Clinical Reasoning for the Infectious Disease Specialist: A Primer to Recognize Cognitive Biases

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Infectious disease specialists are frequently consulted for diagnostic and therapeutic advice on challenging cases. When evaluating patients, the infectious disease specialist is well positioned to offer an appropriate diagnostic approach but is also at risk of not recognizing the correct diagnosis for a variety of reasons. We believe it is important to provide infectious disease specialists and trainees with a fundamental understanding of diagnostic errors, clinical reasoning, and cognitive biases. We present 2 cases demonstrating common cognitive biases leading to diagnostic errors, and we reflect on strategies that may aid in their prevention. We hope to provide knowledge and tools that may help prevent diagnostic errors in the future.

Keywords. cognitive biases; clinical reasoning; histoplasmosis; granulomatosis with polyangiitis.

Infectious disease (ID) specialists are frequently consulted for diagnostic and therapeutic advice regarding challenging cases [1]. An ID consult is oftentimes one of last resort for puzzling cases that may or may not contain an infectious component. Members of the Clinical Affairs Committee of the Infectious Diseases Society of America described the ability to direct care of difficult and perplexing cases as one of the most valuable qualities of the specialty [2]. While evaluating patients, the ID specialist is well positioned to offer an appropriate diagnostic approach but may also be at risk of not recognizing the correct diagnosis for a variety of reasons that we address here.

Diagnostic errors are common in practice and usually are multifactorial in origin [3]. We believe it is important to provide the ID specialists and trainees with a fundamental understanding of clinical reasoning, cognitive biases, and diagnostic errors. We present 2 cases demonstrating common cognitive biases leading to errors and reflect on strategies that may aid in their prevention. We hope to provide knowledge and tools that may help prevent diagnostic errors in the future.

DIAGNOSTIC ERROR

Attention has focused in recent years on diagnostic errors, defined as missed or delayed diagnoses. Studies suggest they occur in up to 15% of cases seen in medical fields [3]. No physician is immune to diagnostic errors, no matter how experienced or knowledgeable he or she is. Approximately 7.4% of US physicians are involved in medical malpractice claims each year, and diagnostic errors are a leading cause of litigation [4].

Diagnostic errors most commonly occur because of breakdowns in the healthcare system (system errors), clinical reasoning (cognitive biases), or both [5]. Graber and colleagues analyzed 100 cases of diagnostic error and found their etiologies were often multifactorial and involved both system errors and cognitive biases. Interestingly, lack of knowledge about the disease process was exceedingly uncommon [5]. Examples of system errors include a breakdown in communication, lack of
errors and cognitive errors are common and overlap [6]. Most evaluated 583 cases of misdiagnosis and also found that system
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rare diseases. Cognitive biases often go unrecognized by physi-
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errors and cognitive errors are common and overlap [6]. Most
errors were the consequence of a failure or delay in considering
the correct diagnosis, failure or delay in ordering necessary
tests, failure to follow up on tests, and placing too much weight
on a competing or coexisting diagnosis. These 2 studies and
others have found that most diagnostic errors occur in patients
with common pathologies and not necessarily in those with
rare diseases. Cognitive biases often go unrecognized by physi-
cians [7], and several can occur to reinforce each other until the
physician ultimately ends up with an incorrect diagnosis [8].

CLINICAL REASONING

Cognitive psychology studies mental processes. The science of
cognitive psychology has found applications in many disci-
plines, including economics and medicine. Cognitive psychology
has also become very popular in the nonmedical press with
several books published on this topic. Two examples of excel-
ent books are Thinking, Fast and Slow, by Nobel Laureate
Daniel Kahneman (Farrar, Straus and Giroux, 2011), and Predic-
tably Irrational: The Hidden Forces That Shape Our Deci-

In recent years, the field of cognitive psychology has been
applied to try to understand how clinicians reason through
data and arrive at a decision, diagnostic or therapeutic. It can
help us comprehend the process of clinical reasoning and how
we reach a proposed diagnosis in a patient. The dual process
theory, studied among others by Daniel Kahneman, proposes
that clinicians use 2 approaches when making diagnostic deci-
sions: the intuitive approach (system 1) and the analytical
approach (system 2) [9–11]. The intuitive approach is based on
pattern recognition and the use of previous knowledge or expe-
riences. It is quick and usually requires little cognitive effort.
For example, a patient with thrush warrants testing for human
immunodeficiency virus (HIV). This decision is based on the
pattern recognition of thrush as a common marker of immuno-
suppression and thus required minimal contemplation.

The analytical approach is more often used when one is con-
fronted with complex or diagnostically challenging cases. This
process is slower and more deliberate and uses significant cog-
nitive effort to reason through decisions, and can thus be ineffi-
cient. For example, an HIV-infected patient with a CD4 count
of 50 cells/μL presents with fever, lymphadenopathy, pulmo-
nary nodules, weight loss, and pancytopenia. This patient
presentation includes many diagnostic possibilities with a
broad differential diagnosis and possible coexisting pathologies,
and will thus require significant cognitive effort to diagnose
and treat. The dual process theory can be applied to many
other areas and is not restricted to medical disciplines.

The novice physician is more likely to use the analytical
approach, and the experienced physician the intuitive approach.
One approach is not thought to be superior to the other; the 2
are felt to exist on a cognitive continuum and to complement
each other [12]. Ideally, physicians should utilize both processes
in the evaluation of patients; some authors have proposed that
an excellent physician recognizes when it is appropriate to slow
down and shift from an intuitive approach to an analytical
approach [11,13,14]. Although described here as 2 separate enti-
ties, they are somewhat interdependent and integrated in the
problem-solving scheme. Both approaches can be subject to the
cognitive biases that are discussed below.

ANCHORING, HEURISTICS, AVAILABILITY, AND
OVERCONFIDENCE BIASES: CASE 1

A 63-year-old man presented to another institution with fever
and chest pain. He had a history of pacemaker insertion, aortic
stenosis with aortic valve replacement (St Jude’s, 3 years prior),
and a pacemaker generator exchange 1 month prior. Two
weeks later he developed fever, purulence, and dehiscence from
his pacemaker site. He received ampicillin/subbactam and me-
tronidazole for presumed pocket infection. Chest imaging
showed bilateral pulmonary nodules, thought to be caused by
septic emboli from pacemaker endocarditis (Figure 1). Anti-
biotic coverage was changed to vancomycin, gentamicin, and ce-
fepime. Transthoracic and transesophageal echocardiography
and bronchoalveolar lavage were unrevealing. He underwent
pocket revision and pacemaker generator exchange. A comput-
ed tomography–guided lung biopsy showed inflammatory
changes. All cultures remained negative; however, with the

Figure 1. Chest computed tomography demonstrating bilateral pulmo-
nary nodules in a 63-year-old man (case 1).
available records it was not possible to determine if initial cultures were obtained before initiation of antibiotics. He was transferred to our institution after developing progressive renal failure, eosinophiluria, and hematuria. Renal consultation suggested the diagnosis of interstitial nephritis from antibiotics. A repeated transthoracic echocardiogram showed normal valvular function and no vegetations. He required hemodialysis, and his pacemaker was replaced. Repeated cultures were negative. Infectious disease consultation agreed with the diagnosis of culture-negative endocarditis. Chest imaging was reported as “increase in size and number of nodules with cavitation, most likely septic; other noninfectious causes of cavitary disease should be excluded, but septic emboli are more likely given history of endocarditis.” Transesophageal echocardiography was again unrevealing. The patient remained on antibiotics and had additional complications. Three months after the initial presentation, a new team reevaluated the patient and considered the possibility of an alternative diagnosis to explain the clinical findings. Based on the findings of negative cultures, cavitary pulmonary nodules, renal failure, and hematuria, a diagnosis of granulomatosis with polyangiitis (formerly known as Wegener’s granulomatosis) was proposed. Cytoplasmic anti-neutrophil cytoplasmic antibody and antiproteinase 3 antibody levels were positive, and a surgical lung biopsy confirmed the diagnosis. Unfortunately, the patient died shortly after diagnosis secondary to multiorgan failure.

DISCUSSION OF CASE 1
This case exhibits a complex patient who was seen by multiple specialists for months. He was initially diagnosed with culture-negative pacemaker endocarditis, which was a reasonable initial conclusion. However, many cognitive errors were present after the initial evaluation, and the diagnosis of endocarditis was not challenged enough, despite many atypical features such as repeated negative cultures and unrevealing echocardiography. An alternative diagnosis was not entertained until too late in the course of his illness, leading to a fatal outcome. We discuss in the next paragraphs some of the cognitive biases that led to diagnostic errors in this case.

Anchoring bias is the tendency to lock onto a diagnosis early on and fail to reconsider after receiving contradictory information. It occurs when we “fall in love” with a diagnosis. This patient’s physicians diagnosed the patient with culture-negative endocarditis given his initial presentation and failed to adjust their impression when new information surfaced (such as worsening of cavitary lung lesions, persistently negative cultures, and progression of renal failure with hematuria). Physicians tend to latch on to a certain piece of history of physical exam finding (in this case, his recent presumed pacemaker infection or the presence of eosinophiluria after receiving antibiotics) and remain focused on their initial thoughts. They concentrated on his presumed diagnosis and discounted his repeatedly negative blood cultures and cardiac imaging, ultimately leading to misdiagnosis, mismanagement, and a fatal outcome.

Heuristic biases are mental shortcuts used in clinical reasoning to solve problems—“rules of thumb.” These shortcuts are usually correct and appropriate because familiar diagnoses are those that are frequently encountered [15]. While dependable, heuristics are not infallible and may lead to the wrong diagnosis. For example, using heuristics, one considers syphilis in a sexually active individual presenting with a palmar maculopapular rash. However, the same presentation can be seen in patients with erythema multiforme or Rocky Mountain spotted fever. In case 1, the clinicians used the following heuristic: “a patient with fever, purulence from a pacemaker pocket, and pulmonary nodules likely has pacemaker endocarditis.”

The availability bias leads people to judge likelihood by the ease with which examples spring to mind [16], and recent experience with a disease may inflate its likelihood of being diagnosed [17]. For example, if a physician recently read about or frequently treats “disease X,” then he or she is more likely to think about this disease first when seeing a new case. This cognitive bias can lead the physician to believe that a particular disease is more prevalent than it truly may be.

Overconfidence bias is the inclination to believe we know more than we do. This bias suggests that one’s subjective confidence in their assessment is reliably greater than their accuracy. Most errors are caused by faulty judgment rather than a fundamental lack of knowledge. Overconfidence bias reflects a tendency to act on incomplete information, intuitions, or hunches [17]. Overconfidence places a great deal of trust in opinion instead of carefully gathered evidence and is often amplified by the anchoring and availability errors [17].

PREMATURE CLOSURE, DIAGNOSTIC MOMENTUM, COGNITIVE OVERLOAD, SYSTEM ERRORS: CASE 2
A 41-year-old woman with known HIV infection was found unresponsive at home. Her family reported a 3-week history of the patient feeling poorly and experiencing dyspnea, and a 2-day history of odynophagia. The patient was taking no medications. Upon presentation, her temperature was 38.7°C, heart rate 152 beats per minute, blood pressure 102/62 mm Hg, and respirations 30 breaths per minute. She was afebrile, had rales in her oral mucosa, and had mild wheezing bilaterally. She had no meningeal signs or neurological deficits. Her skin exam showed coalescent erythematous papules and plaques on her neck, chest, and extremities (Figure 2). White blood cell count was 2400 cells/mm³ (34% neutrophils, 5% bands, 50% lymphocytes, and 5% monocytes; absolute neutrophil count
Pseudomonas aeruginosa cells/mm³ (1%), and tazobactam, azithromycin, sulfamethoxazole/trimethoprim, thickening. Lumbar puncture showed normal results. The lactic acid level 7.3 mmol/L, and lactate dehydrogenase level 576 U/L. Chest radiography showed bilateral peribronchial thickening. Hematocrit was 20%, and the platelet count was 19,000 platelets/mm³. Other laboratory evaluations showed the following results: serum creatinine level 1.9 mg/dL, international normalized ratio 1.7, fibrinogen level 282 mg/dL, lactic acid level 7.3 mmol/L, and lactate dehydrogenase level 6438 U/L. The patient received empiric therapy with vancomycin, piperacillin/tazobactam, azithromycin, sulfamethoxazole/trimethoprim, and fluconazole.

On the second hospital day, her CD4 count returned at 6 cells/mm³ (1%), and Pseudomonas aeruginosa grew in all blood culture bottles. The ID team was consulted and agreed with the antibiotic selection. On day 3, she became obtunded and severely acidemic and progressed to acute respiratory failure. Dermatology consulting physicians thought her rash to be of likely infectious etiology (fungal) or possibly a drug rash. Her condition continued to deteriorate. No consultant suggested medication changes. On hospital day 5, skin biopsy results revealed histoplasmosis. The same day, a member of the team realized that starting on day 2, the laboratory technician had added comments reporting intracellular yeasts; this information was missed until then. Lipid amphotericin was begun; however, the patient died the following day. Histoplasma urine antigen level was positive at >39 ng/mL.

DISCUSSION OF CASE 2

This patient with immunosuppression had a diagnosis (Pseudomonas sepsis) that did not explain all the findings. The presence of an atypical rash, pancytopenia, and very high lactate dehydrogenase suggested the presence of an additional diagnosis—disseminated fungal infection. This diagnosis was not considered early enough in her hospital stay.

Premature closure bias occurs when one accepts a diagnosis with insufficient information. In this scenario, the patient had documented Pseudomonas aeruginosa infection; however, this condition failed to explain all findings. This patient was at risk for numerous opportunistic infections. The possibility of her having more than one disease process was not sufficiently considered. In the setting of clinical deterioration the teams exercised premature closing and did not modify the management of the patient because she was thought to already have a diagnosis.

Diagnostic momentum bias begins once a patient receives a diagnosis. A patient becomes “labeled” and each team member carries the label on without question. This cognitive bias is done unconsciously and must be intentionally overcome to avoid misdiagnosis. Diagnostic momentum of Pseudomonas sepsis likely contributed to the premature closure bias.

Cognitive overload bias occurs when the amount of information exceeds the cognitive capacity for clinical reasoning. In this patient, the variety of symptoms, physical exam findings, and laboratory abnormalities may have overwhelmed the clinicians. In such situations, the cognitive effort needed to challenge the proposed diagnosis or to develop new diagnostic possibilities is significant.

We would also like to emphasize the importance of system errors in this case. The patient’s peripheral blood smear showing yeast forms was not recognized by treating physicians until day 5, despite being mentioned in the laboratory report on day 2. There are many possible reasons to explain why the physicians missed this vital piece of data, including information overload and failure to follow up on all ordered tests. However, this is also an example of a system error, or an imperfection in the healthcare system that contributes to a diagnostic error. In the electronic medical record, the comments mentioning yeast forms were not included in the main report for the complete blood count, but rather in a link labeled “comments” that had to be opened separately. There were no policies implemented for the laboratory to alert the treating physicians with such a finding. Technical failures, organizational lapses, faulty tests or data, and policy inadequacies contribute to system errors. Healthcare system changes can reduce their incidence, but system errors will not be eliminated completely because improvements degrade over time and each new renovation creates the opportunity for new errors to occur. [18]. As discussed above, system errors can contribute significantly to diagnostic errors, frequently coexist and overlap with cognitive bias, and are present in all fields of medicine.

Both of these cases display common cognitive biases that lead to diagnostic errors and demonstrate how cognitive errors can affect patient care, safety, and outcomes. We only discussed
Table 1. Common Cognitive Biases

<table>
<thead>
<tr>
<th>Cognitive Bias</th>
<th>Description</th>
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<tbody>
<tr>
<td>Anchoring</td>
<td>The inclination to lock onto a diagnosis early on and failing to reconsider after receiving contradictory information</td>
</tr>
<tr>
<td>Availability</td>
<td>The tendency to judge things as being more likely to occur due to recent exposure to similar situations</td>
</tr>
<tr>
<td>Base-rate neglect</td>
<td>The tendency to ignore the true prevalence of disease and therefore either inflating or reducing its base-rate; often practiced in the strategy of “ruling out the worst-case scenario”</td>
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<tr>
<td>Diagnosis momentum</td>
<td>Patients receive their diagnostic “label” and their diagnosis is carried on from person to person without being challenged</td>
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<tr>
<td>Gender bias</td>
<td>The predisposition to believe that gender plays a role in the likelihood of diagnosis when no such trend exists</td>
</tr>
<tr>
<td>Heuristics</td>
<td>Mental shortcuts used in cognitive reasoning to solve problems with minimal effort, ie, “rules of thumb.” Based on previous knowledge and experiences but may lead to mistakes</td>
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<tr>
<td>Outcome bias</td>
<td>The predisposition to make diagnostic decisions that will lead to good outcomes; physicians lean toward making decisions targeted toward what they hope might happen rather than what they really believe might happen</td>
</tr>
<tr>
<td>Overconfidence bias</td>
<td>The tendency to believe we know more than we do, or that we are correct more frequently than we really are</td>
</tr>
<tr>
<td>Premature closure</td>
<td>The tendency to accept a diagnosis before it has been fully confirmed</td>
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Source: Adapted from Croskerry [17].

some of the cognitive biases present in each case because our main objective was to use these examples to provide explanations on how these biases affect the diagnostic process. If the clinicians had been mindful about cognitive biases, perhaps the outcome for each patient may have been better.

**SUMMARY**

Missed or delayed diagnoses are often explained by cognitive biases and/or system errors and rarely by lack of knowledge. Cognitive biases are inevitable, and the first step to avoiding them is to recognize their common presence in medical decision making. More than 50 cognitive biases have been proposed in the literature [17], and this article is only focused on the very common cognitive biases that are likely to be encountered in our daily practices (Table 1). Fundamental knowledge of common cognitive biases is essential to attempt to prevent their occurrence and ultimately improve diagnosis and patient safety. It has been postulated that physicians can counteract cognitive biases by increasing awareness of their own thought processes and clinical reasoning. This “thinking about thinking”—also referred to as metacognition—allows physicians to reflect their medical decision-making skills and sharpen their ability to identify and prevent cognitive biases. Groopman and Hartzband have suggested the use of 3 simple questions to enhance medical decision-making skills and hopefully minimize diagnostic errors [8]:

1. What else could this be? Stopping to ask what other diagnoses may exist will allow time to steer clear of premature closing and availability biases by keeping an open mind. Give consideration to extreme circumstances. Ask yourself, “What is the diagnosis I don’t want to miss?” [15]

2. Is there something that does not fit? Raising this question allows the physician to reason through each key data point to ensure it fits appropriately into the presumed diagnosis. Asking this question will allow one to step back from the immediate problem and ensure that all pieces of the puzzle align correctly, allowing the physician to overcome premature closing and anchoring biases.

3. Is there more than one diagnosis? Diagnoses may coexist with one another and considering only one diagnosis can lead physicians to delay or miss diseases. This question brings focus to the entire clinical decision-making picture and can aid in the avoidance of anchoring and diagnosis momentum biases.

Asking each of these questions with every case encountered can attempt to safeguard physicians from the dreaded misdiagnosis. Pausing to ask these pertinent questions allows physicians time to reflect on their thinking and thus can aid in the prevention of cognitive biases that lead to incomplete or incorrect diagnoses. We believe that awareness of cognitive biases and system errors will add to the fundamental knowledge of clinical reasoning. These additional tools should be emphasized both in fellowship training and thereafter. Many excellent reviews on teaching clinical reasoning are available [11, 13, 17, 19–21], including case-based discussions [22–24].

**Notes**

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