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Gathering evidence to determine the place for a new diagnostic test in equine practice

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Declarations

Conflict of interest declaration

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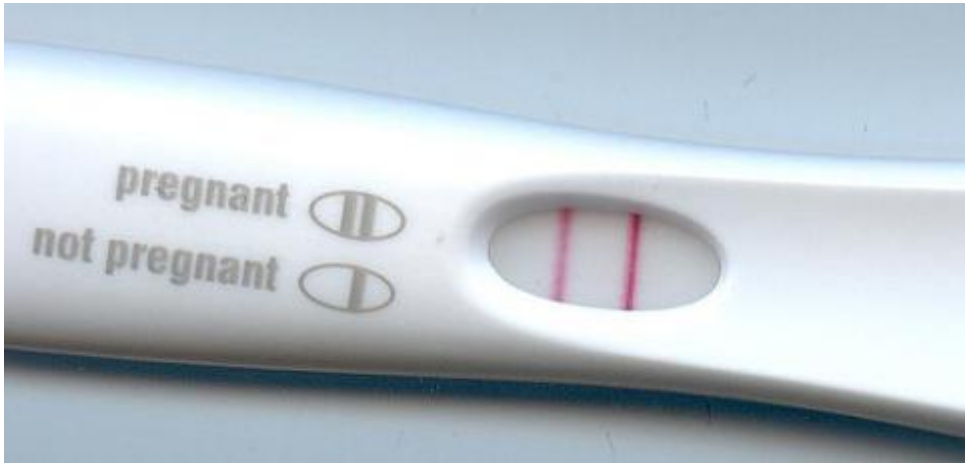
Lateral flow immunoassay



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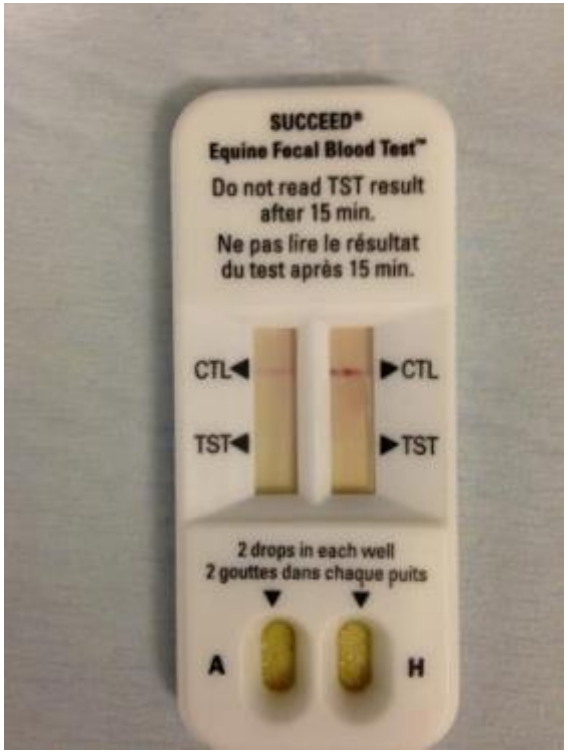
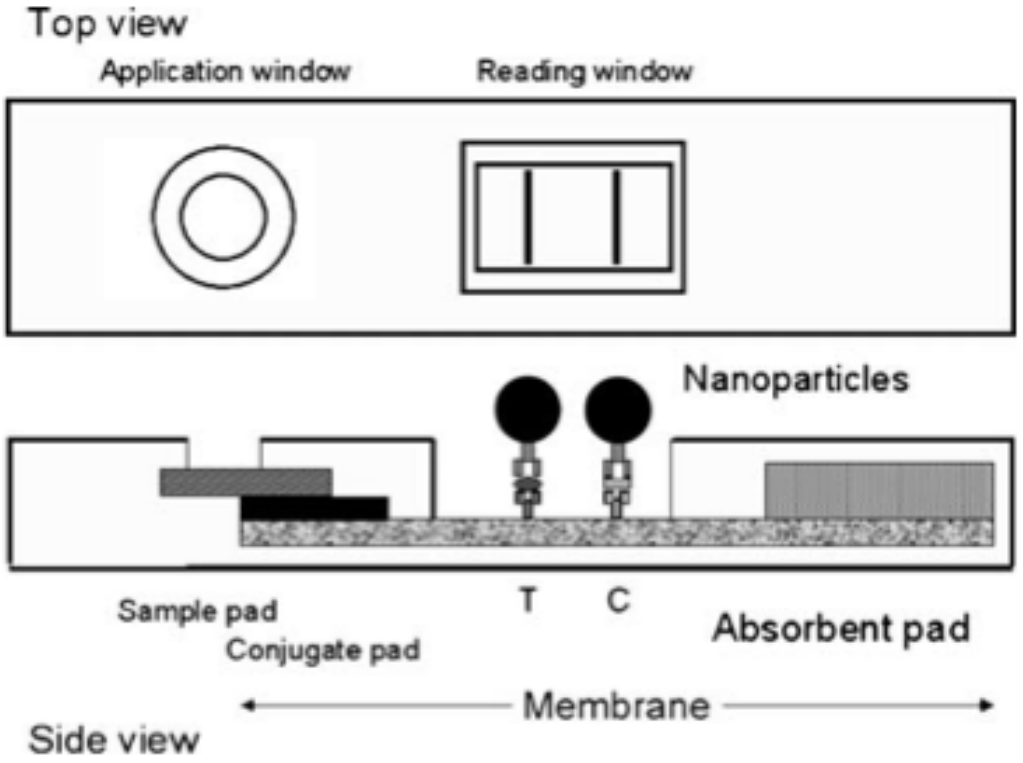
Lateral flow immunoassay

- Qualitative or semi-quantitative
- Strip of carrier material containing dry reagents which are activated upon application of a fluid sample





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Succeed faecal blood test (FBT)

- Commercially available lateral flow immunoassay
- Marketed to ‘aid diagnosis of GI tract conditions’
- ‘Helps differentiate foregut and hindgut conditions’
- Detects both albumin & haemoglobin in faeces
- Positive faecal albumin is diagnostic of ‘colonic ulceration’

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‘Colonic ulceration’

- Poorly defined condition
- May represent the end stage of numerous diseases including:
  - parasitic gastroenteritis
  - inflammatory bowel disease
  - right dorsal colitis
- Prevalence of 63% of 545 horses (*Pellegrini 2005)*
- Lesions not defined by histopathology
  - gross appearance only

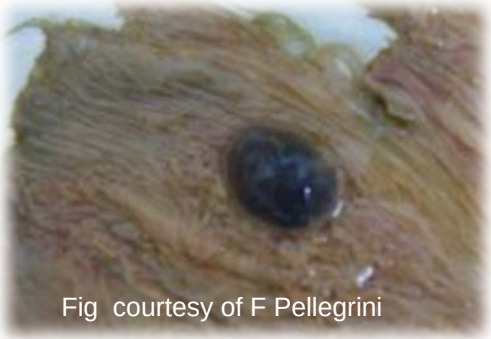

Fig courtesy of F Pellegrini

Pellegrini, F.L., 2005. Results of a large-scale necroscopic study of equine colonic ulcers. J. Equine Vet. Sci. 25, 113–117. doi:10.1016/j.jevs.2005.02.008

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Validation

- Best to compare to ‘gold standard’ diagnostic test
- Problems:
  1. Disease poorly defined- likely multiple disease states could result in a positive test
     - Parasitism
     - IBD
     - Colitis
  2. Potential for false positives
     - Rectal collection of sample
  3. Intestinal disease is difficult to diagnose in horses
     - No gold standard ante-mortem marker of intestinal disease

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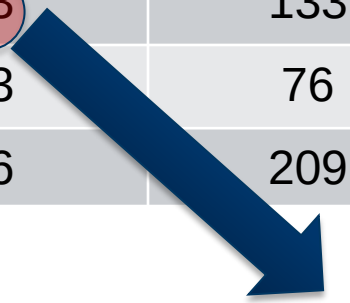
Initial approach to validation

Clinically healthy vs. hospital cases

Test Result	Hospital	Healthy	TOTAL
Alb +	110	23	133
Alb -	53	23	76
	163	46	209



Sensitivity= 23/46 **50%**
Specificity= 53/163 **32%**
Positive predictive value= 23/133 **17%**
Negative predictive value= 53/76 **70%**

Does this represent subclinical disease or false positives?

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Colic cases

TEST RESULT	Colic signs in last 24hrs	No colic	TOTAL
Alb +	20	113	133
Alb -	4	72	76
	24	185	209

Sensitivity= 20/24 **83%**
Specificity= 72/185 **39%**
Positive predictive value= 20/133 **15%**
Negative predictive value= 72/76 **95%**

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Faecal haemoglobin following epistaxis

TEST RESULT	Epistaxis	No epistaxis	TOTAL
Hb +	5	96	101
Hb –	0	109	109
	5	205	210

Sensitivity: 5/5 **100%**
Specificity: 109/205 **53%**
Positive predictive value=5/101 **5%**
Negative predictive value=109/109 **100%**

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High sensitivity / low specificity

Common scenario in veterinary medicine to have an indicator of disease with a high sensitivity and low specificity:

- Pyrexia
- Tachycardia
- Anaemia

High negative predictive values mean that this test has the potential to be used as a screening test….

Next question: Does a positive faecal haemoglobin or albumin reflect intestinal disease or could it be a 'normal' finding?

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Post mortem study

- Detailed examination of the entire intestinal mucosal surface in horses euthanised for non GI related reasons
- Faecal haemoglobin and albumin status determined prior to euthanasia
- Post mortem performed within 30minutes of death to minimise post mortem change

Time consuming and messy!

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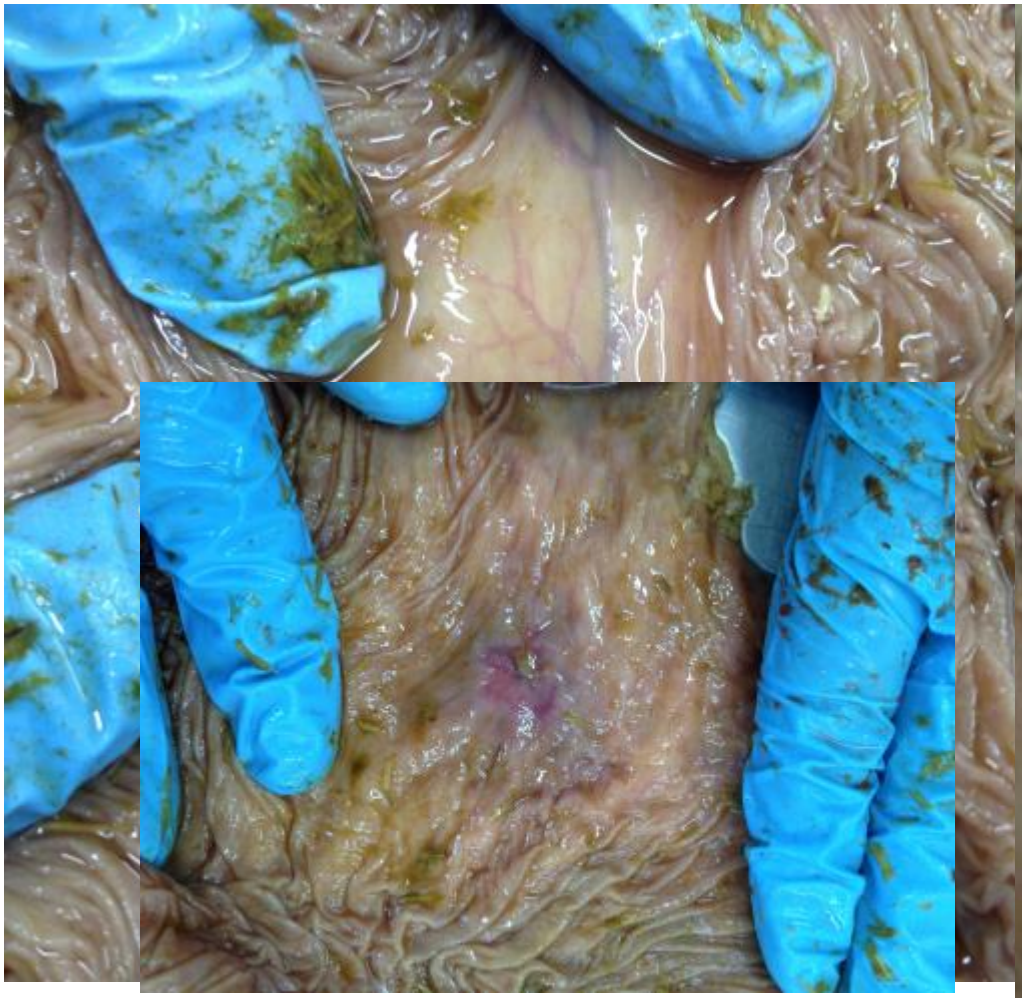
Intestinal lesions



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Evaluation of faecal albumin as a marker of colonic pathology

Colonic mucosal pathology detected in 13/14 horses euthanised for reasons other than GI disease

	Colonic pathology	Normal colon
Albumin +	11	1
Albumin -	2	0

Sensitivity= 11/13= **85%**
Specificity= 0/1= **0%**
PPV=11/12= **92%**
NPV=0/2= **0%**

The prevalence of colonic pathology has previously been grossly underestimated

We need to find more normal horses!

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Evaluation of faecal haemoglobin as a marker of colonic pathology

	Colonic pathology	Normal colon
Haemoglobin +	8	5
Haemoglobin -	0	1

Sensitivity= 8/8 **100%**
Specificity= 1/6 **17%**
PPV=8/13 **62%**
NPV=1/1 **100%**

Haemoglobin negative is rare
difficult to draw conclusions at this stage.

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Intended use of test

- Manufacturers design this test to be interpreted in combination i.e. the combination of Hb and Alb + and – should indicate the location of the pathology.
- Not enough data to validate this yet.

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Conclusions

- Colonic mucosal pathology has previously been grossly underestimated
- Initial analysis suggests a positive faecal albumin has a high PPV for colonic pathology
- Defining the spectrum of observed pathology is currently being undertaken- with view to being able to determine the likely clinical significance of these lesions