What do I stand to gain by participating in this “Case challenges” webinar?

Richard A. Squires,
James Cook University,
Australia.

What do I stand to gain?

1. Have some fun, challenging myself by reviewing some fairly ‘tricky’ cases…

http://www.amazon.co.uk/Feline-Internal-Medicine-Secrets/Michael/dp/1560534613
http://www.amazon.co.uk/s/ref=sr_1_1?s=books&ie=UTF8&qid=1314736659&sr=1-1&keywords=canine+internal+medicine+secrets&x=0&y=0

What do I stand to gain?

2. A chance, perhaps, to discover some small animal internal medicine ‘secrets’ that are new to me…

http://www.amazon.co.uk/Feline-Medicine-Self-assessment-Colour-Review/dp/1840760478/ref=sr_1_1?s=books&ie=UTF8&qid=1314736659&sr=1-1&keywords=canine+internal+medicine+secrets&x=0&y=0

What do I stand to gain?

3. A chance to ‘benchmark’ my knowledge and understanding against that of my friends and other colleagues in a friendly, non-threatening environment…


What do I stand to gain?

4. Most importantly (in this presenter’s view), a chance to analyse your own diagnostic ‘way of thinking’. What happens in your brain when you are working through a ‘confusing’ case?

“Case challenges” webinar

“This Case Just Doesn’t Make Sense!”

Some fun medicine case challenges

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What do I stand to gain?

4. Most importantly (in this presenter’s view), a chance to analyse your own diagnostic ‘way of thinking’.

Do you have a systematic approach to ‘the confusing case’, just as you have a systematic approach to interpretation of your radiographs?

If not, would you like to begin to develop one tonight?

Socrates

γνῶθι σεαυτόν, gnōthi seauton

“Know thyself”

- The aphorism has actually been attributed to at least the following species:
  - Bias of Priene
  - Chilon of Sparta
  - Cleobulus of Lindus
  - Heraclitus
  - Myson of Chenae
  - Periander
  - Pittacus of Mitylene
  - Pythagoras
  - Socrates
  - Solon of Athens
  - Thales of Miletus

http://en.wikipedia.org/wiki/Know_thyself

Diagnostic Reasoning

Jerome P. Kassirer, MD

Annals of Internal Medicine
1989 110: 893-900

Richard.Squires@jcu.edu.au

Forms of diagnostic reasoning

- Probabilistic
- Causal
- Deterministic

“…the ‘microscope’ that can enable detection of mental processes in live time has yet to be invented.”
Cognitive errors: Faulty knowledge (11 occasions); faulty data gathering (45); faulty information processing (159) and faulty verification (106).

Some well-recognised sources of diagnostic error

- Jumping to conclusions, narrowing down too soon, i.e., reaching ‘closure’ too quickly
  (i.e., we stop thinking as we go on through the case management process when we must continue)

Some well-recognised sources of diagnostic error

- Not considering enough differential diagnoses (and therefore missing the right one).

If the correct diagnosis is not in our ‘basket’ at the end of generating differential diagnoses, we are likely to neglect it for the rest of the diagnostic process and thus make a misdiagnosis.

Some well-recognised sources of diagnostic error

- Adhering with remarkable tenacity to one or more diagnostic misconceptions in the face of growing evidence that we are on the wrong track! *(Why?)*

The Diagnostic Process

- SIGNALMENT (species, age, breed, sex)
- HISTORY (general and problem-specific)
- PHYSICAL EXAMINATION
- GENERATION OF A PROBLEM LIST
- CONTEMPLATION / FURTHER QUESTIONS
- DIFFERENTIAL DIAGNOSES
- PLAN (diagnostic, therapeutic, client education)
- EXECUTION OF THE PLAN
- PROBLEM LIST REFINEMENT
- FINAL DIAGNOSIS / DIAGNOSES
Some well-recognised sources of diagnostic error

- Not taking sufficient advantage of what we already know or can easily get:
  - Problem-based reasoning
  - DAMNIT-V scheme (a handle on the drawer)
  - Mechanisms of disease algorithms
  - ‘6th sense’ etc

Law of Parsimony

“…the assertion that no more causes or forces should be assumed than are necessary to account for the facts”

Etymology

ME f. L parsimonia, parcimonia f. parcere, pars - spare

Some well-recognized sources of diagnostic error

- Not taking sufficient advantage of:
  - our capacity for ‘probabilistic’ reasoning
  - Remembering that ‘common things occur commonly’
  - our capacity for cause-and-effect reasoning (a chance to grow!)
- Not thinking enough about ‘diagnostic parsimony’

Some well-recognized sources of diagnostic error

- Not considering that a clinical finding might be normal for this particular patient
- Not recognizing, or failing to consider the possibility of, artifacts in diagnostic test results
- Missing, misidentifying or failing to consider the possibility of ‘human error’ in other people (or in self - v. difficult)

Some well-recognized sources of diagnostic error

- Gaps in knowledge and skills
- Problem with attitude or attention
  - esp. overconfidence. 94% of doctors think they perform in the top half of their profession
- ‘Panicking’ or ‘going blank’ (i.e. not having a systematic approach to a confusing situation to fall back upon [CPR metaphor]
The most beautiful colour in this bird’s plumage is the:

a) Turquoise  
b) Yellow-Orange  
c) Cinnamon  
d) Russet  
e) Puce

Try it out: Your demographics...

1. I graduated within the last 3 years
2. I graduated 3 - 5 years ago
3. I graduated 5 - 10 years ago
4. I graduated 10 - 20 years ago
5. I graduated >20 years ago

Based on probabilistic reasoning and pattern recognition, this 10-year-old FS DSH cat most likely has:

a) Hypernatraemia  
b) Hypocalcaemia  
c) Hyperphosphataemia  
d) Hypercalcaemia  
e) Hypokalaemia

The microhaematocrit tube on the left was from a normal dog. The one on the right was from an anorexic, depressed 6-year-old male German shepherd dog. It had a PCV of 13. What does the image reveal to you?

a) Lipaemia, maybe pancreatitis  
b) Most likely lymphoid leukaemia  
c) I need to look at a buffy coat smear  
d) I need to test for IgA deficiency  
e) Most likely extreme neutrophilia

The microhaematocrit tube on the left was from a normal dog. The one on the right was from an anorexic, depressed 6-year-old male German shepherd dog. It had a PCV of 13. What does the image reveal to you?

a) Lipaemia, maybe pancreatitis  
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c) I need to look at a buffy coat smear  
d) I need to test for IgA deficiency  
e) Most likely extreme neutrophilia
A colleague is seeking your opinion on the radiographs of this 8-month-old male BSH cat with acute onset of hindlimb lameness.

No reported possibility of trauma.

Vaccination and diet reportedly normal.

This case is about double checking...

The kitten has actually been fed nothing but kidneys since a very early age!!!
Renal secondary hyperparathyroidism

Nutritional secondary hyperparathyroidism

A Quickie…

Based on probabilistic reasoning and pattern recognition, this 10-year-old FS Labrador retriever most likely has:

a) Mitral endocardiosis with pulmonary oedema
b) A large pleural effusion
c) A nasopharyngeal foreign body
d) Laryngeal paralysis
e) Tetanus

Another Quickie…

Based on pattern recognition, this little dog most likely has:

a) A nasopharyngeal tumour
b) Reverse sneezing
c) Nasal mite infestation
d) Eversion of the laryngeal saccules
e) Chronic bronchitis
Not sufficiently considering the possible Dx errors of others…

5-year-old, female intact, Rhodesian Ridgeback

Chronic back pain, vomiting once daily for two weeks. Had her last litter of puppies two years ago, no signs of oestrus since then.

15 months ago, exploratory laparotomy for suspected pyometra. No abnormalities found, OVH not done. PCV/TPP: 43/100. WBCC: 28.27x10⁹/L 18.9 neutrophils, 7.6 lymphocytes.

5-year-old, female intact, Rhodesian Ridgeback

10 months ago, referred to a surgeon because was not willing to go upstairs, was manifesting back pain and exercise intolerance.


8 months ago: recheck, no better. 6 months ago: carprofen started. Discussed referral. Owner thinks PU/PD may have developed in the weeks prior to referral to VTH.

5-year-old, female intact, Rhodesian Ridgeback

Problem list, differential diagnoses, plan

Selected lab. results

Mature neutrophilia (31.3x10⁹/L)
TOTAL PROTEIN  105 gm/L
ALBUMIN  30 gm/L

Urine analysis

Light yellow, slightly hazy
S.G.  1.009
pH  6.5
Hb  2+
Urobilinogen  0.2
Few transitional / squamous cells
Rare granular casts
15-20 RBCs / hpf,  0-2 WBCs / hpf

Serology

Aspergillus titre:  negative
Aspergillus terreus

- The major cause of disseminated aspergillosis in dogs (also A. deflectus)
- Mainly GSDs
- Mainly in hot climates (but…)
- Poor humoral immune response (low IgA, high, nonspecific IgG)

Update

- Seen in cooler climates
- Affects several breeds
- Favours bone, kidneys, eyes
- Vasculotropic (aneurysms)

Osteosarcoma?

6-year-old female spayed black Labrador retriever

6-week history of left forelimb lameness

Biopsy: osteosarcoma with “osteochondrous dysplasia”
Osteosarcoma?

6-year-old female spayed black Labrador retriever

6-week history of left forelimb lameness

Biopsy: osteosarcoma with "osteochondrous dysplasia"

Silver stain: the bone was full of branching, septate, fungal hyphae

Quickie – thinking mechanistically (causal reasoning)

• 11-year-old FS Terrier X with acute onset dyspnoea (9 kg)
• Too ill and unstable to manipulate very much
• Grade 4/6 holosystolic heart murmur radiating widely from the left apex. Tachycardic (200 bpm)
An 8-year-old female Fox Terrier

- Presented this morning for acute depression and anorexia of 24 hours’ duration
- T° 39.3°C, tense abdomen
- Haemorrhagic diarrhoea began six hours after admission.

Problem list, Differential diagnoses, Plan

An 8-year-old female Fox Terrier

- PCV 41
- WBCC 143 x 10⁹/L (bands 11.4, Segs 124, Lymphs 2.86, Eos 4.29)
- Platelets adequate
- ↑ serum amylase & lipase
- Positive cPLI

What do you want to do now?
An 8-year-old female Fox Terrier

• 48 hours later: muffled lung sounds
• PCV 33, TPP 52.1, retics 9.1 x $10^9$/L
• WBCC 252 x $10^9$/L (bands 22.68, segs 214.2, lymphs 7.56, monos 5.04, eos 2.52)

An 8 year-old female Fox Terrier

• Many neutrophils show toxic changes, some lymphs look active
• ALP 232, amylase 1976, lipase 3538, bilirubin 11.4, albumin 22.1
• Urinalysis non-remarkable

What does the presence of ‘toxic changes’ in PMNs indicate to you?
Your interpretation?

Cytology of pleural fluid

• “Suppurative inflammation with toxic changes in PMNs. Recommend bacterial culture.”
Faecal culture

- Negative for Salmonella, Campylobacter and parasites

Ultrasound-guided aspirate of the cranial mediastinal mass
Your thoughts at this stage?
Your interpretation?

Most plausible mechanism of the extreme neutrophilia?

1. Tumour necrosis
2. Pancreatitis
3. Acute myelogenous leukaemia
4. Paraneoplastic
5. Infectious
Neutrophil chemotactic factors produced by malignant fibrous histiocytoma cell lines.

British Journal of Cancer
67(3):508-13, 1993

Inflammatory fibrous histiocytoma presenting leukemoid reaction.

Pathology, Research & Practice.
184(5):498-506, 1989

Inflammatory fibrous histiocytoma: an important variant of malignant fibrous histiocytoma highly responsive to chemotherapy.

Annals of Internal Medicine
97(6):858-63, 1982

Extreme leukocytosis

- Usually a neutrophilia, with or without a left shift
- Usually no fever
- ~60-330 x 10⁹/L PMNs
- Synthesis of haematopoietic growth factors by the tumour e.g., G-CSF, GM-CSF, IL-3
- Need to remove the underlying cause

Malignant fibrous inflammatory histiocytosis

CASE REPORT
Paraneoplastic leukocytosis in a dog with a renal carcinoma


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Key Words: Paraneoplastic leukocytosis, Renal carcinoma, Neoplastic hyperplasia, Hematopoiesis

Abstract: A 7-month-old male German shepherd dog was presented due to the presence of a large, irregular, and irregularly shaped right kidney. The dog developed severe anemia, neutropenia, and leukocytosis, with a peak value of 330 x 10⁹/L. The dog also developed diuresis and renal failure. The kidney was resected, and hematopoietic hyperplasia was observed. The dog died 3 weeks later due to renal failure.

Keywords: Paraneoplastic leukocytosis, Renal carcinoma, Neoplastic hyperplasia, Hematopoiesis
Quickie…

• 11-year-old male neutered Boxer with a history of persistent haematuria despite several weeks of antibiotic therapy.

Your interpretation?

A. Benign prostatic hypertrophy
B. Prostatic adenocarcinoma
C. Paraprostatic cyst
D. Cystic calculi
E. Transitional cell carcinoma of bladder apex
George
A 10 year-old MC black Labrador Retriever

• It is 9:00am. He seized at 7:30 this morning, apparently for the first time in his life. It lasted for about 2 minutes, says the owner.
• Now he’s a bit quieter than usual, but otherwise normal.

• No previously detected illnesses apart from a low grade elbow lameness that has been present for several years
• He receives carprofen whenever he is thought to be uncomfortable

George
A 10 year-old MC black Labrador Retriever

• T° 39.4 °C, pulse 110, RR 24 (intermittently panting)
• Normal skin turgor
• Warm, moist, ‘very’ red mucous membranes

Not George, of course

• Large palpable mass or masses in the cranial, dorsal abdomen

Your next step(s)
Least appropriate next step at this stage?
1. Routine haemogram, serum chemistry profile, urinalysis
2. PCV / TPP / Glucose (in-house)
3. Abdominal imaging
4. Thoracic imaging
5. Serum erythropoietin

Well-recognised sources of diagnostic error in ‘human’ medicine
“Narrowing down too soon”

George
A 10 year-old MC black Labrador Retriever
• PCV 75  TPP 78
• Glucose normal

Does this look like a relative or an absolute erythrocytosis to you?
A. Relative
B. Absolute
C. What does that mean?
D. Neither
E. I’m just taking the Micky by pressing “E”.

High PCV
  / \ High TPP / Normal TPP
  \ / relative erythrocytosis absolute erythrocytosis
     (dehydration)

George
A 10 year-old MC black Labrador Retriever
• PCV 75  TPP 78
In another animal, could figures like these ever reflect a ‘relative’ erythrocytosis?
Updated problem list

- History of lameness / carprofen
- ‘Seizured’ this morning
- Palpable abdominal mass(es)
- Absolute erythrocytosis

Differential diagnoses for absolute erythrocytosis

- Relative erythrocytosis (dehydration + hypoproteinaemia)
- Breed variation
- Hyperadrenocorticism
- Some longstanding cardiovascular and pulmonary diseases

Differential diagnoses for absolute erythrocytosis

- Some non-neoplastic renal diseases (cysts, hydronephrosis)
- Polycythaemia vera (primary erythrocytosis)
- Paraneoplastic causes

Paraneoplastic erythrocytosis

*Pathogenesis*

- Tumour itself produces erythropoietin
- Tumour causes renal ischaemia / tissue hypoxia, leading to an increase in release of erythropoietin by the kidney(s)

Tumour-associated erythrocytosis

*Pathogenesis*

- Tumour causes arterial hypoxaemia (lung? heart? airways?), the kidneys respond ‘appropriately’ by releasing more erythropoietin.
George
A 10 year-old MC black Labrador Retriever

Your updated plan?

Abdominal imaging
• Bilaterally symmetrical, marked renomegaly
• Kidneys are diffusely and severely infiltrated
• Lymphoma is considered a likely diagnosis

Thoracic radiography
• No abnormalities detected

Routine haemogram, serum biochemistry and urine analysis
• USG 1.019
• Creatine kinase 1209
• Otherwise, normal
What would you most like to do now?

A. Refer him BUT OWNER SAYS NO!
B. Hit the books and read about approaches to absolute erythrocytosis
C. Remove a unit or two of blood, replace with crystalloid, and think again
D. Trucut biopsy one or both kidneys

Updated Plan…

- Admit and monitor
- Lower his HCT so he is in better shape for further investigations (could save the blood?)
- FNAB kidney
- Check haemostatic status, blood pressure; then biopsy kidney
- ± Serum EPO measurement

Paraneoplastic erythrocytosis

**Kinds of tumours previously associated**

- Renal tumours
- Liver tumours
- Nasal fibrosarcoma *How?*
- T.V.T.
- Others

Typical clinical features

- Lethargy, depression, inappetence
- PU/PD
- Red mucous membranes
- ± Seizures
So why did George seize?

Choose the least plausible reason
1. Cerebrovascular accident
2. Cerebral hyperoxygenation (essentially, oxygen toxicity)
3. Increased blood viscosity
4. Poor cerebral blood flow
5. Idiopathic epilepsy

So why did George seize?
• Poor blood flow, despite high O₂ carrying capacity, leads to poor tissue oxygenation (becomes a vicious circle)
• Mainly affects the brain, eyes, kidneys, heart
• May also see systemic hypertension or heart failure

Paraneoplastic erythrocytosis

Management
• Identify the underlying cause and remove it (if possible) or treat it
• Periodic phlebotomy
• ± Hydroxyurea (40-50 mg/kg PO × BID)
Other cause(s) of hyperviscosity?

1. Multiple myeloma
2. Lymphoma
3. Lymphoid leukaemia
4. “Benign” or primary gammopathy
5. All of the above
Most likely neoplastic cause of this kind of anaemia?

1. Sertoli cell tumour
2. Multiple myeloma
3. Large splenic haemangiosarcoma
4. Nasal fibrosarcoma
5. Bleeding caecal leiomyoma

Another tricky “quickie”

A microcytic, hypochromic, mildly regenerative anaemia with a high platelet count

Iron Homeostasis and Disorders in Dogs and Cats: A Review

Iron is an essential element for nearly all living organisms, and disruption of iron homeostasis can lead to a myriad of clinical manifestations. Iron is used in the formation of heme, the oxygen-transporting component of hemoglobin, as well as numerous enzyme systems of the body. Disorders of iron in the body include iron deficiency anemia, anemia of inflammatory diseases, and iron overload. This article reviews normal iron metabolism, disease syndromes of iron imbalance, diagnostic testing, and treatment of either iron deficiency or excess. Recent advances in determining iron deficiency using novel objective indicators are reviewed. [PDF]
Another tricky “quickie”

A 10 year-old MC Golden retriever presented for acute collapse with apparent abdominal enlargement, bilaterally symmetrical, non-pruritic truncal alopecia, white, warm, moist gums, good pulse quality, PCV 10, TPP 69.

Most likely cause of this kind of anaemia

1. Sertoli cell tumour
2. Multiple myeloma
3. Bleeding splenic haemangiosarcoma
4. Nasal fibrosarcoma
5. Bleeding gastric carcinoma