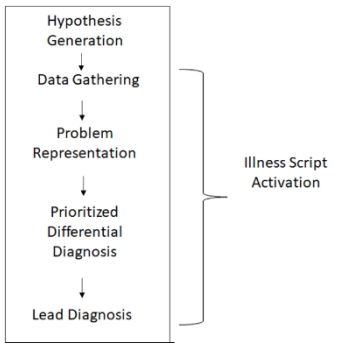
RENE Score Interpretation Guide

Overview of the Clinical Reasoning Exercise: Background and Objectives

Clinical reasoning is the cognitive process by which clinicians gather, interpret, and synthesize data to arrive at a working diagnosis and management plan. The outcome of this process is not certainty, but rather a reduction in diagnostic uncertainty sufficient enough to make optimal decisions about management.

Clinical reasoning skills are mental (and often unconscious) processes, and therefore, difficult to observe in daily practice. That is why the Reasoning Evaluation in Nephrology Education (RENE) exercise is designed to capture these cognitive steps through a "show-your-work" approach. Through simulation of an acute kidney injury consult, RENE aims to assess diagnostic reasoning skills. Scoring is in three domains— Problem Representation, Differential Diagnosis with Justification, and Diagnostic Plan with Justification. Each domain represents a linear sequence along the clinical reasoning pathway (Figure 1). Deficient performance in a given category can help identify steps along the pathway that might benefit from targeted intervention.

Figure 1



Medical knowledge is necessary but insufficient to execute sound clinical reasoning. This exercise is not designed to assess the fellow's fund of knowledge. However, a fellow's performance might suggest some knowledge deficiencies. These deficiencies should be explored and addressed in tandem with deficits in the clinical reasoning pathway.

RENE is intended as a formative assessment tool—that is, a way to screen fellows' clinical reasoning skills in the beginning of their nephrology training. Early identification of deficient reasoning skills creates an opportunity for early intervention.

Explanation of the Scoring Domains

Problem Representation

A problem representation (colloquially known as the "one-liner" on rounds) is a concise statement that incorporates key findings from the history, physical, and diagnostic tests to characterize the patent's primary problem. It paints a picture of who the patient is (i.e., demographics), the temporal pattern of the illness, and the features of the clinical syndrome. A well-constructed problem representation triggers illness scripts, which are mental representations of previously learned diagnoses that incorporate epidemiology, pathophysiology, and signs/symptoms. In turn, the illness scripts are a foundation for development of a differential diagnosis, and ultimately, selection of a lead or working diagnosis. An effective problem representation must be concise. Excessively wordy problem

representations with irrelevant data can lead to cognitive overload (for both the person generating the problem representation and for those listening to it) and fail to activate the proper illness scripts.

The problem representation is preceded and informed by two earlier steps on the clinical reasoning pathway: hypothesis generation and data gathering. Therefore, these steps are indirectly assessed by the problem representation.

Differential Diagnosis with Justification

The objective of this domain is to assess the fellow's ability to generate a differential diagnosis that is appropriately sized (including both common and "cannot miss" diagnoses) and that indicates both a lead diagnosis and alternate diagnoses.

The written justification provides insight into the cognitive steps used in this process. Phrases such as "most likely" and "less likely" indicate how the differential is prioritized based on pertinent positives and negatives (also referred to as the discriminating and defining features of competing illness scripts). Clinical data is iteratively compared and contrasted across illness scripts until a lead or working diagnosis emerges. The act of choosing a lead diagnosis is also known as script selection.

Diagnostic Plan with Justification

The objective of this domain is to assess the fellow's ability to further narrow the differential diagnosis by using additional diagnostic testing and procedures. This corresponds with the latter parts of the clinical reasoning pathway (Figure 1), including refinement of hypotheses and selection of a lead or working diagnosis.

What might a low score represent?

Problem Representation

A fellow who has difficulty constructing an effective problem representation might present in a few ways. For example, he or she could appear disorganized—often unready to present patients on attending rounds despite arriving to the hospital early to pre-round. His or her patient presentations might also seem disorganized—long, lacking key findings, and containing irrelevant findings. He or she might struggle with executing effective patient handoffs. Further, in the absence of an effective problem representation—that is, lack of a clear definition of the patient's clinical problem—generation of an adequate differential diagnosis for the clinical problem might be impaired.

Of note, fellows who have difficulty with problem representation do not necessarily have medical knowledge deficits. Rather, they might just have difficulty accessing and applying their knowledge in real-world scenarios. Therefore, their scores on standardized board exams might not reflect their clinical reasoning deficit. However, medical knowledge and clinical experience to build illness scripts are necessary to develop a problem representation, so these two things should also be assessed independently.

Differential Diagnosis with Justification

A fellow with a low score in this Differential Diagnosis with Justification might struggle to do the following: make an appropriately-sized differential diagnosis, justify the inclusion of various diagnoses, and assign relative probabilities to the diagnoses. In other words, the fellow might generate limited differential diagnoses; focus exclusively on rare ("zebra") diagnoses and not consider more common ones; or struggle with prioritizing a differential diagnosis based on available clinical data.

Diagnostic Plan with Justification

A low score in the Diagnostic Plan with Justification might indicate that the fellow struggles with the latter parts of the clinical reasoning pathway—namely, refining initial hypotheses, which helps further narrow the original differential diagnosis and increase confidence in a lead diagnosis. Behaviors that suggest an inability to refine initial hypotheses include exhaustive lists of proposed diagnostic tests/procedures; very short lists of proposed diagnostic tests/procedures; and diagnostic plans that lack prioritization based on pre-test probability and severity of risk.

What are potential reasons for a low score?

Problem Representation

A fellow might have difficulty constructing a problem representation for several reasons.

First, the problem representation is contingent upon the two immediately preceding steps in the clinical reasoning pathway: hypothesis generation (in response to the chief complaint, or in the case of nephrology, the reason for consultation) and data gathering. Hypothesis generation should direct data gathering in a purposeful manner. That is, for example, if the reason for consultation is for peripheral edema, then data should be gathered with this problem in mind. "Peripheral edema" should trigger early hypotheses about the underlying cause—nephrotic syndrome, liver disease, kidney disease with fluid overload, DVT, heart failure, etc. Then, data gathering will be directed towards things that are potentially associated with this clinical problem, such as the serum creatinine trend, urinalysis, serum albumin, and fluid intake and outtake. If data is collected in a haphazard or exhaustive way that fails to connect with the clinical problem, then constellations of key clinical features are less likely to be recognized.

Second, many fellows have not had explicit instruction in constructing a problem representation. The electronic medical record has made it easy to import large amounts of historical data into a consult or progress note. As a result, fellows might not be developing the skill of selecting the most relevant information to succinctly frame the patient's primary problem.

Finally, a knowledge deficit might impair a fellow's ability to effectively perform early hypothesis generation and hypothesis-directed data gathering.

Differential Diagnosis with Justification

A low score in the Differential Diagnosis with Justification domain could stem from a few steps in the clinical reasoning pathway. As discussed previously, struggling with problem representation or the steps upstream to it will likely result in trouble with appropriate differential diagnosis generation. In addition, fellows might score low in this domain if they have limited clinical experience (in the way of stored illness scripts) or lack a structured framework for considering

diagnoses and their relative probabilities. It is also possible that there are psychological barriers to developing an appropriate differential diagnosis. For example, a fellow might experience performance anxiety when faced with a complex case or when placed in a busy clinical environment, and this could impede their ability. Finally, significant deficits in medical knowledge will also impact generation of an appropriate differential diagnosis.

Diagnostic Plan with Justification

A low score in the Diagnostic Plan with Justification domain suggests deficiency in the skill of hypothesis refinement, which can result in an inability to select a correct working or lead diagnosis. Hypothesis refinement can be limited by some cognitive biases. For example, a fellow that succumbs to early confirmation bias—that is, puts disproportionate weight on findings that confirm a diagnosis rather than findings that disconfirm it—he or she might fail to pursue additional diagnostic tests. A fellow who is influenced by this bias will likely also generate a very limited differential diagnosis and "prematurely close" with a lead diagnosis. Similar biases that promote early closure (and therefore, limit effort to reduce diagnostic uncertainty through additional testing) include framing bias, anchoring bias, base rate neglect, and ascertainment bias. Below there is a table with common types of cognitive biases and definitions.

In addition to cognitive bias, fellows might lack certain skills that promote hypothesis refinement. For example, fellows who have not mastered probabilistic reasoning might create very long lists of proposed diagnostic tests and procedures. The fellows might also overemphasize rare diagnoses, and their diagnostic plans will lack prioritization—meaning that the pursuit of certain tests are not contingent on the results of others.

Some fellows who also struggle with hypothesis-driven data gathering will have similar difficulty with generating an appropriate list of additional diagnostic tests and procedures. They often will indiscriminately order tests without linking them to illness scripts.

Finally, there might be psychological barriers to generating an appropriate diagnostic plan. These include personality traits consistent with obsessive compulsive disorder. Fellows who exhibit these traits tend to produce very large differential diagnoses with exhaustive diagnostic plans for fear of missing the correct diagnosis.

Examples of Common Cognitive Biases	
Bias	Definition
Confirmation bias	The tendency to look for evidence to support a diagnosis and to ignore evidence that makes the diagnosis less likely
Anchoring bias	The tendency to lock on to salient features in a patient's early presentation and failure to incorporate new information as it comes to light
Base-rate neglect	The tendency to ignore the true prevalence of disease—either inflating or reducing its base rate
Framing effect	The tendency to be strongly influenced by the way a patient's case is presented by another

	provider
Ascertainment bias	The tendency for a clinician's thinking to be disproportionally shaped by a prior expectation (e.g., gender stereotyping)

What are the next steps to evaluate a low score?

Problem Representation

First, review the fellow's clinical evaluations to see if there are comments that match the clinical phenotype of someone who struggles with problem representation formation: disorganized patient presentations, missing the "forest for the trees," difficulty with patient hand-offs, difficulty with generating an appropriate differential diagnosis.

Second, directly observe the fellow during a patient presentation to screen for signs of struggle with problem representation formation.

Third, in order to isolate and remediate the step(s) in the reasoning pathway that are deficient, there are several exercises that can be done with the fellow.

In addition to these steps, always independently evaluate the fellow's knowledge base by reviewing past standardized test performance, in-training exam scores, using board-style question banks, and asking probing knowledge-based questions on rounds.

Recommended exercises:

Articulate the Summary Statement: Use a case bank to practice creating one to two-problem representations (i.e., summary statement) using key features and semantic qualifiers.

Highlight Key Features: Provide the fellow with written history and physicals and ask him or her to highlight the key clinical features based on possible diagnoses. This allows the fellow to identify the relevant, illness-script-activating data for a problem representation.

Search for Scripts: This is to improve hypothesis generation and hypothesis-driven data gathering. The fellow should propose three potential diagnoses based on the reason for consultation, followed by five history questions and five exam/diagnostic test findings that fit the potential diagnoses.

Differential Diagnosis with Justification

First, review the fellow's clinical evaluations to see if there are comments that meet the clinical phenotype of someone who struggles with generation of a differential diagnosis. Features of this include differentials that are too short or excessively long without prioritization. Some fellows might focus only on common diagnoses and others, only on rare diagnoses. Often, if there is a deficiency in this skill, then there are also deficiencies upstream of it, including in initial hypothesis generation, data gathering, and problem representation formation. Therefore, a fellow who struggles with the differential diagnosis might also score low in the Problem Representation category and exhibit its associated clinical phenotype.

Second, directly observe the fellow in the clinical environment for evidence of the features described above. If present, discuss with the fellow what he or she thinks of his or her performance. Screen for features of performance anxiety or other mental health disorders that might impede clinical performance and address these if necessary.

If it is determined that the fellow struggles with generation of differential diagnoses in the clinical environment, further evaluation is required to ascertain the step(s) in the clinical reasoning pathway that require strengthening. There are several exercises that help both diagnose and treat weaknesses with impaired differential diagnosis generation.

Recommended exercises:

Scaffold the Differential: Starting with the chief complaint and demographics, use an analytical approach for generation of the differential diagnosis with anatomic, pathophysiology, or systems-based schemas or mnemonics.

Structured Reflection: The fellow should reflect on the case to identify features that are concordant with the lead diagnosis and those that are discordant. He or she should also brainstorm features that would support the lead diagnosis, but are missing from the available data.

Identify Findings that Matter: The fellow should identify findings that have the biggest effect on increasing or decreasing the likelihood of a diagnosis. This exercise will help build and link illness scripts to diagnoses.

Play the Role: The fellow will assume the role of the patient and persuade the faculty member of the lead diagnosis by including its most pertinent features. This exercise allows the fellow to develop the skill of prioritizing the differential diagnosis based on the relevant details (script selection).

Cognitive Debiasing/Metacognition: Confirmation bias is a type of cognitive bias that leads to diagnostic error. When someone succumbs to confirmation bias, he or she selects a lead or working diagnosis based on confirming data. However, disconfirming data—that is, pertinent negatives—are ignored. Metacognition (the act of thinking about the way one thinks) will increase awareness of his or her cognitive biases with the goal of avoiding them in future clinical decision-making.

Think Base Rate: The fellow will incorporate probabilistic reasoning into the differential diagnosis generation by considering diagnoses that are common, atypical, rare, and “cannot miss.”

Diagnostic Plan with Justification

First, review the fellow’s evaluations to see if there are comments that suggest the following practices: ordering/recommending extensive diagnostic tests in an apparently indiscriminate fashion; ordering/recommending inappropriately few diagnostic tests; failure to narrow an expansive initial differential diagnosis; failure to prioritize diagnostic plans based on the pre-test probability of a given diagnosis. Fellows with low scores in the Diagnostic Plan with Justification category might also score poorly in Problem Representation and Differential Diagnosis with Justification because the steps required to succeed in Diagnostic Plan with Justification (hypothesis refinement and selection of a lead/working diagnosis) are dependent on successful

completion of the upstream steps (initial hypothesis generation, data gathering, problem representation).

Second, directly observe the fellow in the clinical environment for evidence of the features described above. If present, discuss with the fellow what he or she thinks of his or her performance and address common cognitive biases. Screen for features of mental health disorders that might impede clinical performance, including traits of obsessive compulsive disorder and refer for management as indicated.

If it is determined that the fellow struggles with generation of an appropriate diagnostic plan in the clinical environment, further evaluation is required to ascertain the step(s) in the clinical reasoning pathway that require strengthening. There are several exercises that help both diagnose and treat weaknesses in the clinical reasoning pathway for those who struggle with formulation of the diagnostic plan.

Recommended exercises:

Persuade the MD: Assuming the role of the patient, the fellow attempts to convince the attending nephrologist of the lead diagnosis by providing key discordant and concordant features. This exercise will help develop many clinical reasoning skills, including refining his or her hypotheses and selecting a lead diagnosis.

Structured Reflection: Ask the fellow to list aspects of the case that are concordant and discordant with the lead diagnosis as well as things that are missing from the presentation that, if present, would support the lead diagnosis. For example, if a low fractional excretion of sodium would support a diagnosis of hemodynamic AKI, then this might be a reason to order this test and narrow the differential diagnosis.

Think Base Rate: The fellow will incorporate probabilistic reasoning into the differential diagnosis generation by considering diagnoses that are common, atypical, rare, and "cannot miss." This will guide the fellow in selecting appropriate diagnosis tests.

Question-by-Question Guide

1a. Is the tempo of the overall illness (not just the AKI) described? That is, are words such as "chronic," "subacute," or "progressive" used? Also, "yes" should be granted if a duration of signs and symptoms is given in days or months.

A description of the tempo of a clinical presentation is critical to an effective problem representation. Tempo is a powerful activator of illness scripts. In this case of AKI, the description of the patients symptoms (DOE, edema, anorexia, fatigue, B-symptoms) as "chronic," "progressive," or "subacute" activates a different set of illness scripts than if the tempo was labeled as "acute" or if it was entirely absent from the problem representation. This constellation of progressive symptoms activates scripts related to malignancy, an indolent infection (e.g., tuberculosis or another granulomatous process), or other inflammatory conditions. It helps us place the AKI in the context of the overall illness and hypothesize if the AKI is the primary driver of the illness or a secondary feature.

Although credit is granted if the illness tempo is described in days or months, the ideal problem representation uses terms like "chronic", "progressive," or "subacute." These are examples of

sematic qualifiers. They are words or phrases that translate key features of the patient's presentation in abstract medical terms. Semantic qualifiers are the language of illness scripts—that is, our brain typically encodes our memories of diagnoses using such terms. Therefore, incorporating semantic qualifiers into problem representations is a more efficient way to search and retrieve an illness script from our mental library. It also allows us to communicate about the case more effectively on rounds and during patient handoffs.

1b. Does the problem representation include the appropriate semantic qualifiers? That is, it translates key aspects of the patient's presentation into abstract medical terms. See below for the appropriate semantic qualifiers for this case.

Fatigue, weakness, or malaise (any of these)
B symptoms (or night swears, fever)
Dyspnea on exertion (SOB with exertion)
Edema (or swelling)
Polydipsia
Anorexia/poor appetite
Fever

Semantic qualifiers are words or phrases that translate key aspects of the patient's presentation into abstract medical terms. Semantic qualifiers are the language of illness scripts—that is, our brain typically encodes our memories of diagnoses using such terms. Therefore, incorporating semantic qualifiers into problem representations is a more efficient way to search and retrieve an illness script from our mental library.

The list of sematic qualifiers in the table summarizes the most discriminating features of the case presentation. They should activate illness scripts related to malignancy, indolent infections (e.g., tuberculosis or another granulomatous process), or other inflammatory conditions. Further, the illness scripts triggered by this particular constellation of signs/symptoms also likely include other features of the case, such as hypercalcemia, lymphadenopathy, and unilateral pleural effusion.

Although credit is granted for phrases such as "swelling," or "SOB with exertion," translating the patient's words into medical terms is ideal. This means using terms and phrases like edema (instead of swelling), dyspnea (instead of SOB), anorexia (instead of lack appetite), or B symptoms (instead of night sweats and fever). Again, semantic qualifiers are the language of illness scripts and therefore, allow us to search and retrieve scripts from our library more efficiently.

1c. Are relevant historical data included in the problem representation? See below for relevant historical data.

Diabetes mellitus
Hypertension

The most relevant pieces of the patient's past medical history should be included in the problem representation. In this case, they are diabetes and hypertension. This information helps provide a context for who the patient is, and therefore, how her characteristics will influence her susceptibility to disease as well as how disease may uniquely present and progress in her.

It is important to be judicious about what past medical history to include in a problem representation. An effective problem representation is succinct and activates illness scripts. Problem representations that have exhaustive lists of irrelevant history can activate the wrong illness scripts and lead to cognitive overload. In this case (and nearly all cases of AKI), diabetes and hypertension are relevant past/current diagnoses. It would also be reasonable to include arthritis or GERD if NSAID or PPI use were key contributors to the differential diagnosis.

1d. Are relevant physical findings included in the problem representation? See below for relevant physical findings.

Fever (or B symptoms)
Lymphadenopathy
Hepatosplenomegaly
Edema (or swelling)
Reduced breath sounds at the right base (or a pleural effusion)
Oliguria

A problem representation should include relevant physical findings that will trigger illness script activation. In this case, the findings listed in the table are the most discriminating physical features of her presentation. Taken collectively, they should activate illness scripts for lymphoproliferative disorders, autoimmune conditions, and infections.

1e. Are relevant diagnostic test results included in the problem representation? See below for relevant diagnostic test results.

Elevated creatinine (compared to baseline creatinine)[†]
Hypercalcemia
Microscopic hematuria
Unilateral pleural effusion on CXR
Proteinuria
Hypoalbuminemia
Anion gap metabolic acidosis
Anemia

[†]Can be substituted with AKI

A problem representation should include relevant diagnostic test results that will trigger illness script activation. In this case, the findings listed in the table are the most discriminating diagnostic test results of her presentation. When we combine the diagnostic tests with the

disease tempo and physical findings, we are able integrate the kidney injury into the overall clinical presentation and hypothesize if it is a primary or secondary feature.

For full credit on this question, the inclusion of hypercalcemia is required, which is a particularly discriminating feature of the case. Hypercalcemia can contribute to kidney injury through multiple mechanisms and also can be a feature of several systemic processes, including paraneoplastic and granulomatous. Also, the proteinuria, hypoalbuminemia, and microscopic hematuria make us consider a glomerular process. If these results are absent from a problem representation, then we might not consider this "cannot miss" diagnosis.

1f. How is the problem representation structured?

An effective problem representation is concise. It should convey the most relevant information in the most succinct way possible with the goal of framing the patient's primary problem.

Excessively wordy problem representations lead to cognitive overload. Cognitive overload has negative consequences for both the person creating the problem representation and the person listening to it.

For the creator—in our case, the fellow—it will impair his or her ability to generate, prioritize, and refine a differential diagnosis. Also, the fellow will have trouble juggling multiple complex patients at once because he or she will have difficulty retrieving information on them efficiently. This is because there is a limit to how much information our brains can process at a given time. We need to store a concise representation of each patient in our brains or else we will not be able to simultaneous manage patients in a busy clinical environment.

For the listener—in our case, the nephrology attending or a colleague—the cognitive overload caused by a wordy problem representation can activate the wrong illness scripts and lead to various cognitive biases.

2a. Is there a lead diagnosis with a written justification? A lead diagnosis can be indicated by designating it directly as such, or, by using language such as "most likely" or "probably." Numbered lists alone are not enough to designate a lead diagnosis.

The purpose of this question is to assess the fellow's ability to prioritize a differential diagnosis. Although a diagnosis can never be made with certainty (particularly in the early stages of a clinical presentation), it is important for the fellow to be able to select the lead or a working diagnosis with the data available. In fact, the purpose of the clinical reasoning process is not certainty, but rather a reduction in uncertainty sufficient enough to make optimal decisions about diagnosis and management. Therefore, we are looking for fellows to "put their nickel down" on a lead diagnosis and to provide justification for it. Please note that the clinical case used in RENE is designed to trigger a broad differential diagnosis; there is no certain diagnosis (although there are several discriminating clinical features that must be recognized in order to avoid overlooking "cannot miss" diagnoses).

2b. Is there a differential diagnosis with a written explanation? In other words, is there an explanation about why alternate diagnoses are being considered? The explanation should include why features of these diagnoses are concordant or discordant with the patient's presentation (i.e., pertinent positives and negatives) and how likely they are *relative to the lead diagnosis and/or to other alternate diagnoses*. Note: There should be appropriate use of

pertinent positives and negatives *in general*, but it is not necessary to use both for every item on the differential diagnosis. See the table for examples of data that make a given diagnosis more or less likely.

The purpose of this question is to assess a fellow's ability to generate and prioritize a differential diagnosis. We are looking to see if the fellow can use data for probabilistic reasoning. That is, can they compare and contrast illness scripts to come up with a hierarchal list of diagnostic possibilities.

Again, we are not scoring fellows on correct or incorrect diagnoses, but rather, their ability to apply data to justify the likelihood of any given diagnosis. Table 1 below is a comprehensive (but not exhaustive) list of potential diagnoses along with data that is concordant or discordant with the patient's presentation.

Table 1

Diagnosis	**Data For (Pertinent Positive)**	**Data Against (Pertinent Negative)**
Pre-Renal		
• Hemodynamic AKI (hypotension/volume depletion related to hypercalcemia/anorexia, hypercalcemia-induced renal vasoconstriction)	• Hypotension with tachycardia • ACE-I +/- NSAID use • Few hyaline casts • Hypercalcemia • Oliguria	• Spg 1.010 • Lack of a response to 2.5 L NS
• Cardiorenal syndrome	• Hypotension • LE edema • DOE • Has indicated that she sleeps in a chair (although no clear suggestion of orthopnea)	• Hypercalcemia • Unilateral effusion rather than bilateral • Lack of JVD • Fever, lymphadenopathy
• Hepatorenal syndrome	• Hepatosplenomegaly • Unilateral pleural effusion • Hypotension with tachycardia • Granular casts on U/A	• Fever, lymphadenopathy • Hypercalcemia • No other stigmata of liver cirrhosis such as ascites or spider angiomas (this would make a hepatic hydrothorax less likely) • Spg 1.010 (in HRS, the spg should be extremely concentrated)
Glomerular etiology		
• Malignancy-related GN (e.g., paraprotein MPGN or	• Lymphadenopathy • Hypercalcemia	• Proteinuria could be due to underlying

light-chain deposition disease)	• Sub-nephrotic range proteinuria (dipstick) • Heme (dipstick) • B-symptoms • LE edema	diabetes • Microscopic hematuria must be confirmed by microscopy and could be due to urinary catheter
• Membranous nephropathy (lymphoma vs. solid malignancy vs. sarcoidosis)	• Lymphadenopathy • B-symptoms • Unilateral pleural effusion • Hypercalcemia • Sub-nephrotic range proteinuria (dipstick) • LE edema • Hypoalbuminemia	• Proteinuria is sub-nephrotic and could be due to underlying diabetes • Edema could be due to DVT or fluid retention in setting of reduced GFR • Alone, might not explain significant elevation in creatinine
• Minimal change disease (lymphoma, other malignancy)	• Lymphadenopathy • B-symptoms • Proteinuria (by dipstick) • LE edema • Hypoalbuminemia • NSAID use	• Proteinuria is sub-nephrotic • Proteinuria could be due to underlying diabetes • LE edema and hypoalbuminemia have other explanations • Although NSAIDs are present, there are many other potential insults that are more likely to be responsible for the clinical presentation
• Infection-related GN	• Low-grade fever • Lymphadenopathy • Sub-nephrotic range proteinuria (by dipstick) • Heme (dipstick)	• Proteinuria could be due to underlying diabetes • Microscopic hematuria must be confirmed by microscopy and could be due to urinary catheter • No evidence (yet) of bacteremia
• Lupus nephritis	• Fatigue • Cytopenias • Pleural effusion • Microscopic hematuria • Proteinuria	• Age is older than one would expect for a de novo presentation of lupus • Does not explain hypercalcemia

		• Microscopic hematuria must be confirmed by microscopy and could be due to urinary catheter • Although SLE may present with diffuse lymphadenopathy, this would be an atypical presentation
• ANCA Vasculitis	• Fatigue • Microscopic hematuria • Proteinuria • Generally affects older adults	• Absence of signs of diffuse alveolar hemorrhage • Absence of purpura
• Thrombotic microangiopathy (TMA)	• Microscopic hematuria • Proteinuria • Thrombocytopenia • Anemia • Possible malignancy (part of a paraneoplastic syndrome)	• Splenomegaly could also explain thrombocytopenia
Tubulointerstitial etiology		
• Acute tubular injury/ATN	• Potentially, prolonged ischemic insults (hypotension, hypercalcemia leading to vasoconstriction, NSAIDs, ACEI) • Oliguria • Spg 1.010 • No response to 2.5 L NS • Few granular casts	
• Tumor lysis syndrome (TLS) related to malignancy	• Lymphadenopathy • B-symptoms • Unilateral pleural effusion • Hyperkalemia	• Hypocalcemia is typically a feature of TLS (not hypercalcemia; although hypercalcemia could be driven by a separate malignancy-related process)
• Interstitial nephritis (granulomatous from infection vs. sarcoidosis or acute viral infection like HIV)	• Hypercalcemia • Lymphadenopathy • Recent trip to Texas (like coccidiomycosis) • Fever	• Presentation seems sub-acute; less likely timeline of sarcoidosis • Lack of classic lung features (nodules,

		hilar adenopathy, cavitary lesions) despite unilateral pleural effusion
• Interstitial nephritis (medication-mediated)	• PPI, NSAIDS	• This does not explain the other systemic features of the case (e.g., adenopathy)
• Cast nephropathy from multiple myeloma	• Hypercalcemia • Fatigue	• Lymphadenopathy is rarely a presenting feature of multiple myeloma
• Infiltrative disease	• Suggestion of lymphoproliferative disorder (fever, lymphadenopathy, hepatosplenomegaly)	• Does not account for the impact of hypotension, hypercalcemia, and other hemodynamic insults
Post-Renal		
• Above-the-bladder obstruction related to lymphadenopathy; tumor; stones from TLS (crystal formation) or hypercalcemia	• Lymphadenopathy • Hypercalcemia • Oliguria despite fluid resuscitation and urinary catheter placement	• Does not account for the impact of hypotension, hypercalcemia, and other hemodynamic insults

2c. Are common diagnoses considered? Common diagnoses are considered to have a high base rate in the hospitalized population.

Because "common things are common," failing to consider diagnoses such as acute tubular injury/ATN or something on the pre-renal spectrum can lead to diagnostic error. It is important to use a framework that reminds the fellow to consider both common diagnoses as well as rarer, "cannot miss" diagnoses (see below at 2d).

In this case, there are several risk factors for hemodynamic insults to the kidney, including potential ACE-I and NSAID use in the setting of possible relative hypotension and hypercalcemia. This might lend itself to ischemic insults, resulting in acute tubular injury or ATN. Table 1 shows data that is concordant and discordant with these diagnoses.

2d. Are "cannot miss" diagnoses considered? "Cannot miss" diagnoses are those that, while potentially less likely, lead to poor outcomes if not identified and intervened upon expediently.

Just as it is important to use a diagnostic framework that considers common diagnoses, rarer "cannot miss" diagnoses should also be considered. In this case, a malignancy-related kidney injury cannot be missed. As noted before, certain features of this case should activate illness scripts for malignancy—anorexia, B symptoms, hypercalcemia, lymphadenopathy, unilateral pleural effusion. Malignancy-related kidney injury can come in many varieties (glomerular pathology, tumor lysis syndrome, myeloma kidney); credit for considering malignancy-related

kidney injury is granted for mention of any variety. Other “cannot miss” diagnoses include obstruction and acute glomerulonephritis. Obstruction (above and below the bladder) should be considered in all cases because failure to relieve an obstruction in a timely manner can lead to permanent nephron loss. In this case, an upper tract obstruction should be considered due to the lymphadenopathy and possibility of malignancy. Therefore, the observation that an indwelling urinary catheter did not relieve the obstruction does not eliminate obstruction from the differential diagnosis. Acute glomerulonephritis should always be considered when there is evidence of proteinuria and microscopic hematuria.

2e. Are the clinical features from the problem representation (e.g., lower extremity edema, unilateral pleural effusion, hypercalcemia, etc.) clearly incorporated into the justification for the differential diagnosis?

The purpose of this question is to assess the linkage between the problem representation and the differential diagnosis. The problem representation should be engineered to highlight the key clinical features that drive the generation of a differential diagnosis; it should not be a haphazard list of irrelevant details. The problem representation should help us retrieve illness scripts—that is, constellations of features that associate with a given disease state, not solitary features. To score well on this question, the fellows need to demonstrate that the features highlighted in the problem representation are central to the justification for the differential diagnosis. This shows that they have synthesized the clinical features in a purposeful way. For example, if lower extremity edema and a unilateral pleural effusion are mentioned, there should be something on the differential diagnosis that incorporates the two together, such as nephrotic syndrome, heart failure, or lymphatic obstruction from malignancy. Or, if hypercalcemia is mentioned, it should be part of the differential diagnosis for the AKI and (ideally), part of the overall clinical syndrome (e.g., hypercalcemia from a malignancy or a granulomatous process).

3a. Are further tests/procedures recommended?

This question assesses whether fellows designate further diagnostic tests or procedures to narrow the differential diagnosis.

3b. Are the diagnostic tests and/or procedures justified based on the differential diagnosis? Justification is defined by linking a test/procedure to a specific diagnosis and indicating its utility**.** Table 2 has appropriate diagnostic studies for diagnoses that might appear on the differential with their justification. Note: if a diagnostic possibility is not mentioned in the differential diagnosis in the Differential Diagnosis with Justification section, then credit should not be given here. For example, if a renal ultrasound is suggested to “rule-out obstruction,” then credit should only be given if obstruction is mentioned as part of the differential diagnosis in the Differential Diagnosis with Justification section.

In this question, we are assessing fellows ability to justify their reason for a ordering a diagnostic test or procedure. A diagnostic evaluation should always be designed with a purpose. For example, ANCA titers should not be ordered indiscriminately for every patient with AKI. An ANCA titer should be ordered if there is reasonable suspicion for a renal-limited or systemic vasculitis. Supporting features (also listed in Table 2) include evidence of a potential acute glomerulonephritis (rise in serum creatinine, microscopic hematuria, and proteinuria). Other features concordant with an illness script for ANCA vasculitis include purpura, sinus disease, pulmonary hemorrhage, new-onset mononeuropathy or polyneuropathy, and presentation in an older adult. Although ANCA vasculitis might always be on the differential diagnosis for an acute glomerulonephritis, it is not always the most likely etiology based on the presence or absence of the features mentioned and whether there is a more likely diagnosis. Therefore, justifying the

rationale for this test and others is important for narrowing a differential diagnosis with consideration for the disease severity, pre-test probability, and cost of care.

3c. Does the diagnostic plan propose tests to evaluate for common diagnoses? See below for a table of common diagnoses and associated diagnostic tests/procedures.

Common Diagnoses	**Diagnostic Tests/Procedures**
Hemodynamic AKI from hypotension/volume depletion/hypercalcemia (also give credit for "pre-renal" AKI)	Urine microscopy, and/or urine electrolytes; and/or PTH (evaluation for hypercalcemia); and/or SPEP or free light chains (evaluation for hypercalcemia); and/or trial of volume resuscitation with IV fluids
ATN/acute tubular injury	Urine microscopy and/or urine electrolytes

As was discussed for question 2c, it is always important to have a differentia diagnosis that considers common diagnoses. Diagnostic error can occur if we fail to consider the most common diagnoses. Failure to include common diagnoses can be avoiding by using diagnostic frameworks that consider the base rate of a given diagnosis (in this case, for AKI) in a hospitalized population. At the same time, this framework should also include "cannot miss" diagnoses.

To receive credit for this question, the fellow must indicate at least one test for the common diagnoses of acute tubular injury/ATN as well as for pre-renal insults.

3d. Does the diagnostic plan propose certain tests/procedures to evaluate for "cannot miss diagnoses"? See the table for a "cannot miss diagnoses" and associated diagnostic tests/procedures

Cannot Miss Diagnoses	**Diagnostic Tests/Procedures**
Malignancy-related kidney disease (malignancy-related GN, TLS, lymphomatous infiltration, multiple myeloma)	Urine microscopy to assess for glomerular hematuria; and/or urine protein evaluation; and/or renal imaging (CT or ultrasound); and/or SPEP/immunofixation/free light chains
Above-the-bladder obstruction	Renal imaging (CT or ultrasound)
Acute glomerulonephritis	Urine microscopy to assess for glomerular hematuria; and/or urine protein evaluation; and/or kidney biopsy if other tests inconclusive

As was discussed for question 2d, we should also think about what the "cannot miss" diagnoses are in any clinical scenario and consider their likelihood. Even though these diagnoses might be rarer or less likely in a given case, missing them can have devastating consequences for the patient.

To receive credit for this question, the fellow must indicate at least one test for obstruction, acute glomerulonephritis, and a malignancy-related kidney disease.

3e. Does the diagnostic plan consider factors such pre-test probability and test invasiveness?

This question assesses the fellows ability to perform probabilistic reasoning and consider other factors like test invasiveness, risk, and cost.

To score “yes” for this question, there must be a sequence to the proposed diagnostic procedures/tests that considers pre-test probability and/or test invasiveness. For example, are viral serologies and ANA ordered only after a urine protein quantification and microscopy have confirmed proteinuria and possible glomerular hematuria? Or, is a kidney biopsy only considered after less invasive tests are used or after more common diagnoses are excluded?