CLINICAL PRACTICE

Microscopic Hematuria

Robert A. Cohen, M.D., and Robert S. Brown, M.D.

This Journal *feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the authors' clinical recommendations.*

An otherwise healthy 48-year-old woman is found to have microscopic hematuria (5 red cells per high-power field) on a urinalysis performed by a life insurance company. No other laboratory abnormalities are identified; the serum creatinine concentration is 0.8 mg per deciliter (70.7 μmol per liter). The woman reports no symptoms and is a nonsmoker. Her blood pressure is 118/74 mm Hg, and the findings on physical examination are normal. How should she be evaluated?

THE CLINICAL PROBLEM

From the Division of Nephrology, Department of Medicine, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston. Address reprint requests to Dr. Cohen at the Division of Nephrology, Beth Israel Deaconess Medical Center, 330 Brookline Ave., DA517, Boston, MA 02115, or at rcohen@bidmc.harvard.edu.

Microscopic hematuria without proteinuria is often an incidental finding. Since bleeding may arise from any site along the urinary tract, it has a broad differential diagnosis, possibly reflecting an entirely benign cause, such as vigorous exercise just before urine collection, or a malignant, potentially lethal disease, such as bladder or renal cancer. Even with a thorough investigation, the source of the microscopic hematuria frequently is not found. We focus here on the evaluation of microscopic hematuria in persons older than 18 years of age.

DEFINITIONS

We define microscopic hematuria as 2 or more red cells per high-power field on microscopical examination.[1,2] Definitions vary, however, from 1 to more than 10 red cells per high-power field.[2] Dipstick testing for heme may be too sensitive, detecting hemoglobin from 1 or 2 red cells per high-power field. Such testing also lacks specificity, since the presence of myoglobin or hemoglobin may result in a positive test when the urine contains no red cells. Therefore, if the dipstick test is positive, the presence of red cells should be confirmed by microscopical examination.

There have been only a few population-based studies addressing the prevalence of microscopic hematuria, and their results vary according to the age and sex distribution of the populations studied, whether the diagnosis was based on the dipstick test alone or that test coupled with microscopical evaluation, and the number of screening tests performed per patient. In six studies, the prevalence ranged from 0.18 percent to 16.1 percent.[3,4] Only two studies report a higher prevalence among women than among men.[2] Although some studies suggest that there may be an increased prevalence among older persons,[2] others show no difference according to age.[5]

Microscopic hematuria also may be transient. In a study of male soldiers who underwent yearly examinations of urinary sediment over a 12-year period, the cumulative incidence was 39 percent with microscopic hematuria on one examination and 16 percent with microscopic hematuria on two or more examinations.[6] In another study, transient microscopic hematuria was noted in about 13 percent of postmenopausal women.[5] Transient microscopic hematuria may be caused by vigorous exercise before urine collection, by sexual intercourse, by mild trauma, or by menstrual contamination. There are

no data on differences between patients with transient microscopic hematuria and those with persistent microscopic hematuria with regard to the likelihood of underlying urinary tract disease.

CLINICAL RELEVANCE

Causes of isolated microscopic hematuria (without proteinuria) are listed in Table 1 and can be classified as either glomerular or nonglomerular in origin. Because renal biopsies are not typically part of the evaluation of microscopic hematuria, it is difficult to estimate the percentage of cases that are clearly attributable to glomerular bleeding. In a study involving 157 men in whom renal biopsy was performed when no cause of microscopic hematuria had been identified by other tests, a glomerular source was identified in 16 percent of the patients. IgA nephropathy, a form of glomerulonephritis defined histologically by glomerular IgA deposits, accounted for the majority of cases with a glomerular source.[7] In a series of 165 patients, renal biopsies were performed after renal imaging and cystoscopy. No abnormalities were noted on renal biopsy in 87 patients. Of the remaining 78 patients, 49 had IgA nephropathy.[8] Although IgA nephropathy is probably the most common glomerular cause of hematuria,[9] some data suggest that thin basement membrane disease, an inherited glomerular disorder defined histologically by diffuse thinning of the glomerular basement membranes, may be as frequent a cause of isolated glomerular microscopic hematuria.[10] Hereditary nephritis is a less common glomerular cause.

Nonglomerular sources of microhematuria involving the kidney and the upper urinary tract include neoplasm, nephrolithiasis, cystic disease (including polycystic kidney disease and medullary sponge kidney), papillary necrosis, and metabolic defects such as hypercalciuria or hyperuricosuria. The causes involving the lower urinary tract include disorders of the bladder, urethra, and prostate.

Urologic cancers (mainly of the bladder and prostate) are estimated to account for about 5 percent of cases of microscopic hematuria, although estimates vary widely according to whether the study is referral-based (higher percentages) or population-based (lower percentages).[2] The risk of bladder cancer increases significantly with age, particularly after 65 years of age.[11] Risk factors for transitional-cell cancer of the bladder or urinary tract include cigarette smoking, occupational exposure to chemicals used in certain industries (leather, dye, and rubber or tire manufacturing), heavy phenacetin use, past treatment with high doses of cyclophosphamide, and ingestion of aristolochic acid found in some herbal weight-loss preparations.[11-13]

STRATEGIES AND EVIDENCE

The first steps in evaluating microscopic hematuria should be to obtain a pertinent history and perform a physical examination. It should be noted that anticoagulant therapy alone does not cause hematuria, except in the case of a marked overdose of warfarin.[14] The urine should be evaluated for bacteriuria and pyuria. If either is present, a urine culture should be ordered. Serum creatinine should be measured to evaluate the patient for renal insufficiency. If proteinuria is detected on dipstick testing, the ratio of the urinary protein concentration to the urinary creatinine concentration, in milligrams per deciliter, should be determined, or a 24-hour urine collection should be obtained for measurement of total protein excretion. Clinically significant proteinuria (a ratio of urinary protein to urinary creatinine of more than 0.3 or 24-hour urinary protein excretion of more than 300 mg) points to the kidney as a source of microscopic hematuria.

URINALYSIS

The single most important test in the evaluation of hematuria is the microscopical analysis of urine, because it often distinguishes glomerular from nonglomerular bleeding (Fig. 1). If the findings indicate a glomerular site of bleeding, no urologic evaluation is necessary. Documentation of renal insufficiency or proteinuria warrants referral to a nephrologist for evaluation and possible renal biopsy; referral should be prompt if a second measurement of serum creatinine is abnormal or higher than the first. However, renal biopsy in a patient with microscopic hematuria unaccompanied by clinically significant proteinuria or renal insufficiency is not supported by the limited data that are available. In a study involving 75 patients with isolated microscopic hematuria who underwent renal biopsy, 36 percent had thin basement membrane disease, and 23 percent had IgA nephropathy — findings that made little difference in their care.[20]

IMAGING OF THE UPPER URINARY TRACT

If a glomerular source is ruled out or considered unlikely on the basis of the clinical presentation, the upper urinary tract should be imaged. The goal is to

Table 1. Causes of Isolated Microscopic Hematuria.*

Origin	<50 Yr of Age	≥50 Yr of Age
Glomerular	IgA nephropathy (increased incidence in Asians)	IgA nephropathy
	Thin basement membrane disease (benign familial hematuria)	Hereditary nephritis (Alport's syndrome)
	Hereditary nephritis (Alport's syndrome)	Mild focal glomerulonephritis of other causes
	Mild focal glomerulonephritis of other causes	
Nonglomerular		
Upper urinary tract causes	Nephrolithiasis	Nephrolithiasis
	Pyelonephritis	Renal-cell cancer
	Polycystic kidney disease	Polycystic kidney disease
	Medullary sponge kidney	Pyelonephritis
	Hypercalciuria, hyperuricosuria, or both, without documented stones	Renal-pelvis or ureteral transitional-cell cancer
	Renal trauma	Papillary necrosis
	Papillary necrosis	Renal infarction
	Ureteral stricture and hydronephrosis	Ureteral stricture and hydronephrosis
	Sickle cell trait or disease in blacks	Renal tuberculosis
	Renal infarction or arteriovenous malformation	
	Renal tuberculosis in endemic areas or in patients with HIV infection	
Lower urinary tract causes	Cystitis, prostatitis, and urethritis	Cystitis, prostatitis, and urethritis
	Benign bladder and ureteral polyps and tumors	Bladder cancer
	Bladder cancer	Prostate cancer
	Prostate cancer	Benign bladder and ureteral polyps and tumors
	Urethral and meatal strictures	
	Schistosoma haematobium in North Africans	
Uncertain	Exercise hematuria	Exercise hematuria
	"Benign hematuria" (unexplained microscopic hematuria)	Over-anticoagulation (usually with warfarin)
	Over-anticoagulation (usually with warfarin)	
	Factitious hematuria (usually presents with gross hematuria)	

* Disorders causing microhematuria are presented roughly in order of descending frequency of presentation, according to available data. HIV denotes human immunodeficiency virus.

detect any neoplasms, including renal-cell carcinoma and the less prevalent transitional-cell carcinomas of the renal pelvis and ureters, urolithiasis, cystic disease, and obstructive lesions. Excretory urography has been used routinely to examine the upper urinary tract in most studies of microscopic hematuria.[2] Ultrasonography is safer, does not involve exposure to intravenous radiographic contrast medium, is appropriate for use during pregnancy, and is less expensive.[21] Ultrasonography, however, may be limited in its detection of solid tumors that are less than 3 cm in diameter.[22] In a study in which
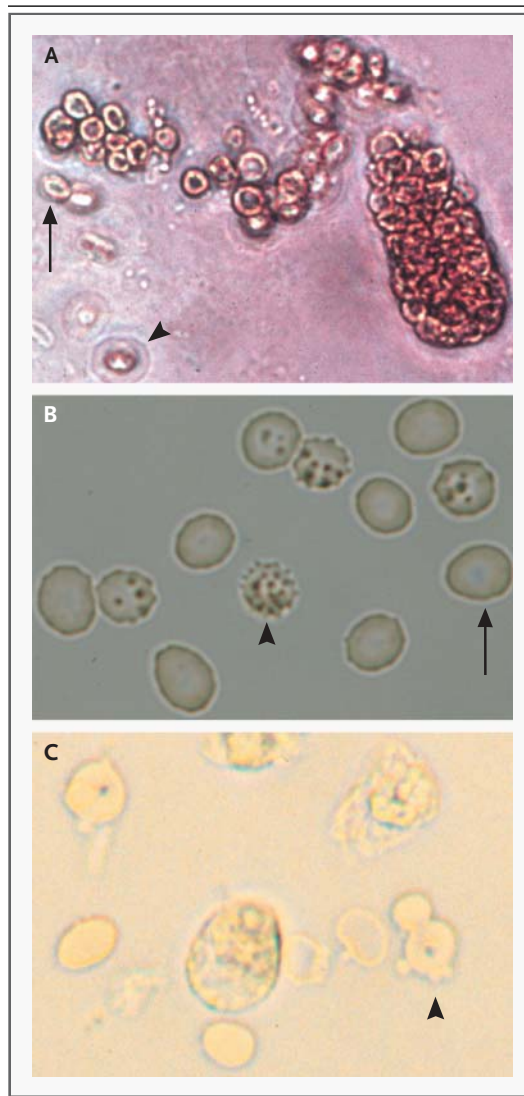
enhanced computed tomography (CT) was used as the standard, the sensitivity and specificity of ultrasonography for the detection of renal parenchymal masses between 2 and 3 cm in diameter were 82 percent and 91 percent, respectively. In the same study, the sensitivity and specificity of excretory urography were 52 percent and 82 percent, respectively.[23] Since excretory urography may miss small renal masses and sometimes cannot differentiate solid from cystic masses, a follow-up study with the use of ultrasonography, CT, or magnetic resonance imaging is often ordered. To our knowledge, no studies have specifically compared the effectiveness of these various imaging techniques in the evaluation of microscopic hematuria.

A CT scan without the use of a contrast agent is appropriate as the first test for patients with suspected stone disease. In one series of patients with renal colic who underwent unenhanced helical CT followed immediately by excretory urography, the sensitivity for the detection of ureteral stones was 100 percent with the former, as compared with 67 percent with the latter.[24] When there is no clinical suspicion of stone disease, CT urography should be performed first without contrast medium and then with it, particularly in patients who might be at increased risk for kidney cancer. Although CT is more expensive than excretory urography or ultrasonography, studies involving the latter techniques are often followed by additional imaging (to confirm that cysts are benign or to reevaluate questionable or negative studies) and thus cannot be considered

Figure 1. Findings in Urinary Sediment.

In Panel A (×440), urinary sediment shows a red-cell cast and red cells. Red-cell casts indicate the presence of glomerular bleeding, a finding that is very specific but rather insensitive. If no red-cell casts are found, urinary red-cell morphology should be examined. The small, dysmorphic red cell (arrow) suggests a glomerular source,[15] and the uniform, biconcave disk shape of normal red cells (arrowhead) suggests nonglomerular bleeding. Some have noted that dysmorphic or abnormally shaped red cells are not reliable enough as a means for distinguishing a glomerular source of bleeding from a nonglomerular source, particularly if mixtures of dysmorphic and normal-appearing red cells are seen.[16,17] (Photomicrograph courtesy of the late Dr. Richard Nesson.) In Panel B (×440), urinary sediment shows normal red cells (arrow) and crenated red-cell forms with spicules (arrowhead). Crenated red cells form in concentrated urine and are not diagnostically relevant. A more specific finding with bleeding of glomerular origin may be the presence of a particular form of abnormal red cells in the urine — acanthocytes,[18,19] doughnut-like cells with membrane blebs attached (Panel C, ×440, arrowhead). With meaningful acanthocyturia defined as the presence of acanthocytes accounting for more than 5 percent of urinary red cells, the sensitivity of phase microscopy for detecting glomerular hematuria was 52 percent in one large series in which glomerulonephritis was documented with renal biopsy and 73 percent in another series, and the specificity for detecting a glomerular source was 98 percent and 100 percent, respectively, in the two series.[18,19] The sensitivity and specificity of light microscopy for identifying acanthocytes have not been reported; since most laboratories do not routinely identify acanthocytes, this test should ideally be performed by an experienced laboratory technologist alerted to look for acanthocytes or by a nephrologist.

cost-saving in general. If CT is unavailable or prohibitively expensive, excretory urography, ultrasonography, or the combination of the two is a reasonable alternative. If a mass suspected to be malignant is identified, the patient should be referred to a urologist. If polycystic kidney disease is found, the patient should be referred to a nephrologist.

EVALUATION OF THE LOWER URINARY TRACT
The source of microscopic hematuria remains obscure in about 70 percent of cases after imaging of the upper urinary tract and examination of urine for evidence of glomerular hematuria. In these cases, it may be necessary to evaluate the lower urinary tract, with particular attention to possible bladder cancer. Cystoscopy is appropriate if risk factors for bladder cancer are present. This procedure is also warranted in older men with asymptomatic microscopic hematuria, but the data are inconclusive regarding the age at which to recommend cystoscopy.

In one community-based study,[25] 1340 men 50 years of age or older (mean age, 65 years) were tested for hematuria with urinary dipsticks daily for two weeks. Twenty-one percent had at least one episode of hematuria. Of these men, 192 underwent complete urologic evaluation. A total of 16 malignant lesions were identified: 9 bladder cancers, 1 renal-cell carcinoma, and 6 prostate cancers. In another community-based study, 3152 men older than 60 years of age were screened for microscopic hematuria by urinary dipstick testing daily or weekly for 10 weeks. Twenty percent had hematuria on at least one dipstick test, and of the 319 men who underwent full urologic evaluation, 22 had cancer (bladder cancer in 17 and prostate cancer in 5).[26] Thirteen of the 17 men with bladder cancer had a history of cigarette smoking. In these two studies, the positive predictive value of dipstick testing for the detection of bladder cancer was 4.7 percent and 5.3 percent, respectively. In a referral-based study involving 100 men younger than 40 years of age with microscopic hematuria, no bladder cancers were identified by cystoscopy.[27] CT studies with the use of radiographic contrast medium may reduce the need for cystoscopy. In a recent series, the sensitivity of this technique was 100 percent and the specificity was 98 percent for the detection of neoplasms of the bladder.[28]

Available data provide less support for cystoscopy in women with asymptomatic microscopic hematuria than in men. No cases of bladder cancer were found in one prospective, referral-based study involving 177 women (mean age, 57.2 years) with asymptomatic microscopic hematuria who underwent cystoscopy.[29] In another referral-based study, involving 1034 adults (75 percent of whom were female), only two cases of bladder cancer were identified in women with microscopic hematuria (one 54 years old and the other 70 years old).[30] In contrast, in a referral-based study involving 484 women with microscopic hematuria, 12 cases of urologic cancer were identified in women between 60 and 89 years of age, and 5 cases were found in women between 40 and 59 years of age. The specific types of cancer and the number of diagnoses made with cystoscopy were unclear.[31]

CYTOLOGIC STUDIES OF URINE
Cytologic analysis of voided urine is less sensitive (66 percent and 79 percent in two large series) than cystoscopy in the detection of bladder cancer[32,33] but has high specificity (95 percent and 100 percent in the two series). The sensitivity is improved if specimens of urine from the first voiding in the morning on three consecutive days are obtained.[34] The sensitivity is higher for the detection of high-grade bladder cancer and carcinoma in situ[33] but lower for the detection of cancers of low histologic grade, and cytologic analysis is insensitive for the detection of renal-cell cancer. Cystoscopy itself had 87 percent sensitivity for the detection of bladder cancer in one large series and is especially limited for the diagnosis of carcinoma in situ.[32] Urinary molecular markers for the noninvasive detection of bladder cancer are currently being evaluated but have not yet been validated.[35]

FOLLOW-UP AFTER NEGATIVE EVALUATION
A thorough evaluation of the urinary system may fail to identify a source of microscopic hematuria. In studies in which both imaging of the upper urinary tract and cystoscopy were performed in patients with microscopic hematuria, a source was not identified in 19 to 68 percent of the patients evaluated.[29,31,36-39] Microscopy was not routinely part of the evaluation in these studies, suggesting that more glomerular causes of microscopic hematuria might be identified with this addition.

Follow-up of patients with unexplained microscopic hematuria has been evaluated in two studies, both without a control group. In one, 191 patients with asymptomatic hematuria that remained unexplained after urologic evaluation with urinalysis, cytologic analysis of voided urine, excretory urog-

raphy, and cystoscopy subsequently underwent excretory urography and cystoscopy. No cancers were detected during follow-up, prompting the authors to suggest that no further studies are necessary unless symptoms develop.[40] This suggestion was corroborated by similar recommendations in another prospective study.[31]

AREAS OF UNCERTAINTY

Currently, the data are inadequate to support clearcut recommendations regarding the evaluation and management of microscopic hematuria. Shortcomings of available studies include inconsistencies in definition, study design, selection criteria, and diagnostic-test techniques and procedures used.[41] Data are lacking on outcomes in patients with microscopic hematuria who did not undergo formal evaluation and those in whom the finding remained unexplained despite evaluation. In addition, there have been no randomized trials comparing the outcomes associated with different strategies.

GUIDELINES

The U.S. Preventive Services Task Force and the Canadian Task Force on the Periodic Health Examination do not recommend routine screening of urine for microscopic hematuria.[11] Regarding bladder cancer, they cite the low predictive value of a positive screening test even in a high-risk population of older adults. They also cite the absence of proof that early detection improves the prognosis in the small number of patients found to have urinary tract cancer.[11]

The American Urological Association has issued guidelines for the evaluation of microscopic hematuria in adults (http://www.aafp.org/afp/20010315/1145.html). According to these guidelines, after microscopical examination of the urine, testing for proteinuria, and measurement of serum creatinine, a full urologic workup should be performed, including radiologic imaging of the upper urinary tract, cytologic analysis of urine, and cystoscopy (recommended for all persons with asymptomatic microscopic hematuria who are older than 40 years).[42]

CONCLUSIONS AND RECOMMENDATIONS

When asymptomatic microscopic hematuria is detected, as in the patient described in the vignette, the urinalysis should be repeated a few days later before any workup is initiated, especially if the patient has had vigorous exercise, menstruation, trauma to the urinary tract, or sexual activity just before the collection. Our recommended approach after a second urinalysis is summarized in Figure 2.

If microscopic hematuria is absent on repeated testing, we do not recommend further evaluation, unless the patient has risk factors for bladder cancer or transitional-cell cancer of the urinary tract, such as cigarette smoking or exposure to toxins. If repeated urinalysis confirms the presence of microscopic hematuria, we recommend microscopical analysis for evidence of a glomerular source, such as acanthocyturia or red-cell casts. Whether or not such a source is found, if microscopic hematuria is accompanied by proteinuria or renal insufficiency, the patient should be referred to a nephrologist for evaluation.

If isolated glomerular microscopic hematuria is identified, we recommend follow-up by a primary care physician, initially at six months and then annually, to check for the development of proteinuria or renal insufficiency (although there are no data supporting a specific interval between follow-up visits). We would not perform a renal biopsy in a patient with isolated glomerular microscopic hematuria, since the limited data available do not suggest that identification of the specific disease makes any difference in management or outcome.

If examination of urine does not suggest a glomerular source and the patient is not pregnant, helical CT urography should be performed, first without and then with radiographic contrast medium, primarily for the detection of occult stone disease or a mass (in the upper urinary tract or possibly in the bladder). An examination without contrast medium would be appropriate if stone disease was suspected clinically. CT is highly sensitive for the detection of disease in the upper urinary tract; we do not recommend excretory urography unless CT is unavailable or deemed too expensive. Ultrasonography can be performed in place of CT (and is advised for patients with renal failure, pregnancy, or hypersensitivity to contrast medium), with the understanding that further imaging may be necessary.

If imaging is unrevealing, we recommend obtaining specimens of urine from the first voiding in the morning on three consecutive days for cytologic analysis in persons older than 40 years of age, but the insensitivity of cytologic analysis for the detection of low-grade bladder cancer should
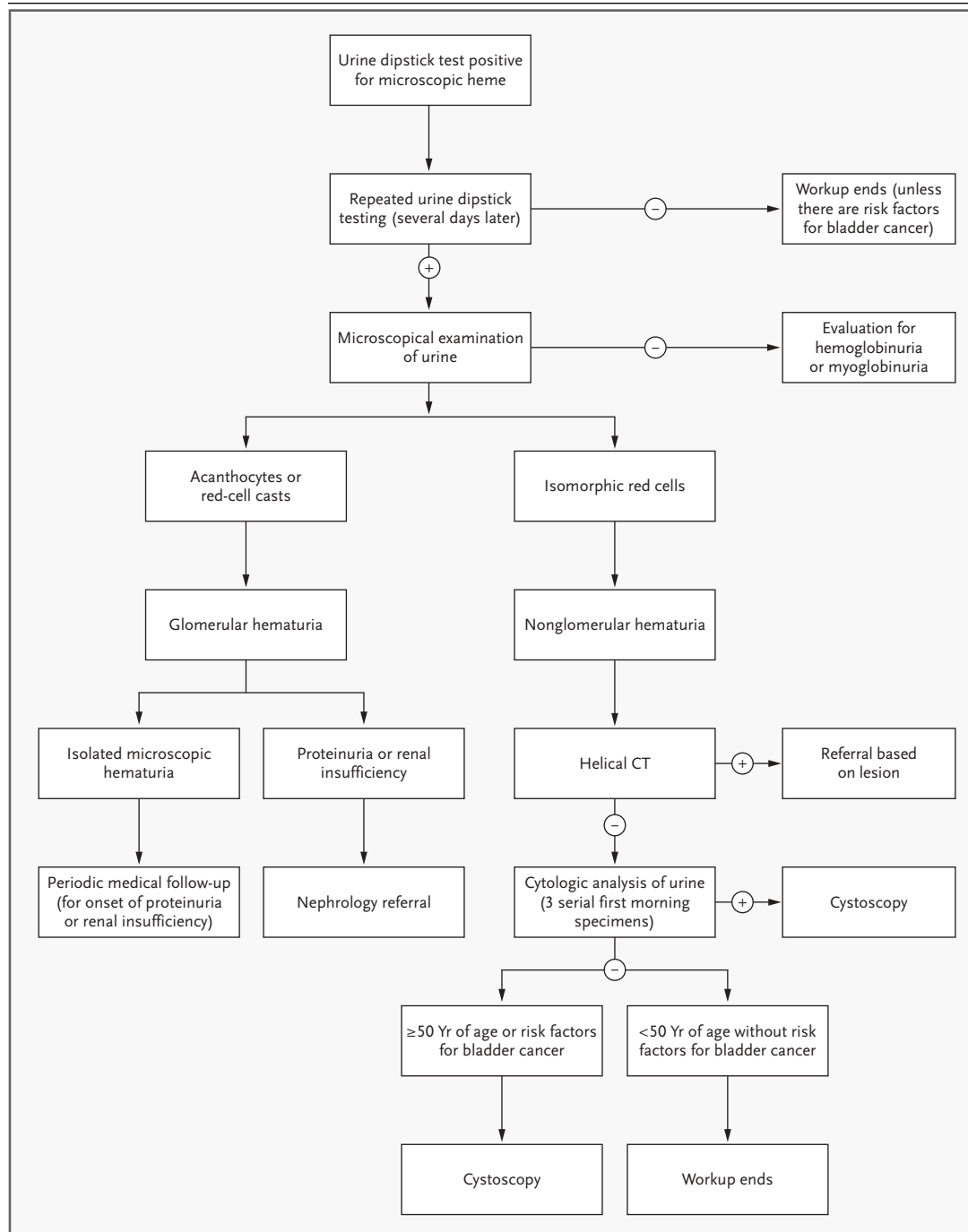
Figure 2. Evaluation of Microscopic Hematuria.

If hematuria is determined to be nonglomerular in origin, computed tomography (CT) should be performed without contrast medium if a stone is suspected to be present or first without and then with contrast medium if no stone is suspected. Ultrasonography should be performed instead of CT in pregnant patients and those with hypersensitivity to contrast medium. Risk factors for bladder cancer include cigarette smoking, occupational exposure to chemicals used in certain industries (leather, dye, and rubber or tire manufacturing), heavy phenacetin use, past treatment with high doses of cyclophosphamide, and ingestion of aristolochic acid found in some herbal weight-loss preparations. Plus signs indicate positive findings, and minus signs negative findings.

be recognized. Cystoscopy should be performed if cytologic analysis of voided urine has identified neoplastic cells or if the patient has risk factors for bladder cancer. In the absence of these factors, the question of the age at which cystoscopy should routinely be performed to evaluate patients of either sex who have microscopic hematuria remains controversial. At variance with the American Urological Association, we would not routinely recommend cystoscopy for all persons older than 40 years of age, since we believe that such a recommendation would lead to unnecessary testing, with the attendant expense and potential risks associated with this invasive procedure; we would, however, recommend yearly follow-up with urinalysis. Recognizing the trend toward a higher incidence of bladder cancer with advancing age, we would advise men and women older than 50 years of age who have persistent microscopic hematuria to undergo cystoscopy. Cystoscopy is also recommended if gross hematuria develops, because this finding is associated with a higher risk of urologic cancer than is microscopic hematuria.[2,31]

REFERENCES

1. Mariani AJ, Mariani MC, Macchioni C, Stams UK, Hariharan A, Moriera A. The significance of adult hematuria: 1,000 hematuria evaluations including a risk-benefit and cost-effectiveness analysis. J Urol 1989; 141:350-5.

2. Sutton JM. Evaluation of hematuria in adults. JAMA 1990;263:2475-80.

3. Woolhandler S, Pels RJ, Bor DH, Himmelstein DU, Lawrence RS. Dipstick urinalysis screening of asymptomatic adults for urinary tract disorders. JAMA 1989;262: 1214-9.

4. Hiatt RA, Ordonez JD. Dipstick urinalysis screening, asymptomatic microhematuria, and subsequent urological cancers in a population-based sample. Cancer Epidemiol Biomarkers Prev 1994;3:439-43. [Erratum, Cancer Epidemiol Biomarkers Prev 1994;3:523.]

5. Mohr DN, Offord KP, Owen RA, Melton LJ III. Asymptomatic microhematuria and urologic disease: a population-based study. JAMA 1986;256:224-9.

6. Froom P, Ribak J, Benbassat J. Significance of microhaematuria in young adults. Br Med J (Clin Res Ed) 1984;288:20-2.

7. Sparwasser C, Cimniak HU, Treiber U, Pust RA. Significance of the evaluation of asymptomatic microscopic haematuria in young men. Br J Urol 1994;74:723-9.

8. Topham PS, Harper SJ, Furness PN, Harris KPG, Walls J, Feehally J. Glomerular disease as a cause of isolated microscopic haematuria. Q J Med 1994;87:329-35.

9. D'Amico G, Imbasciati E, Barbiano Di Belgioioso G, et al. Idiopathic IgA mesangial nephropathy: clinical and histological study of 374 patients. Medicine (Baltimore) 1985; 64:49-60.

10. Tiebosch ATMG, Frederik PM, van Breda Vriesman PJC, et al. Thin-basement-membrane nephropathy in adults with persistent hematuria. N Engl J Med 1989;320: 14-8.

11. Preventive Services Task Force. Guide to clinical preventive services: report of the U.S. Preventive Services Task Force. 2nd ed. Baltimore: Williams & Wilkins, 1996.

12. Piper JM, Tonascia J, Matanoski GM. Heavy phenacetin use and bladder cancer in women aged 20 to 49 years. N Engl J Med 1985;313:292-5.

13. Talar-Williams C, Hijazi YM, Walther MM, et al. Cyclophosphamide-induced cystitis and bladder cancer in patients with Wegener granulomatosis. Ann Intern Med 1996; 124:477-84.

14. Van Savage JG, Fried FA. Anticoagulant associated hematuria: a prospective study. J Urol 1995;153:1594-6.

15. Birch DF, Fairley KF. Haematuria: glomerular or non-glomerular? Lancet 1979;2: 845-6.

16. Pollock C, Lui P-L, Gyory AZ, et al. Dysmorphism of urinary red blood cells — value in diagnosis. Kidney Int 1989;36:1045-9.

17. Offringa M, Benbassat J. The value of urinary red cell shape in the diagnosis of glomerular and post-glomerular haematuria: a meta-analysis. Postgrad Med J 1992;68: 648-54.

18. Kohler H, Wandel E, Brunck B. Acanthocyturia — a characteristic marker for glomerular bleeding. Kidney Int 1991;40: 115-20.

19. Kitamoto Y, Tomita M, Akamine M, et al. Differentiation of hematuria using a uniquely shaped red cell. Nephron 1993;64:32-6.

20. McGregor DO, Lynn KL, Bailey RR, Robson RA, Gardner J. Clinical audit of the use of renal biopsy in the management of isolated microscopic hematuria. Clin Nephrol 1998;49:345-8.

21. Corwin HL, Silverstein MD. The diagnosis of neoplasia in patients with asymptomatic microscopic hematuria: a decision analysis. J Urol 1988;139:1002-6. [Erratum, J Urol 1988;140:1558.]

22. Jamis-Dow CA, Choyke PL, Jennings SB, Linehan WM, Thakore KN, Walther MM. Small ($\leq$ 3-cm) renal masses: detection with CT versus US and pathologic correlation. Radiology 1996;198:785-8.

23. Warshauer DM, McCarthy SM, Street L, et al. Detection of renal masses: sensitivities and specificities of excretory urography/linear tomography, US, and CT. Radiology 1988;169:363-5.

24. Sourtzis S, Thibeau JF, Damry N, Raslan A, Vandendris M, Bellemans M. Radiologic investigation of renal colic: unenhanced helical CT compared with excretory urography. AJR Am J Roentgenol 1999;172:1491-4.

25. Messing EM, Young TB, Hunt VB, et al. Home screening for hematuria: results of a multiclinic study. J Urol 1992;148:289-92.

26. Britton PJ, Dowell AC, Whelan P, Harris CM. A community study of bladder cancer screening by the detection of occult urinary bleeding. J Urol 1992;148:788-90.

27. Jones DJ, Langstaff RJ, Holt SD, Morgans BT. The value of cystourethroscopy in the investigation of microscopic haematuria in adult males under 40 years: a prospective study of 100 patients. Br J Urol 1988;62:541-5.

28. Lang EK, Macchia RJ, Thomas R, et al. Computerized tomography tailored for the assessment of microscopic hematuria. J Urol 2002;167:547-54.

29. Bard RH. The significance of asymptomatic microhematuria in women and its economic implications: a ten-year study. Arch Intern Med 1988;148:2629-32.

30. Murakami S, Igarashi T, Hara S, Shimazaki J. Strategies for asymptomatic microscopic hematuria: a prospective study of 1,034 patients. J Urol 1990;144:99-101.

31. Khadra MH, Pickard RS, Charlton M, Powell PH, Neal DE. A prospective analysis of 1,930 patients with hematuria to evaluate current diagnostic practice. J Urol 2000;163: 524-7.

32. Rife CC, Farrow GM, Utz DC. Urine cytology of transitional cell neoplasms. Urol Clin North Am 1979;6:599-612.

33. Koss LG, Deitch D, Ramanathan R, Sherman AB. Diagnostic value of cytology of voided urine. Acta Cytol 1985;29:810-6.

34. Badalament RA, Hermansen DK, Kimmel M, et al. The sensitivity of bladder wash flow cytometry, bladder wash cytology, and voided cytology in the detection of bladder carcinoma. Cancer 1987;60:1423-7.

35. Stein JP, Grossfeld GD, Ginsberg DA, et al. Prognostic markers in bladder cancer: a contemporary review of the literature. J Urol 1998;160:645-59.

36. Greene LF, O'Shaughnessy EJ Jr, Hen-

dricks ED. Study of five hundred patients with asymptomatic microhematuria. JAMA 1956;161:610-3.

37. Carson CC III, Segura JW, Greene LF. Clinical importance of microhematuria. JAMA 1979;241:149-50.

38. Davides KC, King LM, Jacobs D. Management of microscopic hematuria: twenty-four-year experience with 150 cases in a community hospital. Urology 1986;28:453-5.

39. Ritchie CD, Bevan EA, Collier SJ. Impor-

tance of occult haematuria found at screening. Br Med J (Clin Res Ed) 1986;292:681-3.

40. Howard RS, Golin AL. Long-term followup of asymptomatic microhematuria. J Urol 1991;145:335-6.

41. Köhler C, Varenhorst E. Mikroskopisk hematuri hos vuxna — ett diagnostiskt dilemma: vetenskapliga riktlinjer för handläggning saknas visar litteraturgenomgång. Lakartidningen 1999;96:4911-6.

42. Grossfeld GD, Litwin MS, Wolf JS Jr, et

al. Evaluation of asymptomatic microscopic hematuria in adults: the American Urological Association best practice policy. II. Patient evaluation, cytology, voided markers, imaging, cytoscopy, nephrology evaluation, and follow-up. Urology 2001;57:604-10.

Copyright © 2003 Massachusetts Medical Society.