INSTITUTE FOR DEFENSE ANALYSES

Lack of Experimental Data Limits the Use of Diagnostic Systems to Detect Biological Attacks and Outbreaks

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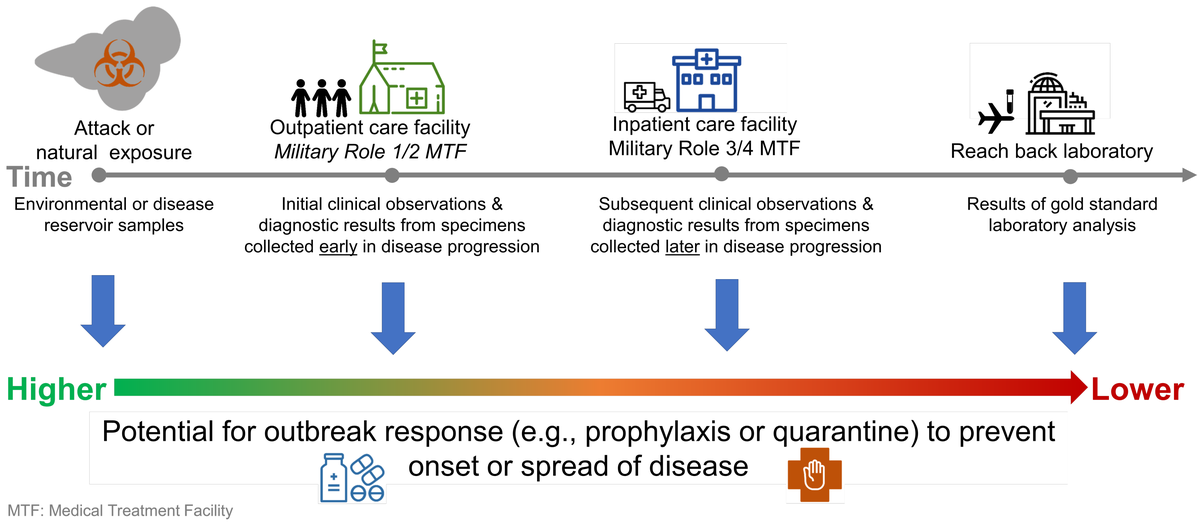
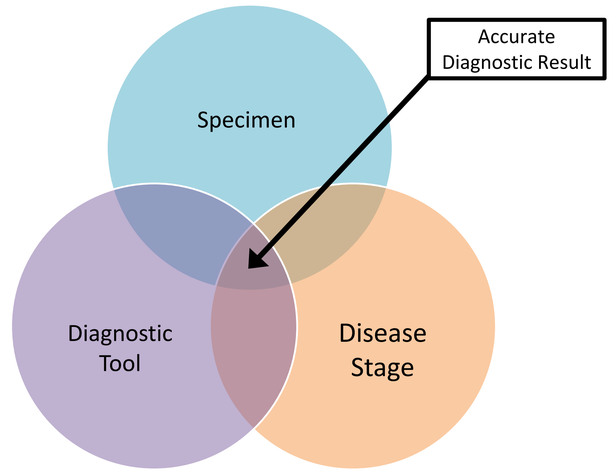
Diagnostics as detectors: medical system provides critical situational awareness to inform timely and effective outbreak response



MTF: Medical Treatment Facility

How can diagnostics provide the earliest possible warning?

Accurate diagnostic results require: the correct diagnostic specimen, and collecting the specimen at the correct stag



***Early* diagnosis requires diagnostics that work with**

Literature review indicates data on probability of detection over time is rarely available—especially human test data

Disease	Specimen Type	Bacterial/ Viral/Toxin Isolation	PCR (In-House)	PCR (Cartridge)	Antigen (ELISA/ Mass Spec)	Antigen (Rapid)
Plague	Blood	Non-Human Primate Data	Non-Human Primate Data	Insufficient Test Data Found	Insufficient Test Data Found	Insufficient Test Data Found
	Sputum	Insufficient Test Data Found	Insufficient Test Data Found	Insufficient Test Data Found	Insufficient Test Data Found	Insufficient Test Data Found
Q Fever	Blood	Test Does not Exist	Non-Human Primate Data	Insufficient Test Data Found	Test Does not Exist	Test Does not Exist
Tularemia	Blood	Non-Human Primate Data	Non-Human Primate Data	Non-Human Primate Data	Insufficient Test Data Found	Test Does not Exist
	Sputum	Insufficient Test Data Found	Insufficient Test Data Found	Insufficient Test Data Found	Insufficient Test Data Found	Test Does not Exist
Ebola	Blood	Insufficient Test Data Found	Insufficient Test Data Found	Human Data	Human Data	Insufficient Test Data Found
VEE	Blood	Non-Human Primate Data	Insufficient Test Data Found	Insufficient Test Data Found	Insufficient Test Data Found	Test Does not Exist
Anthrax	Blood	Insufficient Test Data Found	Insufficient Test Data Found	Insufficient Test Data Found	Insufficient Test Data Found	Insufficient Test Data Found
SEB	Blood	Test Does not Exist	Test Does not Exist	Test Does not Exist	Insufficient Test Data Found	Insufficient Test Data Found
Influenza	TNS	Human Data	Human Data	Insufficient Test Data Found	Insufficient Test Data Found	Human Data
	NPA	Human Data	Human Data	Insufficient Test Data Found	Insufficient Test Data Found	Human Data

Sufficient Test Data Found
Insufficient Test Data Found
Test Does not Exist
Human Data
Non-Human Primate Data

TNS: throat/nasal swab
NPA: nasopharyngeal aspirate

Sufficient Test Data = data needed to characterize probability of detection over the course of disease progression

Available data suggests current diagnostics do not provid across all diseases of interest

Probability of detection at given stage of disease: <20% | 20%-80% |

Disease	Test (Specimen)	Detectable Before Symptom Onset	Detectable At Symptom Onset	Detectab Middle of
Plague	In-House PCR (blood)	<20%	<20%	>80%
	Bacterial Isolation (blood)	<20%	<20%	20%-80%
Q Fever	In-House PCR (blood)	20%-80%	>80%	>80%
Tularemia	PCR Cartridge (blood)	<20%	20%-80%	>80%
	Bacterial Isolation (blood)	<20%	20%-80%	20%-80%
Ebola	PCR Cartridge (blood)	<20%	>80%	>80%
	Antigen (blood)	<20%	20%-80%	>80%
VEE	Viral Isolation (blood)	20%-80%	>80%	20%-80%
Influenza	In-House PCR (throat/nasal swab)	>80%	>80%	>80%
	Antigen (throat/nasal swab)	20%-80%	20%-80%	20%-80%
	Viral Isolation (throat/nasal swab)	>80%	>80%	20%-80%

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Recommendations to improve diagnostic systems contribution to detection of biological attacks and outbreaks

1) Conduct longitudinal experiments to characterize diagnostic system sensitivity over course of disease progression
2) Develop clinical specimen collection practices that target specimens with highest bacterial/viral load early in disease progression
3) Train medical personnel to understand how diagnostic probability of detection changes during the progression of a given disease, especially near symptom onset

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14. ABSTRACT

In the absence of effective environmental sampling, the military medical system will likely provide the first indication of a biological warfare attack. Accurate and timely diagnostic results provide critical situational awareness that informs the implementation of disease response measures, revised planning, and treatment of ill individuals. The Institute for Defense Analyses evaluated how various tactics techniques and procedures for the collection and analysis of clinical specimens influence the timing and accuracy of diagnostic test results. The analysis included a scientific literature review, the results of which we used to characterize the times during a given disease's progression that a given diagnostic test can generate accurate results. For multiple combinations of diseases and diagnostic technologies of interest, we were unable to find sufficient data to characterize when during the course of illness the diagnostic technology would generate accurate results. Of the disease and diagnostic technology combinations of interest for which sufficient data was available, high test sensitivity at or before symptom onset was not common. To further assess the disease and technology combinations that we found sufficient data on, we developed a stochastic individual based model to simulate disease progression, patient movement, and clinical specimen collection and analysis following a biological exposure event. We then analyzed the modeling results to determine how changes in tactics, techniques, and procedures for specimen collection and analysis affect the timing and accuracy of diagnostic results.

15. SUBJECT TERMS
diagnostics, bacterial load, viral load, Next Generation Diagnostic System, NGDS, NGDS 2, polymerase chain reaction (PCR), antigen, bacterial isolation, viral isolation

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