmD, University of Washington.

Assessment of Patient Therapy

- The general approach to the patient encounter should follow the problem-oriented medical record (POMR), where data are organized by medical problem (Table 1.2). Problems are listed in order of importance and are supported by subjective and objective evidence gathered during the patient encounter.
- Subjective and objective data provide the clinician with information to assess whether a problem continues to exist and that therapeutic outcomes are being achieved. Assessment of drug therapy and disease-specific problems follows data collection. Assessment is the clinician's justification of the plan. The final step is developing the medication action plan and processing any billing requirements. The SOAP (subjective/objective/assessment/plan) note is a common format used when documenting a patient encounter in the hospital setting.
- Communication of the plan with the patient/caregiver is required to ensure there is an understanding of the medical problem(s) and the goal of all treatment plans.

TABLE 1.2 **Elements of the Problem-Oriented Medical Record**[a]

Problem name: Each "problem" is listed separately and given an identifying number. Problems may be a patient complaint (e.g., headache), a laboratory abnormality (e.g., hypokalemia), or a specific disease name if prior diagnosis is known. When monitoring previously described drug therapy, more than one drug-related problem may be considered (e.g., nonadherence, a suspected adverse drug reaction or drug interaction, or an inappropriate dose). Under each problem name, the following information is identified:

Subjective	Information that explains or delineates the reason for the encounter. Information that the patient reports concerning symptoms, previous treatments, medications used, and adverse effects encountered. These are considered nonreproducible data because the information is based on the patient's interpretation and recall of past events.
Objective	Information from physical examination, laboratory test results, diagnostic tests, pill counts, and pharmacy patient profile information. Objective data are measurable and reproducible.
Assessment	A brief but complete description of the problem, including a conclusion or diagnosis that is supported logically by the above subjective and objective data. The assessment should not include a problem or diagnosis that is not defined above.
Plan	A detailed description of recommended or intended further workup (e.g., laboratory tests, radiology, consultation), treatment (e.g., continued observation, physiotherapy, diet, medications, surgery), patient education (e.g., self-care, goals of therapy, medication use and monitoring), monitoring, and follow-up relative to the above assessment.

[a]Sometimes referred to as the **SOAP** (subjective, objective, assessment, plan) note.

CHAPTER 2

Interpretation of Clinical Laboratory Tests*

General Principles

- Laboratory findings can be helpful in assessing clinical disorders, establishing a diagnosis, assessing drug therapy, or evaluating disease progression.
- The serum, urine, and other fluids of patients are routinely analyzed; however, laboratory tests should be ordered only if the results of the tests will affect decisions about the therapeutic management of the patient.
- Laboratory values must be assessed in the context of the clinical situation. They should not be evaluated in isolation of the subjective and objective findings.
- When interpreting laboratory test results, clinicians should use the normal values listed by their own laboratory facility rather than those published in reference texts, because laboratories may use different methods of assay.
- Laboratory error should always be considered when laboratory results do not correlate with clinical expectations.
- Most countries, other than the United States, report clinical laboratory values in the metric system (SI units).

Reference Values

- Blood chemistry reference values are shown in Table 2.1.
- Hematologic laboratory values are shown in Table 2.2.
- Equations are commonly used to estimate a patient's creatinine clearance (CrCl) in lieu of a 24-hour urine collection.
  - When serum creatinine (SCr) concentrations are <1.5 mg/dL, the Cockcroft–Gault formula is typically used:

$$\text{Estimated CrCl for males (mL/minute)} = \frac{(140 - \text{Age})(\text{Body weight in kg})}{(72)(\text{SCr in mg/dL})}$$

    Ideal body weight is used unless actual body weight is less than the ideal weight. The result is multiplied by 0.85 for females.
  - When SCr concentrations are >1.5 mg/dL, the Jelliffe method is typically used:

$$\text{Estimated CrCl for males (mL/minute/1.73 m}^2) = \frac{98 - [(0.8)(\text{Age} - 20)]}{(\text{SCr in mg/dL})}$$

    The result is multiplied by 0.9 for females.

*The reader is referred to Chapter 2, Interpretation of Clinical Laboratory Tests, written by Catrina R. Schwartz, PharmD, and Mark W. Garrison, PharmD, FCCP, in the 10th edition of *Applied Therapeutics: The Clinical Use of Drugs*, for a more in-depth discussion. All notations to reference numbers are based on the reference list at the end of that chapter. The editor of this handbook expresses her thanks to Drs. Schwartz and Garrison and acknowledges that this chapter is based on their work.

TABLE 2.1 **Blood Chemistry Reference Values**

Laboratory Test	Normal Reference Values: Conventional Units	Normal Reference Values: SI Units	Conversion Factor	Comments
ELECTROLYTES				
Sodium	135–145 mEq/L	135–145 mmol/L	1	Low sodium is usually caused by excess water (e.g., ↑ serum antidiuretic hormone) and is treated with water restriction. ↑ in severe dehydration, diabetes insipidus, significant renal and GI losses.
Potassium	3.5–5 mEq/L	3.5–5 mmol/L	1	↑ with renal dysfunction, acidosis, K-sparing diuretics, hemolysis, burns, crush injuries. ↓ by diuretics, or with alkalosis, severe vomiting and diarrhea, heavy NG suctioning.
CO_2 content	22–28 mEq/L	22–28 mmol/L	1	Sum of HCO_3^- and dissolved CO_2. Reflects acid–base balance and compensatory pulmonary (CO_2) and renal (HCO_3^-) mechanisms. Primarily reflects HCO_3^-.
Chloride	95–105 mEq/L	95–105 mmol/L	1	Important for acid–base balance. ↓ by GI loss of chloride-rich fluid (vomiting, diarrhea, GI suction, intestinal fistulas, overdiuresis).
BUN	8–20 mg/dL	2.8–7.1 mmol/L	0.357	End product of protein metabolism, produced by liver, transported in blood, excreted renally. ↑ in renal dysfunction, high protein intake, upper GI bleeding, volume contraction.
Creatinine	0.6–1.2 mg/dL	53–106 μmol/L	88.4	Major constituent of muscle; rate of formation constant; affected by muscle mass (lower with aging); excreted renally. ↑ in renal dysfunction. Used as a primary marker for renal function (GFR).
CrCl	90–130 mL/minute	1.5–2.16 mL/second	0.01667	Reflects GFR; ↓ in renal dysfunction. Used to adjust dosage of renally eliminated drugs.
Estimated GFR	90–120 mL/minute/1.73 m^2	n/a	n/a	Possibly a more accurate reflection of renal function than CrCl. Still influenced by muscle mass.
Cystatin C	<1.0 mg/dL	<0.749 μmol/L	0.749	Indicator of renal function—not influenced by patient muscle mass, age, or sex. May also help predict patients at risk for cardiovascular disease.
Glucose (fasting)	70–99 mg/dL	3.9–5.5 mmol/L	0.05551	↑ in diabetes or by adrenal corticosteroids.

TABLE 2.1 **Blood Chemistry Reference Values** (Continued)

Laboratory Test	Normal Reference Values: Conventional Units	Normal Reference Values: SI Units	Conversion Factor	Comments
Glycosylated hemoglobin	<4%–5.6%	<4%–5.6%	1	Used to assess average blood glucose during 1–3 months. Helpful for monitoring chronic blood glucose control in patients with diabetes. Values >8% seen in patients with poor glucose control.
Calcium—total	8.5–10.5 mg/dL	2.1–2.6 mmol/L	0.250	Regulated by body skeleton redistribution, parathyroid hormone, vitamin D, calcitonin. Affected by changes in albumin concentration. ↓ in hypothyroidism, loop diuretics, vitamin D deficiency; ↑ in malignancy and hyperthyroidism.
Calcium—unbound	4.5–5.6 mg/dL	1.13–1.4 mmol/L	0.250	Physiologically active form. Unbound "free" calcium remains unchanged as albumin fluctuates. Total calcium ↓ when albumin ↓.
Magnesium	1.5–2.4 mEq/L	0.75–1.2 mmol/L	0.51	↓ in malabsorption, severe diarrhea, alcoholism, pancreatitis, diuretics, hyperaldosteronism (symptoms of weakness, depression, agitation, seizures, hypokalemia, arrhythmias). ↑ in renal failure and hypothyroidism, and with magnesium-containing antacids.
Phosphate[a]	2.5–4.5 mg/dL	0.8–1.45 mmol/L	0.323	↑ in renal dysfunction, hypervitaminosis D, hypocalcemia, hypoparathyroidism. ↓ with excess aluminum antacids, malabsorption, renal losses, hypercalcemia, refeeding syndrome.
Uric acid	<7 mg/dL	<0.42 mmol/L	0.06	↑ in gout, neoplastic, or myeloproliferative, disorders, and with drugs (diuretics, niacin, low-dose salicylate, cyclosporin).
PROTEINS				
Prealbumin	15–36 mg/dL	150–360 mg/L	10	Indicates acute changes in nutritional status, useful for monitoring TPN.
Albumin	3.3–4.8 g/dL	33–48 g/L	10	Produced in liver; important for intravascular osmotic pressure. ↓ in liver disease, malnutrition, ascites, hemorrhage, protein-wasting nephropathy. May influence highly protein-bound drugs.

Continued on following page

TABLE 2.1 **Blood Chemistry Reference Values** (Continued)

Laboratory Test	Normal Reference Values: Conventional Units	Normal Reference Values: SI Units	Conversion Factor	Comments
Globulin	2.3–3.5 g/dL	23–35 g/L	10	Active role in immunologic mechanisms. Immunoglobulins ↑ in chronic infection, rheumatoid arthritis, multiple myeloma.
CK	<150 units/L	<2.5 μkat/L	0.01667	In tissues that use high energy (skeletal muscle, myocardium, brain). ↑ with IM injections, MI, acute psychotic episodes. Isoenzyme CK-MM in skeletal muscle; CK-MB in myocardium; CK-BB in brain. MB fraction >5%–6% suggests acute MI.
CK-MB	0–12 units/L	0–0.2 μkat/L	0.01667	
cTnI	<1.5 ng/mL	<1.5 μg/L	1	More specific than CK-MB for myocardial damage, elevated sooner and remains elevated longer than CK-MB. cTnI >2.0 suggests acute myocardial injury.
Myoglobin	<90 mcg/L	<90 μg/L	1	Early elevation (within 3 hours), but less specific for myocardial injury compared with CK-MB.
Homocysteine	4.6–11.9 μmol/L	4.6–11.9 μmol/L	1	Damages vessel endothelial, which may increase the risk for cardiac disease. Associated with deficiencies in folate, vitamin B_6, and vitamin B_{12}.
LDH	<200 units/L	<3.33 μkat/L	0.01667	High in heart, kidney, liver, and skeletal muscle. Five isoenzymes: LD1 and LD2 mostly in heart, LD5 mostly in liver and skeletal muscle, LD3 and LD4 are nonspecific. ↑ in malignancy, extensive burns, PE, renal disease.
BNP	<100 pg/mL	<100 ng/L	1	BNP >500 ng/L indicates left ventricular dysfunction. Released from heart with ↑ workload placed on heart (e.g., CHF).
NT-proBNP	<60 pg/mL (males) <150 pg/mL (females)	<60 ng/L (males) <150 ng/L (females)	1	Component of a precursor to BNP. NT-proBNP has similar clinical utility to BNP as a marker for cardiovascular disease.
CRP	0–1.6 mg/dL	0–16 mg/L	1	Nonspecific indicator of acute inflammation. Similar to ESR, but more rapid onset and greater elevation. CRP >3 mg/dL increases risk of cardiovascular disease.

TABLE 2.1 **Blood Chemistry Reference Values** (Continued)

Laboratory Test	Normal Reference Values: Conventional Units	Normal Reference Values: SI Units	Conversion Factor	Comments
hs-CRP	0–2.0 mg/L	0–2.0 mg/L	1	More sensitive measure of CRP; concentrations 0.5–10 mg/L; hs-CRP <1.0 mg/L low risk for cardiovascular disease; 1.0–3.0 mg/L average risk; and >3.0 mg/L high risk for cardiovascular disease.
Liver Function				
AST	0–35 units/L	0–0.58 μkat/L	0.01667	Large amounts in heart and liver; moderate amounts in muscle, kidney, and pancreas. ↑ with MI and liver injury. Less liver specific than ALT.
ALT	0–35 units/L	0–0.58 μkat/L	0.01667	From heart, liver, muscle, kidney, pancreas. ↑ negligibly unless parenchymal liver disease. More liver specific than AST.
ALP	30–120 units/L	0.5–2.0 μkat/L	0.01667	Large amounts in bile ducts, placenta, bone. ↑ in bile duct obstruction, obstructive liver disease, rapid bone growth (e.g., Paget disease), pregnancy.
GGT	0–70 units/L	0–1.17 μkat/L	0.01667	Sensitive test reflecting hepatocellular injury; not helpful in differentiating liver disorders. Usually high in chronic alcoholics.
Bilirubin—total	0.1–1 mg/dL	1.7–17.1 μmol/L	17.1	Breakdown product of hemoglobin, bound to albumin, conjugated in liver. Total bilirubin includes direct (conjugated) and indirect bilirubin. ↑ with hemolysis, cholestasis, liver injury.
Bilirubin—direct	0–0.2 mg/dL	0–3.4 μmol/L	17.1	
Miscellaneous				
Amylase	35–120 units/L	0.58–2.0 μkat/L	0.01667	Pancreatic enzyme; ↑ in pancreatitis or duct obstruction.
Lipase	0–160 units/L	0–2.67 μkat/L	0.01667	Pancreatic enzyme, ↑ in acute pancreatitis, elevated for longer period than amylase.
PSA	0–4 ng/mL	0–4 μg/L	1	↑ in benign prostatic hypertrophy (BPH) and also in prostate cancer. PSA levels of 4–10 ng/mL should be worked up. Risk of prostate cancer increased if free PSA/total PSA <0.25.
TSH	0.4–5 μunits/mL	0.4–5 μunits/L	1	↑ TSH in primary hypothyroidism requires exogenous thyroid supplementation.

Continued on following page

TABLE 2.1 **Blood Chemistry Reference Values** (Continued)

Laboratory Test	Normal Reference Values: Conventional Units	Normal Reference Values: SI Units	Conversion Factor	Comments
Procalcitonin	<0.5 ng/mL	<0.5 μg/L	1	↑ in bacterial infections—low risk of sepsis if <0.5 ng/mL; high risk of severe sepsis if >2.0 ng/mL. May assist in when to start/stop antibiotic therapy.
TOTAL				
Cholesterol	<200 mg/dL	<5.2 mmol/L	0.02586	Desirable = Total <200; LDL 70–160 (depends on risk factors); HDL >45 mg/dL; ↑ LDL or ↓ HDL are risk factors for cardiovascular disease. Consult NCEP and ATP guidelines for most current target goals and description of patient risk factors.
LDL	70–160 mg/dL	<4.13 mmol/L	0.02586	
HDL	40 mg/dL	1.03 mmol/L	0.02586	
Triglycerides (fasting)	<150 mg/dL	<1.70 mmol/L	0.0113	↑ by alcohol, saturated fats, drugs (propranolol, diuretics, oral contraceptives). Obtain fasting level.

[a]Phosphate as inorganic phosphorus.

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ATP, Adult Treatment Panel; BNP, brain natriuretic peptide; BPH, benign prostatic hypertrophy; BUN, blood urea nitrogen; CHF, congestive heart failure; CK, creatine kinase (formerly known as creatine phosphokinase); CrCl, creatinine clearance; CRP, C-reactive protein; cTnI, cardiac troponin I; ESR, erythrocyte sedimentation rate; GFR, glomerular filtration rate; GGT, γ-glutamyl transferase; GI, gastrointestinal; HDL, high-density lipoprotein; IM, intramuscular; LDH, lactate dehydrogenase; LDL, low-density lipoprotein; MI, myocardial infarction; NCEP, National Cholesterol Education Program; NG, nasogastric; PE, pulmonary embolism; PSA, prostate-specific antigen; SI, International System of Units; TPN, total parenteral nutrition; TSH, thyroid-stimulating hormone.

TABLE 2.2 **Hematologic Laboratory Values**

Laboratory Test	Normal Reference Values: Conventional Units	Normal Reference Values: SI Units	Comments
RBC count			
Male	4.3–5.9 × 10^6/μL	4.3–5.9 × 10^{12}/L	
Female	3.5–5.0 × 10^6/μL	3.5–5.0 × 10^{12}/L	
Hct			↓ with anemias, bleeding, hemolysis. ↑ with polycythemia, chronic hypoxia.
Male	39%–49%	0.39–0.49	
Female	33%–43%	0.33–0.43	
Hgb			Similar to Hct.
Male	14–18 g/dL	140–180 g/L	
Female	12–16 g/dL	120–160 g/L	
MCV	76–100 μm^3	76–100 fL[a]	Describes average RBC size; ↑ MCV = macrocytic, ↓ MCV = microcytic.
MCH	27–33 pg	27–33 pg	Measures average weight of Hgb in RBC.

TABLE 2.2 **Hematologic Laboratory Values** (Continued)

Laboratory Test	Normal Reference Values: Conventional Units	Normal Reference Values: SI Units	Comments
MCHC	33–37 g/dL	330–370 g/L	More reliable index of RBC hemoglobin than MCH. Measures average concentration of Hgb in RBC. Concentration will not change with weight or size of RBC.
Reticulocyte count (adults)	0.1%–2.4%	0.001–0.024	Indicator of RBC production; increase suggests ↑ number of immature erythrocytes released in response to stimulus (e.g., iron in iron-deficiency anemia).
ESR			Nonspecific; ↑ with inflammation, infection, neoplasms, connective tissue disorders, pregnancy, nephritis. Useful monitor of temporal arteritis and polymyalgia rheumatica.
Male	0–20 mm/hour	0–20 mm/hour	
Female	0–30 mm/hour	0–30 mm/hour	
WBC count	4–11 × $10^3/\mu L$	4–11 × 10^9/L	Consists of neutrophils, lymphocytes, monocytes, eosinophils, and basophils; ↑ in infection and stress.
ANC	2,000 cells/μL		ANC = WBC × (% neutrophils + % bands)/100; if <500 ↑ risk of infection, if >1,000 ↓ risk of infection.
Neutrophils	40%–70%	0.4–0.7	Increase in neutrophils suggests bacterial or fungal infection. Increase in bands suggests bacterial infection.
Bands	3%–5%	0.03–0.05	
Lymphocytes	20%–40%	0.20–0.40	
Monocytes	0%–11%	0–0.11	
Eosinophils	0%–8%	0–0.08	Eosinophils ↑ with allergies and parasitic infections.
Basophils	0%–3%	<0.03	
Platelets	150–450 × $10^3/\mu L$	150–450 × 10^9/L	<100 × $10^3/\mu L$ = thrombocytopenia; <20 × $10^3/\mu L$ = ↑ risk for severe bleeding.
Iron			
Male	80–180 mcg/dL	14–32 μmol/L	Body stores two-thirds in Hgb; one-third in bone marrow, spleen, liver; only small amount present in plasma. Blood loss major cause of deficiency.
Female	60–160 mcg/dL	11–29 μmol/L	↑ needs in pregnancy and lactation.
TIBC	250–460 mcg/dL	45–82 μmol/L	↑ capacity to bind iron with iron deficiency.

[a]fL, femtoliter; femto, 10^{-15}; pico, 10^{-12}; nano, 10^{-9}; micro, 10^{-6}; milli, 10^{-3}.

ANC, absolute neutrophil count; ESR, erythrocyte sedimentation rate; Hct, hematocrit; Hgb, hemoglobin; MCH, mean corpuscular hemoglobin; MCHC, mean cell hemoglobin concentration; MCV, mean cell volume; RBC, red blood cell; SI, International System of Units; TIBC, total iron-binding capacity; WBC, white blood cell.

Medication Monitoring

- Therapeutic drug monitoring assists with appropriate dosing adjustments to optimize therapy (Table 2.3).
- Laboratory monitoring for common therapeutic agents are shown in Table 2.4.

TABLE 2.3 **Therapeutic Drug Monitoring Reference Ranges**

Drug	Peak Reference Range	SI Units	Trough Reference Range	SI Units	Notes
ANTIBIOTICS[a]					
Amikacin	25–35 mcg/mL	43–60 μmol/L	<10 mcg/mL	<17 μmol/L	Traditional dosing
Gentamicin or Tobramycin	6–10 mcg/mL	13–21 μmol/L	<2 mcg/mL	<4.2 μmol/L	Traditional dosing
Gentamicin or Tobramycin	20 mcg/mL	42.5 μmol/L	Undetectable	Undetectable	Extended dosing
Vancomycin	Not recommended		10 mcg/mL	3 μmol/L	Recommended to keep >10 mcg/mL to avoid development of resistance
			15–20 mcg/mL	10–14 μmol/L	Complicated infections (bacteremia, endocarditis, osteomyelitis, meningitis, and hospital-acquired pneumonia caused by *Staphylococcus aureus*
ANTIEPILEPTIC DRUGS[b]					
Carbamazepine	4–12 mcg/mL[c]	17–51 μmol/L			
Phenobarbital	10–40 mcg/mL	43–170 μmol/L			
Phenytoin	10–20 mcg/mL	40–79 μmol/L			
Primidone	4–12 mcg/mL	18–55 μmol/L			
Valproic acid	50–125 mcg/mL	350–690 μmol/L			
ANTIDEPRESSANTS AND RELATED AGENTS[d]					
Amitriptyline	120–250 ng/mL	433–903 nmol/L			
Clozapine	200–350 ng/mL	0.6–1 μmol/L			
Desipramine	100–300 ng/mL	281–1125 nmol/L			
Doxepin	100–250 ng/mL	107–537 nmol/L			
Imipramine	125–300 ng/mL	446–893 nmol/L			
Lithium	0.6–1.2 mEq/L	0.6–1.2 nmol/L			
Nortriptyline	50–170 ng/mL	190–646 nmol/L			
ANTIARRHYTHMICS[e]					
Amiodarone	0.5–2.5 mcg/mL	1.5–4 μmol/L			
Digoxin	0.8–2 ng/mL	0.9–2.5 nmol/L			
Flecainide	0.2–1 mcg/mL	0.5–2.4 μmol/L			
Lidocaine	1.5–6 mcg/mL	6.4–26 μmol/L			
Procainamide	4–10 mcg/mL	17–42 μmol/L			
Quinidine	2–5 mcg/mL	6–15 μmol/L			

[a]Peak and trough targets may vary with dosing interval, type or severity of infection, and patient-specific factors.
[b]Therapeutic targets may vary with seizure control and patient-specific factors.
[c]From this point onward, the value in this column indicate therapeutic reference level.
[d]Therapeutic targets may vary with response and patient-specific factors.
[e]Clinically therapeutic targets may vary with response and patient-specific factors.

TABLE 2.4 **Laboratory Monitoring for Common Therapeutic Agents**[a]

Drug or Drug Class	SCr, CrCl	BUN	Na	K	CO_2	Ca	Mg	Phos	Glu	CBC	WBC Indices	RBC Indices	LFT(s)	Lipids	TSH	Drug Level	Other	Notes
ACEI, ARB	✓			✓														
Acitretin									✓				✓	✓				
Aldosterone antagonists	✓	✓		✓														
Amiodarone				✓			✓								✓		Free T_4	Chest x-ray
Atypical antipsychotics									✓					✓				*Also see clozapine*
Calcipotriol/ calcipotriene						✓												
Carbamazepine	✓	✓								✓			✓			✓	Calcium and vit D levels	Genotyping, drug interactions possible
Clozapine									✓		✓						Absolute neutrophil count	
DMARDs	✓									✓			✓					
Digoxin	✓		✓	✓	✓	✓	✓									✓		
Diuretics	✓	✓	✓	✓	✓	✓	✓		✓								Uric acid	
Enoxaparin	✓																Platelets	Anti-Xa (obesity, renal dysfunction, pregnancy)
Ethosuximide													✓			✓		
Felbamate										✓								
Fenofibrate													✓					CK if muscle symptoms
Fexofenadine	✓																	Dose-adjusted CrCl <80 mL/ minute

Continued on following page

TABLE 2.4 **Laboratory Monitoring for Common Therapeutic Agents**[a] (Continued)

Drug or Drug Class	SCr, CrCl	BUN	Na	K	CO_2	Ca	Mg	Phos	Glu	CBC	WBC Indices	RBC Indices	LFT(s)	Lipids	TSH	Drug Level	Other	Notes
Flecainide				✓												✓		
Gemfibrozil										✓			✓					CK if muscle symptoms
Glitazones													✓					
Glyburide	✓								✓								A_{1c}	Not recommended CrCl <50 mL/minute
HMG-CoA inhibitors													✓				Lipids, baseline CK	CK, TSH if muscle symptoms
Lithium	✓	✓	✓	✓	✓	✓				✓					✓	✓		Pregnancy test
Metformin	✓											✓					Hgb, Hct, vit B_{12}, folic acid	
Niacin				✓				✓	✓				✓				Uric acid	CK if muscle symptoms
NSAIDs	✓									✓			✓					
Oxcarbazepine			✓												✓			
Phenytoin										✓						✓	Albumin, calcium, and vit D levels	
PPIs																	Vit B_{12}	
Ranitidine	✓																Vit B_{12}	Dose-adjusted CrCl <50 mL/minute
Retinoids (oral)									✓				✓	✓				Monthly pregnancy test
Theophylline																✓		Drug interactions possible

Thyroid replacement				✓	Free T_4	
Topiramate					Bicarbonate	Ammonia if symptomatic
Valproic acid	✓		✓	✓	Plt count, coagulation tests	Ammonia if symptomatic
Warfarin					INR, Hct	Genotyping, drug interactions possible

[a]Frequency and type of monitoring may vary based on clinical situation.

A_{1c}, hemoglobin A_{1c}; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BUN, blood urea nitrogen; CBC, complete blood count; CK, creatine kinase; CrCl, creatinine clearance; DMARDs, disease-modifying antirheumatic drugs; Hct, hematocrit; Hgb, hemoglobin; HMG-CoA, 3-hydroxy-3-methylglutaryl-coenzyme A; INR, international normalized ratio; LFTs, liver function tests; NSAIDs, nonsteroidal anti-inflammatory drugs; Plt, platelet; PPIs, proton-pump inhibitors; RBC, red blood cell; SCr, serum creatinine; T_4, thyroxine; TSH, thyroid-stimulating hormone; Vit, vitamin; WBC, white blood cell.

Adapted from Therapeutic Research Center. Recommended lab monitoring for common medications. *Pharm Lett*. 2010;26(260704).