Teaching Clinical Reasoning

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No financial disclosures
Clinical reasoning

The cognitive process necessary to evaluate and manage a patient’s medical condition. It involves knowledge, intuition (developed by experience), critical thinking and reflection on the process.

Clinical reasoning is the sum of the thinking and decision-making process associated with clinical practice, it enables clinicians to take the best judged action in a specific patient context.

Barrows HS, Tamblyn RM. Problem based learning: Springer 1980
HiggsJ, Jones M. Clinical Reasoning in the Health Professions 3rd ed
Clinical reasoning: metacognition is crucial

Thinking about how you think, while you think, albeit within the limitations of your thinking mind.
Teaching clinical reasoning

One approach:
1 Understand the processes involved in clinical reasoning
2 Recognize your own process of clinical reasoning in real time
3 Be cognizant of predictable pitfalls in clinical reasoning
4 Apply real time strategies to avoid pitfalls in clinical reasoning
5 Make your thinking visible to your learners in real time
6 Personalize your approach
Teaching clinical reasoning

You will not become an expert at teaching clinical reasoning after this one session. Need to practice, practice, practice and practice! Need to reflect, reflect, reflect and reflect! Need to seek constant feedback.
Clinical reasoning (CR)

Synthesis of info and data → Problem representation → Illness script in our database

55 yr homeless man presents with 5 weeks of cough, hemoptysis, wt loss, fevers and nights sweats. CXR and CT: bilateral cavitary lesions. Quantiferon + HIV negative.
Clinical reasoning (CR)

Dual process theory: 2 cognitive systems involved in reasoning

<table>
<thead>
<tr>
<th>Intuitive (type 1)</th>
<th>Analytic (type 2)</th>
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<tbody>
<tr>
<td>Reflex system</td>
<td>Deliberate and rational</td>
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<td>Experiential – inductive</td>
<td>Hypothetico-deductive</td>
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<tr>
<td>Gestalt</td>
<td>Critical logical thought</td>
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<tr>
<td>Heuristics</td>
<td>Normative reasoning</td>
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<td>Low effort</td>
<td>High effort</td>
</tr>
<tr>
<td>High emotional attachment</td>
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</tr>
<tr>
<td>Low cognitive control</td>
<td>High cognitive control</td>
</tr>
<tr>
<td>Low scientific rigor</td>
<td>High scientific rigor</td>
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Clinical reasoning: dual process model

Adapted from P Croskerry. Healthcare Quarterly Vol. 12 2009
Clinical reasoning: dual process model

The bulk of our clinical reasoning is done in the intuitive mode

Adapted from P Croskerry. Healthcare Quarterly Vol. 12 2009
Clinical reasoning (CR)

Dual process theory: 2 cognitive systems involved in reasoning

Intuitive (type 1)  
- Reflex system
- Experiential – inductive
- Gestalt
- Heuristics
- Low effort
- High emotional attachment
- Low cognitive control
- Low scientific rigor

Analytic (type 2)  
- Deliberate and rational
- Hypothetico-deductive
- Critical logical thought
- Normative reasoning
- High effort
- Low emotional attachment
- High cognitive control
- High scientific rigor

Heuristics

Heuristics

Heuristics refers to shortcuts in reasoning

Influenced by prior experience

These are typically correct

Prevent extensive deliberation and excessive testing

Produce desired results with minimum delay, cost and anxiety

We spend > 90% of our conscious time in a heuristic mode
Common heuristics

Availability heuristic
- The ease with which a particular idea can be brought to mind

Representativeness heuristic
- Based on similarity to prototype of a category

Anchoring and adjustment heuristic
- Relying heavily on an initial bit of information and all further adjustments are made relative to the “anchor” e.g. buying a car: sticker price is the anchor

Affect heuristic
- Based on feelings (shorter than mood): fear, pleasure, dread
Diagnostic errors: delayed or missed diagnoses

Occur due to pitfalls in clinical reasoning: subconscious biases

We make mistakes when we encounter complex problems

Everyday situations are sufficiently complex to elicit mistakes

Errors occur due to flawed reasoning much more than due to knowledge deficiency

*Surveys of physicians report error rates resulting in serious harm as high as 35 to 40%

* Blendon et al. NEJM 2003
Bias or cognitive disposition to respond (CDR)

Biases are predictable deviations from rationality

CDR is a tendency to react *unconsciously* to contextual clues that may lead to flawed reasoning

Biases lead to diagnostic errors

Most biases occur in the intuitive type 1 reasoning processes

Biases can only be dealt with by activating type 2 reasoning processes

P Croskerry et al. BMJ Qual Saf 2013
# Pitfalls in clinical reasoning

Commonly due to biased judgment and fallacies of heuristics

| TABLE 3. Failed Heuristics, Biases, and Cognitive Dispositions to Respond |
| Aggregated bias | Confirmation bias | Multiple alternatives bias | Posterior probability error | Sutton’s slip |
| Anchoring | Diagnosis momentum | Order effects | Premature closure | Triage-cueing |
| Ascertainment bias | Fundamental attribution error | Omission bias | Psych-out error | Unpacking principle |
| Availability and non-availability | Gambler’s fallacy | Outcome bias | Representativeness restraint | Vertical line failure |
| Base-rate neglect | Gender bias | Overconfidence bias | Search satisfying | Visceral bias |
| Commission bias | Hindsight bias | Playing the odds | | Yin-yang out |
| | | | | Zebra retreat |

32 biases and heuristics pitfalls in clinical reasoning
Cognitive biases: some examples

**Blind spot bias**
- We believe we are less susceptible to bias than others

**Search satisfying**
- Calling off a search once something is found

**Gamblers fallacy**
- Assuming a sequence of diagnosis will not continue

**Sunk cost bias**
- The more we have invested in a diagnosis, the less we can let go

**Triage cueing bias**
- AKA geography is destiny: admitted to surgery limits to surgical perspective

**Diagnostic momentum**

**Bandwagon effect**
- Group thinking, “that's what they do in CCU”

**Visceral bias**
- Feelings towards patients impact decisions
Classifications of CDRs in clinical reasoning

Error of overattachment to a particular diagnosis
- Anchoring, confirmation bias, premature closure, sunk costs

Error due to failure to consider alternative diagnoses
- Multiple alternatives bias, representativeness restraint, search satisficing, Sutton’s slip

Error due to inheriting someone else’s thinking
- Diagnosis momentum, framing effect, ascertainment effect, bandwagon effect

Errors in prevalence perception or estimation
- Availability bias, base-rate neglect, gambler’s fallacy,
Classifications of CDR

Errors associated with physician affect, personality, or decision style
- Commission bias, omission bias, outcome bias, visceral bias, overconfidence/under confidence, vertical line failure, ego bias, sunk costs

Errors involving patient characteristics or presentation context
- Fundamental attribution error, gender bias, psych-out error, triage cueing, contrast effect, yin-yang out
Pitfalls in clinical reasoning: heuristics

<table>
<thead>
<tr>
<th>Pitfall</th>
<th>Description</th>
</tr>
</thead>
</table>
| Availability            | Ease of recalling past cases  
                        | Subject to base rate neglect                                               |
| Anchoring               | Relying on initial impressions and  
                        | Ignoring inconsistencies in data                                           |
|                         | Generates **diagnosis momentum**                                           |
| Framing                 | Swayed by wording                                                          |
| Blind obedience         | Undue deference to authority or technology                                  |
| Premature closure       | Narrow-minded belief in 1 diagnosis                                         |

### Pitfalls in clinical reasoning: biases

<table>
<thead>
<tr>
<th>Bias</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Representative bias</strong></td>
<td>Inclination to estimate probability based on how well it fits the typical characteristics of a category than on the true base rate of that category</td>
</tr>
<tr>
<td><strong>Overconfidence bias</strong></td>
<td>Over reliance on self or experts opinion</td>
</tr>
<tr>
<td><strong>Confirmation bias</strong></td>
<td>Focus on data that supports our expectations and ignoring conflicting data</td>
</tr>
<tr>
<td><strong>Illusory correlation bias</strong></td>
<td>Thinking events are causally related, when in fact the connection is coincidental</td>
</tr>
<tr>
<td><strong>Hassle bias</strong></td>
<td>Tendency to take the easy way out</td>
</tr>
</tbody>
</table>

*Jill Klien. BMJ Volume 330, 2005*
Back to the patient . . .
Pitfalls in clinical reasoning: heuristics

55 yr homeless man presents with 5 weeks of cough, hemoptysis, weight loss, fevers and nights sweats. Quantiferon + CXR and CT: bilateral cavities, HIV negative

Plan:
Isolated, AFB x 3 negative, fungal culture and cytology -ve

Plan:
BAL AFB -ve, fungal stains and culture negative

Plan:
ATB meds, seen in clinic 7 weeks later: “doing ok” cultures –ve for TB

Plan:
Seen in clinic 12 weeks later, hematuria, pyuria

Plan:
Diagnosis GPA!

Availability
Premature closure
Anchoring
Illusory correlation
Confirmation bias
Diagnostic momentum
## Heuristics: corrective strategies

| Availability | Base rates: appropriate pretest probability?  
| | Does anything argue against my initial impression?  
| | How is this different from prior cases?  
| | What are the next 2 likely diagnosis? How do I exclude?  
| Anchoring | Reconsider in light of new data  
| | Always explain and reconcile inconsistencies  
| Framing | Examine case from alternate perspective  
| | Reframe: would it change inclination?  
| Blind obedience | Asses test accuracy or tactfully seek a second opinion  
| Premature closure | Return to case when refreshed: sleep on it if possible  

*Cognitive Psychology of Missed Diagnosis. Ann Intern Med 2005*
## Biased judgment: corrective strategies

<table>
<thead>
<tr>
<th>Biased Judgments</th>
<th>Strategies</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Representative bias</strong></td>
<td>Be aware and seek true base rates</td>
</tr>
<tr>
<td><strong>Overconfidence Bias</strong></td>
<td>Be aware of limitations of your knowledge</td>
</tr>
<tr>
<td></td>
<td>You are wrong more often than you think</td>
</tr>
<tr>
<td><strong>Confirmation bias</strong></td>
<td>Seek inconsistencies and strive to reconcile them even if it means re-visiting diagnosis</td>
</tr>
<tr>
<td><strong>Illusory correlation bias</strong></td>
<td>Question “correlations” objectively!</td>
</tr>
<tr>
<td><strong>Hassle bias</strong></td>
<td>Inconvenience is part of medicine</td>
</tr>
<tr>
<td></td>
<td>“The best way out is always through”</td>
</tr>
</tbody>
</table>

Jill Klien. BMJ Volume 330, 2005
Cognitive Debiasing

Bias is triggered

Awareness of bias

Motivated to correct bias

Aware of direction and magnitude of bias

Able to apply appropriate debiasing strategy

Successful debiasing

Optimal decision making

Debiasing Failure

Distortion of clinical reasoning

T Wilson, N Brekke. Psychol Bull. 1994
Clinical reasoning: debiasing

P Croskerry. Academic Medicine 2009
Teaching clinical reasoning

A game of numbers . . .
Clinical reasoning: testing and treatment thresholds

Testing threshold

0% Probability of disease/s

5%

Treatment threshold

90%

100% Probability of disease/s
Clinical reasoning: testing and treatment thresholds

Testing threshold

- Pre test probability of disease: 5%

Tests/investigations:
- Sensitivity
- Specificity
- Positive predicative valves
- Negative predicative values
- Positive likelihood ratio
- Negative likelihood ratio

Treatment threshold

- Post test probability of disease: 90%
Clinical reasoning: testing and treatment thresholds

Testing threshold

Pre test probability of disease: 5%

Tests/investigations:
- Sensitivity
- Specificity
- Positive predicative values
- Negative predicative values
- Positive likelihood ratio
- Negative likelihood ratio

Post test probability of disease

Treatment threshold

Pre test probability of disease: 90%
Clinical reasoning: applying tests:

Tests/investigations:
- Sensitivity
- Specificity
- Positive predictive values
- Negative predictive values
- Positive likelihood ratio
- Negative likelihood ratio

Values known for most tests

Depends on prevalence of disease

Independent of prevalence of disease

Very useful to generate post test probability
Diagnostic utility of tests

Sensitivity and specificity generate likelihood ratios

<table>
<thead>
<tr>
<th>LR</th>
<th>Δ In post test probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>↑ 45%</td>
</tr>
<tr>
<td>5</td>
<td>↑ 30%</td>
</tr>
<tr>
<td>2</td>
<td>↑ 15%</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>0.5</td>
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<td>0.2</td>
<td>↓ 30%</td>
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<tr>
<td>0.1</td>
<td>↓ 45%</td>
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\[ LR_+ = \frac{\text{Sensitivity}}{1 - \text{Specificity}} \]

\[ LR_- = 1 - \frac{\text{Sensitivity}}{\text{Specificity}} \]

How do we then determine what our pre test probability is?
Clinical reasoning

- History from patient
- Physical examination
- Known prevalence of disease
- Prediction modules

Help generate a pre test probability
Clinical reasoning

- History from patient
- Physical examination
- Known prevalence of disease
- Prediction modules

- Diagnostic tests
  - blood, urine and stool
  - Xrays, CT scans, MRIs
  - Ultrasounds and special imaging

Help generate a pre test probability

Help generate a post test probability
Let’s practice...
A 56 year old woman with a history of hypertension, presents to the ED with 2 weeks of shortness of breath (SOB). She gets SOB while walking, associated with chest tightness but no pain. She has noticed a cough productive of whitish sputum but has not had any fevers. Though, 3 weeks ago she had a “cold” after a long flight from China. No history of tobacco use. Her hubby has noticed that she wakes up SOB at night and sits up to open the windows. Her legs are also swollen but the right is more swollen than the left leg.

**Differential diagnosis:**
Heart failure
Pulmonary embolism
Pneumonia
Others: anemia, pleural effusions, overactive thyroid etc.
Case: physical exam and labs and CXR

BP 168/105, HR 115, Respiratory rate 22/min, 97% pulse oximetry
JVD+
Heart sounds normal
Lungs clear
Both legs swollen R = 38 cm L 37cm

Blood count is normal  TFT and blood chemistry is normal and CXR shows a borderline enlarged heart but otherwise normal, no pneumonia seen.
Case:

Differential diagnosis:
Heart failure
Pulmonary embolism
Both?
Pneumonia
Others: anemia, cancer, pleural effusions, overactive thyroid etc.
Clinical reasoning

History from patient
Physical examination
**Known prevalence of disease**
Prediction modules

[Diagram showing]

Diagnostic tests
- blood, urine and stool
- X-rays, CT scans, MRIs
- Ultrasounds and special imaging

Help generate a pre test probability
Help generate a post test probability
Breathing Not Properly Study
- 1600 adults that presented to ED with SOB in 5 countries
- Ultimately 47% had heart failure as the diagnosis
- No finding of heart failure in 49%
## Does she have a PE? Wells Score for PE

<table>
<thead>
<tr>
<th>Clinical feature</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous PE or DVT</td>
<td>1.5 points</td>
</tr>
<tr>
<td>HR &gt; 100</td>
<td>1.5 points</td>
</tr>
<tr>
<td>Surgery or immobilization within 4 wks</td>
<td>1.5 points</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>1 point</td>
</tr>
<tr>
<td>Active cancer</td>
<td>1 point</td>
</tr>
<tr>
<td>Clinical signs of DVT</td>
<td>3 points</td>
</tr>
<tr>
<td>Alternate diagnosis less likely than PE</td>
<td>3 points</td>
</tr>
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Our patient had a score of 1.5

Wells et al. Thrombo Haemost 2000
Wells Score for PE pretest probability

Pooled probability based on a systemic review of 29 studies and 31,200 patients

<table>
<thead>
<tr>
<th>Score</th>
<th>Risk</th>
<th>Pretest probability of PE</th>
</tr>
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<tbody>
<tr>
<td>0 - 1</td>
<td>low</td>
<td>6% (4 - 8%)</td>
</tr>
<tr>
<td>2 - 6</td>
<td>Intermediate</td>
<td>23% (18 - 28%)</td>
</tr>
<tr>
<td>≥ 7</td>
<td>high</td>
<td>49% (43 – 56%)</td>
</tr>
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</table>

Two level Wells Score for PE

<table>
<thead>
<tr>
<th>Score</th>
<th>PE unlikely</th>
<th>Pretest probability of PE</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 4 points</td>
<td>PE unlikely</td>
<td>8.4% (6 – 11%)</td>
</tr>
<tr>
<td>≥ 5 points</td>
<td>PE likely</td>
<td>34.4% (29 – 40%)</td>
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ceriani et al. J Thromb Haemo 2010
Clinical reasoning: testing and treatment thresholds

Testing threshold
- PE: 10 - 25%
- HF: 47%

Treatment threshold
- 90%

0% Probability of disease/s

100% Probability of disease/s
Diagnostic utility of tests

Sensitivity and Specificity generate Likelihood ratios

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D-dimer for suspected PE (sensitivity 95% specificity 40%)

Pre-test prob = 20%

D dimer = negative
LR 0f 0.1

If negative Post-test probability = 2%

If positive = LR of 1.58
Post test probability = 35%
BNP for diagnosis of heart failure (sensitivity 90% spec 76%)

Pre-test probability = 50%

BNP > 100 = LR+ of 4

Post-test probability = 80%

BNP < 100 = LR- of 0.1
Post test probability of 9%
Case: Diagnosis

D-dimer was < 0.5 taking the post test probability of having a pulmonary embolus down to 2%

BNP was 550 taking the post test probability of heart failure to 80%

An echocardiogram showed reduced systolic function

Symptoms were caused by heart failure.
Teaching clinical reasoning

Grab a worksheet
The movie: Inception
The story. . .

- Chapter I; there will be blood...
- Chapter II; you give me fever...
- Chapter III; the liver leads...
Chapter I; there will be blood....admission #1

• 35 year old male with a history of ETOH use disorder

• Off alcohol for 8 months

• 2 weeks of fatigue, DOE and anorexia

• 121/70 98 18 100% 98F

• Icteric++, no LN, moderate splenomegaly
Chapter I; there will be blood.... admission #1

- **Labs**
  - HB 4.9, MCV 143, WBC 3.6, PLT 108, retic 31
  - Bilirubin 9.4/2.4, LDH 400, ALP 350, GGT 300
  - Haptoglobin <6, Coombs test +

- **Team**
  - Autoimmune hemolytic anemia
  - Pancytopenia: hypersplenism?
  - Alcohol liver disease
Chapter I; there will be blood….admission #1

- **Hematology**
  - Underlying liver disease with pancytopenia due to hypersplenism
  - Now with an autoimmune hemolytic anemia
  - LFTs consistent with hemolysis
  - Rule out systemic connective tissue disease

- **Plan**
  - Transfuse PRBC
  - High dose prednisone
  - Send for B12, folate, ANA et al
Chapter I; there will be blood.... admission #1

- **Further labs**
  - ANA, ANCA negative, HIV and hepatitis screen negative
  - B12 and folate normal
  - Warm and cold antibodies detected

- **Hospital course**
  - Prednisone 80mg/day
  - PRBC x 4
  - HB 8.1 on discharge
Chapter I; there will be blood....admission #2

• 1 week of DOE, fatigue and 102F fevers
• Splenomegaly and jaundice
• **HB 5**, WBC 0.9, PLT 100, retic 23

• **Hematology**
  - Idiopathic AIHA flare; start solumedrol
  - Bone marrow biopsy
  - Thrombocytopenia due to hypersplenism
Chapter I; there will be blood….admission #2

• **Bone marrow**
  - Hyper cellular marrow
  - No atypical infiltrates, normal flow cytometry
  - All consistent with peripheral destruction and sequestration

• **Hospital course**
  - PRBC x 6 (warmed up)
  - Solumedrol x 4 days, discharged on prednisone of 60mg
Chapter I; there will be blood....admission #3

• HB 4.6, WBC 4.5, PLT 40
• Fevers 101F

• AIHA flare
• Hepatosplenomegaly on ultrasound

• PRBC x 7
• Rituximab and iv dexamethasone
• Prednisone 80mg
Chapter I; there will be blood....admission #4

- HB 5.9, WBC 0.8, PLT 50
- Body aches, fevers 101F
- PRBC x 5
- Cyclosporine 100mg bid and prednisone 60mg
Chapter I; there will be blood....admission #5

- Aches, pains and fevers 103F
- HB 5.7, WBC 7.2, PLT 85
- CT #1: HSM, splenic infarcts and aortic LN's
- PRBC x 2
- Cyclosporine stopped but steroids continued
Chapter I; there will be blood....admission #6

- RUQ pain, aches and fevers 101 – 103F
- HB 6.5, WBC 2.0, PLT 39
- CT #2: new hypo dense liver lesions, aortic LNs
- PRBC x 5, PLTS x 30 units, IVIG, prednisone
- Surgery consulted for splenectomy: “wait till infection clears”
Chapter I; there will be blood....admission #7

• Aches and pains, fevers 100 – 102°F

• **HB 6.3, WBC 2.2, PLTS 62**

• CT #3: HSM, slight reduction in liver lesions, stable aortic LN

• PRBC x 3, prednisone 60mg

• Surgery: planning elective splenectomy
Chapter I; there will be blood....admission #8

- RUQ pain, aches and fevers 101 – 103F
- HB 5.8, WBC 1.9, PLT 105
- PRBC x 3, IVIG, prednisone 60mg
Chapter I; there will be blood….admission #9

• Aches and pains, no fevers

• **HB 5.5, WBC 5.9 PLT 102**

• PRBC x 3, IVIG, prednisone 60mg
Chapter I; there will be blood....admission #10

- RUQ pains, fevers 101 – 103F
- **HB 6.2, WBC 9, PLT 145**
- CT #4: splenic infarcts, reduced liver lesions, aortic LN
- PRBC x 6, prednisone 100mg
- **Splenectomy DONE!** which shows normal pathology
Chapter I; there will be blood….admission #11

• Fevers 102 – 103F

• HB 6… yes hemolysis! after splenectomy

• CT #6: larger left hepatic lobe lesion

• PRBC x 9, prednisone 60mg

• IR guided biopsy is planned
Chapter I; there will be blood....

- To be continued...
Chapter II; you give me fever...

*Life does fade as the fever rages.*...
Chapter II; you give me fever...admission # 2

- 39yr old male with AIHA and ETOH liver disease

- RUQ pains, fevers 101 – 102F

- All cultures negative, CXR normal, USS without cholecystitis

- No antibiotics given
Chapter II; you give me fever...admission # 3

- RUQ pain, fevers 101 – 102F
- All cultures negative, CXR normal
- Ceftriaxone and metronidazole for 5 days
- No antibiotics on discharge
Chapter II; you give me fever...admission # 4

- AIHA + leucopenia
- Aches, pains and fevers 101 – 103F.
- Urine culture: E Faecalis but no urinary symptoms
- CT #1: HSM, splenic infarcts, no pyelonephritis
- ID consult: E faecalis UTI; ampicillin x 7 days
Chapter II; you give me fever...admission # 6

- AIHA, WBC 2 (ANC 540: lowest ever)
- Aches and pains, fevers 102F
- All cultures and CXR negative
- Started on imipenem by primary team
- CT #2 shows new liver hypo densities and splenic infarcts?
Chapter II; you give me fever...admission # 6

• **ID consult service**
  - Hepatosplenic candidiasis vs histoplasmosis vs blastomycosis (less likely)
  - Concern for brucellosis, Q fever and leptospirosis
  - Blood and urine cultures, urine histo antigen
  - Serum crypto antigen, brucella and leptospira serology
  - IR biopsy of hepatic lesions
  - Continue imipenem and start fluconazole

• **ID consult service (2 days later)**
  - Still febrile
  - Add vancomycin, switch to itraconazole
Chapter II; you give me fever...admission # 6

• Now afebrile for over 72hrs

• **ID consult service**
  - Splenic + hepatic lesions with fevers, now improved
  - Negative cultures; improvement likely from antifungals or steroids
  - Risk for disseminated candidiasis is low given absence of severe prolonged neutropenia
  - Endemic mycosis like histoplasmosis more likely
  - Tissue needed; IR guided biopsy
  - Stop imipenem, vanco and itraconazole, start voriconazole
Chapter II; you give me fever...admission # 6

- Patient remains afebrile
- Combined IR and Hem conference; “biopsy after repeat CT”
- At this time platelets 50

- CT #3: read by IR as showing slight interval resolution of lesions, likely fungal micro abscesses

- IR decide to hold on biopsy

- Patient discharged on voriconazole
Chapter II; you give me fever...admission # 7

- AIHA, WBC 2.4
- Fevers 101 – 102F
- CT #4: decrease in size of liver lesions, stable aortic LNs

- ID consult
  - Urine histo and brucella serology negative
  - Lesions have decreased in size on CT
  - Hepatosplenic azole responsive lesions; consistent with hepatosplenic candidiasis
  - Continue voriconazole
Chapter II; you give me fever...admission # 8 & 9

- AIHA

- RUQ pain, fevers 101 – 103F

- All cultures negative

- No ID consult

- Voriconazole continued
Chapter II; you give me fever...admission # 10

- Post op (splenectomy) fevers 101 – 102°F

- **ID consult**
  - Probable hepatosplenic candidiasis
  - Off voriconazole for 2 weeks?
  - Change voriconazole to fluconazole
  - Post op fevers with negative cultures
  - Hold antibiotics
Chapter II; you give me fever...admission # 11

- Still febrile
- Now on fluconazole
- All cultures negative

- CT #7: confluent large lesion in left hepatic lobe

- **ID consult**
  - All cultures negative
  - Uncontrolled fungal infection?
  - Start amphotericin to serve as induction therapy
  - Liver biopsy
Chapter II; you give me fever...admission # 11

• Still high grade fevers 101 – 103°F

• IR liver biopsy done

• ID
  - Ampho changed to fluconazole
Chapter II; you give me fever...admission # 12

• Aches, abdominal pains

• Fevers 101 – 103F

• To be continued. . . .
Chapter III; the liver leads...

Is life worth living? It all depends on the liver

Williams James
Chapter III; the liver leads...CT #1

CT shows marked splenomegaly
Chapter III; the liver leads...CT #1

CT shows left para – aortic lymphadenopathy
Chapter III; the liver leads...CT #2

Multiple liver hypodensities

Splenic infarcts
Chapter III; the liver leads...CT # 2 and 3

CT #2

CT #3 “improved” per IR

Platelet count was 50
Chapter III; the liver leads...CT #4

CT shows a reduction in the liver lesions
Chapter III; the liver leads...CT #6

Worsening liver lesions

Worsening liver lesions
Chapter III; the liver leads...CT #6

Worsening of para – aortic lymphadenopathy

To be continued . . .
Back to our story. . .
Chapter III; the liver leads...

- Ultimately a CT guided liver biopsy was done 4 months after the liver lesions were identified.

- Hodgkin's Lymphoma (lymphocyte depleted)

- No evidence of hepatic candidiasis, fungal, bacterial infection or ETOH liver disease

- **Final diagnosis**
  Stage IV Hodgkin’s Lymphoma presenting with cold and warm antibody auto immune hemolytic anemia that led to splenomegaly resulting in thrombocytopenia and leucopenia.
Post (first) chemotherapy

Resolution of left para – aortic LNs

Marked reduction in liver lesions

No more evidence of a hemolytic anemia
Small bowel obstruction due to surgical adhesions
Delayed diagnosis

- **Consequences**
  - approx 60 units of PRBC
  - approx 60 units of platelets
  - $$$$$ of IVIG
  - Courses of iv solumedrol
  - 494 days of prednisone = 296 grams
  - courses of rituximab, cyclosporine and cyclophosphamide
  - 127 days of antifungal treatment (azoles + ampho)
  - splenectomy
  - small bowel obstruction due to post surgical adhesions
  - MRSA bacteremira with endocarditis
Delayed or missed diagnosis

• Occur due to pitfalls in clinical reasoning

• We make mistakes when we encounter complex problems.

• Everyday situations are sufficiently complex to elicit mistakes
Back to our patient

• We focused more on his hemolysis than on the cause of it; perhaps we missed the forest for the trees.

• We encountered recognized and predictable pitfalls in clinical reasoning:
  - Availability bias
  - Illusory correlation
  - Premature closure
  - Anchoring+++++
  - Diagnostic momentum
  - Overconfidence on experts
  - Hassle bias
Immune hemolysis

- AHA is rare, prevalence of 17/100,000
- 85% are due to warm antibodies, 15% cold
- Overall 50% are idiopathic and 50% are secondary

<table>
<thead>
<tr>
<th>Warm</th>
<th>Cold</th>
</tr>
</thead>
<tbody>
<tr>
<td>lymphomas 10 – 40%</td>
<td>lymphomas 10 - 35%</td>
</tr>
<tr>
<td>SLE 30 – 40%</td>
<td>cold disease agglutinin dx 30%</td>
</tr>
<tr>
<td>CLL 7%</td>
<td>Waldenstrom’s disease 15%</td>
</tr>
<tr>
<td>Drugs, infections, PCH, CVID</td>
<td>CLL, infections, drugs</td>
</tr>
</tbody>
</table>
Our patient

• Presented with severe hemolytic anemia
• ANA, HIV, SPEP etc were all negative

• Framing: pt with warm and cold immune hemolytic anemia with negative serology tests (as above)

• Anchored: idiopathic AIHA

• Challenges (inconsistencies) to anchor and responses:
  Persistent high fevers: cultures negative therefore due to his AIHA
  Abnormal LFTS: always considered consistent with hemolysis
Some facts on hemolysis

• LFTs in hemolysis:

<table>
<thead>
<tr>
<th>Increased</th>
<th>No change/reduced*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilirubin</td>
<td>Alkaline Phosphatase*</td>
</tr>
<tr>
<td>LDH</td>
<td>GGT*</td>
</tr>
<tr>
<td>AST</td>
<td>ALT</td>
</tr>
</tbody>
</table>

• Total serum bilirubin is never > 4 – 5mg/dl

• Total bilirubin rarely ever > 5mg/dl and direct usually < 15% of total

• Fevers more likely in secondary AIHA

C Packman, Blood Reviews Vol 22 June 2008

Harrison’s Principles of Medicine
Our patient: labs for 11 months before abnormal CT

- **Alk Phos**
  - Up to 3 x normal

- **GGT**
  - Up to 16 x normal

- **AST**
  - Up to 16 x normal

**Events**:
- **Stopped ETOH**

**Graphs**:
- **Alk Phos** graph shows values up to 3 x normal.
- **GGT** graph shows values up to 16 x normal.
- **AST** graph also shows values up to 16 x normal.
Our Patient

Bilirubin Total

Up to 14mg/dl

Bilirubin Direct

Up to 35% of total
Our patient

- Alternate framing:

  39 year old male with warm and cold AIHA who presents with fevers, hepatosplenomegaly, para – aortic lymphadenopathy and LFTs suggestive of an infiltrative disease pattern without biliary dilatation.

- Would have raised the question of a liver biopsy (months before the CT was even abnormal) to evaluate for a secondary cause of AIHA such as a lymphoma
Our Patient

- RUQ pain and fevers with negative cultures
- CT showed multiple liver hypo densities

**Framing #1**

*Given immunosuppressive Rx, leucopenia, CT findings are concerning for hepato splenic candidiasis vs histoplasmosis vs blastomycosis*

- Became afebrile transiently after antibiotics and antifungals

**Framing #2**

*now seemingly improved; given negative cultures, improvement seems most likely from antifungal or prednisone therapy.*

- IR liver biopsy recommended
Our patient

- **Blind obedience to authority/technology**
  His CT “improved” per IR (**hassle bias**) within 9 days of treatment, so discharged

- **Framing #3 and final anchoring**
  *Urine histo negative. Hepatosplenic azole responsive lesions; consistent with hepatosplenic candidiasis.*

- **Diagnosis momentum;** each time he came in febrile he got more or different anti fungals, in addition, he got antibiotics
Clinical reasoning

• Diagnostic reasoning is limited by our ability to assign the appropriate pretest probability to clinical presentations

• Our appropriate pretest generating ability can be restricted by our clinical experience

• The gap can be narrowed by actively questioning our assumptions to ensure we achieve consistency
Hepatosplenic candidiasis

• First reported in 1969

• Occurs almost exclusively in patients with acute leukemia who develop severe neutropenia post chemo

• Very few prolonged neutropenic patients with lymphoma and sarcomas

• Only 6 reported cases in non neutropenic patients; usually single large abscesses or complicating abdominal surgery

• Radiologic improvement takes a minimum of 4 weeks to months which lags behind clinical response

Thaler et al, Annals 1988 Vol 108
Kontoyiannis et al, Infect Dis North America 2000
Shirkhoda et al, Radiology 1986 Vol 159
Our patient

- **Challenges (inconsistencies) to anchor**
  - He had RUQ pain and fevers for 5 months before the abnormal CT
  - Lowest ANC 540 for 1 day ONLY
  - He had no established leukemia or lymphoma
  - He improved radiologically within 10 days of treatment
  - He never improved clinically; fevers and RUQ pain persisted for months

**Not consistent with hepatosplenic candidiasis**
Pel-Ebstein fever: fevers that cyclically increase then decrease over an average period of one or to weeks in patients with Hodgkin's lymphoma.

Pel PK. Zur first reported cases in 1885 and Ebstein W. Das described cases in 1887.

In 1959 Richard Alan John Asher declared it mythical in his Lancet making sense series.

You decide; myth or reality?
Teaching clinical reasoning

Steps involved

1 Understand the process of clinical reasoning ✓
2 Recognize your own process of clinical reasoning in real time ✓
3 Be cognizant of pitfalls in clinical reasoning ✓
4 Apply real time strategies to avoid pitfalls in clinical reasoning ✓
5 Personalize your approach
6 Make your thinking visible to your learners in real time
Personal approach

My real time cognitive approach to cases with learners:

**Acronym: A DIVA PR²OF**

A = Assign appropriate pretest probability
D = Determine most effect discriminating factor to narrow field
I = Internal consistency
V = Validate assumptions
A = Anticipate response to both possible test results: + vs –
P = Probe to disprove your hypothesis
R = Reframe your framing
R = Reconcile inconsistencies
O = Often wrong
F = Figure out why we were wrong
Acronym: A DIVA PR²OF

A = Appropriate pretest probability
  - Counters availability and representative biases

D = Determine most effect discriminating factor to narrow field
  - Narrows differentials and enables focused testing

I = Internal consistency
  - Counters anchoring, premature closure, confirmatory bias and diagnosis momentum

V = Validate! assumptions
  - Counters anchoring, premature closure, confirmatory bias and diagnosis momentum

A = Anticipate response to both possible test results: + vs –
  - Counters confirmatory bias, anchoring and premature closure
Acronym: A DIVA PR²OF

P = Probe to disprove your hypothesis
   - Counters over confidence, anchoring and premature closure

R = Reframe your framing
   - Counters premature closure

R = Reconcile inconsistencies
   - Counters anchoring, confirmatory bias, illusory correlation and hassle bias and premature closure

O = Often wrong
   - Counters over confidence and inspires life long learning

F = Figure out why we were wrong
   - Counters over confidence and inspires life long learning
Acronym: A DIVA PR²OF

39 year old male with warm and cold AIHA who presents with fevers, hepatosplenomegaly and para – aortic lymphadenopathy

Assign appropriate pretest probability
- Secondary causes of AIHA are just as common as idiopathic AIHA
- Of all secondary causes: lymphoma is the commonest

Determine most effective discriminating factor to narrow the field
- His LFT pattern suggested an infiltrative pattern and not hemolysis or alcohol liver disease

AIHA + infiltrative LFT pattern = liver biopsy
ADVAIR

A: Appropriate pretest probability
D: Discriminating factor
V: Validate assumptions
A: Anticipate both possible test results
I: Internal consistency always
R: Reconcile internal inconsistencies
Clinical Reasoning: the KTTL cycle

Know → Learn → Teach → Think → Know

MAKE IT ALL VISIBLE

MAKE IT ALL VISIBLE

MAKE IT ALL VISIBLE

MAKE IT ALL VISIBLE
Of one thing be certain; always think about how you think while you think, albeit within the limitations of your thinking mind.

Of questions and answers, strive to answer questions always but pause to question answers often.

We should always assume that our presumption about our assumptions is just that; an assumption that needs to be validated and clothed in certainty.

Strive for consistency always; to ignore facts does not change the facts.
Thank you

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