Proteinuria and Hematuria

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Faculty

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Faculty Disclosure

Contributing faculty, Carol Whelan, APRN, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

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The division planner and director have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Audience

This course is designed for nurses caring for patients who may present with proteinuria or hematuria.

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Course Objective

The purpose of the course is to provide healthcare professionals with the information necessary to accurately diagnose and manage the conditions of proteinuria and hematuria, thereby improving patient outcomes.

Learning Objectives

Upon completion of this course, you should be able to:

1. Define proteinuria and describe the pathophysiology of the finding.
2. Analyze the clinical presentation of proteinuria and possible co-occurring signs, including aspects of the physical examination.
3. Describe the diagnosis and management of patients with proteinuria.
4. Assess the clinical findings of and appropriate diagnostic techniques for hematuria.
5. Discuss the management of hematuria and related conditions.

Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also included so you may determine the validity or relevance of the information. These sections may be used in conjunction with the course material for better application to your daily practice.

INTRODUCTION

Proteinuria and hematuria can be relatively common, with rates of transient hematuria exceeding 38% [1]. However, hematuria and especially proteinuria can be signs of serious disease or neoplasm [2; 3; 4; 5; 6]. In particular, the presence of proteinuria in patients with diabetes can be an important indication of unsuccessful disease management. Therefore, a careful evaluation is essential. However, according to one study, physicians do not always adhere to the guideline-endorsed recommendations for testing urine protein content in these patients [7]. Furthermore, in men older than 50 years of age, even transient hematuria is often an indication of more serious disease, with up to 2.4% of this population having urinary tract malignancy [2]. This course will review the diagnosis and treatment of proteinuria and hematuria, including considerations for various etiologies.

DEFINITION AND EPIDEMIOLOGY OF PROTEINURIA

Approximately 15 kg of protein are filtered through the healthy adult kidney each day, with less than 150 mg excreted [2; 5; 8]. Proteinuria is generally defined as urinary protein excretion of more than 150 mg/day (10–20 mg/dL) [9]. The presence of proteinuria is considered the hallmark of renal disease. Moderately increased albuminuria (microalbuminuria) is defined as the excretion of 30–300 mg/day of albumin protein and can be a sign of early renal disease, particularly in patients with diabetes [9; 10]. Severely increased albuminuria (macroalbuminuria) describes albumin excretion rates of more than 300 mg/day. This finding indicates more advanced renal disease [9].

Proteinuria can be classified as transient or persistent. Transient proteinuria is caused by a temporary change in glomerular hemodynamics that results in excess protein. These conditions are usually of a benign or self-limiting nature and include orthostatic (postural) proteinuria, dehydration, fever, exercise, and emotional stress [9; 10]. Congestive heart failure and seizures can also cause transient proteinuria [10]. Persistent proteinuria is defined as 1+ protein on a standard dipstick (which corresponds to approximately 30 mg/dL) two or more times over a three-month period [11]. Persistent proteinuria indicates a pathologic process, and the etiology must be investigated. Possible causes may be genetic, infectious, metabolic, or vascular in nature (***Table 1***).

COMMON CAUSES OF PROTEINURIA	
Category	**Possible Causes**
Drug-induced	Lithium Cyclosporine Cisplatin Nonsteroidal anti-inflammatory drugs (NSAIDs)
Genetic	Polycystic kidney disease Medullary kidney disease
Immune	Drug allergies Collagen vascular disease IgA nephropathy Sarcoidosis
Infectious	Bacterial, fungal, or parasitic infection Tuberculosis
Metabolic	Hyperuricemia Hypercalcemia Amyloidosis
Vascular	Diabetes Hypertension Sickle cell disease Radiation nephritis

Source: Compiled by Author *Table 1*

Although isolated proteinuria is not necessarily associated with excess morbidity and mortality, it can be a sign of serious systemic disease. In the United States, diabetes is the leading cause of end-stage renal disease (ESRD), followed by hypertension [12]. In both type 1 and type 2 diabetes, microalbuminuria is often the first sign of deteriorating renal function [7]. As kidney function declines, microalbuminuria becomes full-fledged proteinuria. ESRD has a yearly mortality rate of approximately 15% and currently affects more than808,500 patients in the United States alone [13]. Proteinuria can also be a sign of nephrotic syndrome, which carries a high risk of morbidity and mortality.

Urinary albumin excretion has also been shown to predict increases in blood pressure in nondiabetic, nonhypertensive individuals and appears to precede progression to higher blood pressure stages [14]. Therefore, proteinuria may be a useful biomarker to identify individuals who are at risk for developing hypertension [14]. In addition, persistent proteinuria in excess of 1 g/day has been associated with increased cardiac morbidity and mortality [15].

Advanced age and overweight/obesity are risk factors for proteinuria. Certain population groups, including African Americans, Native Americans, Hispanic Americans, and Pacific Islanders, are also at increased risk for developing proteinuria [7].

PATHOPHYSIOLOGY OF PROTEINURIA

The normal urine protein profile consists of approximately 40% to 50% Tamm-Horsfall proteins, 30% to 40% albumin, and 20% to 30% various plasma proteins [5; 8]. Protein excretion is affected by three factors: prevention of excretion by the glomerular capillary wall, reabsorption and catabolism by the proximal tubule cells, and production of low-molecular-weight proteins [5; 8]. Depending on the cause of the increased levels, proteinuria is classified as either glomerular, tubular, or overflow [2; 8; 9]. Glomerular proteinuria is the most common type of persistent proteinuria, and albumin is the primary urinary protein present in these cases [9; 10]. Tubular proteinuria results when malfunctioning tubule cells no longer metabolize or reabsorb the protein that has been normally filtered. In this condition, low-molecular-weight proteins are the predominant type of protein, and the amount rarely exceeds 2 g/day [9]. Overflow proteinuria occurs when low-molecular-weight proteins overwhelm the ability of the tubules to reabsorb filtered proteins [9; 10].

DIAGNOSIS OF PROTEINURIA AND RELATED CONDITIONS

CLINICAL PRESENTATION

Patients with proteinuria range from healthy young adults with functional proteinuria related to prolonged exercise to seriously ill diabetic patients with nephrotic syndrome. Therefore, all individuals presenting for primary care should be screened for proteinuria by routine dipstick testing. Especially important is the routine screening of pregnant women. Proteinuria before 20 to 24 weeks' gestation indicates likely glomerulonephritis, whereas proteinuria after 24 weeks' gestation is usually a sign of pre-eclampsia [6].

Persistent proteinuria in patients with diabetes is usually a result of diabetic nephropathy. However, uncontrolled diabetes may cause transient proteinuria, most likely as a result of hyperfiltration and decreased tubular reabsorption [16].

PHYSICAL EXAMINATION

A complete and thorough history is essential for patients with proteinuria. Specific areas of focus should include recent acute or chronic illness, surgery, diagnostic procedures (especially those requiring contrast media), urinary frequency or symptoms suggesting infection, risk factors for human immunodeficiency virus (HIV) infection, medications taken (including over-the-counter medications), family history of renal disease or diabetes, and recent physical activity (especially exercise or cold-weather activities). The physical examination should be comprehensive and thorough. In the case of co-existent diabetes, the severity of the disease should be assessed to determine whether it correlates with the severity of proteinuria [2].

TESTS AND DIFFERENTIAL DIAGNOSIS

Proteinuria is usually detected on routine dipstick testing, and any value of 1+ or greater on two or more occasions should be investigated. Limitations of dipstick testing include false-negative results caused by dilution, an inability to detect low levels of microalbuminuria (although newer ultrasensitive dipstick tests may overcome this problem), false-positive results caused by certain medications, and an inability of dipstick reagents to detect light-chain proteins [2; 9; 17]. Patients with a positive dipstick test (for protein or any other component) should have routine microscopic urinalysis. Abnormalities on urinalysis (e.g., casts and dysmorphic red blood cells suggesting glomerulonephritis; glucose, ketones, or both suggesting diabetes) or disorders suggested by history and physical examination (e.g., peripheral edema suggesting a glomerular disorder) require further work-up [17].

After proteinuria has been identified, unless the cause is readily identified (e.g., pre-eclampsia, nephrotic syndrome, diabetes), the urine should be tested for Bence Jones proteins; if present, Bence Jones proteins suggest multiple myeloma [2]. In addition, a full blood chemistry panel with fasting blood glucose, a lipid profile, urine culture and sensitivity, and complete blood count (CBC) with differential are indicated. Further evaluation of persistent proteinuria usually includes determination of 24-hour urinary protein excretion or spot urinary protein/creatinine ratio, microscopic examination of urinary sediment, urinary protein electrophoresis, and additional assessment of renal function [10; 17].

Another important consideration is whether the proteinuria is persistent or transient [2]. Transient proteinuria secondary to an identifiable cause (e.g., exercise, fever, congestive heart failure) in an otherwise healthy patient may be classified as functional proteinuria and does not require further testing or evaluation [2; 8]. Persistent proteinuria that cannot be classified as functional proteinuria requires further investigation, beginning with a 24-hour measurement of urine protein and creatinine clearance to determine the urinary protein excretion and the protein/creatinine ratio [5; 17]. If the excretion rate is 3.5 g/day or more, the patient by definition has nephrotic syndrome, which is usually accompanied by hypoalbuminemia, hyperlipidemia, and edema [5; 9]. Nephrotic syndrome requires a nephrologist's evaluation [9; 17]. Systemic diseases that affect the kidneys are secondary causes of nephrotic syndrome. Diabetes is the leading secondary cause of nephrotic syndrome and accounts for more than 50% of all cases [2; 18].

If the 24-hour urinary protein excretion rate is less than 3.5 g/day, patients should be classified by their level of renal function (i.e., normal or abnormal). Proteinuria in the presence of normal renal function is referred to as isolated proteinuria. In these patients, the next step is to determine whether the proteinuria is orthostatic or nonorthostatic [2]. Urinary protein excretion can increase after prolonged standing, so three early-morning voids should be checked for protein. If all the results are negative, a diagnosis of orthostatic proteinuria can be made, and no further diagnostic tests are necessary [2]. However, these patients may benefit from referral to a renal specialist, as the condition is poorly understood, although generally benign and self-limited [2; 8; 17].

An alternative to 24-hour urine testing for total protein is the measurement of the urine protein/creatinine ratio obtained by a single spot urine collection. When the ratio of urine protein to urine creatinine is greater than 2 g/g, this corresponds to 3 g of urine protein per day or more [18].

Patients should be given specific instructions for collecting a 24-hour urine specimen [9]. Collection should start after the first morning void (which should be flushed) and continue to the next morning void (which should be collected) [18]. Patients should plan their collection for a day when they will be home to avoid voiding in a place where they cannot collect the urine.

Patients with nonorthostatic proteinuria and normal renal function without an elevation in Bence Jones proteins should be referred to a renal specialist. A renal biopsy may be needed to determine the cause of the proteinuria and subsequent treatment options [18]. If Bence Jones proteins are present, a serum protein electrophoresis test is warranted and a referral should be made for further evaluation to exclude multiple myeloma.

Other diagnostic tests depend on presentation and differential diagnosis. Collagen disease, glomerulonephritis, hepatitis-induced vasculitis, urate-related renal disease, and other systemic disease or structural abnormalities should be considered in the evaluation of proteinuria [6].

MANAGEMENT OF PROTEINURIA

Management of proteinuria obviously depends on the underlying cause, but some general principles apply. A careful medication review should be performed, and any medications implicated in proteinuria should be discontinued. Clinicians should be especially careful to fully question patients regarding all medications being used, as over-the-counter nonsteroidal anti-inflammatory drugs (NSAIDs) can be the cause of renal injury. Also, dietary supplements, protein powders, and body-building supplements should all be investigated for their potential to cause renal injury. Patient education is extremely important; many patients may feel that supplements bought at health food stores or health clubs are inherently safe.

Medications to decrease proteinuria may be prescribed. Angiotensin-converting enzyme (ACE) inhibitors and angiotensin-receptor blockers (ARBs) have been found to reduce proteinuria, most likely by decreasing intraglomerular pressure [2; 9; 19; 20]. Additionally, ACE inhibitors reduce the rate of deterioration of renal function in patients with diabetic and nondiabetic renal disease associated with proteinuria. ARBs protect renal function and delay the onset of ESRD [9]. Calcium channel antagonists (e.g., diltiazem, nifedipine) may help to reduce proteinuria [9].

Diabetes, hypertension, and hyperlipidemia, if present, should be appropriately managed. Patients with chronic renal failure should be treated aggressively to help prevent or delay the onset of ESRD. Sodium, potassium, and/or protein-restricted diets may be indicated for some patients, with associated patient education to help promote dietary compliance [9]. If available, consideration can be given for referral to a dietician and/or support groups for patients with renal disease and/or diabetes. Local hospitals often have a diabetes educator who can be a resource for patient education and referrals. Patients with proteinuria who also have chronic illnesses such as diabetes or hypertension may find disease management overwhelming. A diabetes educator may be able to provide support and serve as an advocate and resource for the patient.

No matter the cause, persistent proteinuria should be aggressively managed, both by controlling the underlying disease and by directing specific therapy (usually ACE inhibitors or ARBs) aimed at reducing protein excretion. The goal for treatment is protein excretion rates of 1 g/day or less (as measured by 24-hour urine sample for total protein) [9]. Higher rates have been shown to increase cardiovascular disease and risk of mortality.

INDICATIONS FOR REFERRAL OR HOSPITALIZATION

All patients with renal disease or abnormal renal function should be referred to a renal specialist for consultation and management guidance. Referrals for patients with isolated orthostatic proteinuria should be based on a thorough risk assessment and evaluation of their general health, lifespan considerations, and concerns for aggressive management. Patients with diabetes should be referred to diabetes education classes and to a dietician or diabetes educator. Patients with uncontrolled or poorly controlled diabetes and those with severe hyperlipidemia may be referred to an endocrinologist.

Any patients with nephrotic syndrome, acute renal failure, renal failure of unknown origin, or unstable vital signs should be urgently referred for hospitalization. New-onset proteinuria in pregnant women

should also be considered a potential medical emergency, and urgent referral to exclude pre-eclampsia is indicated.

PATIENT AND FAMILY EDUCATION

Specific patient education points will depend on the cause of proteinuria, but diet education, disease control strategies for patients with diabetes, and education concerning blood pressure management are necessary for most patients. It is especially critical that the patient and family understand the importance of diagnostic testing and regular follow-up care. Education regarding specific medication regimens is important, as patients will often be taking numerous medications. The clinician should ensure that the prescribed regimen is affordable for the patient. Many of the medications used to control proteinuria, including ACE inhibitors, ARBs, and statins, have at least one generic formulation available.

SPECIAL TOPICS IN PROTEINURIA

NEPHROTIC SYNDROME

Nephrotic syndrome is characterized by proteinuria, serum hypoalbuminemia, and edema. Hyperlipidemia may also be present. Nephrotic syndrome is defined by an excretion of protein in the urine of at least 3.5 g/day/1.73 m^2 of body surface area [21]. The pathophysiology of nephrotic syndrome is dependent on the underlying cause, but it is usually caused by disorders that damage the basement membrane of the glomerulus [1].

Pathophysiology

Studies suggest that primary nephrotic syndrome is likely a disease of the podocytes, a structure in the basement membrane of the glomerulus of the kidney [1]. The mechanism of damage to these structures is unknown, but evidence suggests that T cells either up- or downregulate a factor or factors that increase permeability of glomerular capillaries and cause proteinuria [21]. It is known that edema is most likely caused by reduced oncotic pressure, induced by a loss of protein via the urine and resulting in decreased serum albumin levels [1]. The presence of proteinuria may cause renal inflammation, resulting in increased sodium retention and worsening edema.

Symptoms

Patients most commonly notice edema as the first symptom of nephrotic syndrome [1]. Peripheral and facial edema, weight gain (from fluid retention), and abdominal ascites may be present. Most symptoms are the result of hypoalbuminemia. While patients may only notice the presence of edema, hypoalbuminemia has effects on many systems [18]. Complications can include impaired renal function, increased platelet aggregation, hyperlipidemia, increased drug toxicity, and abnormalities in blood volume [1; 21].

As noted, edema associated with increased protein excretion and resulting hypoalbuminemia is most likely due to the oncotic changes in intravascular pressure. The decreased amount of intravascular protein results in a drop in intravascular oncotic pressure, which then favors the movement of water from the intravascular into the interstitium, resulting in edema [1].

Hyperlipidemia may also be a result of nephrotic syndrome, although the exact mechanism remains unknown. It may be the result of decreased kidney metabolism and excretion of the cholesterol precursor mevalonic acid. Animal studies have demonstrated increased liver defects in nephrotic syndrome that can also result in increased cholesterol synthesis [1].

Nephrotic syndrome is also associated with hypercoagulability due to elevated levels of plasma fibrinogen. It is theorized that this is a result of increased hepatic synthesis [21]. Increased fibrinogen levels tend to correlate with increased plasma cholesterol levels [1]. Currently, no guidelines call for anticoagulation of patients with nephrotic syndrome, but patients with risk factors for cardiovascular disease and those at risk for deep vein thrombosis may be candidates for low-dose aspirin therapy according to their level of risk.

Diagnosis

The first step in evaluating nephrotic syndrome is determining if it is of primary or secondary etiology (***Table 2***). A primary nephrotic syndrome is due to a disease of the kidney, such as minimal change disease (the most common cause in children), focal segmental glomerulosclerosis, or membranous glomerulonephritis (the most common cause in adults) [1; 22]. Secondary nephrotic syndrome can be due to systemic infections (e.g. hepatitis), autoimmune disease (e.g. systemic lupus erythematosus), or diabetes (the most common cause) [22]. The role of testing for secondary causes is controversial because yield may be low. Tests are best done as indicated by clinical context [21]. Definitive diagnosis generally requires referral to a renal specialist, and renal biopsy may be necessary [21; 22].

CAUSES OF NEPHROTIC SYNDROME
Primary Causes
Minimal change disease
Focal segmental glomerulosclerosis
Membranous nephropathy
Secondary Causes
Diabetes
Pre-eclampsia
Hepatitis B or C
HIV
Systemic lupus erythematosus
Sarcoidosis
Sjögren syndrome
Amyloidosis
Hodgkin lymphoma
Leukemia
Malignancy
Infection
Drug reactions (e.g., NSAIDs)
Source: Compiled by Author — *Table 2*

Management

There are no consensus guidelines for the management of nephrotic syndrome. Disease-specific guidelines for secondary causes of nephrotic syndrome (such as those established for diabetes) should always be followed. While specific consensus guidelines for nephrotic syndrome do not exist, expert opinion does, especially for specific areas of syndrome management.

Nutrition

The loss of protein via proteinuria may result in serum hypoalbuminemia, which can alter platelet function. This can be compounded by nutritional deficits, especially when patients are already on restrictive diets due to underlying diabetes or renal disease. Supplementation with protein to correct low serum albumin should be supervised by a registered dietician. Sodium restriction may be necessary, and limits of 2 grams daily or less may be indicated [22]. Patients are often unaware of their true sodium intake, feeling that the elimination of supplemental sodium chloride is enough to attain dietary goals. Patient education is essential, and patients should be taught to properly read food labels. Special attention should be given to determining the total number of servings per container when reading food labels, which will help determine the total sodium content per container (not just per serving).

Pharmacotherapy

While many patients with secondary nephrotic syndrome will already be taking multiple medications, it is often necessary to add medications to address the specific symptoms and complications of the syndrome. Diuretics are generally necessary to control severe edema and fluid balance [18]. When dealing with fluid overload in the outpatient setting, it is important for both patients and clinicians to understand that too rapid of a diuresis can result in acute renal failure due to decreased renal blood flow. Therefore, clinicians should advise patients that a weight loss of approximately 1 to 2 pounds per day is the maximum target. Patients should be instructed to take their weight at the same time every day, preferably before breakfast. The clinician can leave "sliding scale" instructions with the patient for diuretic dosing. For example, if the patient notes a 2-pound weight gain in 24 hours, he or she should take an extra dose of diuretic, or if a 4-pound loss is noted, a dose should be skipped.

The most common diuretics used in the treatment of nephrotic syndrome are loop diuretics such as furosemide [18]. Furosemide is administered at a dose of 1 mg/kg/day, but the dose should be adjusted in the presence of renal failure [23; 24]. Side effects include low potassium and, with larger doses, ototoxicity. Patients should be advised that furosemide has a duration of action of approximately six hours [24]. If they will not have access to a bathroom, either the dose timing or travel plans must be adjusted. Patient compliance can be greatly influenced by the desire not to experience incontinence. Careful education can help avoid this potentially embarrassing complication and promote long-term compliance with the prescribed regimen.

Patients should also be told to report symptoms of low potassium (e.g., muscle cramping) or ototoxicity (e.g., tinnitus). To avoid the side effects of a high-dose single agent and to take advantage of synergistic interactions, combinations of diuretics can be used. Other diuretics include spironolactone (a potassium-sparing diuretic in the class of aldosterone receptor antagonists), hydrochlorothiazide (a thiazide diuretic), or metolazone (a novel quinazoline diuretic) [18]. A loop diuretic in combination with a potassium-sparing diuretic can result in less hypo- or hyperkalemia, common side effects when spironolactone is used as monotherapy. It is important to be aware of the potential side effects of the aldosterone receptor antagonist, as they are quite different than those usually associated with diuretics. The most common side effect is hyperkalemia, and serum potassium levels should be monitored, especially in patients with decreased renal function. Other side effects include gynecomastia in men and menstrual irregularities in women. In men, eplerenone may be preferable to spironolactone as it has the same action without the potential for gynecomastia. However, it is not available in a generic form and is considerably more expensive.

In patients with secondary nephrotic syndrome, ACE inhibitors are often prescribed both for their antihypertensive effect and ability to reduce proteinuria [18]. Many renal specialists will prescribe ACE inhibitors even to normotensive patients with nephrotic syndrome in order to decrease proteinuria. Evidence for benefit exists for the use of both ACE inhibitors and ARBs to help reduce the progression of renal disease in diabetic and nondiabetic patients with chronic renal disease [25]. Both drugs may cause or exacerbate hyperkalemia in patients with moderate-to-severe renal insufficiency [21].

Lipid-lowering agents such as statins may be needed when nephrotic syndrome is accompanied by hyperlipidemia [21]. Disease-specific guidelines should be followed when controlling cholesterol levels in these patients.

Corticosteroids can be useful in the treatment of nephrotic syndrome, particularly in cases of primary nephrotic syndrome that does not respond to conservative treatment, but adverse effects are common [26]. Some small studies have examined the use of corticosteroids in adults with minimal change disease, membranous nephropathy, and focal segmental glomerulosclerosis, with mixed results [27]. Due to the high prevalence of minimal change disease in children with nephrotic syndrome, an empiric trial of corticosteroids is commonly the first step in therapy [28].

Management of Hypertension

Blood pressure management in patients with nephrotic syndrome is important for many reasons. Strict control of blood pressure can decrease the progression of renal disease and the risk for cardiovascular events. Many patients with nephrotic syndrome have multiple risk factors for cardiovascular disease, and it should always be remembered that cardiovascular disease is the leading cause of death in renal failure patients [1].

Antihypertensive regimens may include the use of ACE inhibitors, ARBs, calcium channel blockers, diuretics, or beta-blockers. In particular, agents that block the renin angiotensin system, including ACE inhibitors and ARBs, appear to lower the risk of cardiovascular disease in patients with proteinuria [18; 25]. Goals for blood pressure management specific to patients with nephrotic syndrome do not exist, but experts suggest that a guideline of less than 130/80 mm Hg should be followed in all patients with hypertension and renal disease [25]. Use of a home blood pressure monitoring system and follow-up to ensure response to therapy can be useful in attaining blood pressure goals.

Patient and family education regarding blood pressure is an important aspect of care. Patients may be taking multiple medications, making compliance difficult even for motivated patients. Nurses can be instrumental in forming a therapeutic relationship with the patient that allows him or her to feel comfortable discussing issues of cost, access, side effects, and struggles with compliance.

PROTEINURIA AND PREGNANCY

Even in normal pregnancy, urinary protein excretion increases to a maximum of 300 mg/day, which correlates with approximately 1+ on a standard dipstick. Rates greater than this level require investigation. As noted, excessive proteinuria prior to 20 to 24 weeks' gestation is suggestive of glomerulonephritis, while proteinuria (especially in combination with hypertension) after 24 weeks' gestation is generally indicative of pre-eclampsia. Pre-eclampsia is of particular concern as it can lead to fetal and maternal death if left untreated [1; 29].

Pre-eclampsia is defined as proteinuria greater than or equal to 300 mg in a 24-hour urine specimen, a protein/creatinine ratio of 0.3 mg/dL or higher, or a urine dipstick protein of 1+ and hypertension (systolic blood pressure greater than 140 mm Hg or diastolic blood pressure greater than 90 mm Hg) after 20 weeks' gestation in a woman who was normotensive before 20 weeks' gestation [30; 31]. Higher rates of proteinuria are indicative of more severe disease [31]. Pre-eclampsia affects 2% to 6% of all pregnancies and is a leading cause of maternal death [30; 31]. The global incidence of pre-eclampsia has been estimated at 5% to 14% of all pregnancies [31]. Risk factors include advanced maternal age (older than 35 years), pre-existing hypertension or renal disease, obesity, diabetes, urinary tract infection, and multiple pregnancy. All patients should be screened for pre-eclampsia and treated immediately [1; 31]. The only cure is delivery, and worsening pre-eclampsia may necessitate early delivery [31]. Up to 16% of all eclamptic seizures actually occur more than 48 hours after delivery, so clinicians should be alert to symptoms of impending eclampsia, including headache, visual disturbances, abdominal pain, and increasing edema.

CASE STUDIES: PROTEINURIA

CASE STUDY 1

Patient G is a woman, 54 years of age, who was diagnosed with type 2 diabetes 20 years previously. She is currently taking metformin 1 gram twice every day and glyburide 5 mg twice daily. She is also prescribed amlodipine 10 mg/day for control of hypertension. At her yearly physical, Patient G is found to have a blood pressure of 154/86 mm Hg and a body mass index of 31. Her laboratory tests reveal a glycosylated hemoglobin (HbA1c) level of 9.4%, blood urea nitrogen (BUN) of 38 mg/dL, and a serum creatinine of 1.2 mg/dL. A routine urine dipstick performed in the office is negative. A urine test for microalbumin is sent to the laboratory, and the results show urine albumin of 125 mg/day, indicating microalbuminuria.

***Comments and rationale**: Proteinuria is one of the first signs of renal disease in patients with diabetes, and all type 2 diabetics should be screened yearly for microalbuminuria. It is unclear when Patient G was last screened, but she may be at risk for diabetic nephropathy.*

Patient G is started on lisinopril 5 mg per day. She is asked to return in two weeks for a blood pressure check and to get repeat laboratory studies drawn.

At her return appointment, Patient G's blood pressure is 143/78 mm Hg, and her blood workup reveals a potassium level of 4.6 mEq/L and a serum creatinine level of 1.3 mg/dL.

***Comments and rationale**: ACE inhibitors, such as lisinopril, can cause a mild elevation in serum creatinine, likely due to decreased glomerular filtration, but this is not indicative of damage. Although it may appear that the patient's disease is worsening, ACE inhibitors are renal protective, as they appear to decrease the hyperfiltration that causes continuing renal injury. However, clinicians should always be aware of the need to modify prescribing based on a patient's renal function. Metformin is contraindicated in patients with elevated serum creatinine. Generally, women with a serum creatinine greater than 1.3 mg/dL and men with a serum creatinine greater than 1.4 mg/dL should not be prescribed metformin due to the increased risk of lactic acidosis.*

Patient G is eventually titrated up to a dose of 40 mg of lisinopril. Although her blood pressure is now within the goal range at 124/73 mm Hg and her proteinuria has decreased to 40 mg/day, she has developed a persistent, dry cough that is worse at night.

***Comments and rationale**: The development of a persistent, non-productive cough is a common occurrence in patients taking ACE inhibitors. Although the exact rate is unknown due to likely under-reporting, up to 20% of all patients taking ACE inhibitors develop a cough. The only known curative treatment for ACE inhibitor-associated cough is stopping the medication, and resolution of the cough may take several weeks after the discontinuation of the medication. However, there are several medications that have been reported to be of benefit for cough suppression in patients for whom halting use of the ACE inhibitor is prohibited, including sodium cromoglycate, theophylline, sulindac, indomethacin, amlodipine, nifedipine, ferrous sulfate, and picotamide.*

Patient G and her primary care provider discuss the benefits of ACE inhibitor therapy versus the discomfort of her current cough. Both are quite pleased with the decrease in the patient's proteinuria. The primary care provider discusses possibly switching to an ARB, which has shown benefit in decreasing proteinuria but does not induce cough. After carefully discussing the options and researching the subject, Patient G decides to stay on the ACE inhibitor. She has several relatives on dialysis and is motivated to avoid the consequences of chronic kidney disease. She tells her clinician that her research has revealed that ACE inhibitors have the strongest evidence for the prevention of the progression of renal disease in diabetic patients with proteinuria.

***Comments and rationale**: Clinicians should welcome an educated and motivated patient but also be aware that patients may obtain questionable or biased information in their own searches. It is important that clinicians have an understanding of available Internet resources and suggest reputable sites that can serve as a basis from which patients can begin their searches (**Resources**).*

CASE STUDY 2

Patient K is a man, 52 years of age, who works as a computer programmer. He presents to his primary care practitioner for an initial visit due to lower extremity edema. He denies chest pain, shortness of breath, polydipsia, or polyuria. He states that he is a smoker, having smoked one pack per day for the past 35 years. Patient K's family history is significant for his father dying from myocardial infarction at 64 years of age. He has no siblings. He does admit to occasional binge drinking and previous cocaine use.

On physical exam, Patient K appears tired. His vital signs are: blood pressure 153/67 mm Hg; pulse 84 beats per minute; respirations 18 breaths per minute; temperature 98˚F; weight 223 pounds; and height 6 feet. Physical examination reveals 2+ edema of the lower extremities and slight crackles at the bases of the lungs. Initial laboratory studies reveal a low serum albumin of 2.8 g/dL and an elevated cholesterol of 420 mg/dL. His triglycerides are 1400 mg/dL, and his fasting glucose is 103 mg/dL. His BUN is 28 mg/dL, and serum creatinine is 1.4 mg/dL. A urine dipstick test is performed in the office.

It indicates 2+ protein, but no blood or glucose. A chest x-ray reveals slight bilateral infiltrates.

***Comments and rationale**: Patients with nephrotic syndrome often present with edema as their initial symptom. Although diabetes is the leading cause of nephrotic syndrome, other potential causes include infection (e.g., HIV, hepatitis), autoimmune syndrome, drug toxicity, and primary kidney disease.*

Further laboratory studies reveal that Patient K is positive for hepatitis C, with a viral load of 3 million copies/mL. He is negative for HIV. The patient's HbA_{1c} is 5.9%, and a 24-hour urine is positive for 3.7 grams of protein and a glomerular filtration rate of 57 mL/min/1.73 m^2. He is referred to a nephrologist who confirms the diagnosis of nephrotic syndrome secondary to hepatitis C. The nephrologist starts the patient on an ACE inhibitor in an attempt to reduce the proteinuria, a low-dose diuretic to decrease edema, and atorvastatin to reduce the serum cholesterol level. Patient K is further referred to a liver specialist for treatment of his hepatitis C and to a dietician for diet counseling.

***Comments and rationale**: Treatment of nephrotic syndrome should address the primary cause of the syndrome as well as any associated lipid disorders, proteinuria, and edema. Dietary consultation may be necessary for many reasons, including low serum albumin, hyperlipidemia, weight management, and counseling regarding salt intake.*

Six months later, Patient K has started interferon and ribavirin treatment for hepatitis C and his viral load is now undetectable. His proteinuria and hyperlipidemia have decreased significantly, and he has made significant lifestyle changes, including being tobacco-free for the last two months.

***Comments and rationale**: Lifestyle changes, such as diet, exercise, and eliminating use of drugs (including nicotine) and alcohol, are important in managing nephrotic syndrome. Nurses and dieticians are essential in helping to educate and motivate patients. Frequent visits may be needed, and clinicians should be careful not to overwhelm patients with a large amount of information at one time. Clinicians should also use easily understood printed materials that patients can take home and refer to frequently.*

DEFINITION AND EPIDEMIOLOGY OF HEMATURIA

Hematuria is generally defined as more than three red blood cells (RBCs) per high-powered field (HPF) [32]. Transient hematuria is hematuria that occurs on one occasion, whereas persistent hematuria is present on two or more consecutive tests [2; 10]. Exercise-induced hematuria in healthy young adults is not associated with any known morbidity or mortality, but both transient and persistent hematuria can be signs of serious disease (***Table 3***).

The rates for hematuria in the general population vary with gender and age. Population-based studies have shown prevalence rates from less than 1% up to 21% [33; 34]. One study of 1,000 men 18 to 33 years of age documented rates of transient hematuria of 38.7%, with virtually all patients found to have no serious disease [8]. Other studies have documented rates of transient hematuria up to 13% in postmenopausal women, again with relatively no serious pathologic conditions identified [2]. However, in men older than 50 years of age, even transient hematuria may be an indication of more serious disease, with up to 2.4% of hematuria in this group linked to malignancy [2]. Gross hematuria in older men denotes a significant risk of malignancy, with documented rates as high as 21% [35].

EVIDENCE-BASED PRACTICE RECOMMENDATION

The American College of Physicians recommends clinicians should heme-positive results of dipstick testing with microscopic urinalysis that demonstrates three or more erythrocytes per high-powered field before initiating further evaluation in all asymptomatic adults.

(https://www.acpjournals.org/doi/10.7326/M15-1496. Last accessed May 20, 2024.)

Level of Evidence: Expert Opinion/Consensus Statement

COMMON CAUSES OF HEMATURIA	
Category	**Possible Causes**
Glomerular	Glomerulonephritis Lupus nephritis Interstitial nephritis Pyelonephritis Vasculitis Alport syndrome
Nonglomerular	Infection Neoplasm of the bladder, ureter, prostate, or kidney Renal or bladder calculi Polycystic kidney disease Sickle cell (disease or trait) Trauma Increased bleeding time Hemorrhagic cystitis Schistosomiasis Nutcracker phenomenon
Pseudohematuria	Menstrual contamination Hemoglobinuria Myoglobinuria Porphyrins Red food dyes Certain medications (e.g., phenytoin, quinine, rifampin, phenothiazines)
Miscellaneous	Medication Exercise Endometriosis
Source: Compiled by Author	*Table 3*

PATHOPHYSIOLOGY OF HEMATURIA

Normal urinary excretion of RBCs is approximately 1 to 2 million/day, or one to three RBCs per high-power field [6]. Isolated hematuria (unaccompanied by any other abnormal urine components) can result from bleeding anywhere from the renal pelvis to the urethra, but it is rarely caused by systemic disease [6]. Hematuria related to renal disease begins at the tubular field along the nephron and produces RBC casts that are indicative of the renal origin [5; 6; 36]. Bacterial infections are a common cause of hematuria, and the presence of bacteria on urinalysis is suggestive of an infectious cause. Acute cystitis or urethritis can cause gross hematuria and is more common in women than in men [36; 37]. The presence of both proteinuria and hematuria is suggestive of glomerular or interstitial nephritis [5].

DIAGNOSIS OF HEMATURIA

CLINICAL PRESENTATION

Hematuria is often accompanied by clinically significant symptoms or by abnormalities in the urinalysis that can aid in identifying the source of bleeding. The patient's age, gender, and level of physical activity should always be considered. A high level of exercise is considered a risk factor, and long-distance runners have been documented to have rates of hematuria as high as 18% [6]. Hematuria with pyuria suggests an infectious process, whereas colicky flank pain suggests pain originating from a ureter [6]. A prostatic or urethral source is likely when bleeding occurs only at the beginning or end of micturition [5; 25]. The combination of hemoptysis, acute renal failure, and hematuria is highly suggestive of Goodpasture syndrome, a rare autoimmune disease affecting the lungs and kidneys [38]. Glomerulonephritis is signified by hematuria accompanied by edema, hypertension, and a sore throat or skin infection, although many patients do not report any recent signs or symptoms of infection [37; 39; 40].

PHYSICAL EXAMINATION

For all persons presenting with hematuria, a thorough patient history should be obtained, including urinary patterns; urine color, timing of hematuria (beginning, end, or throughout micturition; transient or persistent); flank or back pain; history of renal calculi, urinary tract infections, hemoptysis, or bloody nasal secretions; recent acute or chronic illness; medications (including over-the-counter and illicit drugs); history of sexually transmitted infection; risk for HIV infection; and history of travel to areas with endemic schistosomiasis (e.g., Africa, Southeast Asia), the leading cause of hematuria outside the United States [32; 41]. A complete family history specifically related to renal disease, sickle cell disease or traits, and congenital deafness (indicating

Alport syndrome) is also necessary [32; 40]. A comprehensive physical examination, including a pelvic examination in women and a prostate examination in men, is warranted [32].

TESTS AND DIFFERENTIAL DIAGNOSIS

The most important diagnostic element for hematuria is the urinalysis [40]. A urinalysis with RBC casts indicates hematuria originating from the renal parenchyma [42]. Further evidence of a renal source is significant proteinuria (more than 1 g/day), dysmorphic RBCs, brown-tinted or cola-colored urine, or renal insufficiency [5; 6]. One major limitation of dipstick testing is that it detects the peroxidase activity of erythrocytes, not RBCs, in the urine. Myoglobin and hemoglobin will also catalyze this reaction, so a positive test may indicate hematuria, myoglobinuria, or hemoglobinuria [40]. If the dipstick is positive for heme but no increased numbers of RBCs are seen by microscopic examination, the urine should be tested for myoglobinuria and hemoglobinuria [25; 40]. All positive dipstick results and all negative results with a high index of suspicion should undergo microscopy and should be evaluated within one hour, before casts begin to disintegrate and RBCs start to lyse [40].

Causes of hematuria can be categorized as glomerular, renal (i.e., nonglomerular), or urologic. Glomerular hematuria is typically associated with significant proteinuria, erythrocyte casts, and dysmorphic RBCs [40]. However, 20% of patients with biopsy-proven glomerulonephritis present with hematuria alone [10]. Immunoglobulin A nephropathy (Berger disease) is the most common cause of glomerular hematuria [10; 40]. Nonglomerular or renal hematuria is due to tubulointerstitial, renovascular, or metabolic disorders. There is often co-existing proteinuria but no dysmorphic RBCs or erythrocyte casts [40]. The evaluation of glomerular and nonglomerular hematuria requires an assessment of renal function and 24-hour urine or spot urinary protein/creatinine ratio. Urologic causes of nonglomerular hematuria include tumors, calculi, and infections. This etiology is distinguished from other types of hematuria by the absence of proteinuria, dysmorphic RBCs, and erythrocyte casts [40]. Up to 20% of older patients with gross hematuria have a urinary tract malignancy, so a full workup, including cystoscopy and imaging of the upper urinary tract, should be completed in patients with hematuria of suspected urologic origin [10]. Despite this recommendation, studies have found that only 18% of patients presenting with hematuria undergo proper evaluation. African American patients are less likely than white patients to undergo any aspect of evaluation, and women are less likely to be referred to a urologist than men [43; 44].

When hematuria originates from the lower urinary tract, intact and uniform RBCs are generally found [8; 36; 45]. The presence of intact RBCs, white blood cells (WBCs), and bacteria suggests hematuria resulting from a urinary tract infection [40]. The decision to obtain a urine culture and sensitivity should be guided by the patient's age and gender and the presence of resistant organisms in the local population [46]. After treatment has been completed, a repeat urinalysis is necessary to ensure that the hematuria has resolved. Failure to follow hematuria to resolution may result in failure to diagnose a serious condition, one that may have contributed to the development of the original urinary tract infection. If symptoms are suggestive of a urinary tract infection despite a negative urine culture, a diagnosis of chlamydia or renal tuberculosis should be investigated [5; 6].

If hematuria resolves after treatment of the urinary tract infection, no further diagnostic testing is indicated. However, repeat urinary tract infections in low-risk populations, such as young men, should always be fully investigated [34]. If hematuria fails to resolve despite resolution of the urinary tract infection or if it is of renal origin, referral for a urologic evaluation is required [36].

In the absence of RBC casts, bacteria, or WBCs, a urologic evaluation should be performed, usually with spiral computed tomography (CT) of the abdomen and pelvis, both with and without contrast [34]. If the CT shows a solid mass or is nondiagnostic, referral to a urologic surgeon for excision and pathologic testing is advised [47]. The presence of renal or bladder calculi generally requires urologic referral for definitive treatment. If the CT is nondiagnostic, the next step in the evaluation is cystoscopy, which includes inspection, biopsy, and culture of the bladder tissue. Cystoscopy is highly diagnostic for uroepithelial neoplasms [32; 48]. Because the probability of urinary tract malignancy is low in patients younger than 35 years of age, for these patients, cystoscopy should be performed at the discretion of the urologist [34]. If the cystoscopy is nondiagnostic, the urologist may request a renal biopsy. If evaluation does not reveal nephrologic or urologic disease, then an annual urinalysis should be performed for a minimum of two years following the initial referral. If no persistent hematuria is detected, the risk of future malignancy is less than 1% and the patient may be released from care. If asymptomatic microscopic hematuria persists, consider performing a full repeat evaluation within three to five years [32; 50; 51].

MANAGEMENT OF HEMATURIA

Management of hematuria consists mainly of identification, diagnosis, and referral. Further management considerations are based on the underlying pathologic condition, not on the presence of the hematuria itself [40]. Treatment of complications may be indicated in some cases. Complications of hematuria depend on the underlying pathologic condition and can include urinary obstruction, renal failure, anemia, infection, and hydronephrosis. Guidelines from the American College of Physicians have advised that clinicians include gross hematuria in their routine review of systems and that they ask all patients with microscopic hematuria about any history of gross hematuria [52]. The American Urological Association advises clinicians to gather a detailed, probative history to aid in the differential diagnosis of hematuria [49].

INDICATIONS FOR REFERRAL OR HOSPITALIZATION

Isolated, transient hematuria and hematuria related to a urinary tract infection do not require urology consultation. However, referral to a renal or urology specialist is indicated to evaluate other causes of hematuria. Patients with large amounts of frank hematuria, severe flank pain suggestive of renal calculi, unstable vital signs, signs of urologic obstruction, or acute renal failure should be referred for urgent evaluation and possible hospitalization.

PATIENT AND FAMILY EDUCATION

Patient education largely depends on the cause of the hematuria; advice and educational material specific to the underlying pathologic process are appropriate. As smoking is a major risk factor for urologic malignancies, smoking cessation assistance should be offered to all smokers. One of the major goals of education in asymptomatic hematuria is to reinforce the importance of the diagnostic evaluation. Other guidance should focus on the explanation of tests, medications, untoward effects, and the need for careful follow-up evaluation when indicated.

SPECIAL TOPICS IN HEMATURIA

NEPHRITIC SYNDROME

Nephritic syndrome, not to be confused with nephrotic syndrome, is an inflammation of the kidneys that causes damage to the podocytes, one of the structures in the glomeruli [53]. The damage causes holes in the podocytes large enough for RBCs to pass through, resulting in hematuria. Nephritic syndrome often results in proteinuria, but usually at rates lower than those seen in nephrotic syndrome. In addition, the presence of RBCs differentiates nephritic syndrome from nephrotic syndrome (proteinuria in the absence hematuria). One of the most common causes of nephritic syndrome in adults is systemic lupus erythematosus (SLE) [53].

LUPUS NEPHRITIS

Lupus nephritis is a common life-threatening symptom of SLE. Lupus nephritis increases the risk for ESRD and can cause serious morbidity and mortality [54]. The goals of treatment of lupus nephritis include early detection, early referral to a nephrologist, attaining and maintaining remission, and preservation of renal function.

Early Detection

Early detection of lupus nephritis should begin with frequent outpatient visits for all lupus patients (including those with no current symptoms) and dipstick analysis of urine at all patient visits, with special emphasis on patients with known risk factors for development of lupus nephritis and patients at increased risk for ESRD [55]. Race may be one of these risk factors. SLE is most common in African American and Hispanic individuals; severe lupus nephritis is more common in African American and Asian patients than in any other ethnic group [54; 55]. Other risk factors for progression of lupus nephritis include genetic predisposition, lower socioeconomic status, elevated serum creatinine, and failure to achieve remission. Early detection is associated with improved outcomes and may help to provide better access to available treatments [55].

Treatment

The goal of treatment for lupus nephritis is to normalize renal function or, at a minimum, to prevent the progressive loss of renal function [55]. The mainstay of treatment for lupus nephritis is corticosteroids and the immunosuppressive medications azathioprine, cyclophosphamide, or mycophenolate mofetil [54; 56; 57]. Two newer therapies include the monoclonal antibody belimumab and the calcineurin inhibitor voclosporin. Belimumab is approved for use in adults with active lupus nephritis who are receiving standard therapy. Voclosporin is approved for use in conjunction with immunosuppressive treatment [24; 55]. Co-existing hypertension should be treated aggressively, and the patient's diet should be altered in the presence of hypertension, hyperlipidemia, and renal insufficiency. Calcium supplementation may be offered if the patient is on long-term corticosteroid therapy. Avoid NSAIDs in patients with elevated creatinine levels [55]. Patients with active lupus nephritis should avoid pregnancy, as it may worsen their renal disease and certain medications used in treatment may be teratogenic [55; 58; 59; 60].

While mild lupus with arthritis symptoms may be treated with NSAIDs or hydroxychloroquine, lupus nephritis is life-threatening and demands a rapid response. Referral to a rheumatologist is essential. Unfortunately, high-dose corticosteroid treatment often results in multiple side effects, and patient adherence may suffer as a result. Patients may experience weight gain, steroid-induced diabetes, osteoporosis, cataracts, and psychiatric side effects including mania, psychosis, and depression.

CASE STUDIES: HEMATURIA

CASE STUDY 1

Patient W is a man, 59 years of age, with a history of smoking one pack per day for 40 years. He presents to his primary care provider with a 24-hour history of gross hematuria. Urinalysis reveals 30 RBCs per HPF. He denies burning on urination, flank pain, frequency, or fever. Patient W's primary care provider orders a CT of the pelvis with and without contrast and sends urine for cytology. She also arranges for urologic consultation.

***Comments and rationale**: Although hematuria is generally a benign finding, Patient W has several factors that are predictive of increased risk of malignancy, including older age, male gender, and greater hematuria (more than 25 RBCs per HPF). Gross hematuria is generally a urologic problem. While hematuria in men younger than 40 years of age is generally a benign finding, gross hematuria in men older than 50 years of age is a result of neoplasm in up to 25% of cases.*

Although the CT scan and urine cytology are both negative, Patient W's urologist recommends a cystoscopy, due to his history of smoking and age. Cystoscopy shows a small superficial growth on the bladder wall, and pathology is positive for transitional cell cancer.

***Comments and rationale**: Smoking is associated with one-half of all bladder cancers. While there are identifiable risk factors for bladder cancer, such as smoking, there are currently no recommendations for routine screening of at-risk individuals.*

Patient W's urologist reviews the cystoscopy findings and pathology report with him, as well as his previous CT report. Based on the results of these tests, the patient is diagnosed with transitional cell cancer of the bladder wall that does not involve the bladder muscle, classified as non-muscle-invasive disease. His urologist further informs him that while his disease has a potentially far better outcome than muscle-invasive disease, his staging is still based on the pathology of the tumor as well as the presence or absence of positive regional lymph nodes and the presence or absence of distant metastatic disease. He is told that his tumor is a T1 tumor that has invaded the subepithelial connective tissue. Because there are no positive regional lymph nodes or distant metastatic disease, his complete staging is T1N0M0. Patient W is scheduled for transurethral resection of the bladder tumor (TURBT).

***Comments and rationale**: Outcomes for bladder cancer patients vary widely depending on disease progression at time of presentation. Disease can be as low grade as noninvasive papillary carcinoma or as high grade as tumors that have invaded the pelvic and abdominal wall and have distant metastatic disease.*

TURBT is the first step in the management of non-muscle-invasive bladder cancer. A TURBT is accomplished via cystoscopy, and it allows for both visualization and removal of suspicious tissue, thereby aiding both diagnosis and treatment. Tumors are completely resected, and other than for superficial appearing low-grade tumors, muscularis propria must be included in the removed tissue to ensure resection of all cancerous tissue. Management might include directed bladder biopsies of abnormal appearing urothelium or biopsies of the prostatic urethra to exclude difficult to visualize cancer. Biopsy or resection of the prostatic urethra also should be considered if the patient has tumor of the bladder neck or if the tumor is within the prostatic urethra.

CASE STUDY 2

Patient S is a woman, 35 years of age, who was diagnosed with lupus 12 years previously. She has had a reasonably mild course, having been treated with hydroxychloroquine and low-dose ibuprofen as needed for joint pain. She presents to her primary care practitioner with fatigue and peripheral edema. Laboratory analysis reveals a BUN of 68 mg/dL, serum creatinine of 2.8 mg/dL, hematocrit of 28%, and serum albumin of 2.3 g/dL. A urine dipstick performed in the office is positive for blood and 1+ protein. A tentative diagnosis of lupus nephritis is made, and Patient S is urgently referred to her rheumatologist.

***Comments and rationale**: Early detection of lupus nephritis is essential to reduce morbidity and mortality. The goals of treatment should include reduction in proteinuria and slowing of the disease progression. Corticosteroids in combination with immunosuppressants (cyclophosphamide, azathioprine, and mycophenolate mofetil) are the mainstay of treatment. Use of immunosuppressants is associated with reduced mortality and improved renal outcomes. Clinicians should be aware of the side effects of prescribed medications and should educate patients both of possible side effects and management techniques. While patients may initially resist referral to a mental health provider, the provision of mental health services can be very beneficial, both in helping to manage the psychiatric side effects of treatment and to support the patient in the long term. Many patients with systemic lupus erythematosus experience stress and severe depression. Corticosteroids can cause multiple side effects ranging from insomnia, weight gain (with resultant change in body image), hypomania, psychosis, depression, and irritability.*

Few diseases call for as much clinician support and education as systemic lupus erythematosus. Patients with lupus nephritis may feel overwhelmed and hopeless, but a caring clinician can help empower patients by educating them regarding disease management, proper diet and medication adherence, and a healthy lifestyle.

CONCLUSION

Although isolated proteinuria and hematuria are not necessarily associated with excess morbidity and mortality, they can be signs of serious systemic disease. Certain population groups, including African Americans, Native Americans, Hispanic Americans, and Pacific Islanders, are at increased risk for developing these signs. Aging and obesity are also risk factors. As clinicians' patient populations diversify and age, proteinuria and hematuria will become more common. The information provided in this course should assist healthcare professionals in fully appreciating the wide range of conditions that can result in proteinuria and/or hematuria. Early identification and treatment of underlying causes of these seemingly common findings can help save lives and improve quality of life.

RESOURCES

American Cancer Society
https://www.cancer.org

American Diabetes Association
https://www.diabetes.org

American Kidney Fund
https://www.kidneyfund.org

Lupus Foundation of America
https://www.lupus.org

National Cancer Institute
https://www.cancer.gov

National Kidney Foundation
https://www.kidney.org

National Institute of Diabetes and Digestive and Kidney Diseases
https://www.niddk.nih.gov

Implicit Bias in Health Care

The role of implicit biases on healthcare outcomes has become a concern, as there is some evidence that implicit biases contribute to health disparities, professionals' attitudes toward and interactions with patients, quality of care, diagnoses, and treatment decisions. This may produce differences in help-seeking, diagnoses, and ultimately treatments and interventions. Implicit biases may also unwittingly produce professional behaviors, attitudes, and interactions that reduce patients' trust and comfort with their provider, leading to earlier termination of visits and/or reduced adherence and follow-up. Disadvantaged groups are marginalized in the healthcare system and vulnerable on multiple levels; health professionals' implicit biases can further exacerbate these existing disadvantages.

Interventions or strategies designed to reduce implicit bias may be categorized as change-based or control-based. Change-based interventions focus on reducing or changing cognitive associations underlying implicit biases. These interventions might include challenging stereotypes. Conversely, control-based interventions involve reducing the effects of the implicit bias on the individual's behaviors. These strategies include increasing awareness of biased thoughts and responses. The two types of interventions are not mutually exclusive and may be used synergistically.

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