CRITICAL LIMITS

By Gerald J. Kost, MD, PhD, MS, FADLM

Critical limits define the quantitative boundaries of life-threatening diagnostic test results. Critical results falling outside high and low critical limits must be reported to clinicians urgently, so the patient can be treated promptly if necessary. Critical value reporting was implemented by George Lundberg, MD, and published in MLO in 1972.[1] Analysis of the impact of critical notifications on patient outcomes appeared in MLO in 1993 with follow-up articles calling for national harmonization and standards of care for critical notification practices.[2-4]

These tables reflect recent research by Gerald Kost, MD, PhD, MS, FADLM of the POCT•CTR, School of Medicine, UC Davis, and his UC Honors Program student team. The research entailed a review of web-posted critical limits/values at 26 university hospitals[5] with comparison to 1990-93 data compiled through the first three national surveys of critical limits used by 92 responding U.S. medical centers, including 20 trauma centers and 39 children's hospitals.[6-8] Most hospital policies posted on the Web defined what a critical value is and stated that a licensed provider must be informed immediately.[5]

Statistically significant differences in 2023 versus 1990-93 critical limits were observed for blood gas (pO_2, pCO_2), chemistry (glucose, calcium, magnesium), and hematology/coagulation (hemoglobin, platelets, PTT, WBC) tests, and for newborn glucose, potassium, pO_2, and hematocrit, as indicated in bold in the tables. Notable were INR and cardiac troponins, although not all hospitals listed the latter. Fourteen listed troponin (6), troponin I (3), hs-TnI (3), or troponin T (2).[5] The number of qualitative critical values increased substantially, including bioterrorism threats and high-risk pathogens.[5] While COVID-19 was not listed frequently, it should be in view of the risk of infected patients spreading the disease to care providers, families, and other patients.

Table 1: Clinical chemistry critical limits.[5]

Test	Listing freq., %		Units	Low mean (SD)		Low median (range)		High mean (SD)		High median (range)	
	2023	1990		1990	2023	1990	2023	1990	2023	1990	2023
Glucose	100	100	mmol/L	2.6 (0.4)	2.7 (0.3)	**2.5 (1.7-3.9)**	**2.78[a] (2.2-3.3)**	26.9 (8.0)	24.9 (2.6)	27.8 (6.1-55.5)	25.0 (19.4-27.8)
			mg/dL	46 (7)	49 (6)	**45 (30-70)**	**50[a] (40-60)**	484 (144)	449 (46)	501 (110-1,000)	450 (350-500)
Potassium	100	100	mmol/L	2.8 (0.3)	2.8 (0.2)	2.7 (2.5-3.6)	2.8 (2.5-3.0)	6.2 (0.4)	6.1 (0.2)	6.0 (5.0-8.0)	6.0 (6.0-6.5)
Sodium	100	100	mmol/L	120 (5)	121 (2)	120 (110-137)	120 (120-125)	158 (6)	159 (2)	160 (145-170)	160 (155-160)
Calcium	96	100	mmol/L	1.65 (0.17)	1.56 (0.10)	**1.62 (1.2-2.15)**	**1.56[b] (1.25-1.75)**	3.22 (0.22)	3.19 (0.12)	3.24 (2.62-3.49)	3.24 (2.99-3.49)
			mg/dL	6.6 (0.7)	6.3 (0.4)	**6.5 (5.0-8.6)**	**6.3[b] (5.0-7.0)**	12.9 (0.9)	12.8 (0.5)	13.0 (10.5-14.0)	13 (12-14)
Magnesium	81	33	mmol/L	0.41 (0.16)	0.43 (0.03)	0.41 (0.21-0.74)	0.41 (0.41-0.49)	2.02 (0.82)	2.10 (0.53)	**1.75 (1.03-5.02)**	**2.02[a] (1.44-3.70)**
			mg/dL	1.0 (0.4)	1.0 (0.08)	1.0 (0.5-1.8)	1.0 (1.0-1.2)	4.9 (2.0)	5.1 (1.3)	**4.3 (2.5-12.2)**	**4.9[a] (3.5-9.0)**
Ionized calcium	77	57	mmol/L	0.82 (0.14)	0.81 (0.05)	0.80 (0.50-1.07)	0.8 (0.75-0.90)	1.55 (0.19)	1.55 (0.09)	1.50 (1.30-2.00)	1.55 (1.41-1.80)
Phosohorous	77	33	mmol/L	0.39 (0.10)	0.35 (0.05)	0.32 (0.26-0.65)	0.3 (0.29-0.48)	2.87 (0.48)	2.92 (0.22)	3.22 (2.26-3.23)	2.89 (2.58-3.23)
			mg/dL	1.2 (0.3)	1.1 (0.1)	1.0 (0.8-2.0)	1.0 (0.9-1.5)	8.9 (1.5)	9.0 (0.68)	10.0 (7.0-10.0)	9.0 (8.0-10.0)
CO_2 content	69	75	mmol/L	11 (2)	10.5 (1.1)	10 (5-20)	10 (10-14)	40 (3)	41 (4)	40 (35-50)	40 (36-50)
Lactate	58	5	mmol/L	—	—	—	—	3.4 (1.3)	4.1 (1.0)	3.0 (2.3-5.0)	4.0 (2.0-5.0)
			mg/dL	—	—	—	—	30.6 (11.7)	36.8 (8.96)	27.0 (20.7-45.0)	36.0 (18.0-45.0)
Osmolality	38	20	mmol/kg	250 (13)	243 (19)	250 (230-280)	250 (190-251)	326 (18)	333 (22)	320 (295-375)	325 (320-390)
Cerebro-spinal fluid glucose	38	16	mmol/L	2.1 (0.6)	1.8 (0.4)	2.2 (1.1-2.8)	1.9 (1.1-2.2)	24.3 (11.4)	18.3 (5.4)	16.7 (13.9-38.9)	16.7 (13.9-27.8)
			mq/dL	37 (10)	33 (7.7)	40 (20-50)	35 (20-40)	438 (206)	330 (97)	301 (250-700)	300 (250-500)
Chloride	31	20	mmol/L	75 (8)	77 (4)	80 (60-90)	78 (70-81)	126 (12)	123 (4.6)	120 (115-156)	121 (119-130)
Creatinine	23	10	µmol/L	—	—	—	—	654 (380)	698 (218)	884 (177-1,326)	769 (442-884)
			mg/dL	—	—	—	—	7.4 (4.3)	7.9 (2.5)	10 (2.0-15.0)	8.7 (5.0-10.0)
Urea nitrogen	15	20	mmol/L	—	—	—	—	37.1 (21.1)	34.4 (3.92)	33.9 (14.3-107.1)	35.9 (28.6-37.1)
			mg/dL	—	—	—	—	104 (59)	96 (11.0)	95 (40-300)	101 (80-104)
Uric acid	8	20	µmol/L	—	—	—	—	773 (119)	773	892 (595-892)	773
			mg/dL	—	—	—	—	13 (2)	13	15 (10-15)	13
Bilirubin	0	25	µmol/L	—	—	—	—	257 (86)	—	257 (86-513)	—
			mg/dL	—	—	—	—	15 (5)	—	15 (5-30)	—

[a]p<0.05: differences were considered significant, [b]p<0.01: differences were considered highly significant. Cell entries in the Table are boldface when significantly different.

The Joint Commission identifies timely reporting of critical tests results as a National Patient Safety Goal (NPSG.02.03.01) in its accreditation programs.[9] Clinical laboratories can develop notification practices collaboratively with emergency physicians, hospitalists, and point-of-care specialists to achieve timely, effective, and focused patient care. For example, the statistically significant increase in the low critical limit for glucose, which increases the notification frequency, may reflect recognition of the level two threshold [54 mg/dL (3.0 mmol/L)] at which neuroglycopenic symptoms require immediate action.[10]

In the recent survey, the number of tests listed varied from 21 to as high as 116 with a median of 62.[5] Hospitals are advised to review their notification practices, quantitative decision thresholds, and qualitative critical value notifications to assure that effective life-saving alerts improve patient outcomes without excessively burdening laboratory, bedside, critical care, or emergency staff.

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Table 2: Blood gas and pH critical limits.[5]

Measurand	Listing freq., %		Units	Low mean (SD)		Low median (range)		High mean (SD)		High median (range)	
	2023	1990		1990	2023	1990	2023	1990	2023	1990	2023
pH	85	35	pH Units	7.21 (0.06)	7.21 (0.03)	7.20 (7.00-7.35)	7.20 (7.15-7.30)	7.59 (0.03)	7.59 (0.02)	7.60 (7.50-7.65)	7.60 (7.55-7.60)
Arterial pO_2	81	26	mm Hg	43 (6)	46 (6)	**40 (30-55)**	**44[a] (39-60)**	—	—	—	—
			kPa	5.7 (0.8)	6.1 (0.8)	**5.3 (4.0-7.3)**	**5.9[a] (5.2-8.0)**	—	—	—	—
Arterial pCO_2	73	30	mm Hg	19 (3)	20 (3)	**20 (9-25)**	**20[a] (9-25)**	67 (6)	65 (4)	70 (50-80)	65 (60-70)
			kPa	2.5 (0.4)	2.7 (0.4)	**2.7 (1.2-3.3)**	**2.7[a] (1.2-3.3)**	8.9 (0.8)	8.7 (0.5)	9.3 (6.7-10.7)	8.7 (8.0-9.3)
Venous pH	23	—	pH Units	—	7.16 (0.08)	—	7.19 (7.00-7.23)	—	7.56 (0.03)	—	7.57 (7.52-7.59)
Capillary pCO_2	12	—	mm Hg	—	23 (4)	—	23 (20-25)	—	65 (5)	—	65 (60-70)
			kPa	—	3.1 (0.5)	—	3.1 (2.7-3.3)	—	8.7 (0.7)	—	8.7 (8.0-9.3)
Capillary pH	12	—	pH Units	—	7.20 (0.05)	—	7.20 (7.15-7.25)	—	7.58 (0.03)	—	7.60 (7.55-7.60)
Venous pCO_2	12	—	mm Hg	—	24 (5)	—	24 (19-28)	—	71 (12)	—	65 (64-85)
			kPa	—	3.2 (0.7)	—	3.2 (2.5-3.7)	—	9.5 (1.6)	—	8.7 (8.5-11.3)

[a]p<0.05: differences were considered significant, [b]p<0.01: differences were considered highly significant. Cell entries in the Table are boldface when significantly different.

Table 3: Hematology and coagulation critical limits.[5]

Test	Listing freq., %		Units	Low mean (SD)		Low median (range)		High mean (SD)		High median (range)	
	2023	1990		1990	2023	1990	2023	1990	2023	1990	2023
INR	92	—	—	—	—	—	—	—	4.9 (0.7)	—	5 (4-7)
Platelets	92	45	10^9/L	37 (21)	27 (13)	**30 (10-100)**	**20[a] (10-50)**	894 (206)	941 (112)	1,000 (100-1,000)	1,000 (600-1,000)
Hemoglobin	92	42	g/dL	7 (2.2)	6.2 (0.7)	7 (4-15)	6 (5-7)	19 (4.4)	20.7 (1.1)	**20 (20-30)**	**20[a] (20-22.5)**
Partial thrombo-plastin time	89	33	Sec	50 (–)	18 (–)	50 (–)	18 (–)	80 (33)	120 (32)	**80 (40-150)**	**120[b] (70-200)**
Fibrinogen	77	27	g/L	0.85 (0.26)	0.88 (0.16)	1 (0.08-1)	1 (0.6-1)	7.8 (2.6)	—	8 (5-10)	—
WBC	73	42	10^9/L	2.02 (0.7)	1.33 (0.5)	**2 (1-5)**	**1.25[b] (0.5-2.0)**	37 (22)	52 (32)	**30 (9.5-100)**	**50[a] (15-149)**
Hematocrit	65	29	%	20 (8.1)	18 (2.5)	18 (41)	20 (15-21)	60 (12.8)	59.4 (3.8)	60 (20-80)	60 (54-65)
Absolute neutrophil count	31	—	10^9/L	—	0.56 (1.8)	—	0.5 (0.5-1.0)	—	—	—	—
WBC count in CSF	23	—	WBC/ mm^3	—	—	—	—	—	70 (71)	—	45.5 (0.01-200)
Band count	15	—	%	—	—	—	—	—	20 (7)	—	22.5 (10-25)

[a]p<0.05: differences were considered significant, [b]p<0.01: differences were considered highly significant. CSF, cerebrospinal fluid; INR, international normalized ratio; WBC, white blood cell count. Cell entries in the Table are boldface when significantly different.

Table 4: Qualitative critical values.[5]

Laboratory disciplines and critical values	Detection methods (if identified)	Freq., %
Microbiology		
Blood, cerebrospinal fluid, or body cavity fluid	Culture	85
Cryptococcus species	Culture, RAgT	65
Blood, cerebrospinal fluid, or body cavity fluid	Gram stain	62
Acid-fast Bacillus (AFB)	Culture, stain	54
Dimorphic fungal pathogens (e.g., *Histoplasma capsulatum, Blastomyces dermatitidis, Coccidioides* species)	Culture, PCR, smear	31
Group A *Streptococci*	Culture, RAgT	19
Mycobacterium tuberculosis	Culture, PCR	19
Neisseria meningitidis	Culture, RAgT	19
Bordetella pertussis (any specimen from a neonate)	Culture, PCR	15
Neisseria gonorrhea	Neisseria gonorrhea	15
Haemophilus influenzae B	Culture, RAgT	12
Legionella pneumophilia	Culture, RAgT	12
Group B *Streptococci*	Culture, RAgT	8
MRSA (Methicillin Resistant *Staph Aureus*)	Culture	8
Vancomycin Intermediate/ Resistant *Staphylococcus*	Not listed	8
VRE (Vancomycin Resistant *Entercoccus*)	Not listed	8
Positive India Ink preparation	—	4
Virology		
Herpes simplex virus (HSV) in newborns or term pregnant mothers	Culture, PCR	35
Herpes simplex virus (HSV) in CSF	PCR	31
HIV (Human Immunodeficiency virus)	PCR, RAgT	23
Cytomegalovirus (CMV)	PCR, RAgT	19
Varicella zoster virus (VZV)	PCR	19
Epstein-Barr virus (EBV)	PCR	15
COVID-19 (SARS-CoV-2) detected	Not listed	12
Influenza A&B	Culture, PCR, RAgT	12
Hepatitis A, B, or C	PCR, RAgT	12
Syphilis	RPR, VDRL	12
Respiratory Syncytial virus (RSV)	PCR	8
Parasitology		
Malarial parasites	Smear	35
Parasites in sterile body fluid	Smear	23
Microfilaria	Smear	15
Babesia	PCR, smear	12
Blood Bank		
Positive transfusion reaction	—	27
Positive direct coombs test/ direct antiglobulin test (DAT)	—	23
Maternal titers of significant red cell antibodies during pregnancy	—	15

Laboratory disciplines and critical values	Detection methods (if identified)	Freq., %
Blood Bank (continued)		
Blood product associated with a transfusion reaction	Culture	12
Incompatible crossmatch	—	12
Indirect Coombs positive/Indirect antiglobulin test (IAT)	—	12
Crossmatches unable to locate compatible red cells	—	8
Blood product associated with a transfusion reaction	Gram stain	8
Hemoglobinemia in post-transfusion reaction specimen	—	8
Hematology		
Presence of blasts in blood	Smear	27
Positive Heparin-induced platelet antibody	—	23
New diagnosis or findings of leukemia	Smear	4
Presence of band cells	Smear	4
Presence of sickle cells or aplastic crisis	Smear	4
Anatomic pathology		
Unexpected diagnosis of malignancy (as determined by the clinical infor-mation provided)	—	15
Significant disagreement between the frozen section and final diagnosis	—	12
Significant discrepancy between outside diagnosis and the review diagnosis	—	12
Pneumothorax	X-ray	12
All revised or amended reports reflecting a significant change in diagnosis with potential to impact treatment or outcome	—	8
Clinical microscopy		
Presence of malignant cells, blasts, or microorganisms in cerebrospinal fluid or body fluids	Smear	15
Presence of organisms by microscopic examination	Smear	8
Surgical pathology		
Any findings likely to reflect unrecognized perforation of an organ (e.g. fat in endometrial curettage or endo-scopic polypectomy specimen)	—	12
Significant discrepancy between the FNA rapid assessment diagnosis and the final diagnosis	—	12
Crescents in kidney biopsy specimens	—	8
Unexpected absence of chorionic villi in uterine curetting	—	8
Fungi in FNA of immunocompromised patients	—	4
Urinalysis		
Combination of strongly positive test results for glucose and for ketones in urine	—	12
Presence of RBC casts	—	12
Presence of reducing substances	—	12

COVID-19, Coronavirus disease 2019; CSF, Cerebrospinal fluid; FNA, fine needle aspiration; PCR, Polymerase Chain Reaction; RAgT, rapid antigen test; RBC, red blood cells; RPR, rapid plasma reagin; SARS-CoV-2, severe acute respiratory syndrome-Coronavirus-2; VDRL, Venereal Disease Research Laboratory.

Table 5: Frequency of listings of bioterrorism threats and pathogens.[5]

Categories and Threats	Frequency, %
A. Bioterrorism threats listed as critical values	
Category A: Detection of threats that are easily disseminated, result in high mortality, cause public panic, and require special action[a,b]	
Tularemia (*Francisella tularensis*)	27
Anthrax (*Bacillus anthracis*)	23
Plague (*Yersinia pestis*)	23
Botulism (*Clostridium botulinum* toxin)	15
Smallpox (*Variola major*)	12
Viral hemorrhagic fever	8
Category B: Detection of threats that are moderately easy to disseminate, low mortality rates, and require enhanced disease surveillance[a,b]	
Brucellosis (*Brucella* species)	23
Escherichia coli O157:H7 or shiga-toxin tests	19
Burkholderia mallei or *pseudomallei*	15
Epsilon toxin of *Clostridium perfingens*	8
Salmonella species	8
Shigella	8
Cholera (*Vibrio cholerae*)	8
Q fever (*Coxiella burnetii*)	8

Pathogens (and resistance)	CDC	WHO	NIH	Frequency, %
Tuberculosis, including drug-resistant tuberculosis			X	58
Coccidioides species			X	27
Meningitis	X	X		27
Human immunodeficiency virus			X	23
Plague (*Yersinia pestis*)		X	X	23
Streptococcus, group A			X	19
Bordetella pertussis			X	15
Listeria	X		X	15
Antimicrobial resistance			X	12
Coronavirus disease 2019 (COVID-19)	X			12
Viral hemorrhagic fever		X	X	8
Salmonella	X		X	8
Cholera (*Vibrio cholerae*)		X		8
Shigellosis (*Shigella* species)		X	X	8
Influenza A		X	X	8
Hepatitis A	X		X	8
Hepatitis C	X		X	4
Cyclospora cayatanensis			X	4
Rubeola (measles)	X		X	4
Monkeypox		X		4
Norovirus	X			0
Ebola virus disease		X	X	0
Marburg virus disease		X	X	0
Zika virus disease		X	X	0

CDC, Centers for Disease Control and Prevention; COVID-19, Coronavirus Disease 2019; NIH, National Institutes of Health; WHO, World Health Organization.
[a]Centers for Disease Control and Prevention (CDC), Bioterrorism Agents/Diseases (by category)|Emergency Preparedness & Response. Published May 15, 2019. https://emergency.cdc.gov/agent/agentlist-category.asp#catdef [Accessed June 26, 2024].
[b]Homeland Security. Biological Attack Fact Sheet. Department of Homeland Security. Published July 8, 2015. https://www.dhs.gov/publication/biological-attackfact-sheet [Accessed June 26, 2024].

Table 6: Newborn critical limits.[5]

Test	Listing freq., %		Units	Low mean (SD)		Low median (range)		High mean (SD)		High median (range)	
	2023	1990		1990	2023	1990	2023	1990	2023	1990	2023
A. Clinical chemistry											
Bilirubin	88	9	µmol/L	—	—	—	—	239 (34)	257 (34)	257 (171-308)	257 (205-342)
			mg/dL	—	—	—	—	14 (2)	15 (2)	15 (10-18)	15 (12-20)
Glucose	73	42	mmol/L	1.8 (0.4)	2.2 (0.4)	**1.7 (1.1-2.8)**	**2.2[b] (1.7-3.1)**	18.1 (6.0)	14.5 (5.3)	16.7 (11.1-38.9)	12.5 (8.3-27.8)
			mg/dL	32 (7)	39 (7)	**31 (20-50)**	**40[b] (30-55)**	326 (108)	261 (95)	301 (200-700)	225 (150-500)
Potassium	31	32	mmol/L	2.6 (0.2)	2.7 (0.3)	2.5 (2.5-3.5)	2.8 (2.0-3.0)	7.7 (0.7)	7.1 (0.7)	**8.0 (5.5-8.0)**	**7.0[a] (6.0-8.0)**
Calcium	15	—	mmol/L	—	1.46 (0.35)	—	1.56 (0.95-1.75)	—	2.95 (0.19)	—	2.99 (2.74-3.12)
			mg/dL	—	5.8 (1.4)	—	6.3 (3.8-7.0)	—	12 (0.8)	—	12 (11-13)
Sodium	12	—	mmol/L	—	120 (9)	—	125 (110-125)	—	155 (9)	—	160 (145-160)
B. Blood gas and pH											
pH	31	—	—	—	7.16 (0.11)	—	7.20 (7.00-7.25)	—	7.57 (0.07)	—	7.60 (7.50-7.65)
Arterial pO_2	23	8	mm Hg	37 (7)	47 (5)	**35 (30-50)**	**50[a] (40-50)**	92 (12)	94 (5)	100 (70-100)	90 (90-100)
			kPa	4.9 (0.9)	6.3 (0.7)	**4.7 (4.0-6.7)**	**6.7[a] (5.3-6.7)**	12.3 (1.6)	12.5 (0.7)	13.3 (9.3-13.3)	12.0 (12.0-13.3)
Arterial pCO_2	23	2	mm Hg	35 (7)	28 (4)	35 (30-40)	30 (20-30)	55 (7)	66 (11)	55 (50-60)	65 (50-80)
			kPa	4.7 (0.9)	3.7 (0.5)	4.7 (4.0-5.3)	4.0 (2.6-4.0)	7.4 (0.9)	8.8 (1.5)	7.4 (6.7-8.0)	8.7 (6.7-10.7)
C. Hematology											
Hemoglobin	27	7	g/L	95 (35)	87 (23)	85 (50-150)	81 (60-120)	223 (23)	226 (10)	210 (210-250)	225 (211-240)
Hematocrit	23	7	%	33 (6)	25 (7)	30 (24-45)	21 (20-36)	**71 (4)**	**66[bND] (4)**	70 (65-75)	68 (60-70)

[a]$p<0.05$: differences were considered significant, [b]$p<0.01$: differences were considered highly significant. Cell entries in the Table are boldface when significantly different. [ND]normally distributed.