

Veterinary Bioscience: Digestive System

DVM Year 1

VETS30016/VETS90120



THE UNIVERSITY OF
MELBOURNE

FACULTY OF
VETERINARY
SCIENCE

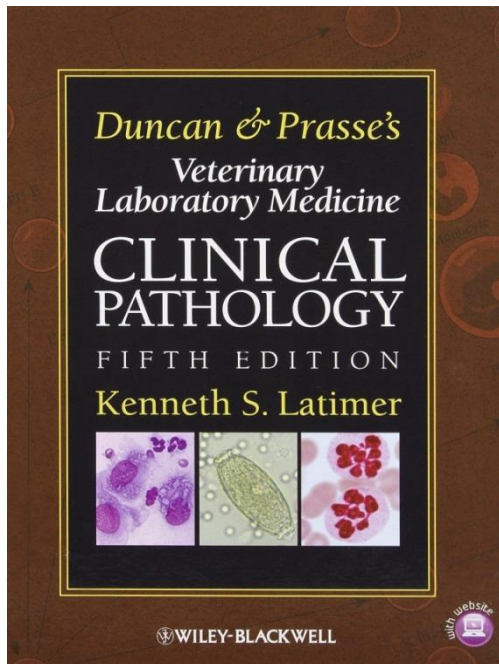


Clinical Pathology of the Gastrointestinal Tract

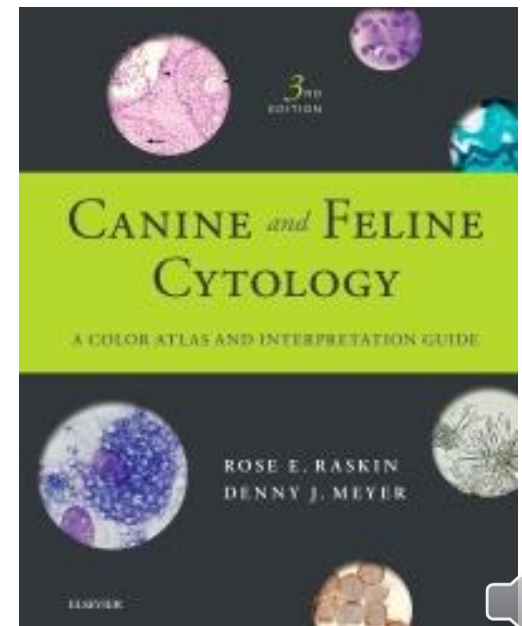
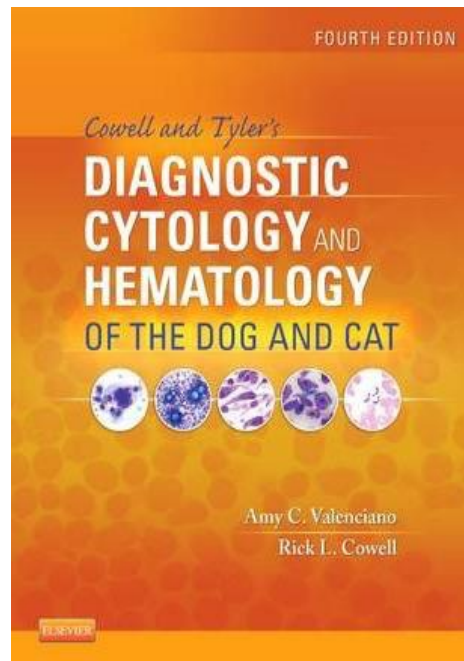
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Chapter 8 for the digestive system



Clinical pathology reference texts available for download from your library...



Learning objectives

- Explain how clinical pathology can help in defining and diagnosing gastrointestinal disease
- Describe in basic terms how blood values may change in response to some common GI diseases
- Explain the diagnostic tests for exocrine pancreatic insufficiency
- Describe what disease mechanisms may result in changes to peritoneal fluid



Lecture overview

1. Introduction to clinical pathology
2. Laboratory evaluation of GI

Case studies:

Vomiting

Diarrhoea

Protein-losing enteropathy (PLE)

Exocrine pancreatic insufficiency (EPI)

- Evaluating data and considering further tests



What is clinical pathology?

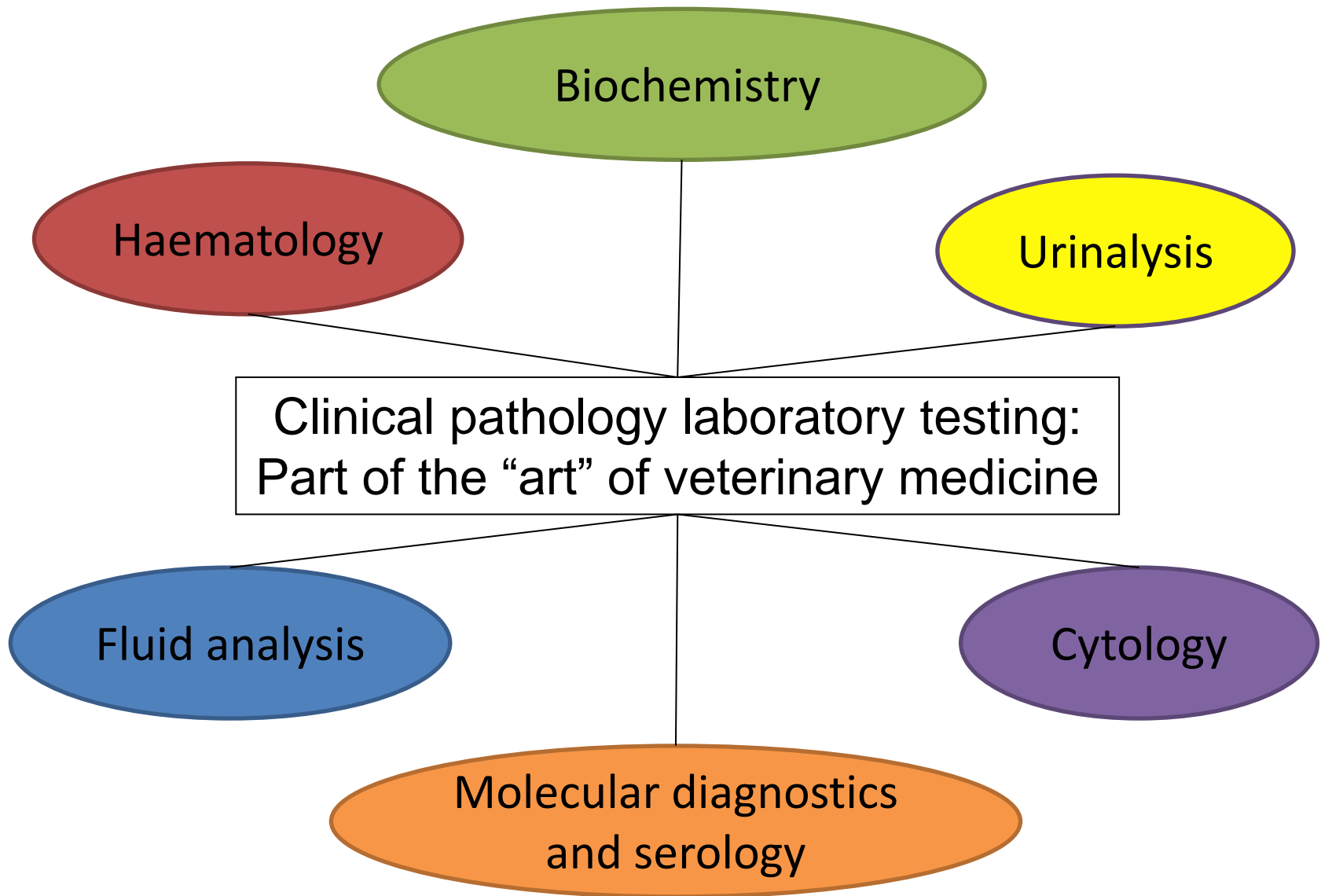
- Utilisation of laboratory tests to:
 - Diagnose disease
 - Narrow down differential diagnoses (DDx)
 - Direct further investigations
 - Monitor disease progression or response to therapy
 - Screen for underlying disease in clinically healthy animals



How to use clinical pathology

- Appropriate laboratory tests are selected after a full history and complete physical examination
 - Identify a problem list first, to ensure selection of appropriate and cost effective tests
- Laboratory tests are frequently used in conjunction with other diagnostic procedures, as part of an integrated diagnostic approach:
 - e.g. imaging, endoscopy, laparotomy, biopsy, treatment trial





Learning the lingo

Common clinical pathology acronyms (CCPA just joking!)

- Haematology
 - PCV: packed cell volume
 - Hct: haematocrit
 - Hb (or Hgb): haemoglobin concentration
 - RCC: red cell count
 - MCV: mean corpuscular volume
 - MCHC: mean corpuscular Hb concentration
 - RDW: red cell distribution width



Learning the lingo

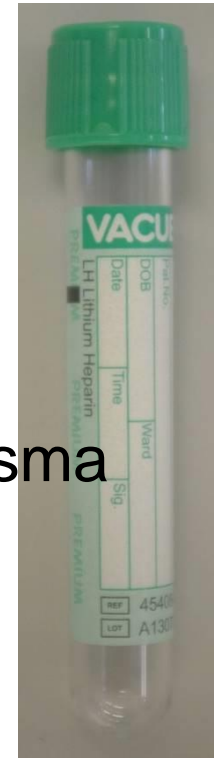
- WCC: white cell count (aka leukocyte count)
- TNCC: total nucleated cell count
- Neut: neutrophil (aka seg or polymorph)
- Lym (or Lymph): lymphocyte
- Mono: monocyte
- Eo: eosinophil
- Baso: basophil
- PLT: platelets (platelet count)
- PDW: platelet distribution width



Learning the lingo

- Biochemistry: Electrolytes
 - Na: sodium
 - K: potassium
 - Cl: chloride
 - Mg: magnesium
 - Ca: calcium (may also be “Total calcium”)
 - Ca^{++} : ionised calcium
 - PHOS: Phosphate
 - Anion Gap: calculated value: $(\text{Na} + \text{K}) - (\text{Cl} + \text{n})$

Plasma



Serum



Learning the lingo

- Biochemistry
 - Urea: measured as BUN (blood urea nitrogen) in USA
 - Cr (or CREAT): creatinine
 - Gluc: glucose
 - Chol: cholesterol
 - Bili: bilirubin, usually “total bilirubin”
 - Bili Total ~ Unconjugated + Conjugated
 - BA: (serum total) bile acids



Learning the lingo

- Biochemistry: Enzymes
 - ALT: alanine aminotransferase (previously SGPT)
 - AST: aspartate aminotransferase (previously SGOT)
 - AP: alkaline phosphatase (aka ALP, AlkPhos)
 - GGT: gamma glutamyltransferase (aka gamma GT, γ GT)
 - SDH: sorbitol dehydrogenase
 - GLDH: glutamate dehydrogenase
 - CK: creatine kinase (previously CPK)



Learning the lingo

- Biochemistry: More enzymes
 - TLI: (serum) trypsin-like immunoreactivity
 - Amylase: sometimes AMYL
 - Lipase: sometimes LIP
 - cPL: canine pancreatic-specific lipase
 - cPLI: canine pancreatic lipase immunoreactivity



Learning the lingo

- Biochemistry: Proteins
 - TP: total protein (measured biochemically)
 - TS: total solids (refractometer total protein value)
 - Alb: albumin
 - Glob: total globulins
 - A:G (ratio): Alb/Glob
 - Fib: fibrinogen
 - SPE: serum protein electrophoresis



Learning the lingo

- Urinalysis (UA):
 - USG: urine specific gravity ('concentration')
 - RBC: red blood cells (erythrocytes)
 - WBC: white blood cells (leukocytes)
 - #/LPF: number per low power field (x100 magnification)
 - #/HPF: number per high power field (x400 magnification)
 - TNTC: too numerous to count (lots and lots!)



Learning the lingo

- Miscellaneous:
 - Ag: antigen
 - Ab: antibody
 - EDTA: ethylene diamine tetraacetic acid
 - Ig: immunoglobulin
 - SDMA: symmetric dimethyl arginine
 - T₄: thyroxine
 - T₃: triiodothyronine



Learning the lingo

- Miscellaneous:
 - TPR: temperature, pulse (rate) and respiration (rate)
 - MN or MC: desexed male
 - FS: spayed female
 - NAD: no abnormalities detected
 - NS: not stated
 - WRI: within reference interval
 - WNL: within 'normal' limits
 - (AbN: abnormal; N: normal)

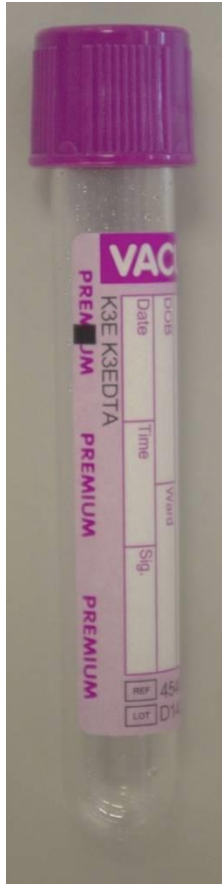


Learning the lingo

- Diagnoses:
 - EPI: exocrine pancreatic insufficiency
 - DM: diabetes mellitus
 - DKA: diabetic ketoacidosis
 - DI: diabetes insipidus
 - HyperA: hyperadrenocorticism
 - HypoT: hypothyroidism
 - etc, etc, etc!!

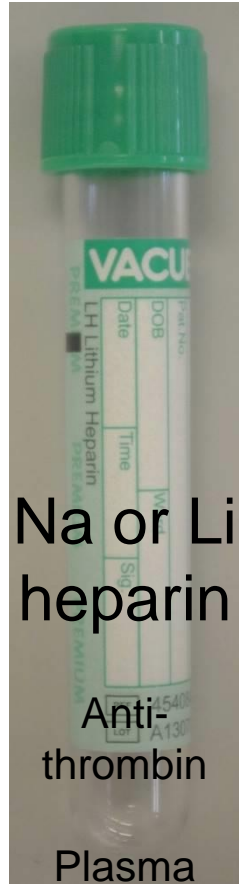


Choosin' the tube



Na or K
EDTA

Chelates Ca^{++}
Haematology



Na or Li
heparin

Anti-thrombin

Plasma

General
biochemistry



“Plain”
tube

Clots

Serum

General
biochemistry
Some specific
tests



Fluoride
Oxalate
tube

Plasma

Glucose
(Lactate)



Haematology

- PCV and TS
- Complete blood count (CBC)
 - Erythrocytes
 - Hct (PCV), Hb, RCC, MCV, MCHC
 - Leukocytes
 - Total and differential cell counts
 - Platelets
- Blood smear examination
 - Cell morphology and validation of analyser results
- Reticulocyte count



Coagulation tests

- ACT: activated coagulation time
- APTT: activated partial thromboplastin time
- PT: prothrombin time
- TT: thrombin time
- Fibrinogen
- vWf (VWF): von Willebrand factor
- FVIII: Factor VIII (similar for other Factors)



Transfusion medicine

- Blood typing
 - Performed when reagents (Ab) are available
 - DEA 1.1 in dogs
 - A, B and AB in cats
- Cross-matching for compatibility
 - Major crossmatch
 - Donor's RBC tested against recipient's serum
 - Minor crossmatch
 - Donor's serum tested against recipient's RBC



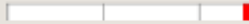

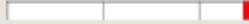










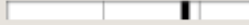



Diagnostic 'groupings'

- Renal disease: urea, Cr, USG, SDMA
- Electrolytes: Na, K, Cl
- Acid Base: pH, bicarbonate, anion gap
- Minerals: Ca, Phos, Mg
- Muscle injury: CK, AST
- Liver: ALT, GLDH, AST, ALP, GGT, bilirubin, bile acids
- Pancreatic function: amylase, lipase, TLI
- Energy metabolism: glucose, cholesterol
- Proteins: TP, albumin (globulins)



Biochemistry 'profiles'

- Larger groupings of biochemistry tests
 - Will vary between laboratories

| | | | | |
|-----------------------|---------------------|---------------------------|-------------|---|
| CREATININE | 0.48 | 0.05 - 0.15 mmol/L | HIGH |  |
| CALCIUM | 2.9 | 1.9 - 2.9 mmol/L | |  |
| PHOSPHATE | 2.6 | 0.8 - 2.1 mmol/L | HIGH |  |
| CA:P RATIO | 1.1 | 1.2 - 3.0 | LOW |  |
| PROTEIN, TOTAL | 70 | 52 - 80 g/L | |  |
| ALBUMIN | 31 | 23 - 40 g/L | |  |
| GLOBULIN | 39 | 25 - 45 g/L | |  |
| A:G RATIO | 0.8 | 0.6 - 1.4 | |  |
| BILIRUBIN, TOTAL | 0 | 0 - 7 umol/L | |  |
| ALP | 57 | 1 - 150 IU/L | |  |
| ALP STEROID ISOENZYME | 4 | IU/L | | |
| AST | 38 | 18 - 80 IU/L | |  |
| ALT | 29 | 16 - 90 IU/L | |  |
| CK | 224 | 73 - 510 IU/L | |  |
| CHOLESTEROL | 8.1 | 3.5 - 9.0 mmol/L | |  |
| AMYLASE | 3170 | 333 - 1500 IU/L | HIGH |  |
| LIPASE | 2000 | 77 - 750 IU/L | HIGH |  |
| SAMPLE APPEARANCE | Slightly Haemolysed | | | |
| T4 TOTAL | 32 ⁻¹ | 13 - 52 nmol/L | |  |



Urinalysis

- Testing the physical and chemical characteristics of fresh urine
- Collection may be free-catch, catheter or cystocentesis
- Assessment of:
 - Gross appearance and odour
 - Urine specific gravity (USG)
 - Urine 'Dipstick' chemistry
 - Urine sediment (microscopy)



Image: Amrls.cvm.msu.edu

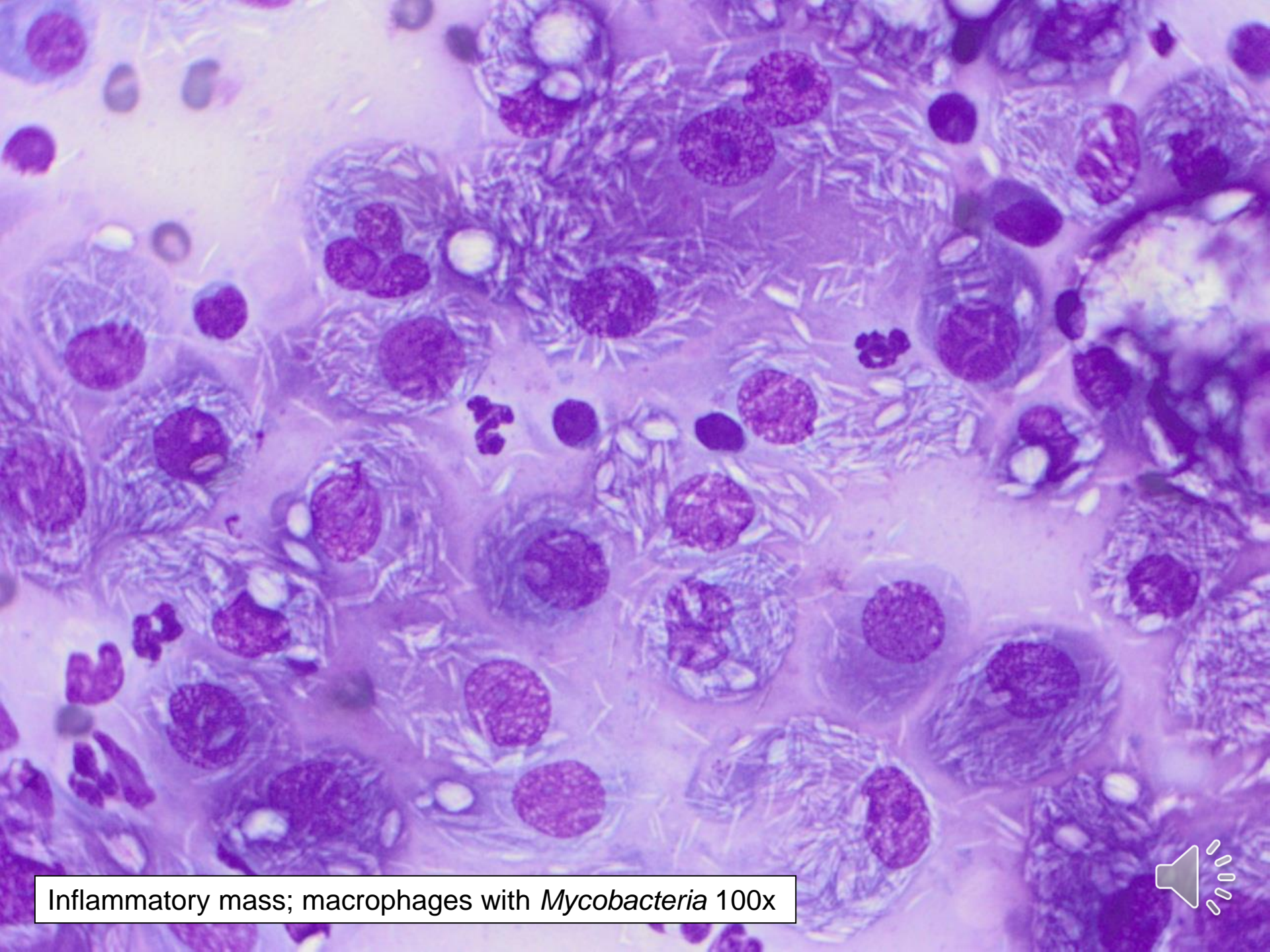


Cytology

The study of cells:

- Fine needle aspirate (FNA) or impression smear
 - Skin masses, lymph node (LN) or tissue
- Body fluids
 - Effusions: peritoneal, pleural, pericardial, synovial
 - Cerebrospinal fluid (CSF)
- Washes
 - Tracheal, prostatic, BAL
- Swabs
 - Vaginal, skin lesions, ears, conjunctiva



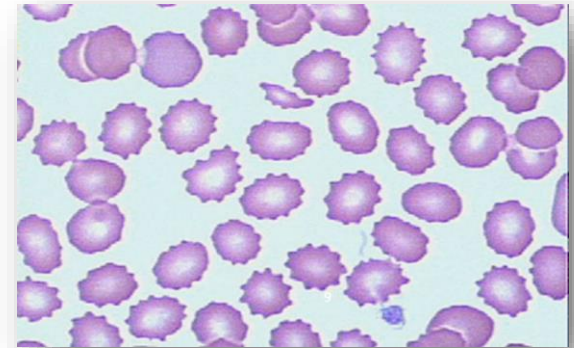


Inflammatory mass; macrophages with *Mycobacteria* 100x



Sample collection

- Avoid artifactual changes
 - Good venepuncture technique
 - Correct blood tube
 - Correct ratio of blood to anticoagulant
 - Harvest plasma or serum asap
 - Make 'fresh' blood smears
 - Gentle preparation techniques for tissue cytology

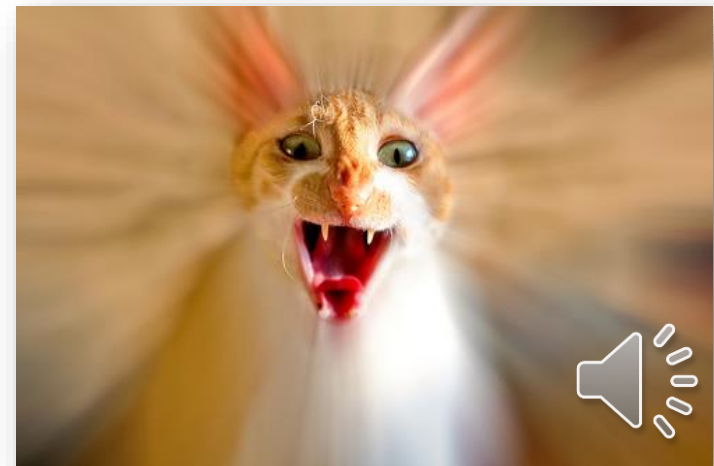


Echinocytes?
Crenation?



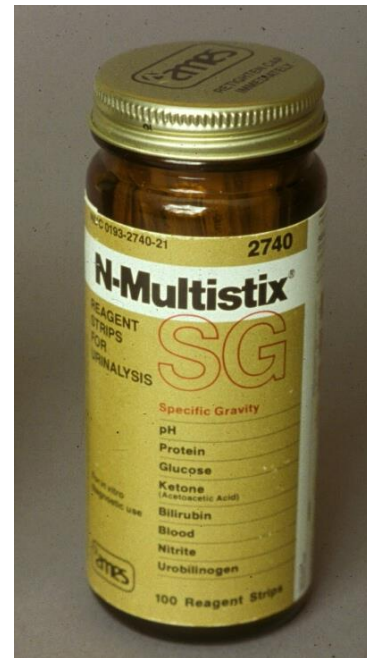
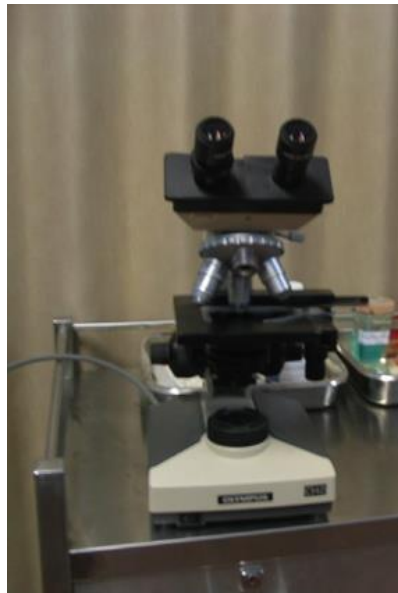
The ideal patient

- Is fasted and rested
- Post-prandial samples may have:
 - Lipaemia
 - Hyperglycaemia
 - Mild azotaemia
- Excited animals may have:
 - Erythrocytosis
 - Physiological leukocytosis
 - Hyperglycaemia



In-house Laboratory

- Simple



In-house Laboratory

- More sophisticated



Referral Laboratory

- ‘Out-sourcing’
 - Quality control (QC) still begins with YOU!
- Larger range of tests
- Provides interpretative support
- Contacts for referring samples



Remember the old adage



=



Interpretation of data

- Providing a pertinent history is important!
 - The more information given to the laboratory, the better the interpretation and comments



vs



Interpretation of data

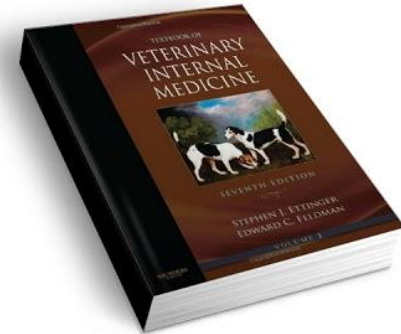
- Ultimate responsibility for interpretation of lab results rests with you, the practitioner
- You must understand the units, reference intervals and significance of abnormalities

| Test | Results | Reference Interval | LOW | NORMAL | HIGH | |
|--------------------------------|-------------|---------------------|-----|--------|------|-------------------|
| Catalyst Dx[®] | | 14/05/2011 3:57 PM | | | | 1/12/2010 1:11 PM |
| GLU | 11.8 mmol/L | HIGH (3.9 – 8.8) | | | | 4.6 |
| BUN | 16.4 mmol/L | HIGH (5.7 – 12.8) | | | | 7.6 |
| CREA | 318 µmol/L | HIGH (70 – 211) | | | | 78 |
| PHOS | 1.67 mmol/L | (0.81 – 2.20) | | | | 2.00 |
| BUN/CREA | 13 | | | | | 16 |
| Ca | 2.52 mmol/L | (1.95 – 2.82) | | | | 2.55 |
| TP | 67 g/L | (57 – 89) | | | | 61 |
| ALB | 30 g/L | (23 – 39) | | | | 27 |
| GLOB | 37 g/L | (28 – 51) | | | | 34 |



Units of measurement

- Australia, Canada, Europe use SI units
- USA still use 'conventional' units
- For example:
 - PCV in SI of 0.45 L/L = 45% in USA
 - Total cell count $10 \times 10^9/\text{L} = 10,000/\mu\text{l}$
 - Glucose of 5.5 mmol/L = 100 mg/dL
 - TP of 75 g/L = 75 g/dL
 - Urea of 2.1 mmol/L = Urea nitrogen of 6 mg/dL



Reference values

- Reference values (or reference intervals) are results derived from a specified population of clinically healthy animals
- They may vary according to:
 - Species
 - Breed
 - Age
 - Sex
 - Method of collection
 - Method of analysis

Lost dog found on Chamberlin rd, no collar, and seems to be a bit aggressive. Also doesn't like baths but she was pretty dirty. Took most of the night, but she's resting comfy now on the bed.



Reference intervals

- Define your population



Reference intervals (values)

- Reference intervals usually represent the test results from 95% of the reference ('healthy') population
- Therefore
~ 2.5% of 'healthy' animals have values above,
and ~ 2.5% below,
the reference interval

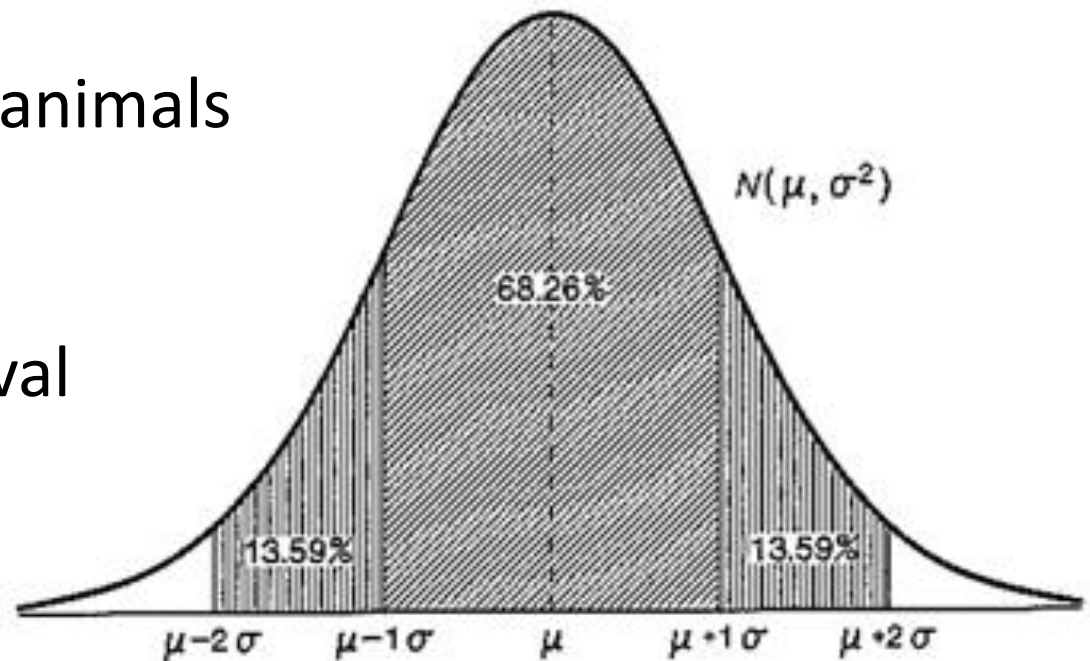


Fig. 1. The Gaussian distribution.



Warnings!

- Always interpret lab results in conjunction with history, clinical findings and other tests
- Anticipate expected findings, so that you can:
 - Question unexpected results
 - Identify pathological processes when lab results are within reference limits
 - e.g., an anaemic animal that is also dehydrated may have a 'normal' PCV



More Warnings!

- Do NOT over interpret mildly increased or decreased test results (especially if they are 'unexpected' or do not fit the clinical diagnosis)

McHUMOR.com by T. McCracken

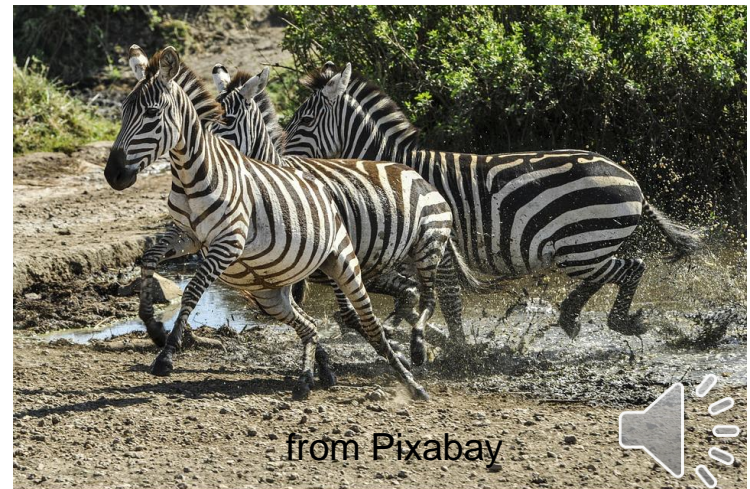


"Off hand, I'd say you're suffering from an arrow through your head, but just to play it safe, I'm ordering a bunch of tests."

Final advice

- The more information that you have steering you in the one diagnostic direction, the more certain you can be of the diagnosis
- **However**, remember that common things occur commonly and do not succumb to the paralysis of over-analysis

If you hear hoof-beats.....
Think horses not zebras!
You'll be right 99% of the time
(unless you're on safari!)



Laboratory evaluation of gut disease

- Laboratory investigations are an important component of the diagnostic approach to gastrointestinal disease by:
 - Narrowing the list of differential diagnoses (DDx)
 - Providing a diagnosis in some cases
 - Directing further investigations
- Baseline data:
 - Routine haematology, biochemistry, urinalysis



Laboratory evaluation of GI disease

- Possible other tests/procedures:
 - Imaging (radiographs, ultrasonography, etc.)
 - Effusion analysis (TNCC/TP, cytology)
 - Endocrine (hyperthyroidism, hypoadrenocorticism)
 - Pancreas (pancreatitis, EPI)
 - Folate/Cobalamin (intestinal function)
 - Mass lesions: FNA for cytology
or surgical biopsy for histopathology
 - Faecal tests



V & D

- How do vomiting and diarrhoea affect haematology and biochemistry values?



Image: Vetmednat



Case 1: Vomiting

- **Sandy**; 3-year-old, MN, Labrador retriever
- History:
Vomiting for the past 3 days, especially after meals
- Clinical examination:
Moderate depression. Anorexia. Slight skin tenting.
Abdominal guarding on palpation,
with possible mass in the anterior abdomen.

HR 260 beats/min
RR 46 breathes/min



Case 1: Vomiting

DDx include:

- Gastritis/Enteritis
- GI obstruction (e.g., foreign body, GDV)
- Diseases of other systems:
 - Pancreatic, hepatic, renal, endocrine
 - Drugs/toxicity



| CBC | | Patient | Ref. Values | |
|------------------|---------------------|----------|-------------|------|
| PCV | L/L | 0.56 | 0.37-0.55 | ↑ |
| White cell count | x10 ⁹ /L | 41.2 | 6.0-17.0 | ↑↑↑↑ |
| Neutrophils | x10 ⁹ /L | 37.5 | 3.0-11.5 | ↑↑↑↑ |
| Lymphocytes | x10 ⁹ /L | 0.4 | 1.0-4.8 | ↓↓↓ |
| Monocytes | x10 ⁹ /L | 3.3 | 0.2-1.4 | ↑ |
| Eosinophils | x10 ⁹ /L | 0 | 0.1-1.3 | ↓ |
| Basophils | x10 ⁹ /L | 0 | Rare | WRI |
| Platelets | x10 ⁹ /L | Adequate | 200-500 | WRI |
| Total solids | g/L | 76 | 60-80 | WRI |



Case 1: Vomiting

CBC:

- Marginal erythrocytosis
 - A 'relative' increase in RBC is most common
 - Likely secondary to fluid loss (dehydration)
- Inflammatory leukogram, characterized by:
 - Marked mature neutrophilia
 - Mild monocytosis
 - Moderate lymphopenia ('stress')



| Biochemistry | | Patient | Ref. Values | |
|---------------|--------|---------|-------------|------|
| Na | mmol/L | 123 | 144-160 | ↓↓↓ |
| K | mmol/L | 2.8 | 3.5-5.8 | ↓↓↓ |
| Cl | mmol/L | 70 | 109-122 | ↓↓↓↓ |
| Urea | mmol/L | 10.3 | 3.0-7.5 | ↑ |
| Creatinine | μmol/L | 150 | 80 - 170 | WRI |
| Amylase | U/L | 1700 | <2000 | WRI |
| Lipase | U/L | 20 | <200 | WRI |
| Total protein | g/L | 73 | 54-74 | WRI |
| Albumin | g/L | 37 | 29-37 | WRI |



Case 1: Vomiting

Serum biochemistry:

- Increased urea (normal creatinine)
 - Consistent with dehydration (pre-renal azotaemia)
 - Increased urea absorption in renal tubules
 - Decreased glomerular filtration rate (hypoperfusion)
 - Increased urea may also occur with GI bleeding
 - Less likely in this case, as erythrocytosis and 'high normal' albumin support dehydration rather than anaemia



Case 1: Vomiting

Serum biochemistry:

- Decreased electrolytes - Na, K, Cl
 - Electrolyte loss via persistent/severe vomiting
 - Note that there appears to be a more marked decrease in **chloride** compared to sodium
 - Suggests vomiting of gastric contents
 - Pyloric obstruction or gastritis?



Evaluating Na and Cl

- Chloride and sodium should move together when changes only relate to water
- Determining if there is a selective loss or gain of chloride, helps refine DDX and also suggests an acid base disturbance

Calculate “corrected Cl”

$$\text{Cl}_{(\text{cor})} = \text{Cl (measured)} \times (\text{normal Na} \div \text{measured Na})$$

* normal Na is midpoint of Na ref interval

* Cl_{cor} should be within the Cl ref interval



Evaluating Na and Cl

| | | | | |
|----|--------|-----|---------|-------|
| Na | mmol/L | 123 | 144-160 | (152) |
| Cl | mmol/L | 70 | 109-122 | |

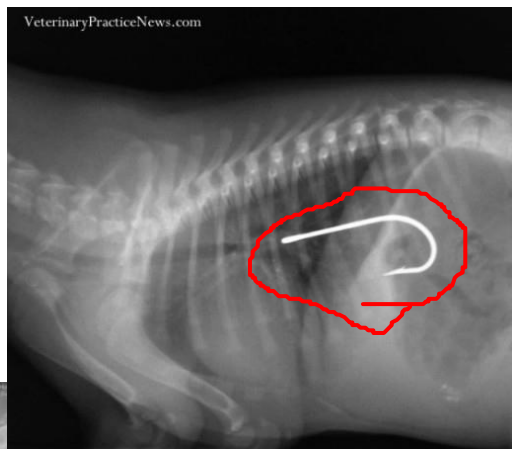
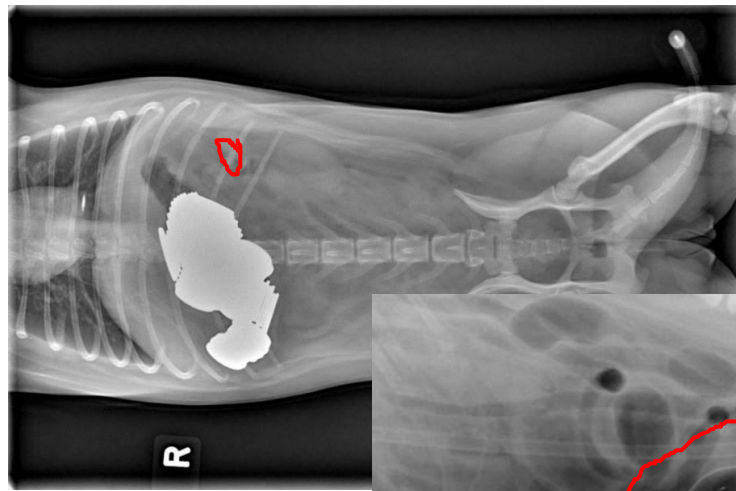
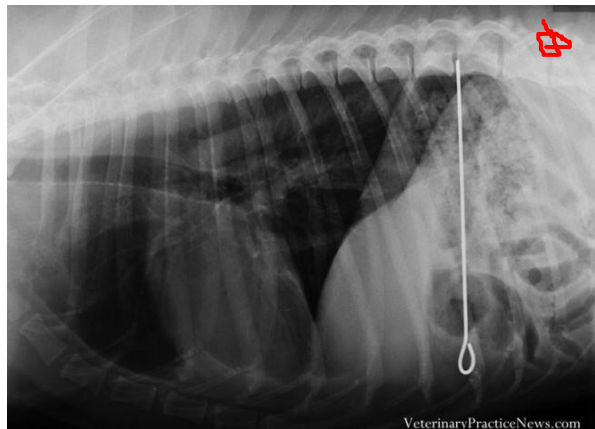
- Corrected Cl = $70 \times (152/123)$
= 86.5
- The corrected Cl value is not within the Cl reference interval – thus **selective** Cl loss is confirmed
 - Gastric vomiting, concern for pyloric obstruction
 - Metabolic alkalosis very likely (need blood gas to confirm)



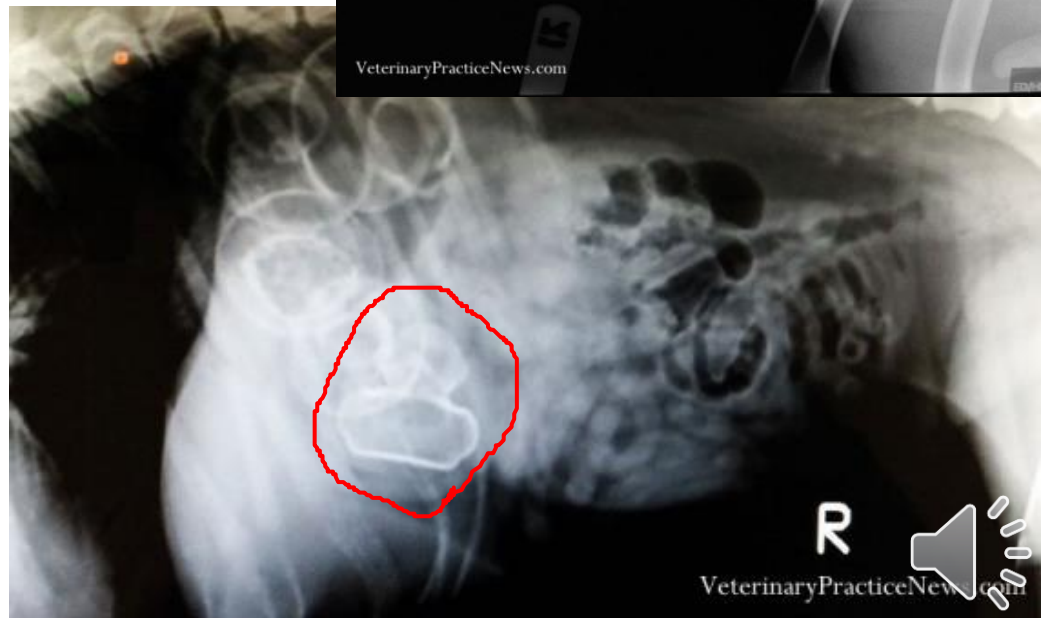
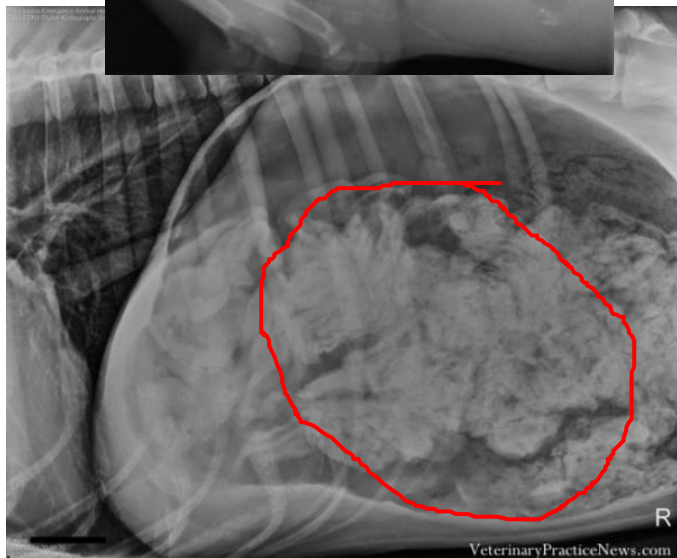
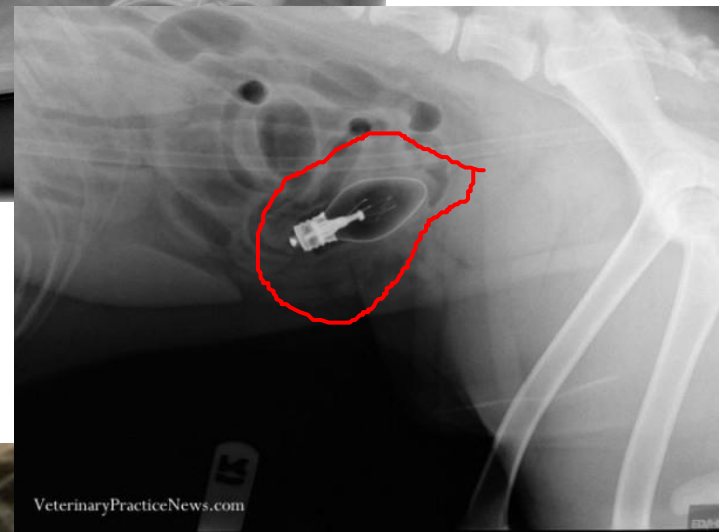
Case 1: Outcome

- Placed on intravenous fluids to correct electrolyte balance and restore hydration
- Imaging revealed a likely foreign body
- Exploratory laparotomy was performed
- A foreign body was found to be obstructing the pylorus
- Sandy made a full recovery!





Guess the FB!



Case 2: Diarrhoea

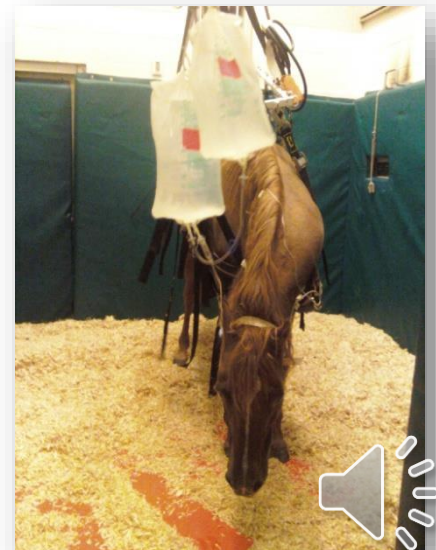
- **Bailey**; 6-year-old, Arabian gelding
- History: Participated in endurance ride yesterday. Today off feed, abdominal discomfort, loose faeces.
- Clinical examination:
Mild to moderate depression. Anorexia.
Increased gut sounds. Moderate skin tenting.
Tacky mucous membranes.
CRT 1.5 sec. HR 55/minute. RR 14/minute.



Case 2: Diarrhoea

In a horse, DDx include:

- Infectious agent
- Antimicrobial induced colitis
- NSAID toxicity
- Sand enteropathy
- Ingestion of toxicant
- Exertional rhabdomyolysis



| CBC | | Patient | Ref. Values | |
|--------------|---------------------|---------|-------------|-----|
| PCV | L/L | 0.57 | 0.32-0.53 | ↑ |
| Leukocytes | x10 ⁹ /L | 2.5 | 5.4-14.0 | ↓↓↓ |
| Bands | x10 ⁹ /L | 1.5 | 0-0.1 | ↑↑ |
| Neutrophils | x10 ⁹ /L | 0.5 | 2.3-8.6 | ↓↓↓ |
| Lymphocytes | x10 ⁹ /L | 0.5 | 1.5-7.7 | ↓↓ |
| Monocytes | x10 ⁹ /L | 0 | 0-1.0 | WRI |
| Eosinophils | x10 ⁹ /L | 0 | 0-1.3 | WRI |
| Platelets | x10 ⁹ /L | 320 | 100-350 | WRI |
| Total solids | g/L | 52 | 60-80 | ↓ |



Case 2: Diarrhoea

CBC:

- Mild erythrocytosis
 - Likely secondary to dehydration
 - Supported by physical exam and increased urea with 'normal' creatinine (pre-renal azotaemia)
- Decreased TS
 - Gastrointestinal protein loss most likely
 - Need TP + Albumin to further characterize



Case 2: Diarrhoea

CBC:

- Leukopenia due to neutropenia with degenerative left shift and lymphopenia
 - Indicates overwhelming inflammatory demand, exceeding the bone marrow's production capacity
 - Immature neutrophils (bands) released (left shift)
 - Bands exceed mature neutrophils (degenerative)
 - A common feature of severe enteritis caused by an infectious agent (e.g., salmonellosis)
 - Lymphopenia: 'stress' response



| Biochemistry | | Patient | Ref. Values | |
|-------------------|--------|---------|-------------|-----|
| Na | mmol/L | 128 | 137-148 | ↓↓ |
| K | mmol/L | 5.7 | 2.8-5.1 | ↑ |
| Cl | mmol/L | 90 | 99-109 | ↓↓ |
| Urea | mmol/L | 10.9 | 4.0-8.0 | ↑ |
| Creatinine mmol/L | | 0.15 | 0.10-0.17 | WRI |
| CK | U/L | 540 | 25-270 | ↑ |
| AST | U/L | 605 | 90-450 | ↑ |
| Total protein | g/L | 50 | 54-74 | ↓ |
| Albumin | g/L | 26 | 29-37 | ↓ |



Case 2: Diarrhoea

Biochemistry:

- Hyponatraemia and hypochloraemia
 - Both are moderately decreased
 - Proportionate loss, likely from GIT
 - Diarrhoea can be explosive event in horses!
 - Massive fluid and electrolyte losses in a short time
- Hyperkalaemia
 - Likely secondary to metabolic acidosis
 - Titration: lactic acid production secondary to hypovolaemia or ischaemia (anaerobic metabolism)



Case 2: Diarrhoea

Biochemistry:

- Mildly increased CK (and AST) indicate muscle damage
 - Consistent with prior strenuous exercise and/or ischaemia from recumbency
 - Unlikely to be due to exertional rhabdomyolysis
 - Values would be much greater (CK likely $> 10,000$ U/L)



Case 2: Outcome

- Presumptive Dx: Salmonellosis
- Supportive management
 - IV fluids
- Made a full recovery after 3 days of treatment



Case 3: Protein-losing enteropathy

Princess; 5-year-old, FS, Poodle

- History: Losing weight for last few months, despite a reasonably good appetite
- Clinical examination: TPR OK.
Abdominal distension.
A fluid wave was palpable.



| CBC | | Patient | Ref. Values | |
|--------------|------------------------|---------|-------------|--------|
| PCV | L/L | 0.46 | 0.37-0.55 | WRI |
| Leukocytes | $\times 10^9/\text{L}$ | 12.1 | 6.0-17.0 | WRI |
| Neutrophils | $\times 10^9/\text{L}$ | 10.0 | 3.0-11.5 | WRI |
| Lymphocytes | $\times 10^9/\text{L}$ | 0.9 | 1.0-4.8 | Marg ↓ |
| Monocytes | $\times 10^9/\text{L}$ | 1.1 | 0.2-1.4 | WRI |
| Eosinophils | $\times 10^9/\text{L}$ | 0.2 | 0.1-1.3 | WRI |
| Basophils | $\times 10^9/\text{L}$ | 0 | Rare | WRI |
| Platelets | $\times 10^9/\text{L}$ | 440 | 200-500 | WRI |
| Total solids | g/L | 34 | 60-80 | ↓↓ |



Hypoproteinaemia: DDx

- Haemorrhage
- Renal loss (protein-losing nephropathy)
- Hepatic 'failure'
- Maldigestion/Malabsorption
- Severe cutaneous exudation
- Starvation
- Marked effusion (usually with 'drainage')
- Gut loss (protein-losing enteropathy)



| Biochemistry | | Patient | Ref. Values | |
|---------------|--------|---------|-------------|-----|
| Na | mmol/L | 153 | 144-160 | WRI |
| K | mmol/L | 3.8 | 3.5-5.8 | WRI |
| Cl | mmol/L | 113 | 109-122 | WRI |
| Urea | mmol/L | 6.8 | 3.0-7.5 | WRI |
| Creatinine | mmol/L | 0.09 | 0.08-0.17 | WRI |
| Cholesterol | mmol/L | 2.6 | 3.6-9.0 | ↓ |
| Glucose | mmol/L | 6.6 | 3.0-7.0 | WRI |
| Total protein | g/L | 32 | 54-74 | ↓↓ |
| Albumin | g/L | 12 | 29-37 | ↓↓↓ |



Hypoproteinaemia – can we rule anything out?

- Haemorrhage
 - Expect panhypoproteinaemia plus anaemia
- Liver failure
 - Expect decreased alb, chol, glu, urea
- Protein-losing nephropathy
 - Expect hypoalb, hyperchol, plus proteinuria
- So this might be a PLE!
 - Expect weight loss, panhypoproteinaemia, hypocholesterolemia



Peritoneal fluid

- Reference values:
 - Volume, colour and turbidity:
Very low volume, colourless and clear
 - TNCC:
< $3.0 \times 10^9/\text{L}$ in small animals
< $5.0 \times 10^9/\text{L}$ in horses
 - Types of cells:
Mostly mononuclear cells (macrophages, lymphocytes, mesothelial cells), with rare neutrophils in small animals
Mostly neutrophils in horses
 - Protein content:
< 25 g/L



Effusion

- Increased volume of fluid in a body cavity:
 - Peritoneal, pleural, pericardial, synovial



Effusions

- Classified according to appearance, TNCC, TS, cytology (and possibly other biochemistry tests)
 - Low protein transudate
 - High protein transudate (modified transudate)
 - Exudate
 - Other
 - Haemorrhagic effusion
 - Chylous effusion
 - Uroperitoneum
 - Neoplastic effusion



Effusions

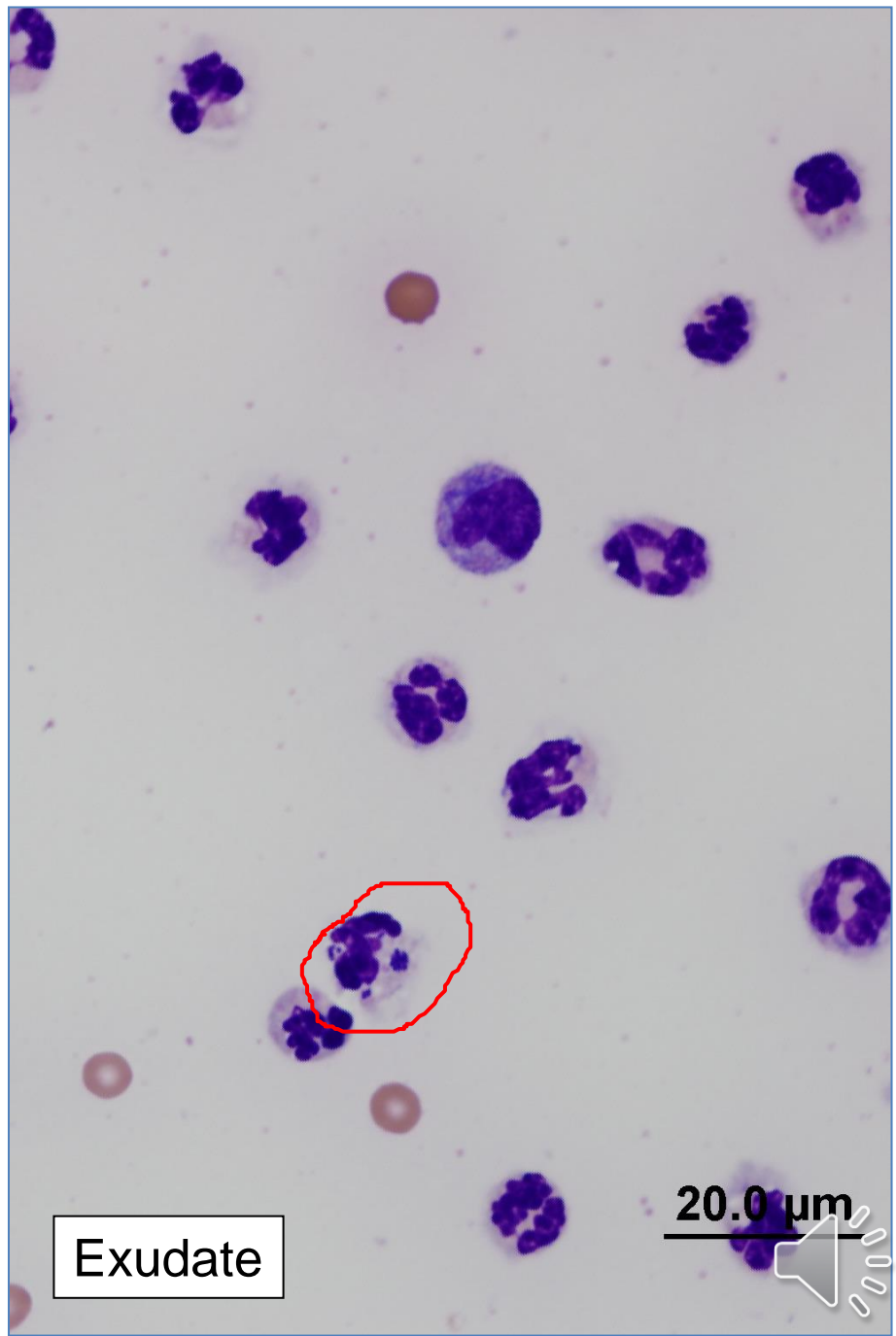
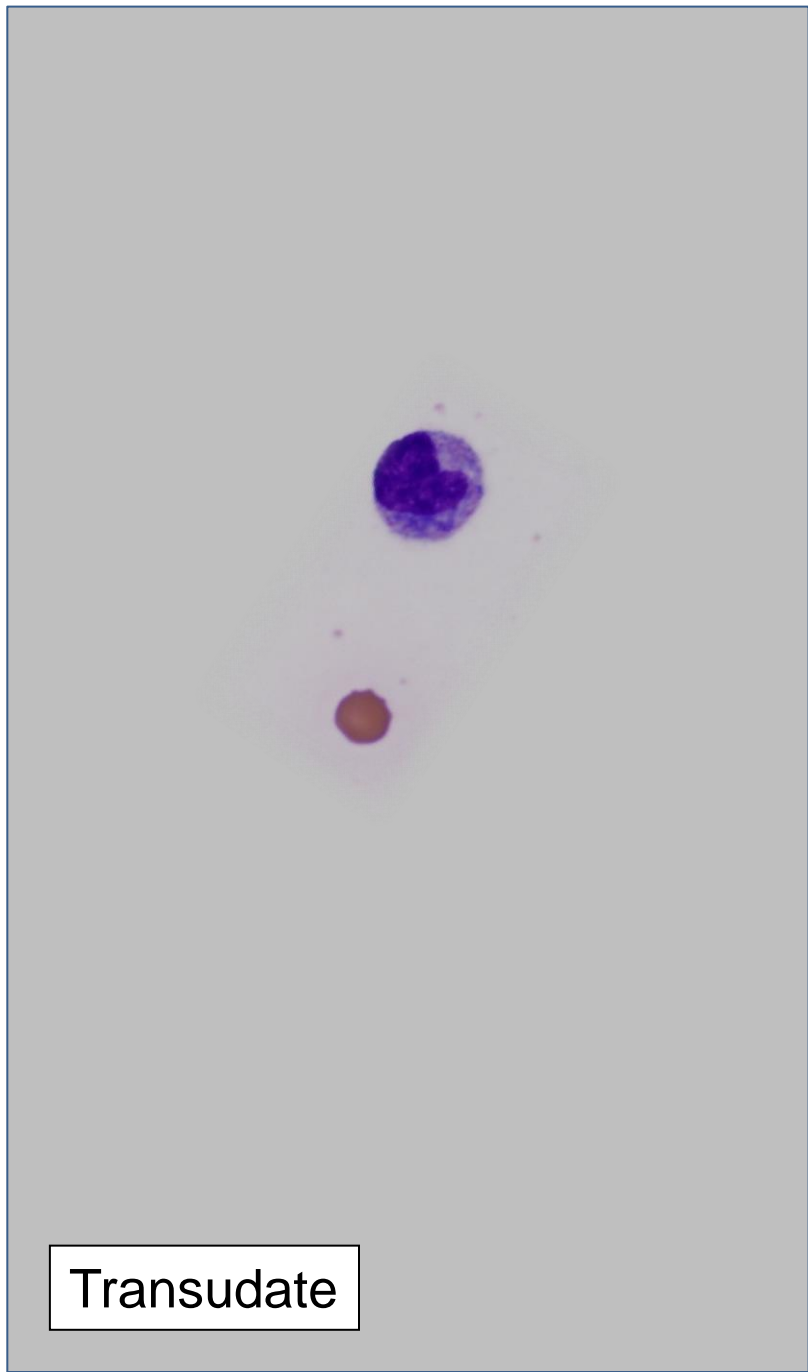
- Transudate
 - ‘Normal’ gross appearance
 - ‘Low’ cell count, ‘low’ protein
 - Hypoalbuminaemia (<15 g/L)
 - Local and systemic venous hypertension, e.g., chronic hepatic disease, such as portosystemic shunt or cirrhosis
 - High protein transudate (modified transudate)
 - Mild increase in protein, ‘normal’ TNCC
 - Congestive heart failure, thrombosis of caudal vena cava, ‘early’ cases of organ torsion



Effusions

- Exudate
 - Usually discoloured and turbid
 - Increased TNCC and TS
 - Inflammation
(increased vascular permeability at serosal surfaces)
 - Neutrophils usually predominate
 - Macrophages may be numerous and phagocytic
 - If cause is bacterial infection *may* see degeneration of neutrophils and presence of organisms
 - Bile leakage, chylous effusion, uroperitoneum and neoplasia may cause an exudate





Effusions

- Haemorrhage
 - Haemorrhage or diapedesis of RBC can be part of an exudate or other effusions
 - ‘A little bit of blood goes a long way’
 - DDx blood contamination at collection
 - Platelets indicate haemorrhage at collection
 - Phagocytosis of RBC and/or haemosiderinophages indicate prior haemorrhage
 - Haemorrhagic effusion may occur in its ‘own right’
 - Usually in a coagulopathy, e.g. vitamin K antagonist poisoning



Effusions

- Other
 - Bile peritonitis
 - Fluid may have a 'gritty' texture
 - Bile is irritant; provokes a good inflammatory response
 - [Total bilirubin] in fluid > blood
 - Chyloabdomen
 - Fluid often opalescent
(likely more so in chylothorax, due to chylomicrons)
 - Initially cells are almost all small lymphocytes
 - With time, increase of neutrophils and macrophages



Effusions

- Other

- Uroperitoneum

- Urine is irritant; provokes an inflammatory response
 - Initially [Urea] in fluid >>> blood; ditto [Creatinine]
 - With time, these substances equilibrate across the peritoneum; urea equilibrates more rapidly
 - In uroperitoneum, fluid [Urea] and [creatinine] will always be greater than the corresponding blood value
 - Cases develop a marked hyperkalaemia (with clinical consequences)



Effusions

- Other

- Neoplasia

- Effusion may appear as a transudate, modified transudate or exudate
 - Neoplastic cells may or may not be visible
 - Causes include: lymphosarcoma, metastatic tumours (especially carcinomas), haemangiosarcoma, mast cell tumour, mesothelioma
 - Mesothelial cells
 - Haemorrhagic effusion



Case 3: Peritoneal fluid analysis

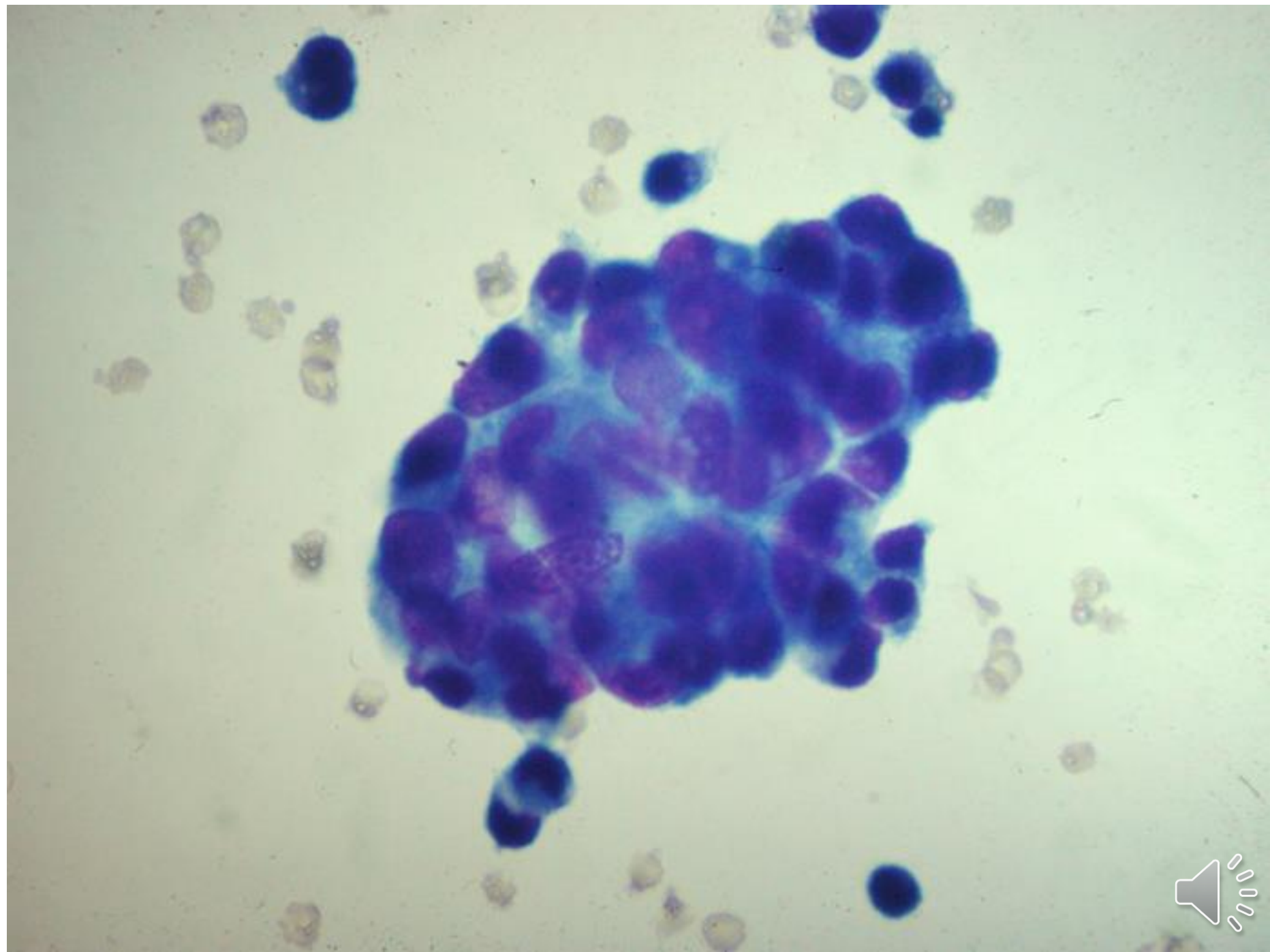
| | Patient | Ref. Values | |
|-------------------------------------|---------|-------------|---------|
| TNCC x10 ⁹ /L | 1.4 | < 1.5 | 'N' |
| Total solids g/L | 12 | < 25 | 'Low N' |

Gross appearance: 20 ml of clear and colourless fluid easily collected

Cytology: Good cell morphology: mostly lymphocytes and large mononuclear cells, little phagocytic activity

Interpretation: Transudate





Case 3: Outcome

- Primary DDx = Protein-losing enteropathy
- Associated with a number of GI disorders
e.g., IBD, lymphangiectasia, lymphoma,
parasitism...
- Need further diagnostics!
- Princess underwent an exploratory laparotomy for intestinal biopsy
- Histopathology report: **Lymphangiectasia**





Lymphangiectasia

- ‘Lacteal dilation’
- Most commonly reported cause of PLE in dogs
- Most cases are idiopathic
 - Some are congenital or secondary to obstruction





Exocrine Pancreatic Insufficiency

- Loss of pancreatic enzymes:
 - Lipase, Amylase and Proteases (e.g., trypsin)
- Leads to maldigestion
- Causes include:
 - Pancreatic acinar atrophy
 - Secondary to chronic pancreatitis



Exocrine Pancreatic Insufficiency

- Extensive loss of pancreatic mass required before signs of EPI evident (~ 90%)
- Clinical signs:
 - Chronic diarrhoea
 - Voluminous, pale, greasy, rancid faeces
 - Weight loss, good appetite (coprophagia)



Exocrine Pancreatic Insufficiency

- Routine clinical pathology diagnostics:
 - Haematology and serum biochemistry usually unremarkable
 - Interestingly amylase and lipase are WRI ... why?
 - Panhypoproteinaemia usually not a feature
- OK, so how do we confirm EPI?
 - Faecal tests for maldigestion have poor Sn/Sp and are no longer used routinely
 - (Faecal fat/starch/mm + faecal proteolytic activity)



Exocrine Pancreatic Insufficiency

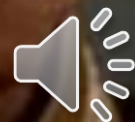
- Serum TLI
 - Trypsin-like Immunoreactivity test
 - High Sn/Sp, species specific
 - EPI is confirmed by subnormal **fasting** sTLI
 - < 2.5 ng/mL (RI healthy dogs: 5.2 – 35 ng/mL)
 - Persistent low normal may be subclinical EPI
 - False negatives:
 - Non-fasted, decreased GFR, active pancreatitis

Dietary supplementation with digestive enzymes is an effective therapy for EPI



But wait!

There's more!



Intestinal function tests



- Serum folate and serum cobalamin
 - Used to evaluate intestinal function (absorption)
 - Vitamin B₁₂ abnormalities are common with EPI
 - 82% dogs, 100% cats can have decreased cobalamin (folate can vary depending on concurrent disease)
 - Recommended to assess folate & cobalamin with TLI
 - Supplementation with vit B₁₂ may be necessary before an optimal response to enzyme supplementation is achieved
 - In addition, if TLI is normal, then finding a decreased folate and cobalamin supports a malabsorption disorder



| | Folate | Cobalamin |
|--|--|--|
| Normal site of absorption | Proximal small intestine (jejunum) | Distal small intestine (ileum) |
| EPI | Normal to increased Acidity increases absorption (pancreas secretes bicarbonate) | Decreased Lack of intrinsic factor, especially in cats (required for absorption) |
| SI bacterial overgrowth (SIBO) | Normal to increased Bacterial production | Decreased Bacterial utilisation |
| Generalised SI disease causing malabsorption (e.g. IBD, lymphoma) | Decreased Jejunal mucosal disease | Decreased Ileal mucosal disease |



... don't forget the faeces



Faecal flotation/sediment

Faecal culture
& sensitivity



ELISA



Faecal PCR



Faecal occult blood test



Faecal cytology

**I HAVE NO IDEA WHAT
HAPPENS TO MY POOP**



**AND AT THIS POINT I'M
TOO AFRAID TO ASK**

