TABLE 480e-1 SELECTED EXAMPLES OF LABORATORY CRITICAL VALUES

Value	Less Than	Greater Than
Chemistry		
Ammonia		>100 µmol/L
Calcium, ionized	<3 mg/dL	>7 mg/dL
Calcium, total	<6 mg/dL	>14 mg/dL
Carboxyhemoglobin		>10%
Creatine kinase, total		>1000 U/L
CO_2, total	<11 mol/L	>45 mmol/L
Digoxin		>2.5 µg/L
Glucose	<40 mg/dL	>500 mg/dL
Glucose—CSF	< 40 mg/dL	
Ketone		>1.5 mmol/L
Lithium		> 2.0 mmol/L
Magnesium		>7 mg/dL
Methemoglobin		>35%
Osmolality	<250 mmol/L	>340 mmol/ L
Phosphorus	<1 mg/dL	
pH	<7.1	>7.6
Pco_2	<20 mmHg	>75 mmHg
Po_2, arterial	<40 mmHg	
Po_2, capillary	<30 mmHg	
Bicarbonate	<11 mol/L	>45 mol/L
Potassium	<2.7 mmol/L	>6 mmol/L
Salicylate		>30 mg/L
Sodium	<120 mmol/L	>160 mmol/L
Troponin		>0.120 µg/L
Hematology		
INR		>6.0
PTT		>105 secs
Hemoglobin	<7 g/dL	
WBCs	<1 $\times 10^9$/L	>50 $\times 10^9$/L
Platelets	<50 $\times 10^9$/L	>1000 $\times 10^9$/L
Microbiology[a]		
Acid fast culture or smear		
Blood culture		
CSF Gram stain/culture		
CSF cryptococcal antigen		
Malarial smear		

[a]Any positive result is critical.

Abbreviations: CO_2, carbon dioxide; CSF, cerebrospinal fluid; INR, international normalized ratio; Pco_2, partial pressure of carbon dioxide; Po_2, partial pressure of oxygen; PTT, partial thromboplastin time; WBCs, white blood cells.

should be reserved for situations in which a result is needed for urgent medical care—a judgment that must be made by the ordering physician. Stat testing should not be used merely for the convenience of either the patient or the health care provider.

SENSITIVITY AND SPECIFICITY IN THE CLINICAL LABORATORY

The commonly used metrics of a clinical laboratory test are the diagnostic sensitivity, specificity, and positive and negative predictive values. These concepts are discussed in Chap. 3. In the clinical laboratory, the terms *sensitivity* and *specificity* have alternative meanings that are applied to tests, and the different uses of these terms may cause confusion. *Analytic sensitivity* can refer to the lowest detectable concentration of analyte that can be measured with some defined certainty or to the rate of change of signal intensity as analyte concentration changes. For example, newer generations of laboratory assays frequently exhibit improved sensitivity over that of earlier generations, i.e., they can detect lower concentrations of the analyte—a feature that is often of value in disease diagnosis. *Analytic specificity* refers to the extent to which other substances in the test system interfere with measurement of the analyte of interest. This concept is frequently applied to immunoassays, in which a detection antibody may also bind with compounds that have a structure similar to the substance sought. For instance, immunoassays for drugs may show cross-reactivity with drug metabolites, and immunoassays for glucocorticoids may show cross-reactivity with other glucocorticoids of similar structure. Certain chemical assays are also subject to nonspecificity. For example, the Jaffe reaction, a chemical method commonly used to measure creatinine, is subject to positive interference from a number of other compounds, including glucose, certain ketones, and cephalosporin antibiotics. Elevated concentrations of bilirubin, free hemoglobin, or turbidity in plasma or serum specimens may also interfere with some assays. The clinical laboratory should be able to provide advice about the presence or magnitude of these effects in the assays it performs.

CLINICAL LABORATORY DIAGNOSTIC PRINCIPLES

Clinical laboratory diagnosis, like all diagnosis, is based on observation of disease-related changes from normality.

1. Tissue injury or necrosis allows leakage of intracellular components into the circulation, with consequent detectable rises in blood levels of these components. Many intracellular molecules are common across tissue types and are therefore not indicative of injury to a specific tissue. Other constituents are selectively expressed in relatively high concentrations—or are even uniquely present—in certain tissues. Therefore, their presence in the blood is evidence of injury to that tissue. This principle forms the rationale for measurement of blood levels of, for example, liver enzymes in evaluating liver disease (Chap. 358), cardiac troponins in acute coronary syndromes (Chap. 295), and myoglobulin in muscle injury. The extent of the rise in blood levels of these markers generally correlates with the extent of tissue damage, although there are exceptions; for example, liver enzyme levels may fall in end-stage liver disease.
2. An increase in blood levels of some analytes indicates failure of normal excretory processes. This principle is illustrated by elevations in conjugated bilirubin that accompany obstruction of the biliary system, by elevations in ammonia in advanced or metabolic liver disease, by rises in creatinine and potassium levels in renal failure, and by increases in Pco_2 in some pulmonary diseases.
3. Increases in the blood concentration of tissue-specific markers may result from expansion of the total volume of that tissue. This principle forms the basis for the measurement of levels of many tumor markers such as PSA (prostate cancer), CA-125 (ovarian cancer), CEA (colon cancer), and CA-19–9 (pancreatic cancer). In practice, the usefulness of these markers varies with the degree to which they are produced by a tumor and by the tumor's size. Small colon cancers, for example, may not produce a significant rise in CEA levels, whereas small prostate cancers often produce detectable rises in PSA concentrations.
4. Disease processes often manifest characteristic patterns of coincident changes in levels of several analytes. These patterns of change can be understood by consideration of the underlying pathophysiology. For example, acute intravascular hemolysis is characterized by a fall in levels of hemoglobin and haptoglobin and by a rise in unconjugated bilirubin. In endocrine diseases, there are often changes in concentrations of several hormones because of disturbance of feedback loops. Primary hyperthyroidism, as an example, is characterized by increases in thyroxine and by suppression of thyroid-stimulating hormone. In diabetic ketoacidosis caused by insulin deficiency, there are concomitant elevations of plasma glucose, ketones, and (frequently) potassium. In response to metabolic acidosis, levels of bicarbonate are typically reduced.
5. Genetic changes underlie many diseases, both inherited and acquired. In the era of molecular medicine, there is increasing recognition of the contribution of hereditary factors to many common diseases. Often, the epidemiology of common diseases such as hypertension is characterized by a minority of families that have