SWVS 2018

The FUTURE of CARE

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San Antonio, Texas

Food Animal Topics

New Diagnostic Advancements: Syndromic Approach to Diagnostic Testing

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Syndromic Approach to Diagnostic Testing

- Reasons to utilize diagnostic testing
- Testing methods
- Interpreting results based on test characteristics
- Improving result interpretation potential

What is the purpose of diagnostic testing?

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- To find out what is wrong with our patients

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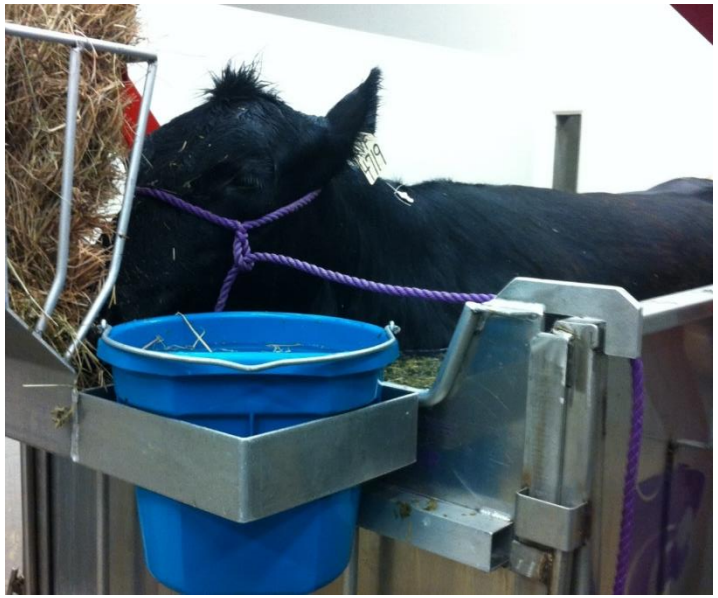
- ~~To find out what is wrong with our patients~~
- Diagnostic tests are tools of prediction, not explanation



What is the purpose of diagnostic testing?

- Diagnosis: to rule in or rule out a specific disease based on pathogen presence, exposure, or physiological effect
- Monitoring: to check response to therapy or the efficacy of preventative, vaccination, or biosecurity programs
- Screening: for genetic diseases, infectious disease carriers, or persistently infected animals
- Research: to understand the pathophysiology of a particular disease process

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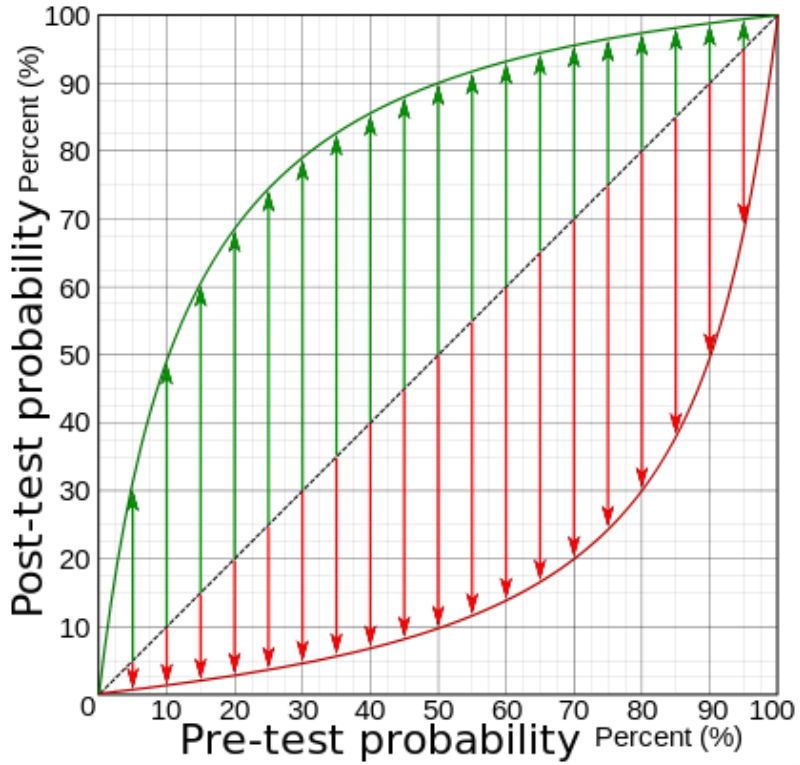
What is the purpose of diagnostic testing

- To gather specific information that closes the gap (amount of uncertainty) between pre-test clinical suspicion and post-test probability of disease
- To inform next steps



Clinicians need to know:

- Should I treat this animal?
  - Probability of treatment success vs. cost of drug + labor
- Do I need to manage risk to herd based on this animal
- Do I need to inform owner of risk to humans based on this animal
- What is the potential benefit to animal and at-risk population of:
  - Treatment/Therapy
  - Vaccination
    - Preventative
    - Outbreak reaction
  - Change in management
  - Change in preventative strategies

Evidence Based Veterinary Medicine

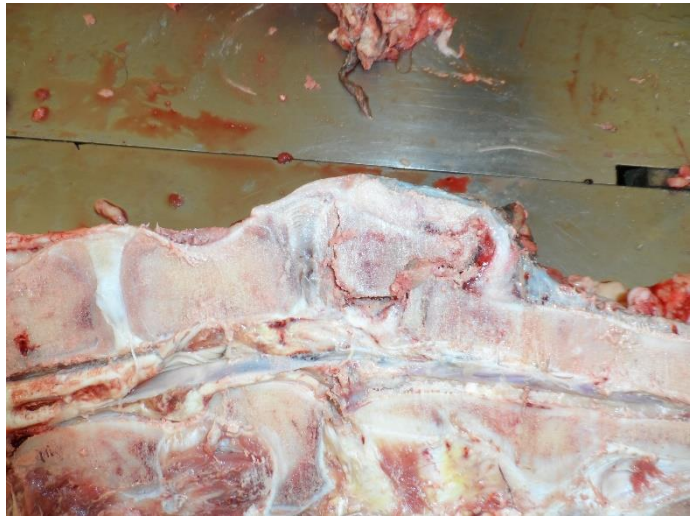
- Bayesian theorem -
  - Pr (H | Data) = Pr (Data | H) * Pr (H) / Pr (Data)
- Provides the basis for obtaining an updated belief ('posterior') about an existing hypothesis ('prior') given new data ('likelihood')
  - Existing hypothesis = differential diagnosis
  - New data = diagnostic test result
  - Updated belief = updated diagnosis or differential list

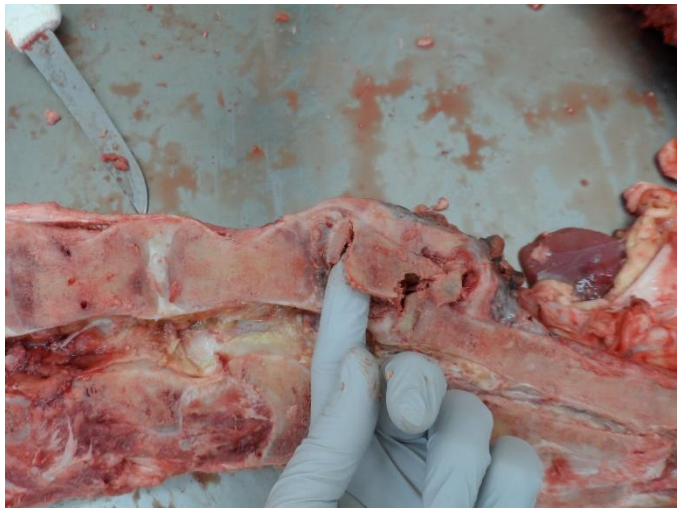
Evidence Based Veterinary Medicine

- Define “pre-test clinical suspicion” → probability estimate
- Incorporate uncertainty if needed → probability range
- Select appropriate test
- Interpret results in light of pre-test probability and test characteristics → post-test probability
- Use information to decide on next action needed

Bayesian Thinking

- Veterinarians are intuitive followers of Bayesian thinking
  - Integrating results of serial procedures to update differential list based on clinical suspicion before and after each procedure until level of uncertainty is minimized





Bayesian Thinking - Patient Assessment

- Signalment
- Clinical History
  - Owner reported abnormalities
  - Management risk factors
  - Environmental risk factors
- Clinical Examination of patient
- Detailed Examination of operation and population (if possible)
- Ancillary/Diagnostic testing

Bayesian Thinking

- Signalment:
  - 5 year old female Boer goat

Bayesian Thinking

- Signalment:
  - 5 year old female Boer goat
  - Genetically valuable

- Clinical Suspicions:

Bayesian Thinking

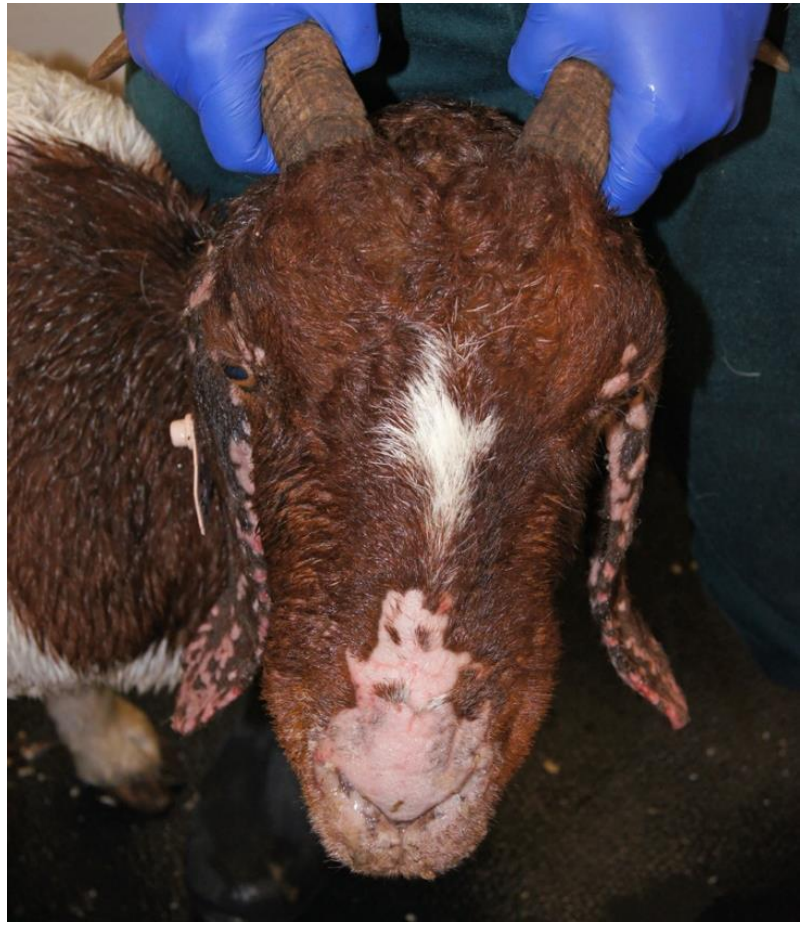
- Clinical History
  - Owner reports that she has been “off” and not eating well
  - She has crusts on her face
  - Now is having problems breathing and won’t stand up (weak?)
- Doe recently purchased and transported several hundred miles 2 weeks ago
- She was inspected before purchase and was fine 8 weeks ago
- Other goats in barn are now developing similar crusts on their heads and ears

Bayesian Thinking

- Clinical Suspicions:

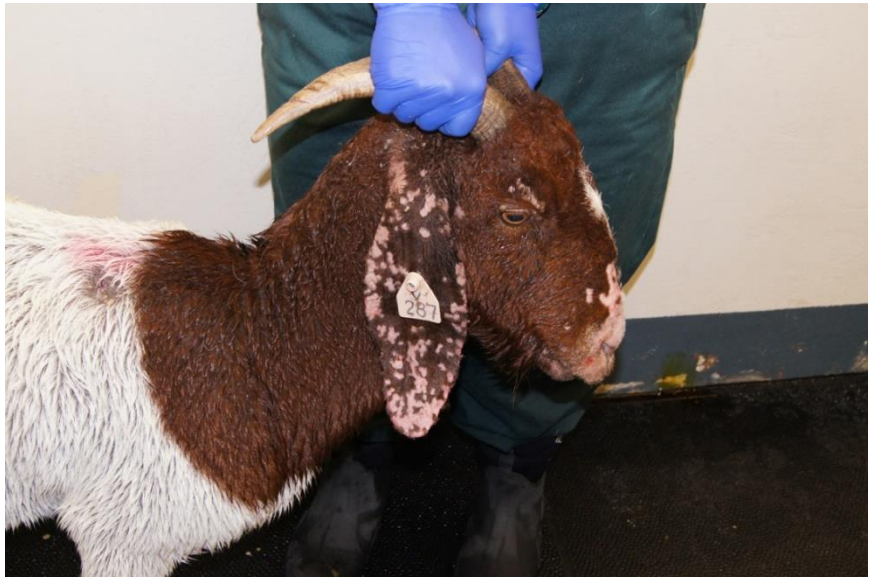
Bayesian Thinking

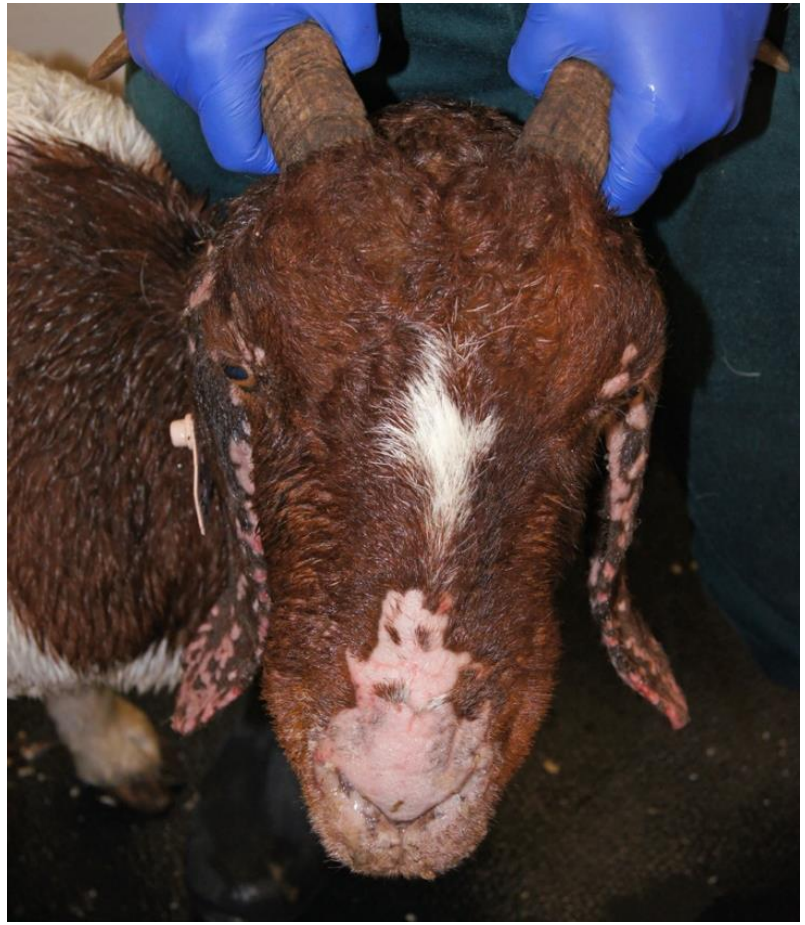
- Clinical Exam
  - Crusts are obstructing nasal airway
  - Multifocal, small, scaly / scabby lesions predominantly around muzzle and ears, but also extending along dorsum and flank.



Bayesian Thinking

- Clinical Exam
  - Elevated respiratory rate and heart rate but no abnormal lung sounds
  - Pale mucous membranes





Bayesian Thinking

- Need more information (testing) but stop and summarize what is known
- Clinical Suspicions:
- Syndrome(s):
- Problems:
- Differentials:

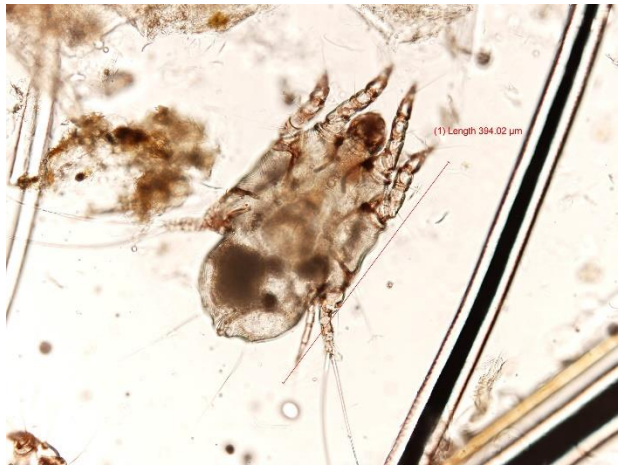
- What do we need to know to be able to finalize patient action plan/treatment protocol?

Bayesian Thinking

- Ancillary/Diagnostic Testing
  - Crusty, proliferative skin lesions – Infectious?
    - Skin Scraping
    - Biopsy
  - Weak/Depressed
  - Recent travel, geographical change, and stress
  - Pale mucous membranes
    - PCV/TP
    - Chemistry Profile
    - Fecal floatation

Bayesian Thinking

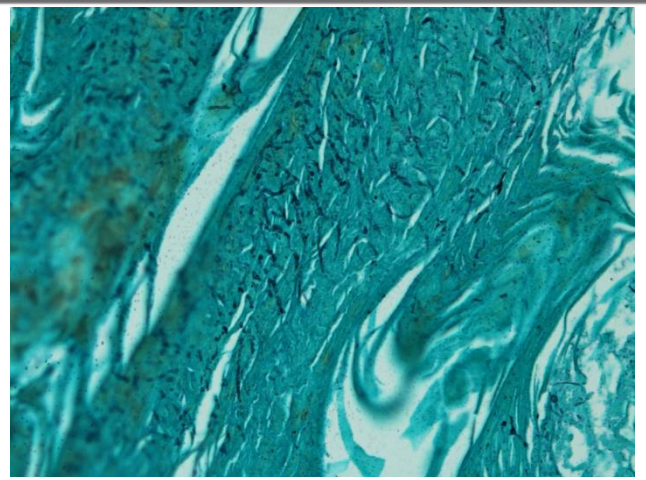
- Ancillary/Diagnostic Testing
  - Crusty, proliferative skin lesions – Infectious?
    - Skin Scraping
  - Chorioptes caprae



- Diagnosis of one patient problem
- Can't stop here:
  - Not all clinical signs fit
  - Why did we find mites?
  - Prevention
  - Herd risks

Bayesian Thinking

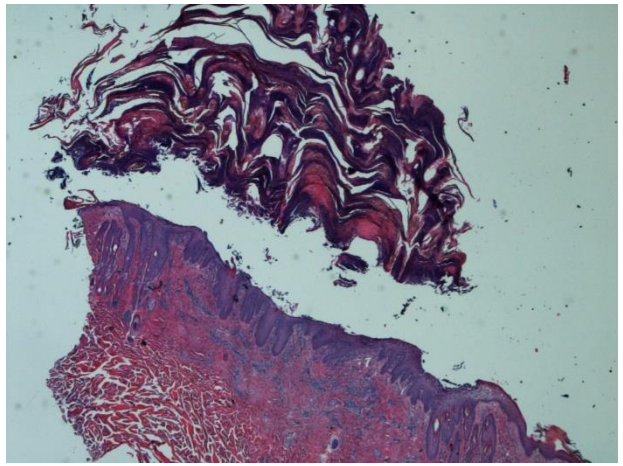
- Ancillary/Diagnostic Testing
  - Crusty, proliferative skin lesions – Infectious?
    - Biopsy

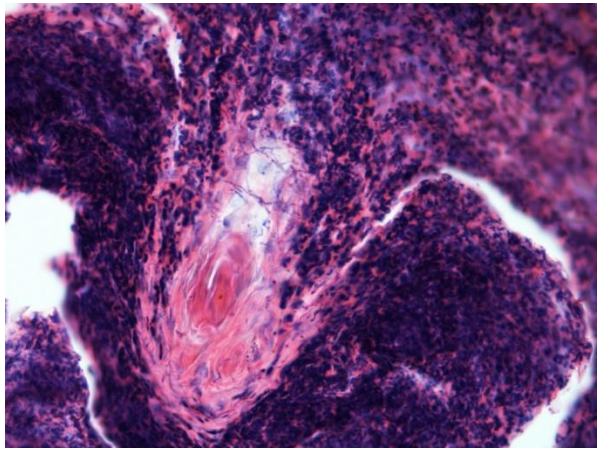


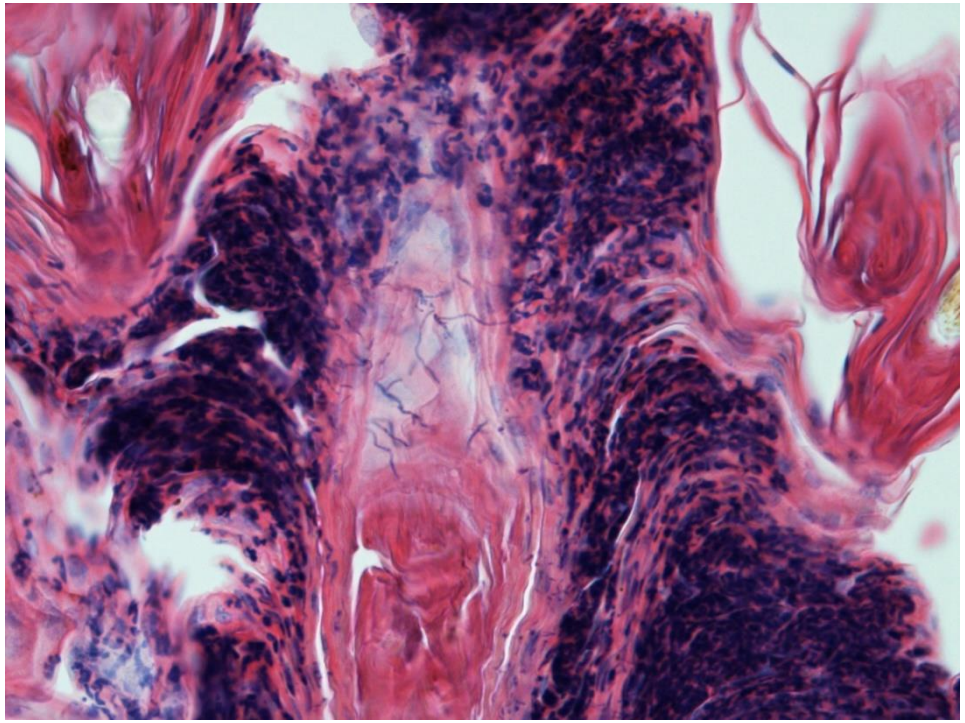
SPECIMEN DESC	Tissue, Fixed
DIAGNOSIS:	Dermatitis with superficial neutrophilic crust and filamentous bacteria typical of Dermatophilus congolensis
COMMENTS:	Morphology of a bacteria is very typical of Dermatophilus congolensis. This is a case of dermatophilosis.
HISTOPATHOLOGIC DESCRIPTION:	Two biopsies of haired skin were submitted. There is a thick crust on the epidermal surface. This crust is composed of layers of degenerating neutrophils, keratin, and accumulations of serum protein. Large numbers of bacterial organisms are present in these crusts. These organisms are tangled, elongate structures composed of individual cells that are perpendicularly arranged to the long axis of the filamentous chain. The epidermis is eroded and hyperplastic. There are accumulations of lymphocytes, plasma cells, and occasional neutrophils within the superficial dermis.

Bayesian Thinking

- Ancillary/Diagnostic Testing
  - Crusty, proliferative skin lesions – Infectious?
    - Biopsy – Dematophilus







Bayesian Thinking

- Ancillary/Diagnostic Testing
  - Weak/Depressed
  - Recent travel, geographical change, and stress
  - Pale mucous membranes
    - PVC/TP – 8/6.5
    - Chemistry Profile
      - High Glucose
      - Low Phosphorus
      - High SDH
    - Fecal floatation
- Why?

Bayesian Thinking

- Ancillary/Diagnostic Testing
  - Weak/Depressed
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PARASITE ID:	STRONGYLE TYPE EGGS 2080 EPG
PARASITE ID:	EIMERIA SPP. 1090 OPG
PARASITE ID:	TRICHURIS 10 EPG

Bayesian Thinking

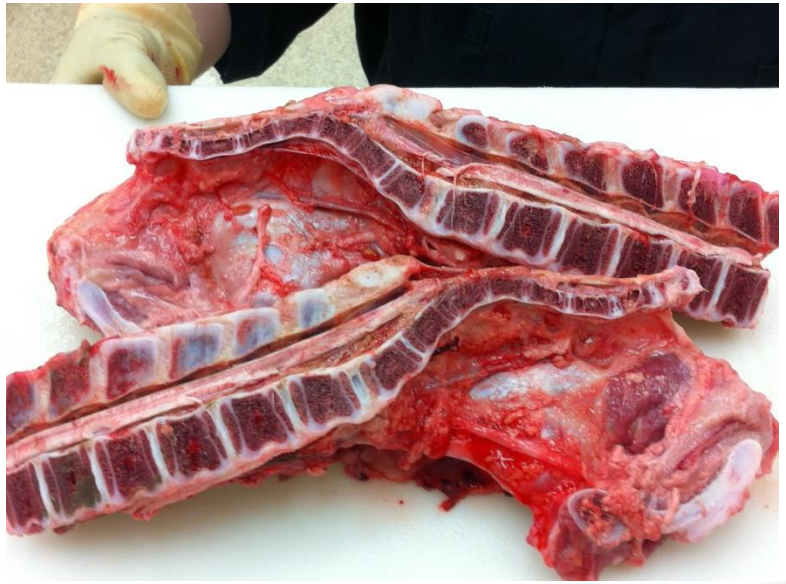
- Combination of information
  - Previous experience
    - Pattern recognition
  - Physical exam findings
  - Knowledge of prevalence of intestinal parasites, chorioptic mange and *Dermatophilus* in small ruminant populations (nationally and regionally)
  - Diagnostic testing information
- Decreases uncertainty
- Leads to confidence in treatment plan

Treatment

- Blood Transfusions
- Topical Ivermectin – whole barn
  - Discussed environmental biosecurity
  - Repeated in 10 days
- Oral anthelmintic
- Non-steroidal anti-inflammatory
- Oxytetracycline
  - Repeated in 14 days

Testing Methods – How to select tests

- Depends on the diagnostic question
- What information is needed to minimize uncertainty and allow action
  - Anatomic, histologic, or clinical pathology correlated with certain disease processes or pathophysiology
  - Exposure or antibody response to pathogen
  - Presence of pathogen



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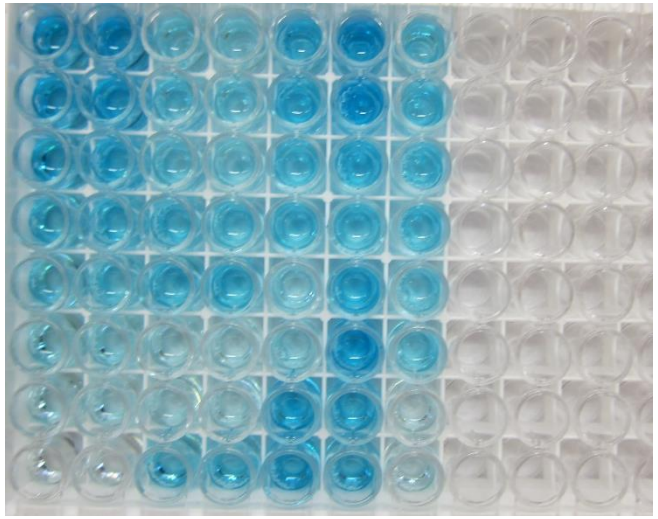

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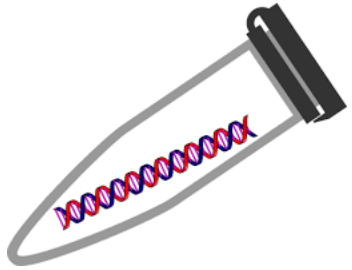
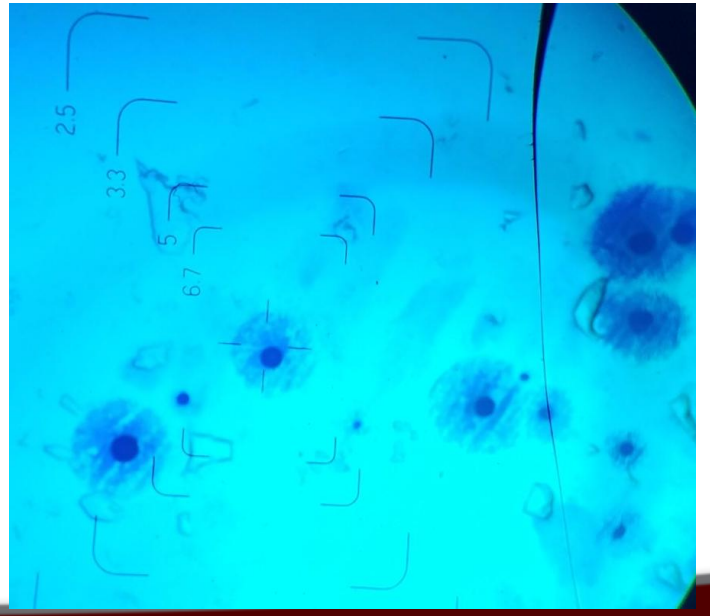




Testing Methods – Diagnostic Question

- What information is needed for the next step?
- Histologic lesions
- Body system function (dysfunction)
- Pathogen detection
- Pathogen isolation

Testing Methods – Pathogen Detection

- Molecular Diagnostics
  - PCR
  - qPCR
- Very sensitive and specific
- Quick answer
- Recent MLV can be detected

Testing Methods – Pathogen Isolation

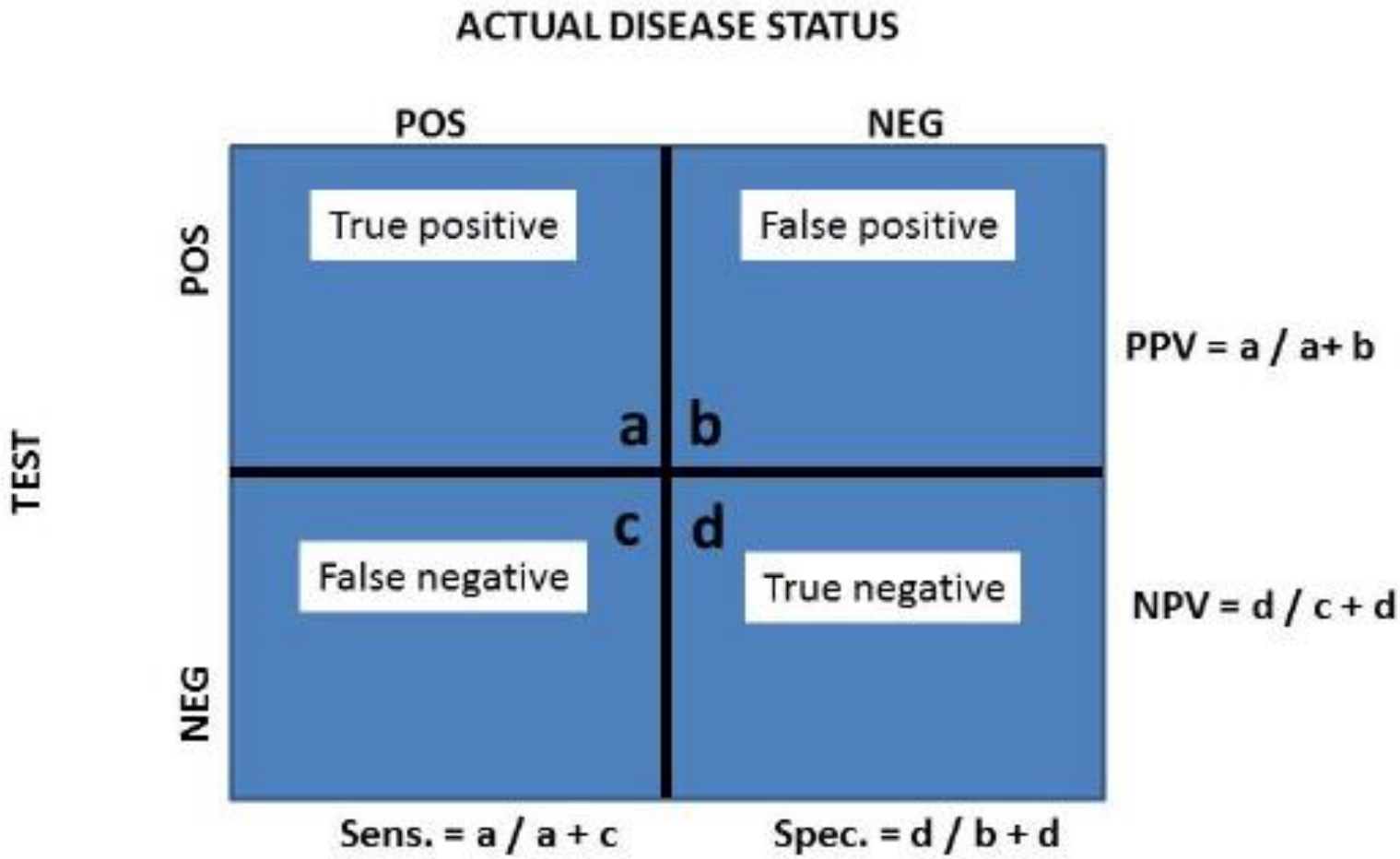
- Virus Isolation
  - Takes longer
  - Dependent on viable virus in the sample
  - Less sensitive than molecular methods
  - Not all viruses can be isolated - BRSV
  - Isolates can be sequenced
  - BRD viral isolates can be from recent MLV

Testing Methods – Pathogen Isolation

- Bacterial Culture
  - Takes longer
  - Dependent on viable bacteria in the sample
  - Affected by antibiotic administration
  - Antimicrobial susceptibility testing can be performed on isolates

How to select tests – Test Characteristics

- Sensitivity – Probability of an animal being test positive given that it is truly disease positive
  - Measure of the likelihood of a positive test in a diseased subject
  - Freedom from false negatives
- Specificity – Probability of an animal being test negative given that it is truly free of disease
  - Measure of the likelihood of a negative test in a healthy subject
  - Freedom from false positives



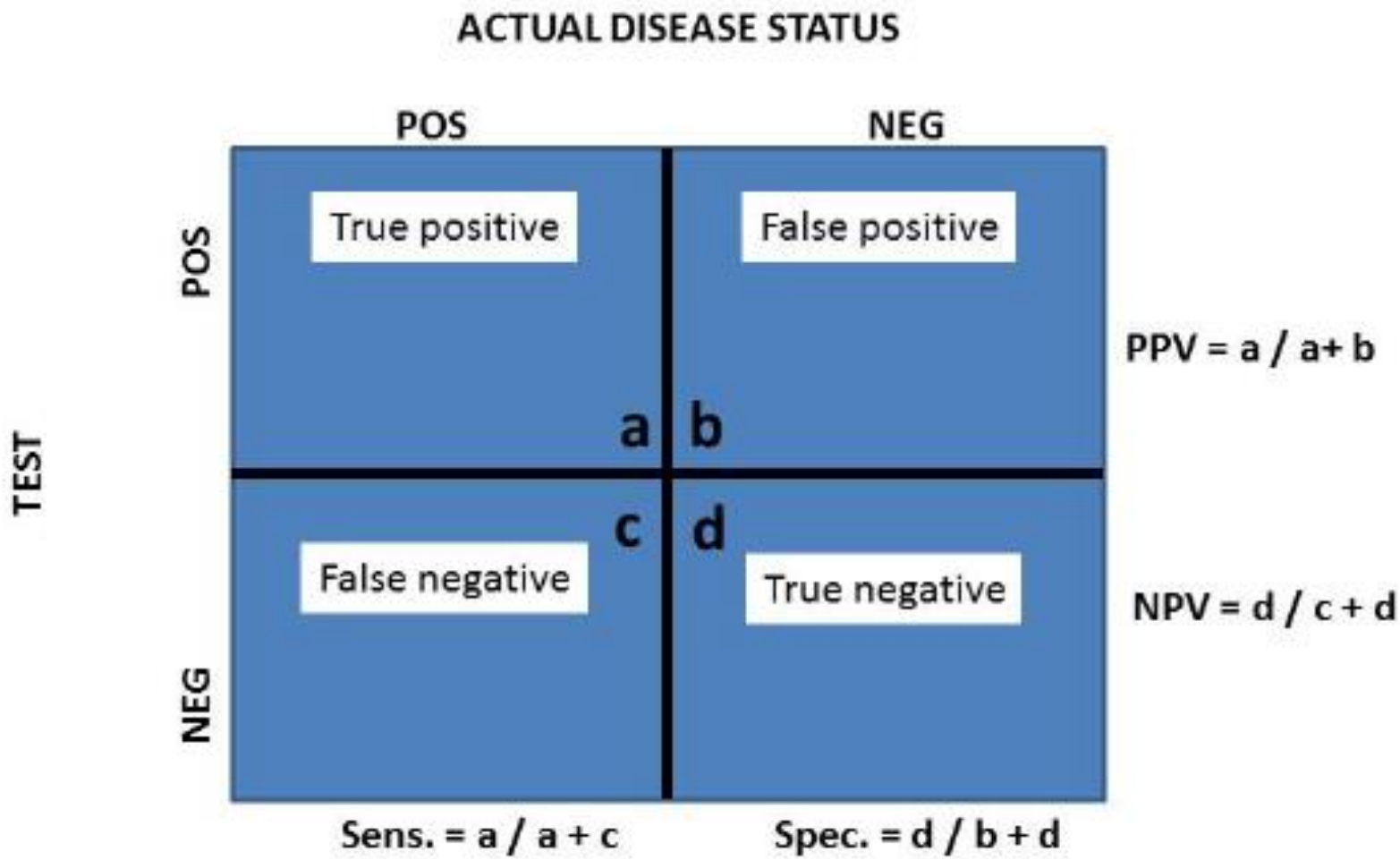
Determined by comparing test results in a population to the results of a gold standard definitive diagnostic test

How to select tests – Test Characteristics

- Sensitivity and specificity are population calculations
- Useful for comparing the performance of one test to another
- Stable to changes in prevalence

How to select tests – Test Characteristics

- Positive predictive value - probability that the disease is present when the test is positive
  - Higher value with high disease prevalence
- Negative predictive value - probability that the disease is not present when the test is negative
  - Higher value with low disease prevalence
- Both are population estimates that do not translate the interpretation of individual animal test results
- Disease prevalence estimates are not always available for external application to individual cases



Increase the likelihood of disease in a given subject before selecting the best test(s) for your goals

How to select tests – Test Characteristics Individual Test Result

- Sensitivity and Specificity
  - "What is the percentage of diseased animals that are correctly classified by the test?"
- What we need to know
  - "What is the percent of test positive animals that are truly diseased?"

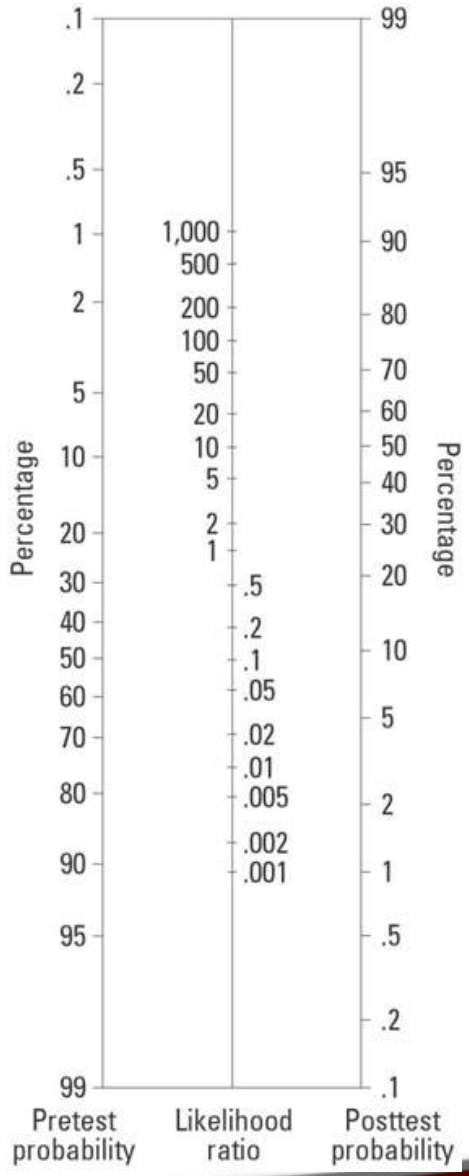
How to select tests – Test Characteristics Individual Test Result

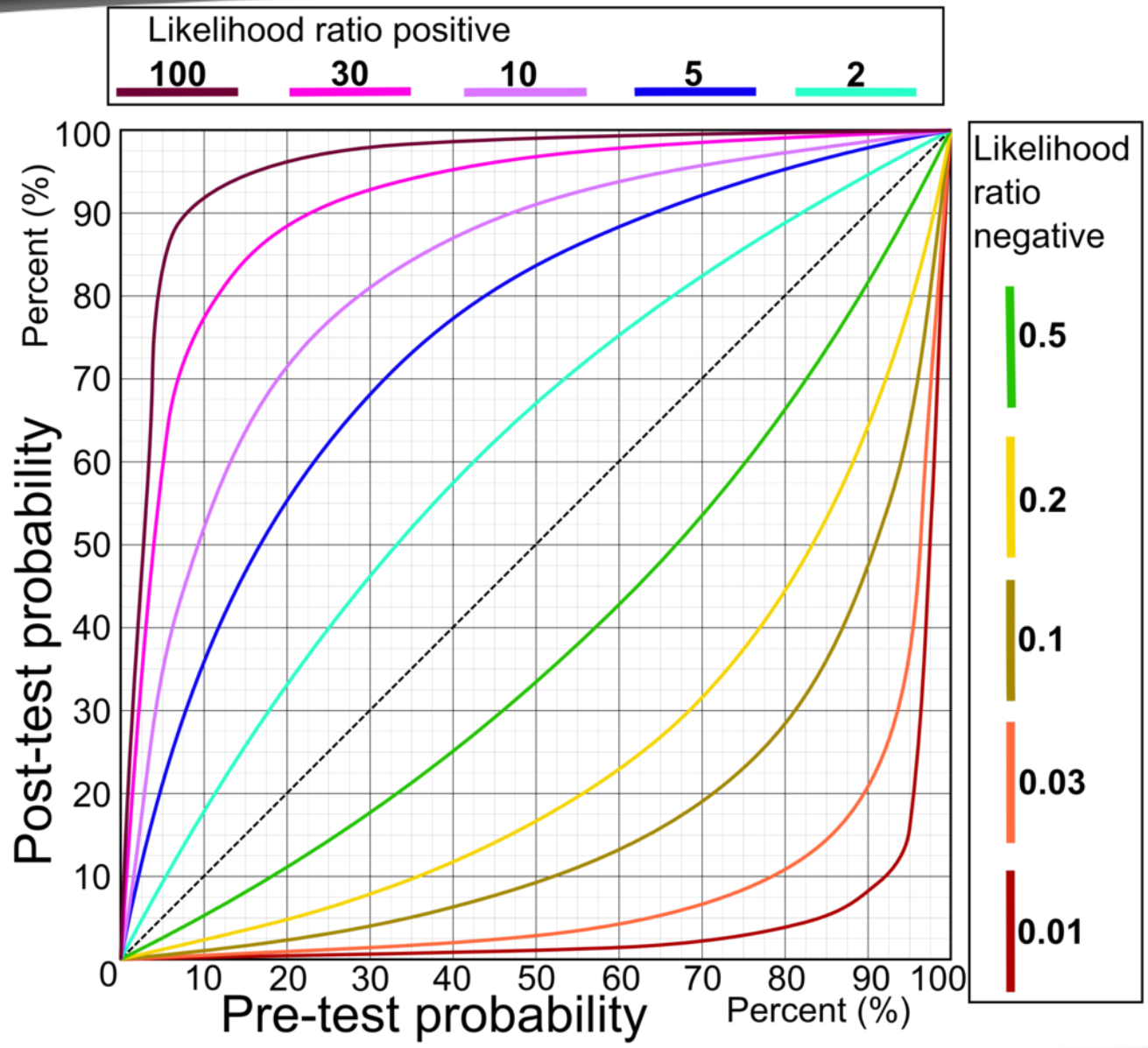
- Likelihood Ratios
  - Quantitate the frequency of positive and negative test results in diseased and disease-free cases
  - Do not depend on disease prevalence
  - Can be applied to cases regardless of population risks and characteristics

Likelihood Ratios

- Used to assess the value of a diagnostic test
- Positive LR (+LR) = Sensitivity / (1-Specificity)
- Negative LR (-LR) = (1- Sensitivity) / Specificity

- Translated into clinical practice via Bayes theorem
- Simplified by using probability revision graph or likelihood ratio normogram





Medical Uncertainty

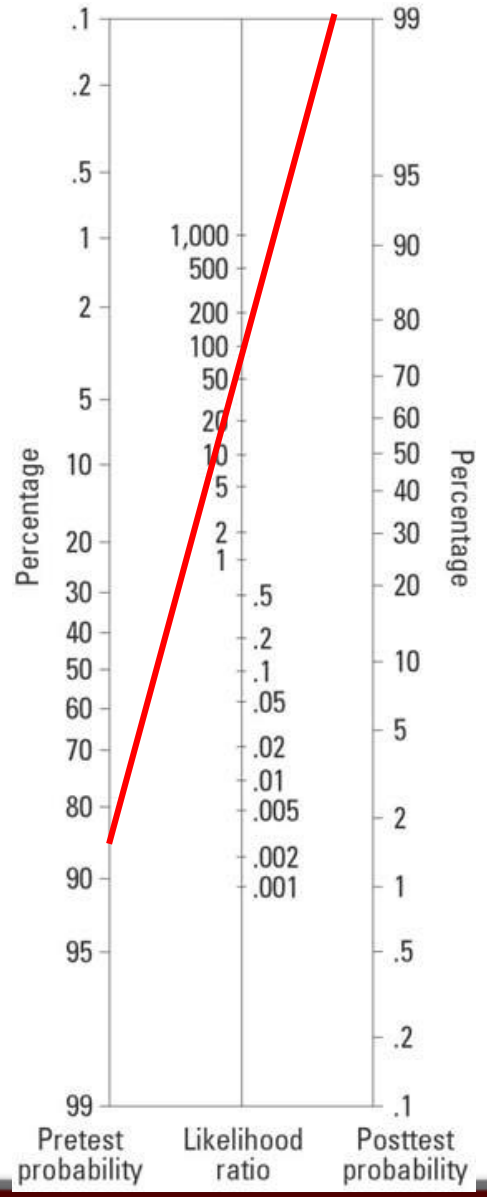
- Test results do not agree with clinical suspicion
- Insufficient evidence to pinpoint pre-test probability → Narrow range
- Lack of experience can lead to inaccurate pre-test probability
- Likelihood normagrams developed to incorporate uncertainty into pretest probability estimates and final diagnostic interpretations
  - visual tool - decide how much "weight" to give a diagnostic test result that contradicts with clinical suspicion

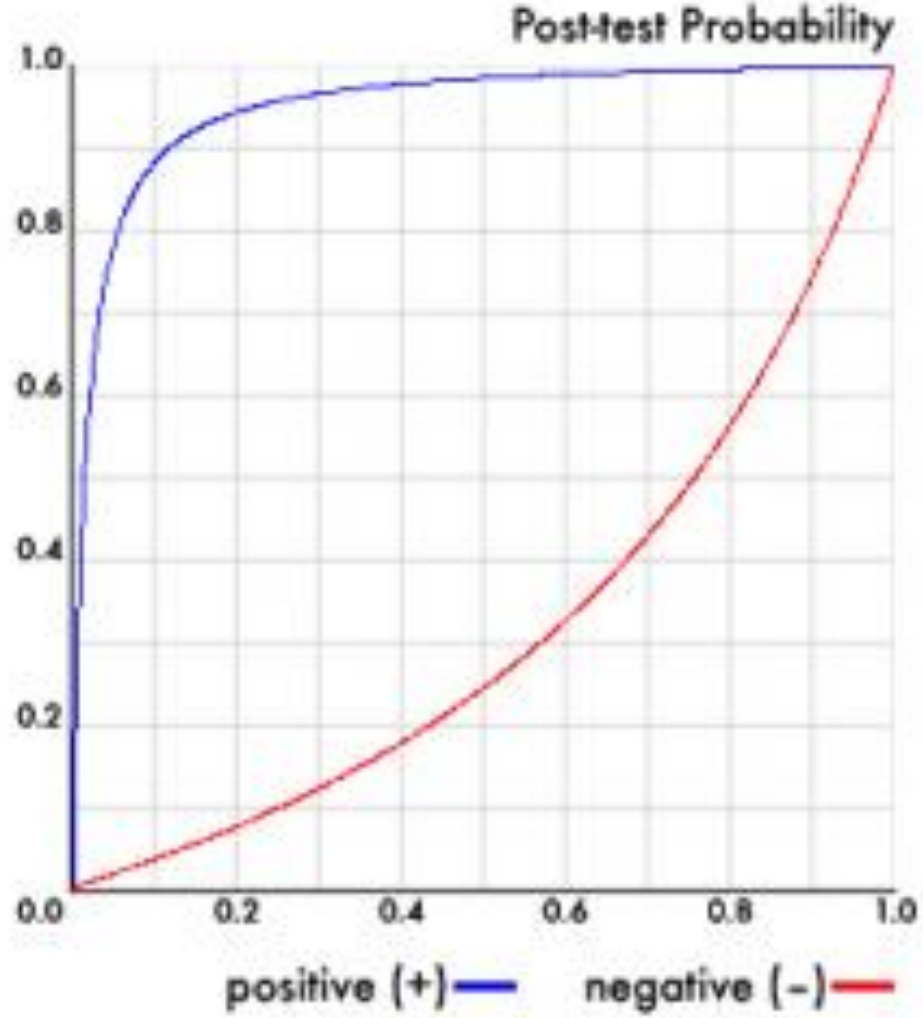
Test	Sensitivity	Specificity	+LR	-LR
Anaplasma marginale cELISA	1.00	1.00	333	0.00
BioPryn PSBP	0.99	0.95	19	0.01
Bovine Leukemia ELISA	0.98	0.99	98	0.02
BVD Ag ELISA ear	0.94	1.00	0	0.06
BVD Ag ELISA serum	0.97	1.00	0	0.03
H. somni qPCR	1.00	0.80	5	0.00
Johne's MAP ELISA	0.68	0.99	68	0.32
Johne's MAP qPCR	1.00	0.80	5	0.00
Leptospira spp. qPCR	0.90	0.95	18	0.11
M. bovis qPCR	0.90	0.92	11	0.11
M. haemolytica qPCR	1.00	0.56	2	0.00
P. multocida qPCR	1.00	0.66	3	0.00
T. pyogenes qPCR	0.89	0.93	13	0.12

Johne's Disease (MAP) ELISA

Pre-test probability = 85%
+LR = 68
-LR = 0.32

Post-test probability = 99.7%



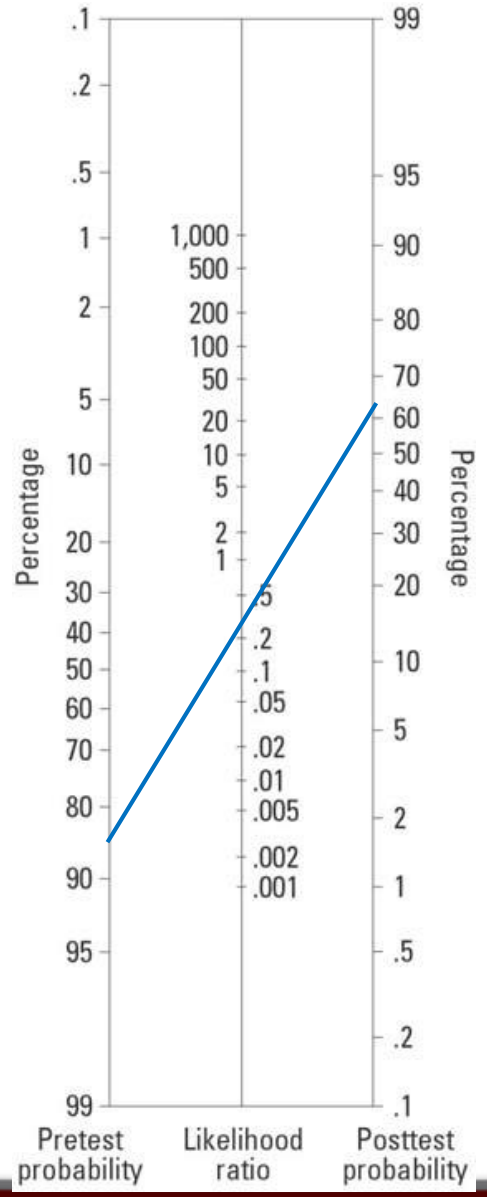


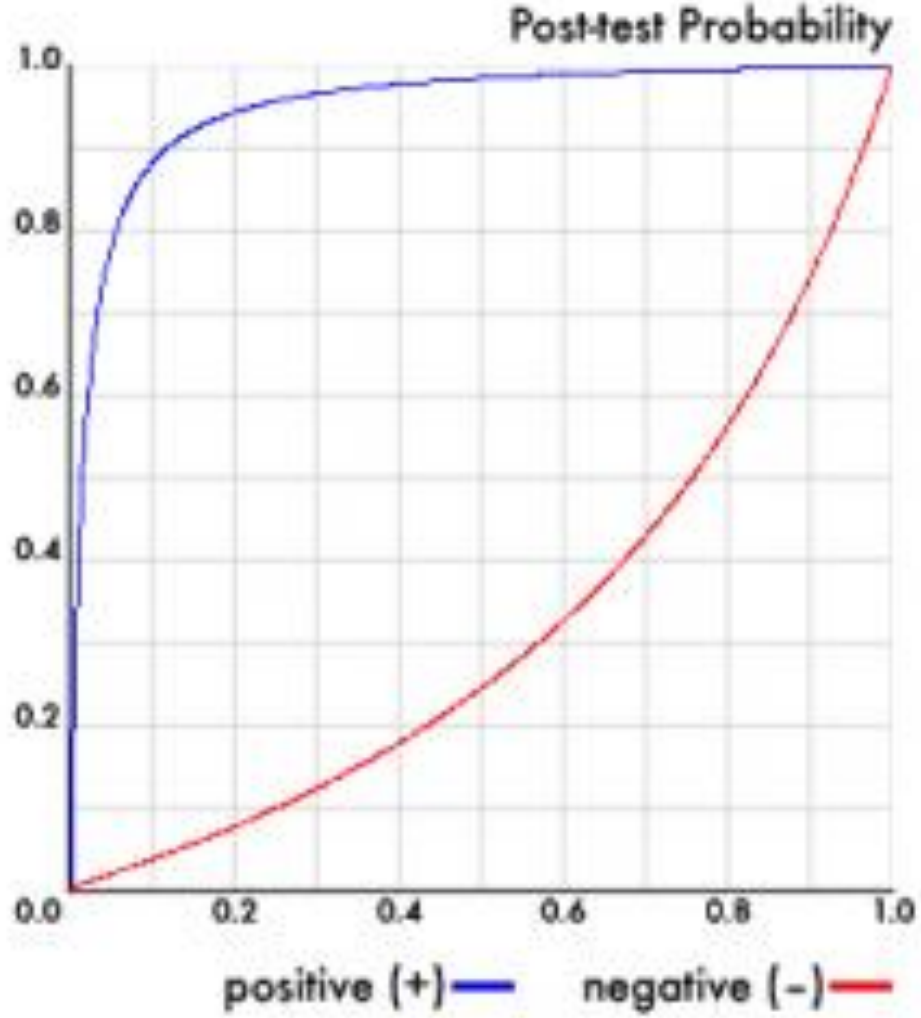
Annals of Emergency Medicine 2003 42, 292-297DOI: (10.1067/mem.2003.274)

Johne's Disease (MAP) ELISA

Pre-test probability = 85%
+LR = 68
-LR = 0.32

Post-test probability = 64.5%





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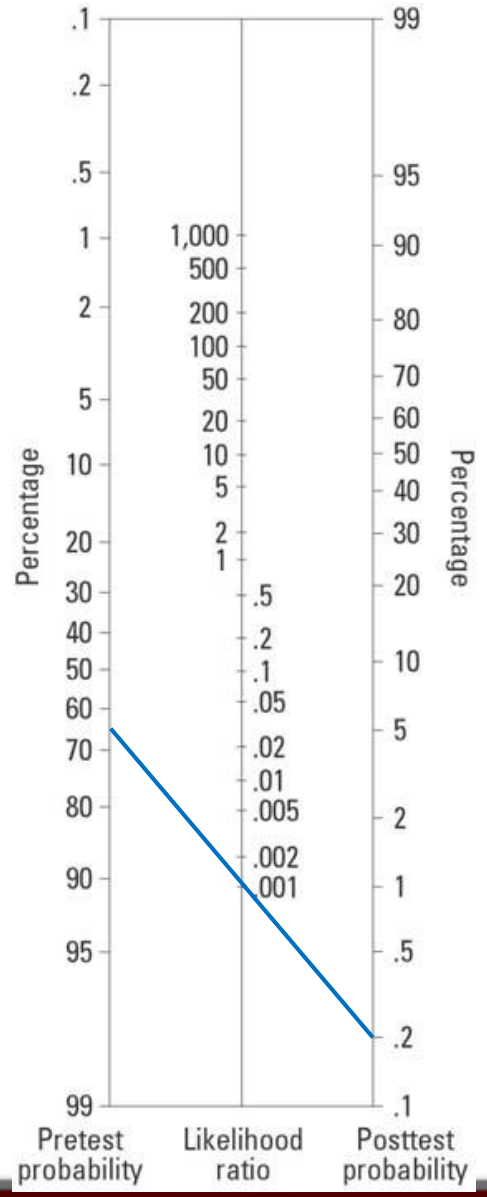
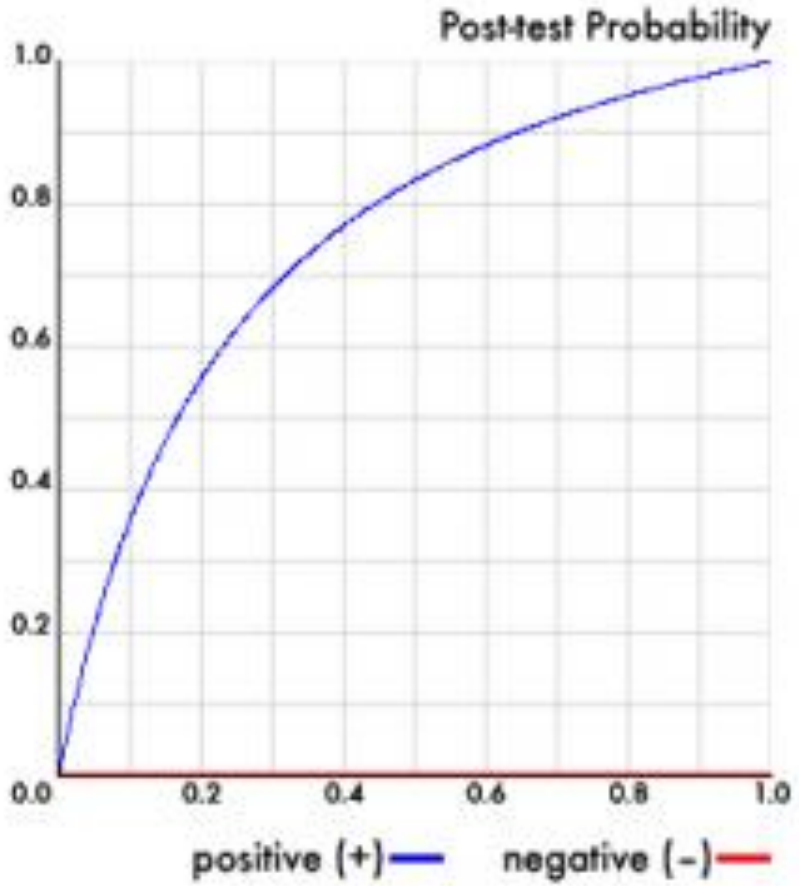
Johne's Disease (MAP) qPCR

Pre-test probability = 64.5%
+LR = 5
-LR = 0.001

Post-test probability = 0.2%





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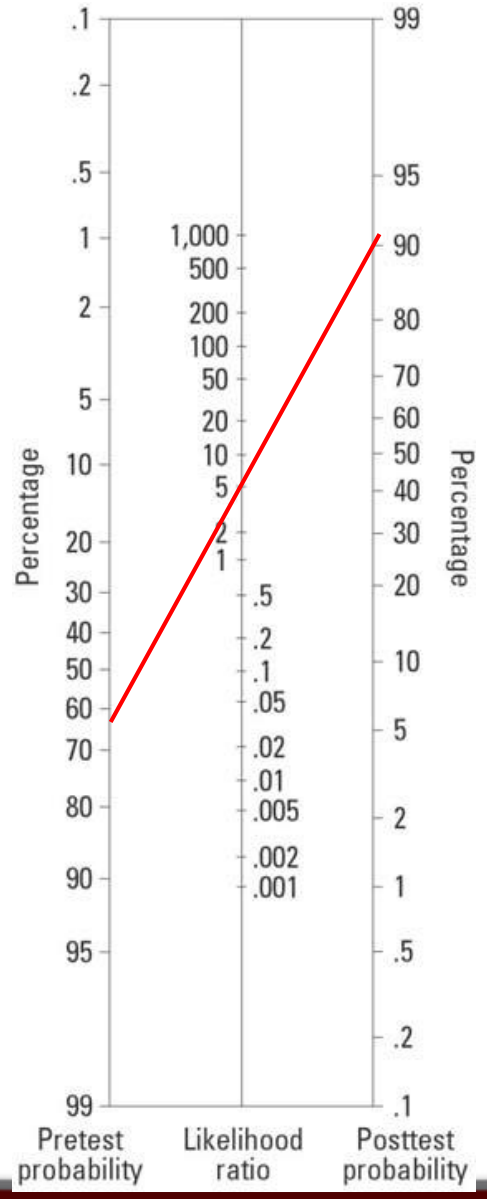
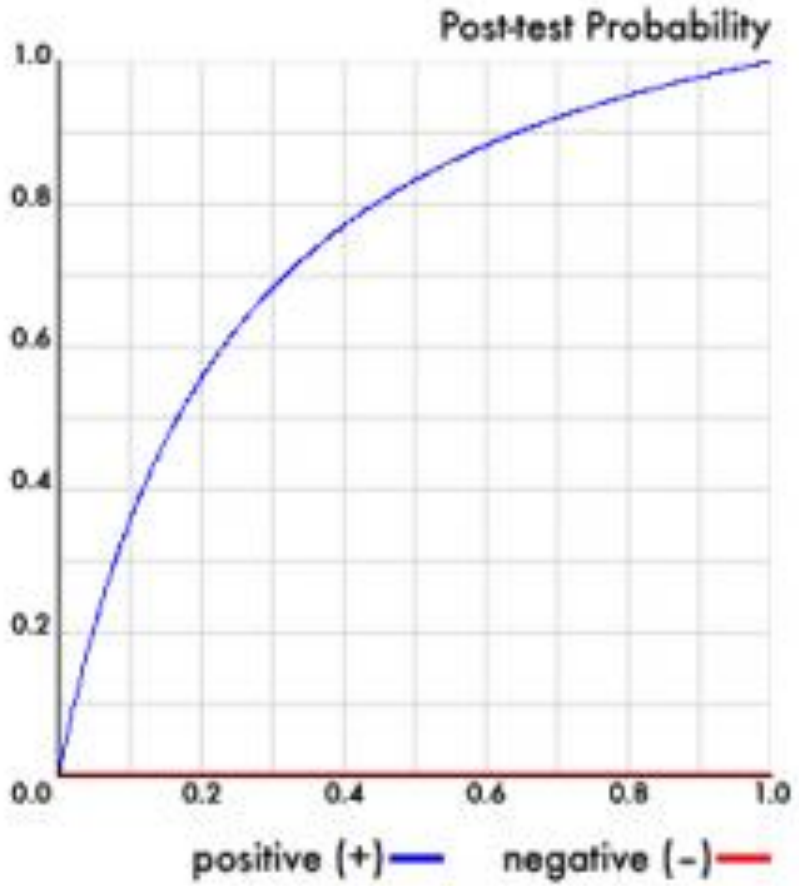
Johne's Disease (MAP) qPCR

Pre-test probability = 64.5%
+LR = 5
-LR = 0.001

Post-test probability = 90.1%





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Improving Interpretation Potential

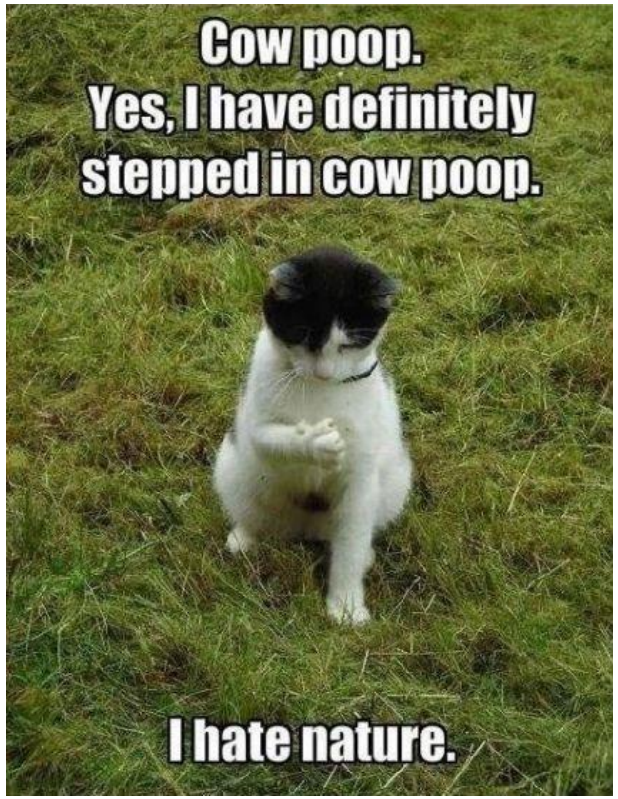
- True or False?
- A diagnostic test is more objective than a patient's history and physical exam.

Improving Interpretation Potential

- **False**
- A diagnostic test is more objective than a patient's history and physical exam.

Improving Interpretation Potential

- Improve pre-test probability estimate as much as possible
- Thorough history – patient, herd, management
- Knowledge of disease prevalence and risk of disease exposure (national or regional)
  - Laboratory summaries or practice databases can potentially be developed
- Complete physical exam
- Diagnostic panels (test clusters) or clinical prediction guides



Questions?

Feel free to contact me with any questions or feedback:

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