Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

CHAPTER 2

Collection and Interpretation of Laboratory Data

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This chapter presents the techniques and procedures for collecting samples for certain laboratory tests (Tables 2-1 to 2-4). Normal values and interpretative guidelines are included. (For normal physiologic values, see Appendix I.)

ANION AND OSMOLAL GAPS

Anion Gap

Definition

I. By the law of electroneutrality, the concentration of circulating anions equals that of circulating cations.
II. Cations and anions are classified as measured or unmeasured.
  A. Measured
    1. Anions: Cl^-, HCO_3^-
    2. Cations: Na^+, K^+
  B. Unmeasured
    1. Anions (UA): albumin, α- and β-globulins, PO_4^{3-}, SO_4^{2-}, organic acids, certain toxins and drugs
    2. Cations (UC): gamma globulins, Ca^{2+}, Mg^{2+}, certain drugs
  C. In electroneutrality:

$$Na^+ + K^+ + UC = Cl^- + HCO_3^- + UA$$

III. Anion gap is the difference between measured cation and anion concentrations.
  A. Denotes an alteration in some unmeasured component of the equation
  B. Anion gap = $(Na^+ + K^+) - (Cl^- + HCO_3^-)$
    1. Normal: 12 mEq/L; range: 8 to 16 mEq/L
    2. May be increased by either a decrease in UC or an increase in UA
    3. Is decreased by either an increase in UC or a decrease in UA
    4. Potassium sometimes deleted from equation because of its low, constant concentration

Causes

I. Causes of increased anion gap
  A. Increase in UA
  B. Increase in serum lactate, ketoacids, and uremia
  C. Certain medications: carbenicillin, penicillin
  D. Dehydration: concentrated normal anions
  E. Alkalemia
  F. Decrease in UC concentrations: Ca^{2+}, Mg^{2+}
  G. Increase in serum albumin
  H. Toxins: ethylene glycol, methanol, salicylate, paraldehyde
II. Causes of decreased anion gap
  A. Increase in normal cations, especially Ca^{2+}, Mg^{2+}, and globulins
  B. Retention of abnormal cations (e.g., multiple myeloma)
  C. Loss of UA: hypoalbuminemia

Clinical Significance

I. Increases index of suspicion that unexpected (or unmeasured) cations or anions are present in serum
II. Allows further definition and classification of metabolic acidotic states
  A. Metabolic acidosis with normal or decreased anion gap is usually caused by renal or intestinal loss of bicarbonate (hyperchloremic acidosis).
  B. Metabolic acidosis associated with an increased anion gap may have various causes.
    1. Diabetic ketoacidosis
    2. Lactic acidosis
    3. Ethylene glycol or paraldehyde intoxication
    4. Acute renal failure

Osmolal Gap

Definition

I. Osmolal gap is the difference between measured serum osmolality and calculated osmolality.
II. Serum osmolality can be measured with an osmometer.
  A. The major osmotically active solutes are Na^+, K^+, glucose, and urea (measured as blood urea nitrogen [BUN]).
  B. Normal osmolality is 285 to 300 mOsm/kg.
III. Calculated serum osmolality is derived from the following equation:

$$2(Na^+ + K^+) + \frac{\text{Glucose}}{18} + \frac{\text{BUN}}{3}$$

IV. A difference of >10 mOsm between the measured and calculated values is significant.

Causes

I. If the calculated value exceeds the measured value, a mathematical or laboratory error exists.
II. If the measured value is normal but the calculated value is low, a decrease in serum water is the usual cause.

TABLE 2-1

Endocrine Assays

TEST	PROTOCOL	SAMPLE REQUIRED	NORMAL VALUES	INTERPRETATION OF ABNORMAL VALUES
Basal T_3, T_4		Serum	*Dog:* T_3 = 80-200 ng/dL = 0.8-2 ng/mL = 1.2-3.1 nmol/L T_4 = 1.3-4 µg/dL = 13-40 ng/mL = 20-52 nmol/L *Cat:* T_3 = 60-150 ng/dL = 0.6-1.5 ng/mL = 0.6-1.9 nmol/L T_4 = 1-4.5 µg/dL = 10-45 ng/mL = 15-58 nmol/L	Suggestive of hypothyroidism: *Dog:* T_3< 30 ng/dL T_4 < 1 µg/dL Hyperthyroidism: *Cat:* T_3 > 200 ng/dL T_4 > 5 µg/dL *Dog:* T_3 > 290 ng/dL T_4 > 4 µg/dL
Free T_4 (FT_4) by dialysis		Serum	*Dog:* 16-30 pmol/L *Cat:* 15-48 pmol/L	*Dog:* FT_4 < 16 pmol/L suggestive of hypothyroidism, but may accompany other diseases *Cat:* FT_4 > 48 pmol/L indicative of hyperthyroidism
TSH response test	*Dog:* 0.1 IU TSH/kg IV *(Thytropar);* TSH inconsistently available	Measure serum T_4 at 0 and 4 or 6 hr after TSH	Post-TSH $T_4 \geq 2 \times$ basal T_4 or >35 nmol/L	Post-TSH $T_4 < 2 \times$ basal T_4 or < 35 nmol/L diagnostic of hypothyroidism
Canine endogenous TSH		Serum	*Dog:* 2-30 µU/L 2.7-7.9 ng/mL	Primary hypothyroidism: T_4 decreased, TSH increased (20-30 ng/mL) Canine assay validated for cats
TRH stimulation test	*Dog:* 0.2 mg TRH IV *Cat:* 0.1 mg TRH IV	Measure serum T_4 at 0 and 4 hr after TRH	*Dog:* Post-T_4 > 2 µg/dL or > basal T_4 + 0.5 µg/dL *Cat:* Post-T_4 increased by > 60%	Hypothyroidism (dog): Post-T_4 < 0.5 µg/dL Hyperthyroidism (cat): Post-T_4 increased by < 50% Equivocal findings (cat): Post-T_4 elevation of 50%-60%
T_3 suppression test	*Cat:* 25 µg T_3 PO TID × 7 doses	Measure T_4, T_3 before and 2-4 hr after last dose of T_3	$T_4 \leq$ 15 ng/mL ≤ 20 nmol/L	Hyperthyroid cats: T_4 does not suppress High T_3: confirms administration of T_3
ACTH response test	A. Synthetic ACTH *(Cortrosyn)* *Dog:* 0.5 U/kg IV, IM (max = 20 U) *Cat:* 0.125-0.25 mg IV, IM B. *Dog or cat:* ACTH gel 2.2 U/kg IM	A. Measure serum cortisol at 0 and 1 hr after ACTH in dogs or at 0, 30, and 60 min in cats B. Measure serum cortisol at 0 and 2 hr after ACTH in dogs and at 0, 1, and 2 hr in cats	≤ 50% of pretreatment values *Dog:* Pre-ACTH = 1.1-5 µg/dL, 25-38 nmol/L Post-ACTH = 6.2-16.8 µg/dL, 200-500 nmol/L *Cat:* Pre-ACTH = 0.33-2.6 µg/dL, 15-72 nmol/L Post-ACTH = 4.8-7.6 µg/dL, 130-210 nmol/L	Hyperadrenocorticism: Pre-ACTH = 4-10.8 µg/dL Post-ACTH = 11.7-50 µg/dL Primary hypoadrenocorticism: Pre- and post-ACTH = ≤1 µg/dL, ≤30 nmol/L

T_3, Triiodothyronine; *T_4,* thyroxine; *TSH,* thyroid-stimulating hormone; *TRH,* thyroid-releasing hormone; *ACTH,* adrenocorticotropic hormone; *max,* maximum.

ACTH assay	Draw sample into chilled syringe and insert into chilled EDTA tube; transfer sample to plastic tube and cool for 20 min in ice water; centrifuge sample for short time, retrieve plasma into another plastic tube, and Trasylol; freeze sample immediately and transport on dry ice		*Dog:* 20-80 pg/mL (avg. 45) 2-8.8 pmol/L *Cat:* 20-61 pg/mL 1-20 pmol/L	Pituitary-dependent hyperadrenocorticism: ACTH ≥40-500 pg/mL >88 pmol/L Functional adrenal tumor: ACTH ≤20 pg/mL ≤4.4 pmol/L
Low-dose dexamethasone suppression test	0.01 mg/kg dexamethasone sodium phosphate IV	Measure serum cortisol at 0, 4, and 8 hr after dexamethasone	*Dog:* Pre = 1.1-5 µg/dL Post = <1 µg/dL (Normal dogs suppress)	Hyperadrenocorticism: no suppression 4 or 6 hr post: 30% of pituitary-dependent hyperadrenocorticism cases suppress
High-dose dexamethasone suppression test	0.1 mg/kg dexamethasone sodium phosphate IV	Measure serum cortisol at 0, 4, and/or 8 hr after dexamethasone	Pre values reflect hyperadrenocorticism (4-10.8 µg/dL)	8 hr post: >1 µg/dL, >30 nmol/L
Urine cortisol:creatine ratio		Fresh urine sample	Urine cortisol (nmol/L):urine creatinine (mmol/L) ratio ≤35 (dog), <28 (cat)	Ratio > normal is suggestive of hyperadrenocorticism
Insulin assay		Measure serum insulin after 24-hr fast or during episodes of hypoglycemia	6-22 µU/mL	Values < normal preclude diagnosis of insulinoma Values > normal are suggestive of insulinoma
GH assay		Serum; assay currently unavailable	*Dog:* 0-10 ng/mL (usually 2-3 ng/mL) *Cat:* 0-8.5 ng/mL (mean = 1.21 ± 1.0 ng/mL)	Values > 90 ng/mL have been associated with neoplasia causing diencephalic syndrome in the dog and acromegaly in the cat Low values are difficult to asses; stimulation tests should be performed
Clonidine stimulation test	10 µg clonidine kg IV *(Catapresan)*	Measure plasma GH at 0, 15, 30, 45, 60, and 120 min after clonidine; keep samples frozen until assayed; GH assay currently unavailable	Normal dogs show increase in GH between 15 and 45 min with a peak of 25-40 ng/mL	Clonidine is a GH stimulant; pituitary dwarfs demonstrate either no or little response to clonidine
Xylazine stimulation test	100 µg/kg IV *(Rompun)*	Measure plasma GH at 0, 15, 30, 45, 60, and 120 min after xylazine; keep samples frozen until assayed GH assay currently unavailable	Normal dogs show increase in GH between 15 and 45 min with a peak of 25-40 ng/mL	Pituitary dwarfs show no response to xylazine

EDTA, Ethylenediamine tetraacetic acid; *GH*, growth hormone.

Continued

TABLE 2-1

Endocrine Assays—*cont'd*

TEST	PROTOCOL	SAMPLE REQUIRED	NORMAL VALUES	INTERPRETATION OF ABNORMAL VALUES
Somatomedin-C; IGF-1		Serum	*Dog:* 280 ± 23 ng/mL (adults) 345 ± 50 ng/mL (immature dogs) 5-45 nmol/L	Pituitary dwarfs have low value (11 ± 2 ng/mL or <5 nmol/L) Acromegaly in cats: Values of 70-100 nmol/L are nondiagnostic; repeat in 3 mos Values > 100 nmol/L are diagnostic
Gastrin assay		Plasma after 12-hr fast	*Dog:* 45-125 pg/mL *Cat:* 28-135 pg/mL	Plasma gastrin levels are increased with primary gastrointestinal tract disease (e.g., functional gastrinomas) or secondary to other systematic diseases, especially chronic renal failure
Antidiuretic hormone response test	Perform water deprivation test first; give desmopressin acetate 2-4 drops intranasally or conjunctivally or 10-20 µg/kg SC (dogs); if available, aqueous vasopressin may be given at 2-5 UIM (dogs)	Empty bladder and collect urine at 60, 120, 180, and 240 min	Normal: sp. gr. >1.025	Central diabetes insipidus: sp. gr. >1.015 Nephrogenic diabetes insipidus or medullary washout: sp. gr. <1.015
PTH assay		Serum	*Dog:* 2-13 pmol/L, 16-136 pg/mL *Cat:* 0-4 pmol/L, 3.3-22.5 pg/mL	Hypoparathyroidism: PTH is low or undetectable, especially if ionized calcium is low Parathyroid adenoma: PTH as high as 45 pmol/L Secondary hyperparathyroidism (renal failure): PTH grossly elevated
Calcitonin assay		Plasma	*Dog:* ≤25 pg-Eq/mL	Values of plasma calcitonin are difficult to interpret at this time; extreme elevations may be caused by calcitonin-producing thyroid tumors
Erythropoietin		Serum	*Dog:* 5-15 mU/mL *Cat:* 5-22 mU/mL	Low: primary polycythemia, chronic renal failure Normal or high: secondary polycythemia Very elevated: asplastic anemia, certain renal tumors
Ionized calcium		Serum	1.12-1.42 nmol/L	Primary hyperparathyroidism: increased values Malignant hypercalcemia; increased values Renal failure: normal or increased values Hypoparathyroidism: decreased values Feline pancreatitis: decreased values

IGF-1, Insulin-like growth factor-I; *sp. gr.,* specific gravity; *PTH,* parathormone.

TABLE 2-2

Gastrointestinal Studies

TEST	PROTOCOL	SAMPLE REQUIRED	NORMAL VALUES	INTERPRETATION
Bile acid assays	1. Fast animal 12 hr 2. Feed a routine or high-protein meal	Serum samples are colleted after 12-hr fast and 2 hr after a meal	*Dog:* Fasting ≤5 µmol/L Postprandial ≤ 15.5 µmol/L *Cat:* Fasting ≤ 2 µmol/L Postprandial ≤ 10 µmol/L	Elevations indicate dysfunction of normal hepatobiliary physiology, with the degree of elevation providing limited quantitative information
Ammonium tolerance test	Give 100 mg/kg NH_4Cl PO (max dose = 3 g)	1. Draw blood sample into EDTA or heparinized saline before and 30 min after NH_4Cl 2. Cool blood on ice immediately	Fasting ≤ 120-150 µg/dL Post-NH_4Cl ≤ 200-250 µg/dL	Elevation of blood ammonia indicates either hepatic dysfunction or shunting of portal blood away from the liver (i.e., portocaval shunt)
Glucagon tolerance test	1. Fast animal 2 hr 2. Give glucagon 0.03 mg/kg IV	Measure serum glucose at 0, 15, 30, 60, and 90 min after glucagon administration	Serum glucose rises in response to glucagon, with peak at 15 min, and returns to normal by 90 min	Glucose curve remains flat with severe hepatic insufficiency, portocaval shunt, glycogen storage disease, and prolonged anorexia or starvation
BT-PABA test	1. Fast animal 18 hr 2. Give 5 mL 1% BT-PABA/kg PO followed by 25-100 mL water 3. Stomach tubing is preferred 4. Avoid concurrent use of chloramphenicol, sulfonamides, diuretics, and pancreatic extracts for 5 days before test	Heparinized plasma is obtained for measuring plasma PABA at 0, 30, 60, 90, and 120 min	*Dog:* >5-35 µg/mL *Cat:* >7.5 µg/mL (at 90 min)	Indirectly measures chymotrypsin activity Values <1.25 µg/mL are compatible with pancreatic exocrine insufficiency and also reflect small intestinal absorption capabilites Values of 1.25-4 µg/mL are compatible with malabsorption
TLI; canine (cTLI) and feline (fTLI) assays available	Fast animal 6-12 hr	Serum	*Dog:* 5-35 µg/L *Cat:* 17-49 µg/L	Maldigestion (exocrine pancreatic insufficiency): <2 µg/L (dog), <8 µg/L (cat) Malabsorption: >5 µg/L (dog) Pancreatitis: >50 µg/L (dog) >200 µg/L (cat)

BT-PABA, N-benzoyl-L-tyrosyl-p-aminobenzoic acid; *TLI,* trysin-like immunoreactivity.

Continued

TABLE 2-2

Gastrointestinal Studies—*cont'd*

TEST	PROTOCOL	SAMPLE REQUIRED	NORMAL VALUES	INTERPRETATION
PLI	Fast animal 6-12 hr	Serum	*Dog:* 0-200 µg/L *Cat:* 2-6.8 µg/L	Poor diagnostic accuracy for pancreatitis Pancreatitis: >400 µg/L (dog) >12 µg/L (cat)
Fecal alpha 1-protease inhibitor assay	Collect fresh fecal specimens	Feces	*Dog:* 0-32 µg/g	Increased with protein-losing enteropathies
Folate levels	Fast animal 6-12 hr	Serum	*Dog:* 6.7-17.4 µg/L *Cat:* 13-4-38 µg/L	Increased with gastrointestinal bacterial overgrowth, pancreatic exocrine insufficiency, folate supplementation, or hemolyzed blood samples Low with small intestine malabsortion
Cobalamin levels	Fast animal 6-12 hr	Serum	*Dog:* 225-660 ng/L *Cat:* 200-1680 ng/L	Low with cobalamin malabsorption (ileal disease), pancreatic exocrine insufficiency, or small intestinal bacterial overgrowth Increased with parenteral supplementation

PLI, Pancreatic lipase immunoreactivity.

TABLE 2–3

Renal Function Tests

TEST	PROTOCOL	SAMPLE REQUIRED	NORMAL VALUES	INTERPRETATION
PSP excretion in urine	A. 1. Empty bladder via catheterization 2. Give 6 mg PSP IV B. Give 1 mg PSP/kg IV	A. Catheterize bladder 20 min later and collect all urine B. Collect 4 mL heparinized plasma before and 60 min after PSP administration	A. Normal: >30% excretion of PSP B. Normal: 80 µg/dL Suspicious: 80-120 µg/dL Abnormal: ≥120 µg/dL	A. Assesses renal blood flow B. Assess renal tubular function; abnormal retention occurs with renal insufficiency
SS clearance	Give 0.2 mL of 10% solution/kg IV after a 12-hr fast	Obtain heparinized blood at 30, 60, and 90 min	Results are expressed as the time needed to clear 50% of dye from the blood ($t_{1/2}$) Normal $t_{1/2}$ = 32-84 min.	SS retention in plasma above normal reflects diminished GFR SS clearance is usually reduced before the development of either azotemia or urine concentration defects
Endogenous creatinine clearance	1. Acclimate animal to metabolism cage 2. Catheterize and empty bladder 3. Allow access to free-choice water 4. Collect all urine for 24 hr; empty bladder again at end of test 5. Avoid contamination of urine with feces 6. Store urine in closed, refrigerated container until test is concluded 7. Record total volume of urine	1. Submit serum sample obtained midway through test for creatinine assay (SC) 2. Submit urine sample from the pooled collection for creatinine measurement (UC) 3. Use equation to calculate clearance: $GFR = \frac{UC\ (mg/dL) \times \text{urine volume (mL)}}{SC\ (mg/dL) \times 1440\ \text{min} \times \text{weight (kg)}}$	Normal, dogs: 2-5 mL/min/kg Normal, cats: 1.6-4 mL/min/kg	Decreased GFR occurs with decreased renal blood flow (prerenal), obstruction of urine outflow (postrenal), and renal parenchymal disease Decreased GFR in an otherwise normal dog indicates renal insufficiency
Urine protein quantitation	Follow protocol outlined for endogenous creatinine clearance Most common assay is trichloroacetic acid–ponceau S method	1. Submit pooled urine sample 2. Protein excretion/24 hr = urine protein (mg/dL) × urine volume (dL) 3. Protein excretion/kg = total protein (mg)/weight (kg)	1. Protein/kg/day ≤30 mg/kg/day 2. Total protein: 333 ± 309 mg/day	Significant proteinuria occurs with glomerular disease Other causes include Bence Jones proteinuria, myoglobinuria, and severe urinary tract trauma
UP/C ratio	Random sample	*Dog:* urine	Normal ≤1.0	Significant proteinuria: UP/C >1.0 Results are affected by both pyuria and gross blood contamination

PSP, Phenolsulfonphthalein; *SS,* sodium sulfanilate; *GFR,* glomerular filtration rate; *UP/C,* urine protein:creatinine.

TABLE 2-4

Interpretation of Selected Serologic Tests

DISEASE	TEST	INTERPRETATION
Brucellosis	A. RSAT	A. Good screening test False positives occur, so perform further seologic assay to confirm the diagnosis; a modification of the test (ME-RSAT) using a less mucoid (M-) variant of *Brucella canis* has fewer false positives; it becomes positive within 3-4 wk, but false negatives can occur up to 8 wk
	B. Tube agglutination tests 1. TAT	B. Most common confirmatory test 1. Becomes positive by 3-6 wk Titer results: 1:50 = early or recovering infection 1:50-1:100 = suspicious ≥1:200 = active infection Occurrence of false positives similar to RSAT
	2. ME-TAT	2. Fewer false positives Becomes positive 1-2 wk after TAT or 5-8 wk post-infection ≥1:200 = active infection
	C. AGID	C. Becomes positive in 8-12 wk Very specific; used to confirm diagnosis, especially in chronic cases Both somatic and cytoplasmic (CPAg-AGID) tests available, but somatic rarely used Results reported as positive, suspicious, or negative Repeat in 4-6 wk if first results are suspicious May remain positive for 1 yr
	D. ELISA	D. Very specific, but less sensitive than TAT tests Becomes positive by 4 wk
	E. IFA	E. Sensitivity is uncertain, so some infected dogs may be missed
Leptospirosis	A. MAT	A. Titers <1:400 may be postvaccinal Titers >1:800 usually indicate infection Paired samples 2-4 wk apart are tested; a fourfold increase in titer is diagnostic Tests for serovar groups, not individual serovars
	B. ELISA	B. IgM titer: develops after 1 wk IgG titer: develops in 2-3 wk Vaccinates: high IgG titer with low or negative IgM titer
Feline infectious peritonitis (FIP)	A. IFA, ELISA	A. Titer >1: 1600 (most laboratories) or fourfold increase over 2-4 wk is compatible with a positive diagnosis Titer > 1: 240 is inconclusive NOTE: This titer cross-reacts with other feline coronaviruses, so is not specific for FIP
	B. PCR assay	B. May help confirm presence of coronavirus in seronegative cats, but false negatives can occur and is not specific for FIP
Canine parvovirus	A. Hemagglutination inhibition, ELISA	A. Positive diagnosis: Single high IgM titer Fourfold rise in IgG titer over 2-4 wk; also considered protective
	B. Fecal ELISA or hemagglutination	B. Sensitive and specific test Shedding of virus is brief and usually not detected by day 10-12 of infection (day 5-7 of clinical illness) Vaccination produces false positives 5-12 days after administration

RSAT, Rapid slide agglutination test; *TAT,* tube agglutination test; *ME-TAT,* 2-mercaptoethane TAT; *AGID,* agar-gel immunodiffusion; *ELISA,* enzyme-linked immunosorbent assay; *IFA,* indirect immunofluorescence antibody; *MAT,* microscopic agglutination test; *IgM,* immunoglobulin M; *IgG,* immuoglobulin G; *PCR,* polymerase chain reaction; *FIP,* feline infectious peritonitis.

TABLE 2-4

Interpretation of Selected Serologic Tests—*cont'd*

DISEASE	TEST	INTERPRETATION
Ehrlichiosis *(Ehrlichia canis)*	A. IFA	A. Becomes positive in 7-28 days Titer >1:80 is considered positive in endemic areas Any measurable titer (>1:10) is significant in dogs in nonendemic areas Submit a second sample 2-3 wk later if suspicious case is negative on first sample Titers persist for 6-9 mo after infection Cross-reactivity occurs with *Neorickettsia* spp., *Helminthoeca* spp., and other ehrlichial agents
	B. Western immunoblotting assay	B. Detects antibodies 2-8 days after exposure Can distinguish *E. canis* from *E. ewingii*
	C. PCR assay	C. Positive within 4-10 days In the future, it may be able to distinguish active infection from titers that persist following successful treatment of disease
Rocky Mountain spotted fever	A. Indirect immunofluorescence test (Micro-IF) or ELISA for IgG	A. Submit acute and convalescent titers 2-3 wk apart Titer ≤1:64 = normal Titer ≥1:1024 in East, ≥1:25 in West = infected Fourfold increase in titers is diagnostic False negatives occur early in disease Titers may stay elevated (1:128) for 5-10 mo
	B. Micro-IF or ELISA for IgM	B. Decreases within 4-8 wk Single high titer indicates active infection
	C. Latex agglutination	C. Sensitivity lower than Micro-IF tests Single high titer (≥132) is diagnostic
	D. PCR assay	D. Can be run on both whole blood and tissues Nested PCR more sensitive in treated dogs
Borreliosis (Lyme disease)	A. IFA, ELISA	A. Titers are difficult to interpret and may indicate exposure rather than active infection Can cross-react with other bacteria, especially other *Borrelia* spp. and *Leptospira* spp. Symptomatic dogs usually have titers >1:128 Measure IgG and IgM titers simultaneously Fourfold increase in paired samples submitted 2-4 wk apart is supportive IgG titers become positive in 4-6 wk and persist for ≥2 yr IgM titers may persist for several months Titers do not distinguish postvaccinal responses from actual infection
	B. Western immunoblotting assay	B. Can distinguish postvaccinal responses from actual exposure/infection and identify false negatives
	C. ELISA for specific outer surface proteins (Osp)	C. Antibodies to OspA and OspB indicate post-vaccinal response Antibodies to OspC indicate active infection C_6 assay way indicate active infection and help assess response to treatment
Toxoplasmosis	A. IHA	A. Becomes positive in 2 wk; detects IgG Relatively insensitive, not species specific Fourfold rise in titer over 2-3 wk supportive
	B. LAT, MAT	B. Become positive in 2 wk, detects IgG MAT more sensitive Positive results: LAT > 1:64 MAT > 1:100 Fourfold rise in titer over 2-3 wk supportive Test may be applied to aqueous humor or CSF

IHA, Indirect hemagglutination; *LAT,* latex agglutination test; *CSF,* cerebrospinal fluid.

Continued

TABLE 2-4

Interpretation of Selected Serologic Tests—*cont'd*

DISEASE	TEST	INTERPRETATION
	C. IFA for IgM, IgG	C. False positives occur IgM elevated within 1-2 wk and IgG detectable after 2 wk Single high IgM titer (1:64), with negative IgG titer, implies active infection Fourfold increase in titers over 2-5 wk supportive Test may be applied to aqueous humor or CSF
	D. ELISA for IgM, IgG	D. More sensitive than IHA or LAT IgM titer >1.256, with negative IgG titer, implies active infection IgM is detected within 1-2 wk IgG is detectable in approximately 2-4 wk Fourfold increase in titers over 2-3 wk supportive Test may be applied to aqueous humor or CSF
	E. All tests	E. NOTE: Use caution when interpreting results; antibodies can occur in the sera of both healthy and diseased cats; therefore serologic tests alone do not confirm the presence of disease; titers may persist for months to years following infection
Blastomycosis	A. AGID	A. If positive, dog has 91% chance of having active disease but test may be negative in acute stages
	B. ELISA	B. May be more sensitive than AGID in cats Accuracy and sensitivity poorly defined
Cryptococcosis	A. LAT	A. *Cat:* Titer >1:12 indicative of active infection *Dog:* Any positive result indicative of infection False negatives can occur with localized disease False positives possible with contamination of assay; test cross-reacts with *Trichosporon* spp. Titers correlate well with extent and course of disease, and response to therapy May be assayed in serum, urine, CSF
	B. PCR	B. May be performed on tissues May be assayed in serum, urine, CSF
Coccidioidomycosis	A. TP test	A. Becomes positive in 2-6 wk Detects IgM; is a qualitative test and fades quickly (within 4-6 wk)
	B. CF test	B. Detects IgG and appears in 8-10 wk Titer ≤1:4 = negative Titer ≥1:16 = suspicious, chronic, or localized disease Titer ≥1:32 = active disease Rise or drop in titer corresponds well with clinical course, but titers remain elevated for months after treatment or disease arrest
	C. LAT	C. Measures IgM, so detects acute infection Some false positives in dogs
	D. AGID-TP, AGID-CF	D. More sensitive assays AGID-TP detects IgM; AGID-CF detects IgG
	E. ELISA	E. Available for detection of both IgM and IgG Some false positives in dogs; cross-reacts with blastomycosis
Histoplasmosis	A. CF titer B. Skin histoplasmin test	Neither test is considered reliable in dogs and cats for definitive diagnosis
Aspergillosis	A. AGDD	A. False positive rate of 6%; cross-reacts with *Penicillum* spp.
	B. CIE	B. Up to 15% false-positive results
	C. ELISA	C. Less reliable than AGDD or CIE
	D. PCR assay	D. Used experimentally; clinical availability limited NOTE: Some infected dogs never seroconvert; false negative rate is higher when only one antigen tested

TP, Tube precipitin; *CF,* complement fixation; *AGDD,* agar gel double diffusion; *CIE,* counterimmunoelectrophoresis.

III. An unmeasured osmole is suggested when both values are elevated and a significant gap exists.
   A. Mannitol, glycerin
   B. Sorbitol, acetone
   C. Ethylene glycol, alcohol
   D. Myeloma protein, hyperlipidemia
   E. Infused hyperosmotic solutions
   F. Activated charcoal containing propylene glycol and glycerol (Burkitt et al., 2005)

Clinical Significance

I. Directs attention to laboratory errors
II. Detects presence of unmeasured osmoles (e.g., ethylene glycol)
III. Can be used to confirm hyperproteinemia and hyperlipidemia

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