"This Case Just Doesn't Make Sense!" Some fun medicine case challenges





Richard A. Squires, James Cook University, Australia. What do I stand to gain by participating in this "Case challenges" webinar?



What do I stand to gain?

1. Have some fun, challenging myself by reviewing some fairly 'tricky' cases...



What do I stand to gain?



2. A chance, perhaps, to discover some small animal internal medicine '*secrets*' that are new to me...

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?

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

- The aphorism has actually been attributed to at least the following ancient Greek sages:

- - 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

ls of Internal Medicine. 1989;110:893-900

- Causal
- Deterministic

Diagnostic error and clinical reasoning Geoffrey R Norman & Kevin W Eva CONTEXT There is a growing literature on diagnostic errors. The consensus of this litera-ture is that most scrops are cognitive and result from the application of one or more gongline biases. Such lisked reasoning is © Blackwell Publishing Ltd 2009. MEDICAL EDUCATION 2010; 44: 94-100 "...the 'microscope' that can enable detection of mental processes in live time has yet to be invented.

ORIGINAL INVESTIGATION

Diagnostic Error in Internal Medicine

Mark L. Graber, MD; Nancy Franklin, PhD; Ruthanna Gordon, Phi

nd: The goal of this study was to determine e contribution of system-related and cogni-

is: One hundred cases of d

Arch Int

rm Med. 2005;165:1493-1499

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?)

Some well-recognised sources of diagnostic error

 Not taking advantage of the easy opportunity to check things for a second time (i.e., double checking things) while thinking hard about the case

Always be second guessing ourselves (while remaining decisive and not developing 'analysis paralysis')

The Diagnostic Process



- SIGNALMENT (species, age, breed, sex
- **<u>HISTORY</u>** (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 <u>what we</u> <u>already know or can easily get</u>:
 - Problem-based reasoning
 - DAMNIT-V scheme (a handle on the drawer)
 - Mechanisms of disease algorithms
 - '6th sense' etc

Some well-recognised 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'

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-recognised sources of diagnostic error

- Not considering that a clinical finding might be normal for this particular patient
- Not recognising, 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-recognised sources of diagnostic error

- Gaps in knowledge and skills [recognised or unrecognised]
- 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]





(?)

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





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



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
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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









Vet Pathol 40:530-539 (2003)

Osteogenesis Imperfecta in Two Litters of Dachshunds

F. SEELIGER, T. LEEB, M. PETERS, M. BRÜGMANN, M. FEHR, AND M. HEWICKER-TRAUTWEIN Department of Pathology (FS. MP, MB, MH), Clinic for Small Domestic Animals (MF), and Department of Animal Breeding and Genetics (TL), School of Veterimary Medicine Hannover, Germany

Interenting and sciencitics (TL). School of Veterinary Medicine Hannover, Hannover, Germany Abstract. A clinical, merphologic, ultrastructural, and genetic study was performed on five rough-coated dachland semistical science of the main spontaneous bose and teeth fractures, joint hyperlaxity, and reduced bone density on radiography. Primary teeth were extremely inhurvailed and brittle. The halfmark of the disease was a severe oscopenia characterized by impairment of lamellar bone formation in the long bones, skull, and vertebral column. No deformity or dwarfism was present. The columns of chordnocytes and primary trabeculue in the epitybes and metaphyses were listologically normal. An alwayf failure of secondary spongiosa and lamellar bone formation was evident in the medullary and cortical zones in all animals. The few existing mathecular consistenced, and small number of large cytoplasmic vascules were present in a few osteoblasts. Molecular analyses of the collagen type I emoduling generative but were not significant for OI. Therefore, OI in these Dachhand litters was characterized by a severe, genentized outpends and dentineopenia. This pattern of reduced bone formation is suggestive of defective production of collagen type I.

Key words: Bone; collagen; Dachshunds; histopathology; osteogenesis imperfecta; reverse transcriptionpolymerase chain reaction.

This case is about double checking...

This case is about double checking...

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

Renal secondary hyperparathyroidism









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





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.



5-year-old, female intact, Rhodesian Ridgeback
Possible back trauma 2 to 3 years ago.
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.



5-year-old, female intact, Rhodesian Ridgeback

10 months ago, diagnosed with discospondylitis. Brucella titre negative. Disc spaces curetted. No bacteria cultured, *Aspergillus flavus* contaminant cultured. Antibiotic prescribed.



5-year-old, female intact, Rhodesian Ridgeback

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

Physical exam: arched back, tense abdomen, very painful spine. Stiff hindlimb gait, reduced epaxial muscle mass, no neurological deficits.



5-year-old, female intact, Rhodesian Ridgeback

Problem list, differential diagnoses, plan

Selected lab. results

Mature neutrophilia (31.3x10⁹/L)

TOTAL PROTEIN ALBUMIN 105 gm/L 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)

Aspergillus terreus



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



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
- 1 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 10⁹/L
- WBCC 252 x 10⁹/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?

















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

























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

Malignant fibrous inflammatory histiocytosis

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

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CASE REPORT

Paraneoplastic leukocytosis in a dog with a renal carcinoma

Claudio Petterino¹, Elisabetta Luzio², Luca Baracchini², Angelo Ferrari⁴, Alessandra Ratto⁴ ¹Organtmet of hubic Neak, Comparative Pathologi and Viterinary Magine, School of Viterinary Madicine, University of hudia, and "gasara (PD), taiyi, ²Sadlo Viterinario Associa Betridi Suci, Gensa, Hai, "Samo Viterinario Mascato Cunno Baracchine, Canton IGI, Baiy, and "gastoan BPD, taiyi, ²Sadlo Viterinario Associa Betridi Suci, Gensa, Hai, "Samo Viterinario Mascato Cunno Baracchine, University ³Sadlo Viterinario Associa Betridi Suci, Gensa, Hai, "Samo Viterinario Mascato Cunno Baracchine, Ligura e Vale D'Aosta, Sesione di Gensa Gensa, taiy

Key Words Ohromophobic cystic papillary renal carcinoma, GM-CSF, hematuria, neutrophilia Correspondence Alassandra Barto, National Reference Centre

Alessandra Ratto, National Reference Centre of Veteninary and Comparative Oncology (CEROVEC), istituto Zooprofilatico Sperimentale del Piemonte, Liguria e Valle D'Aosta, Piazza Borgo Pila 39, int. 24, Torre B, 16129, Genoa, Rafy Evenin Vierort Molforen II. Abstract: A 7-year-old male German Shepherd dog in poor body condition had a 3-month history of intermittent hematuria. Nonregenerative anemia, mild leukcytosis, marked hypoabluminemia, and hematuria pereobserved. Subsequently, marked neutrophilia and moderate monscytosis were noted anemia, hypoabluminemia, and hematuria persisted: and the dog developed disseminated intravascular coagulation. Ultrasonographic examination of the abdomen revealed the presence of an enlarged and irregularly shaped right kidney with a large area of cavitation, and a nephrectomy was performed 0 doays after initial examination. Cytologic examination of fine-needle aspirates and imprints of the right kidney revealed a neodustic cell powulation suggestive of renal cardinoma. The

Vet Clin Pathol 40/1 (2011) 89–94 ©2011 American Society for Veterinary Clinical Pathology



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 seizured 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.

George A 10 year-old MC black Labrador Retriever



- 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



George A 10 year-old MC black Labrador Retriever



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

George A 10 year-old MC black Labrador Retriever Your next step(s)

20

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



?

High PCV High TPP Normal TPP relative erythrocytosis (dehydration)





• PCV 75 TPP 78

In another animal, could figures like these ever reflect a 'relative' erythrocytosis?



Haemorrhagic gastroenteritis

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 <u>most</u> like to do now?

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

Paraneoplastic erythrocytosis

Typical clinical features

- Lethargy, depression, inappetence
- PU/PD
- Red mucous membranes
- ± Seizures

Paraneoplastic erythrocytosis

Typical clinical features

- Lethargy, depression, inappetence
- PU/PD
- Red mucous membranes
- ± Seizures

(?

So why did George seizure?

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 seizure?

- 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











A tricky "quickie"





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

Most likely cause of this kind of anaemia

- 1. Large renal lymphoma
- 2. Multiple myeloma

PMID: 2020011 [PubMed - indexed for MEDLINE]

- 3. Large splenic haemangiosarcoma
- 4. Nasal fibrosarcoma
- 5. Bleeding caecal leiomyoma

REVIEW ARTICLES

Iron Homeostasis and Disorders in Dogs and Cats: A Review

Jennifer L. McCown, DVM*, Andrew J. Specht, DVM, DACVIN

ABSTRACT

Inon is an essential element for nearly all living organisms and disruption of iron homeostasis can lead to a number of clinical manifestations, Iron is used in the formation of both hemoglobin and myoglobin, as well as numerous enzyme systems of the body. Disorders of iron in the body include iron deficiency anemia, anemia of inflammatory disease, and iron overload. This article reviews normal iron metabolism, disease syndromes of iron inbalance, diagnostic testing, and treatment of either iron deficiency or excess. Recent advances in diagnosing iron deficiency using reticulocyte indices are reviewed. (*J Am Anim Hosp* Assoc 2011; 47:151–160, DOI 10.5326/JAMHA-MS-5553)

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