



CLINICAL DIAGNOSIS

Fungal Testing Overview

Fungal antigens, fungal DNA, and anti-fungal antibodies can be used as non-invasive biomarkers for invasive fungal infections (IFIs). MiraVista Diagnostics (MVD) specializes in developing diagnostic tests to detect these biomarkers. These tests provide a rapid, cost-efficient alternative to invasive testing, often required otherwise to diagnose IFIs. Over the past 20 years MVD tests have revolutionized diagnosis and treatment monitoring of IFIs in animals. Use has been reported in many peer-reviewed publications. The reported diagnostic performances are found below.

Diagnostic performance of MVD fungal tests. **Bolded tests** are the recommended first non-invasive diagnostic test(s) to be performed.

Pathogen	Test	Species	Sample	Sensitivity	Specificity#	Min. Vol. (ml) [^]	Test Code	Ref.
<i>Blastomyces</i> *	Antigen EIA	K9	Urine	93	98	0.5	316	1-4
		K9	Serum	91	100	0.8	316	2,3,5
	Antibody EIA	K9	Serum	82	97	0.25	330	2,3
	Antibody ID	K9	Serum	54	100	0.25	322	2,3,6,7
<i>Histoplasma</i>	Antigen EIA	K9	Urine	92	99	0.5	310	8,9
		Feline	Urine	94	98	0.5	310	10,11
		Feline	Serum	73	NA	0.8	310	12
	Antibody EIA	K9	Serum	76	93	0.25	327	MVD
		Feline	Serum	83	95	0.25	328	MVD
	Antibody ID	K9	Serum	28	100	0.25	321	MVD
Feline		Serum	5	100	0.25	321	MVD	
<i>Coccidioides</i> (valley fever)	Antigen EIA	K9	Urine	8	100	0.5	315	13,14
		K9	Serum	27	97	0.8	315	13,14
	Antibody EIA	K9	Serum	89	94	0.25	329	13
		K9	Serum	87	92	0.25	320	13,15,16
	Antibody ID	Feline	Serum	99	NA	0.25	320	17,18
Antibody ID+EIA	K9	Serum	99	95	0.5	329+320	13	
<i>Cryptococcus</i>	Antigen LA	K9	Serum	91	100	0.25	319	19-21
		Feline	Serum	98	NA	0.25	319	19,21,22
<i>Aspergillus</i> (systemic)	Antigen EIA	K9	Urine	88	92	0.8	309	23
		K9	Serum	92	84	0.8	309	23
		K9	Ur+Ser	100	84-92	0.8	309	23
<i>Aspergillus</i> (sinonasal)	Antigen EIA	K9	Serum	24	82	0.8	309	24
		Feline	Serum	23	78	0.8	309	25
	Antibody ID	K9	Serum	76	100	0.25	324	24
		Feline	Serum	43	100	0.25	324	26

For tests with multiple references the combined sensitivity and specificity was provided.

**Blastomyces* antigen test on urine is also the first-choice test for cats.

[^]Minimum sample volume required for testing.

#Specificity was often provided for non-fungal disease.

EIA, enzyme immunoassay; ID, immunodiffusion; LA, latex agglutination

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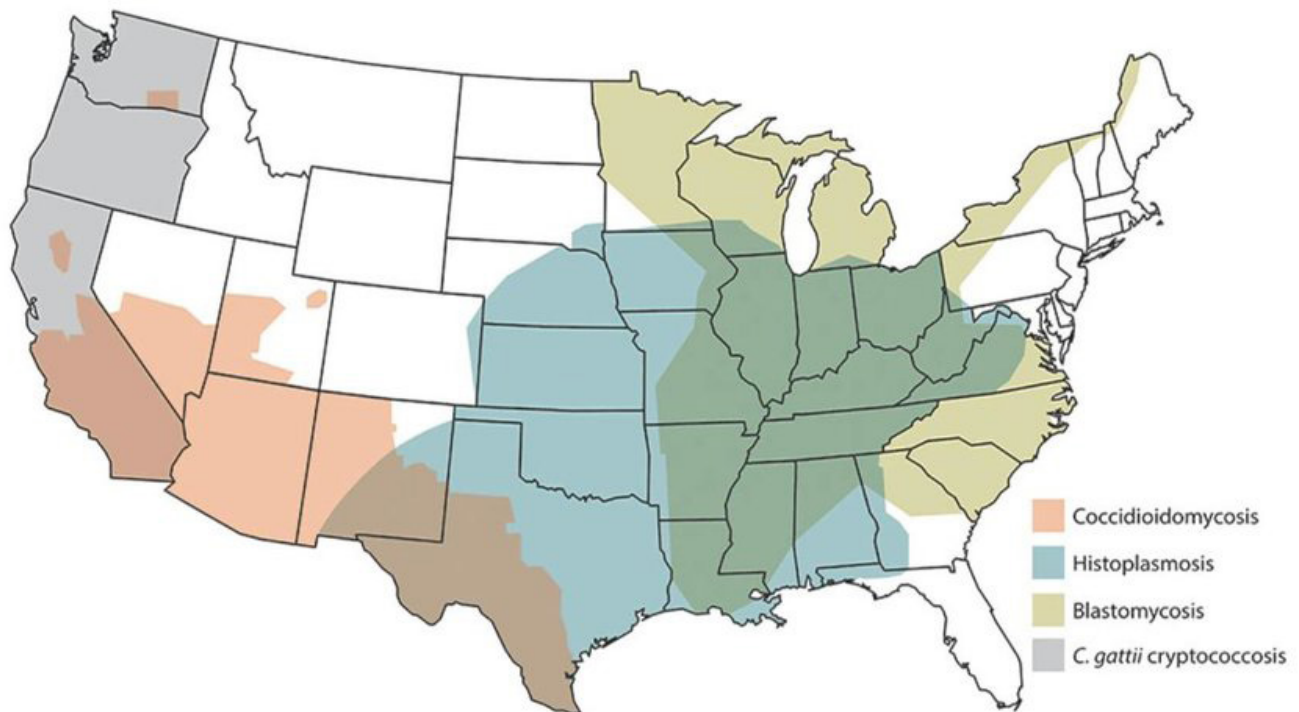
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Geographic location of enzootic invasive fungal infections (IFIs) is an important consideration. Cryptococcosis and aspergillosis, along with other invasive molds, occur anywhere in the U.S. Although infections can occur sporadically anywhere, IFIs due to dimorphic fungi (*Blastomyces*, *Histoplasma*, and *Coccidioides*) are found more commonly in predictable locations. The map below provides a rough estimate of enzootic regions.



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Invasive fungal infections (IFIs) commonly include non-specific findings such as lethargy, anorexia, weight loss, and fever unresponsive to antibiotics. Other more specific findings are also often present and can help guide diagnostic testing. Any IFI can affect any single organ or be multi-systemic, but patterns exist.

Common anatomic locations and clinical signs of invasive fungal infections in dogs and cats.

PATHOGEN	SPECIES AFFECTED	COMMON ORGANS INVOLVED	COMMON CLINICAL SIGNS
<i>Blastomyces</i>	Dog>>>Cat	Lung Lymph nodes Skin Eyes/periocular tissues Bones/joints Testicles/prostate (dog)	Anorexia Weight loss Fever Tachypnea Cough Lameness Vision disturbance Cutaneous Lesions
<i>Histoplasma</i>	Cat>Dog	Lung Lymph node Spleen & Liver Eyes/periocular tissues Bone marrow Bone/joints (cat) GI tract (dog)	Anorexia Weight loss Fever Tachypnea Lameness Vision disturbance Cutaneous lesions Diarrhea
<i>Cryptococcus</i>	Cat>>>Dog	Nasal cavity & sinuses Eyes & periocular tissues Lymph nodes Skin CNS Abdominal viscera (dog)	Nasal discharge Facial deformity Cutaneous lesions Blindness CNS signs Vomiting, diarrhea (dog)
<i>Coccidioides</i> (valley fever)	Dog>>Cat	Lung Lymph nodes Skin Eyes CNS Bones/joints	Anorexia Weight loss Tachypnea Cough Lameness Cutaneous lesions CNS signs
<i>Aspergillus</i> (systemic)	Dog>>>Cat	Bone/joints Vertebral end plates CNS Kidney Lymph nodes Skin Eyes Abdominal viscera	Anorexia Weight loss Fever Lameness Vision disturbance CNS signs Cutaneous lesions PU/PD
<i>Aspergillus</i> (sinonasal)	Dog>>Cat	Nasal cavity Sinuses Orbit CNS	Nasal discharge Nasal depigmentation Facial deformity CNS signs

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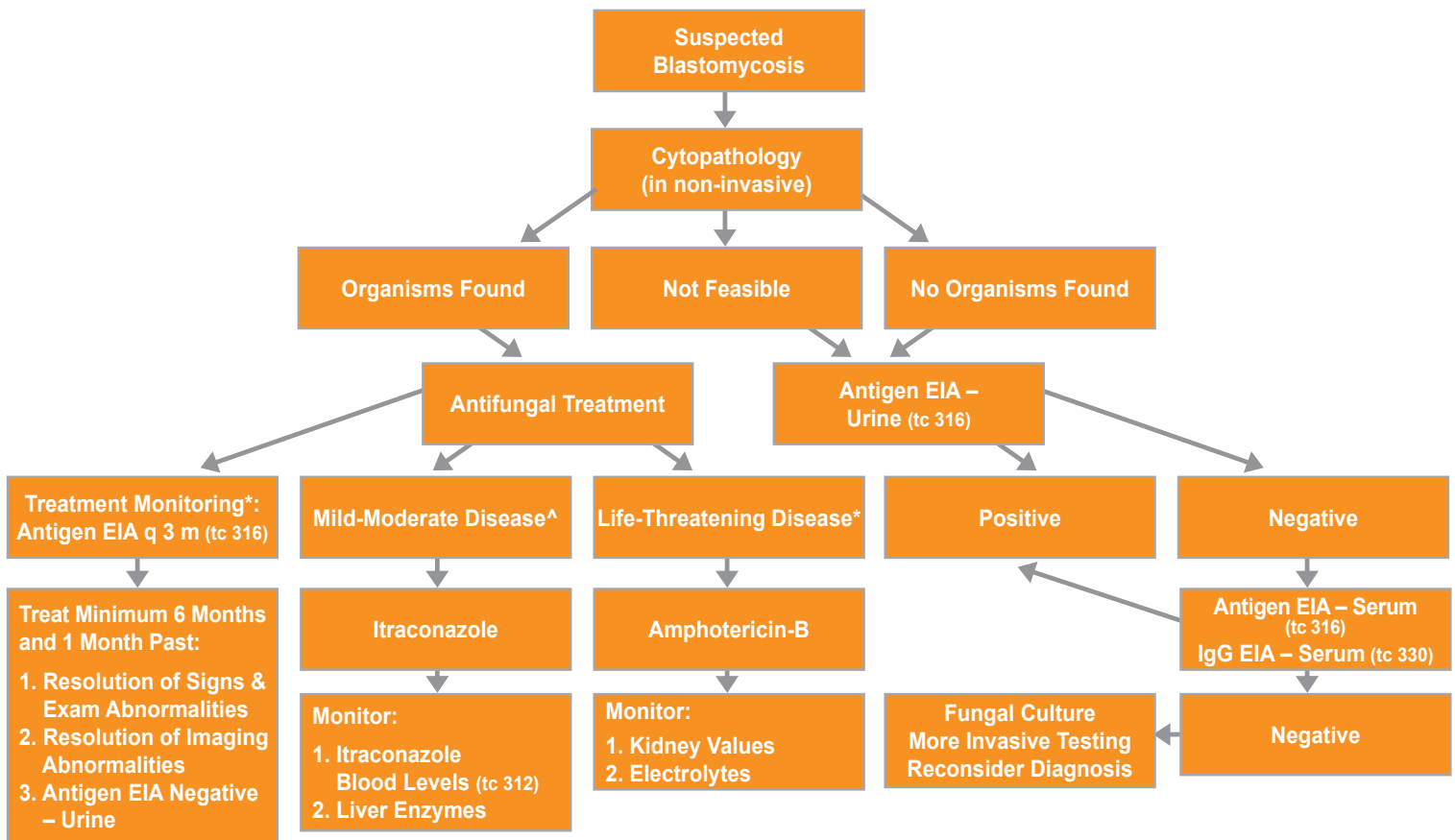
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With many available tests, choosing the best test can be challenging. In some cases, a combination of tests for a specific pathogen is preferred. For others, sequential testing might be needed. Considering the overlap of clinical findings, and enzootic areas, testing for multiple fungal pathogens is appropriate in many cases. To help simplify test selection, and treatment considerations, algorithms are provided below.

Diagnostic and Treatment Algorithm for Blastomycosis in Dogs or Cats



Antibody EIA test is not available for cats and Antibody ID test would be used instead.

*Monitor urine antigen unless above the limit of quantification then monitor serum until urine antigen concentration is quantifiable.

^Mild-moderate disease could be defined as disease which can be treated on an out-patient basis and life-threatening disease requires hospitalization.

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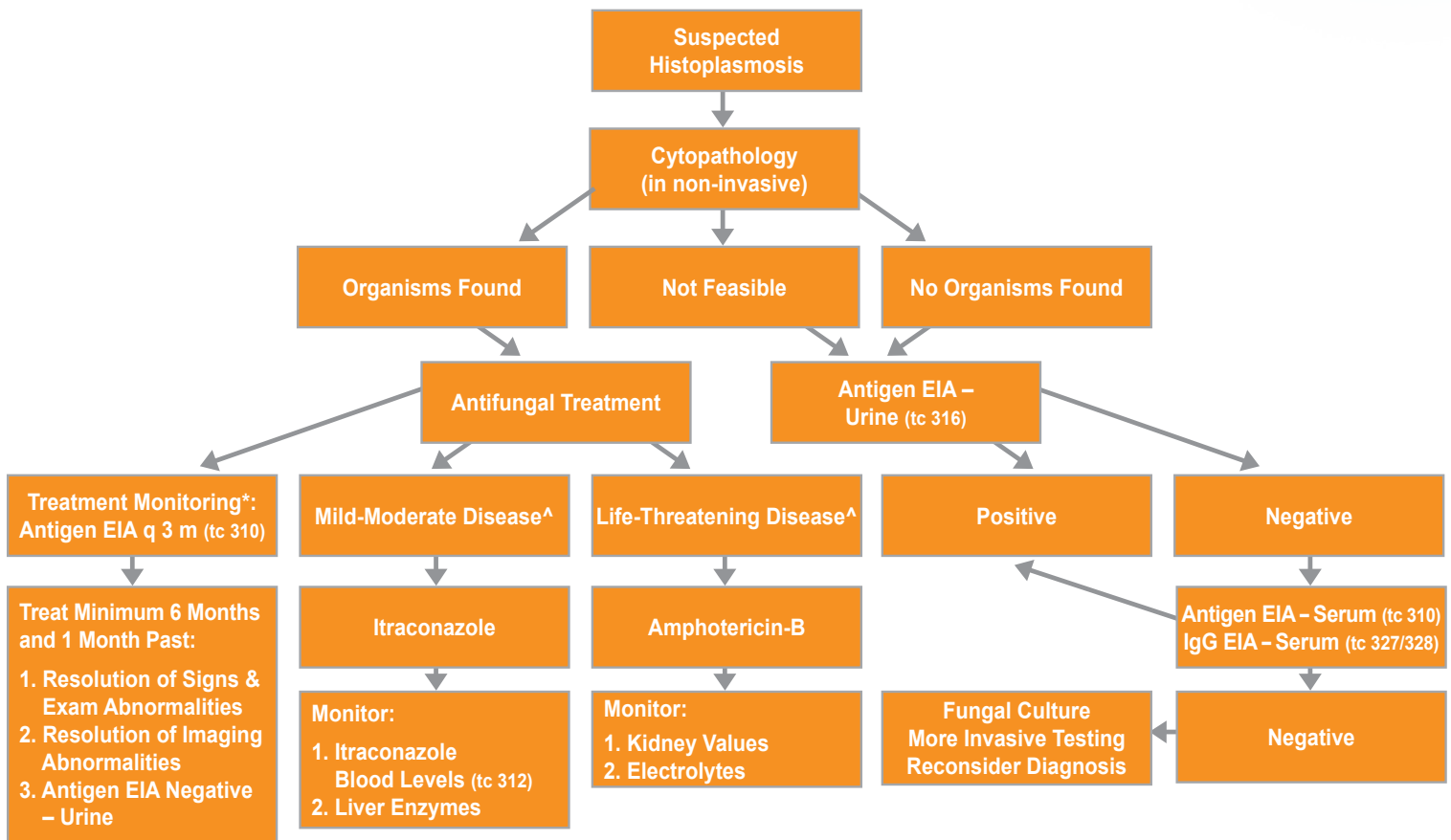
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Diagnostic and Treatment Algorithm for Histoplasmosis in Dogs or Cats



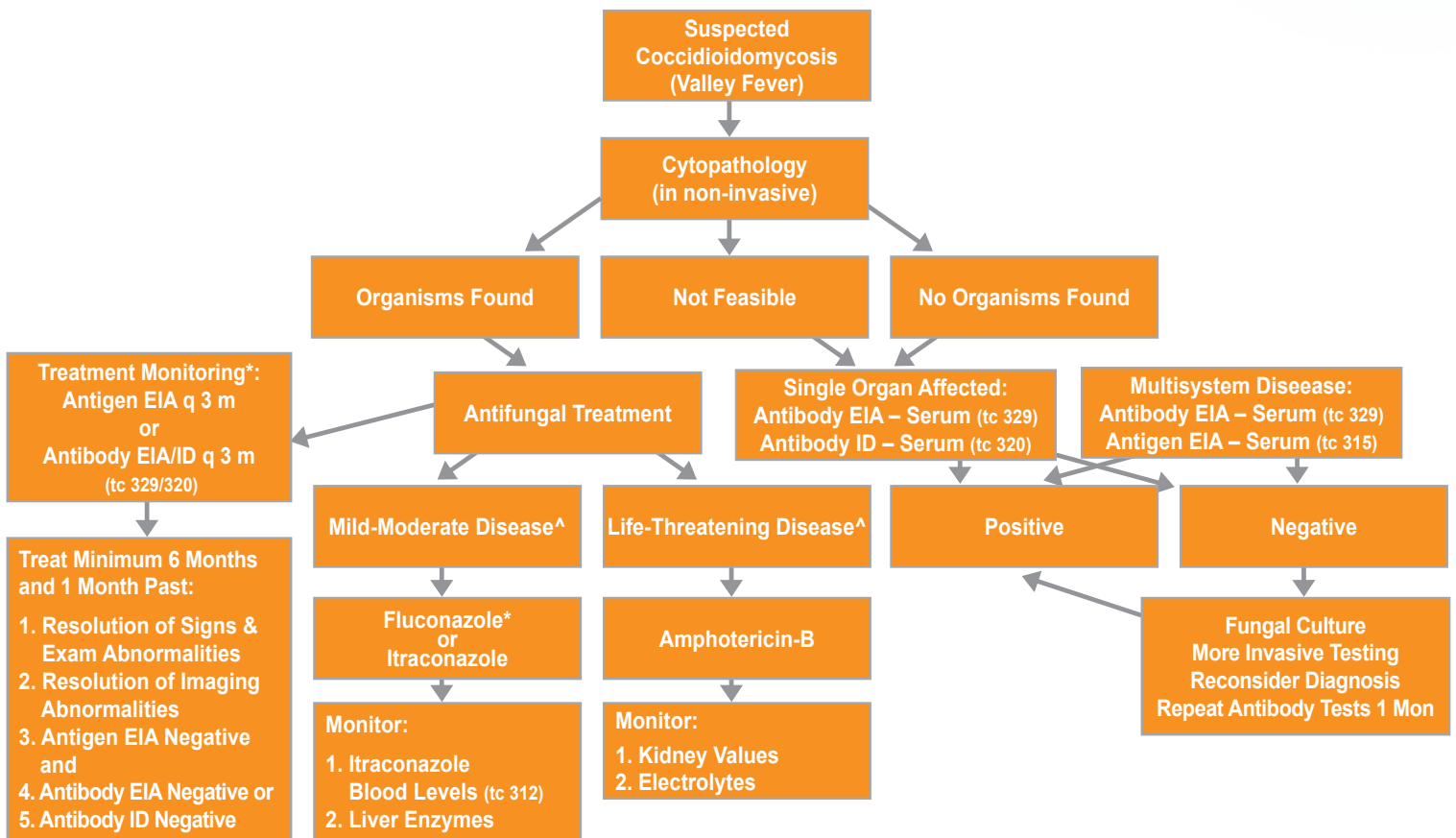
*Monitor urine antigen unless above the limit of quantification then monitor serum until urine antigen concentration is quantifiable.

^Mild-moderate disease could be defined as disease which can be treated on an out-patient basis and life-threatening disease requires hospitalization.



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Diagnostic and Treatment Algorithm for Coccidioidomycosis (Valley Fever) in Dogs or Cats



Antibody EIA test is not available for cats and Antibody ID test would be used as the sole initial screening test.

#Use antigen test for treatment monitoring if positive at baseline. If not use antibody tests for monitoring.

^Mild-moderate disease could be defined as disease which can be treated on an out-patient basis and life-threatening disease requires hospitalization.

*Fluconazole is the most commonly used oral treatment, but in vitro sensitivity data and clinical data from human medicine suggests that itraconazole should be considered as first-line treatment.

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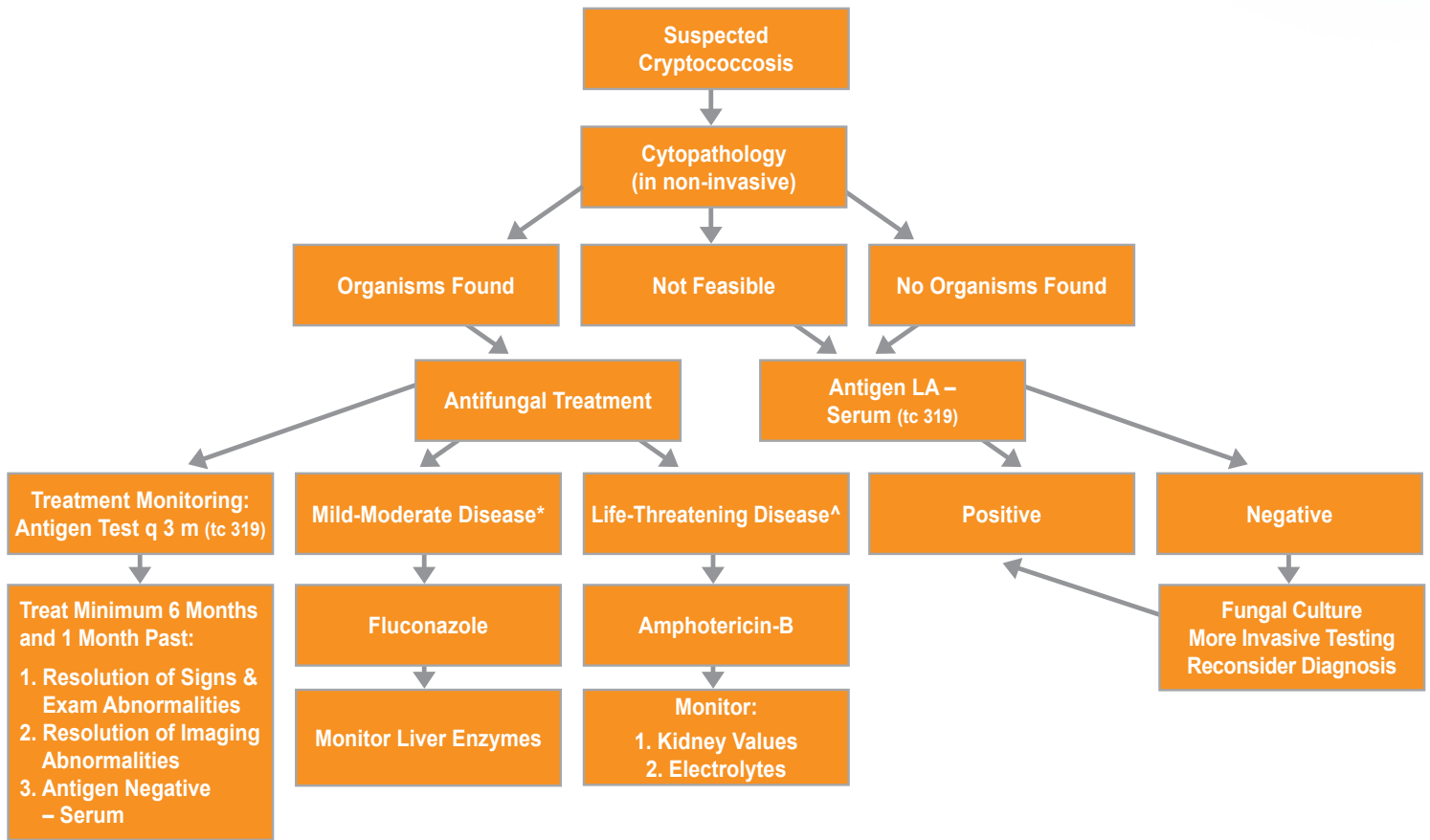
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Diagnostic and Treatment Algorithm for Cryptococcosis in Dogs or Cats

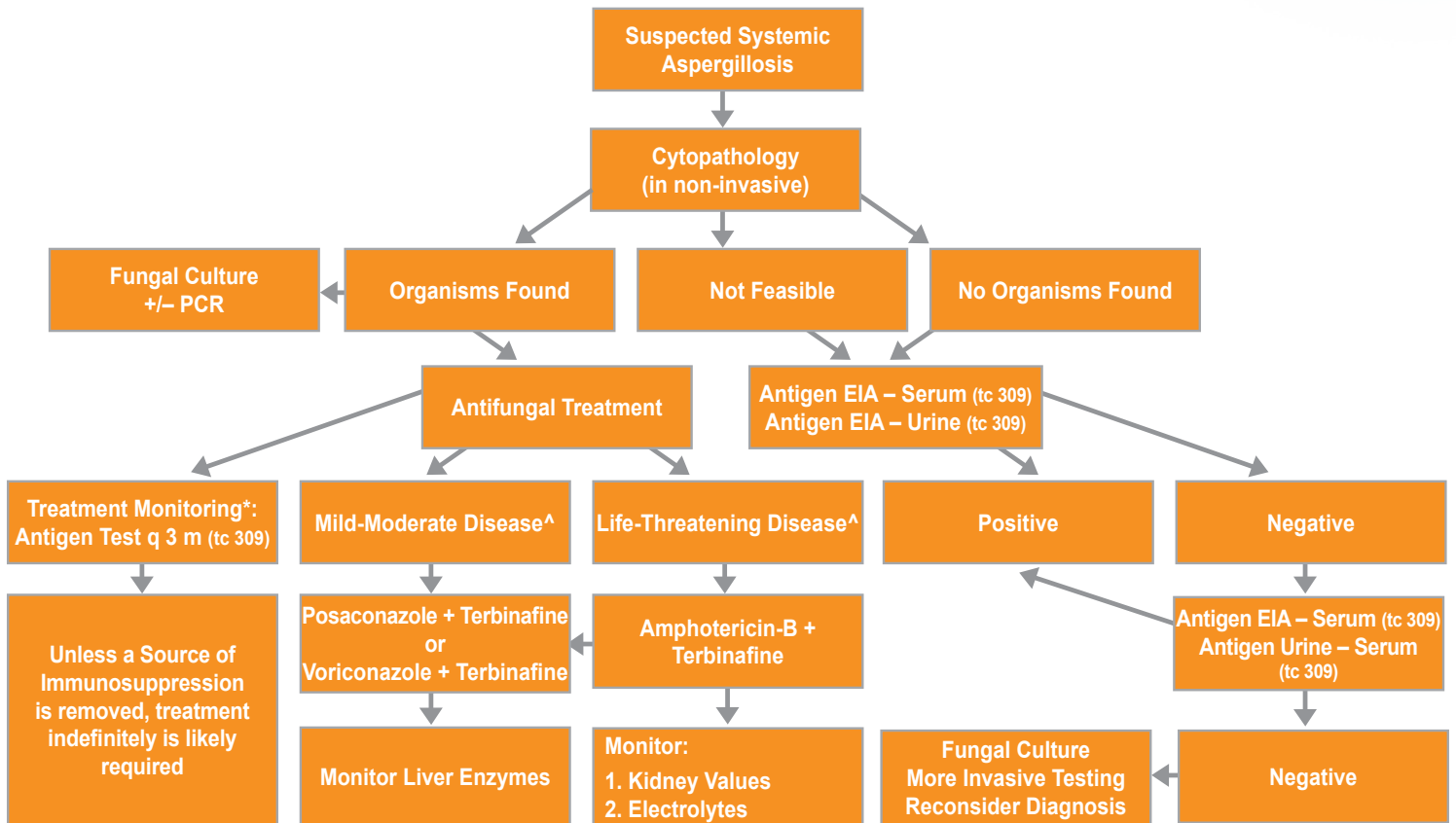


*Mild-moderate disease could be defined as disease which can be treated on an out-patient basis and life-threatening disease requires hospitalization.



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Diagnostic and Treatment Algorithm for Systemic Aspergillosis in Dogs or Cats



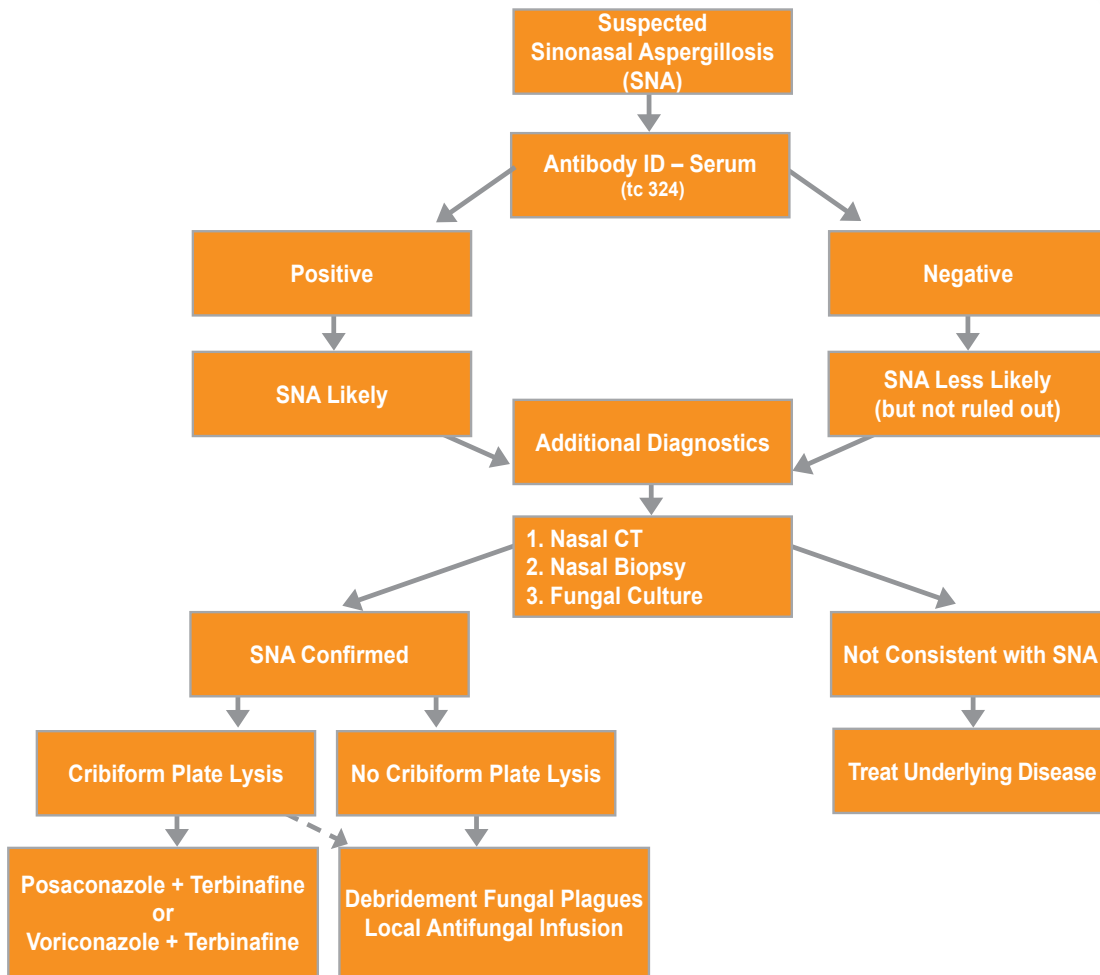
*Use whichever sample had the highest initial antigen concentration for treatment monitoring.

^Mild-moderate disease could be defined as disease which can be treated on an out-patient basis and life-threatening disease requires hospitalization.



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Diagnostic and Treatment Algorithm for Sinonasal Aspergillosis in Dogs or Cats



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