

Diagnosis, Evaluation and Follow-Up of Asymptomatic Microhematuria (AMH) in Adults: AUA Guideline

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Purpose: The purpose of this guideline is to provide a clinical framework for the diagnosis, evaluation and follow-up of asymptomatic microhematuria.

Materials and Methods: A systematic literature review using the MEDLINE® database was conducted to identify peer reviewed publications relevant to the definition, diagnosis, evaluation and follow-up for AMH. The review yielded 191 evidence-based articles, and these publications were used to create the majority of the guideline statements. There was insufficient evidence-based data for certain concepts; therefore, clinical principles and consensus expert opinions were used for portions of the guideline statements.

Results: Guideline statements are provided for diagnosis, evaluation and follow-up. The panel identified multiphasic computed tomography as the preferred imaging technique and developed guideline statements for persistent or recurrent AMH as well as follow-up.

Conclusions: AMH is only diagnosed by microscopy; a dipstick reading suggestive of hematuria should not lead to imaging or further investigation without confirmation of three or greater red blood cells per high power field. The evaluation and follow-up algorithm and guidelines provide a systematic approach to the patient with AMH. All patients 35 years or older should undergo cystoscopy, and upper urinary tract imaging is indicated in all adults with AMH in the absence of known benign causation. The imaging modalities and physical evaluation techniques are evolving, and these guidelines will need to be updated as the effectiveness of these become available. Please visit the AUA website at http://www.auanet.org/content/media/asymptomatic_microhematuria_guideline.pdf to view this guideline in its entirety.

Key Words: hematuria, cystoscopy, urogenital neoplasms, urinalysis, guideline

THIS guideline's purpose is to provide direction to clinicians and patients regarding how to work-up and follow patients with the finding of asymptomatic microhematuria.

METHODOLOGY

A systematic review was conducted to identify published articles relevant to the diagnostic yield of mass screening for mi-

crohematuria as well as the work-up and follow-up of adult patients with AMH. Literature search dates ranged from January 1980 to November 2011. Guideline statements and the accompanying treatment algorithm (see figure) were formed based on this literature review.

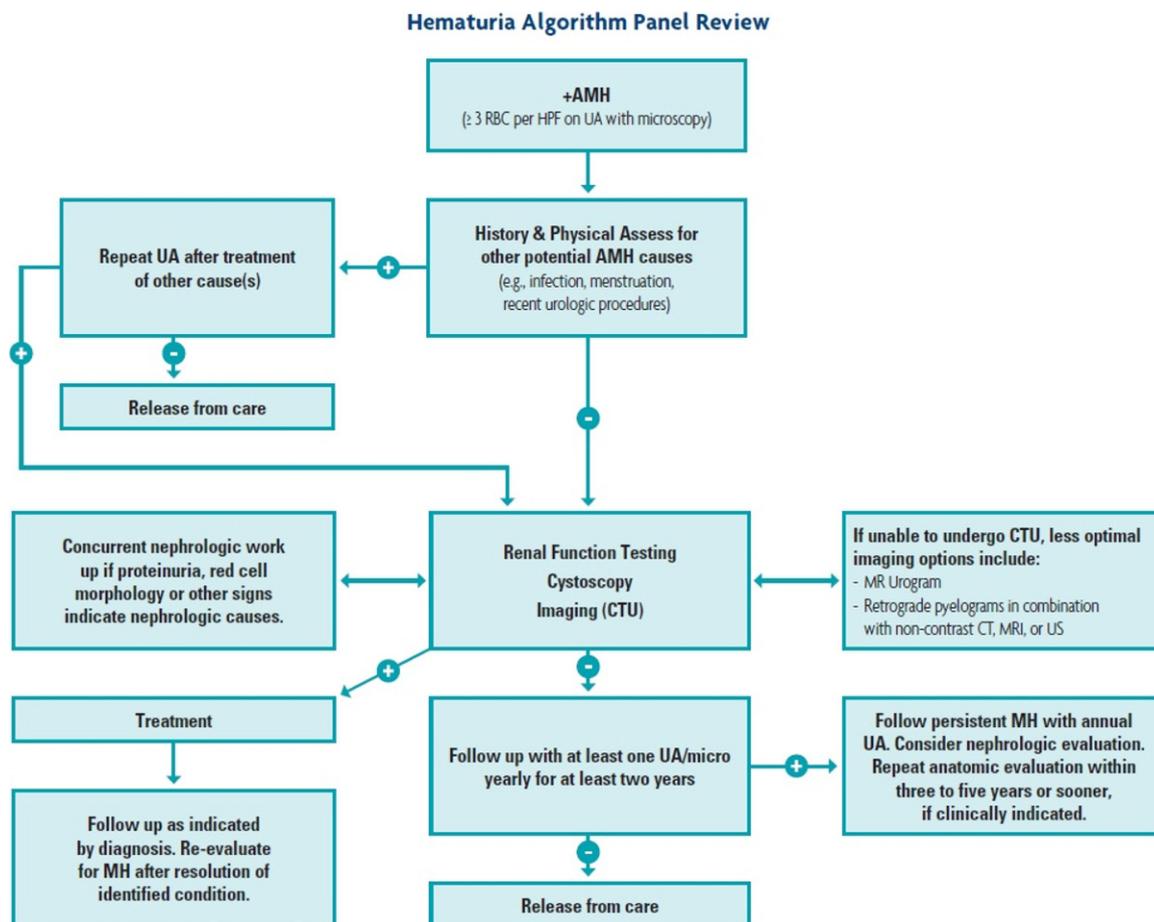
The AUA nomenclature system explicitly links statement type to body of evidence strength and the Panel's judgment regarding the balance between

Abbreviations and Acronyms

AMH = asymptomatic microhematuria
CT = computed tomography
CTU = computed tomography urography
FDA = Food and Drug Administration
IV = intravenous
IVU = intravenous urography
MH = microhematuria
MRI = magnetic resonance imaging
MRU = magnetic resonance urography
RBC = red blood cell
RPG = retrograde pyelogram
US = ultrasound

The complete guideline is available at http://www.auanet.org/content/media/asymptomatic_microhematuria_guideline.pdf.

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benefits and risks/burdens.¹ For a complete discussion of the methodology and evidence grading, please refer to the unabridged guideline available at http://www.auanet.org/content/media/asymptomatic_microhematuria_guideline.pdf.

BACKGROUND

Definition

For the purpose of this guideline, AMH is defined as three or greater red blood cells per high powered field on a properly collected urinary specimen in the absence of an obvious benign cause.

Prevalence

The adult population prevalence of MH varies depending on age, gender, frequency of testing, threshold used to define MH and study group characteristics, such as the presence of risk factors (i.e., past or current smoking).

Origins and Causes

The origins of MH are either urologic or nephrologic. The most common urological etiologies are benign prostatic enlargement, infection and urinary calculi.

The most common risk factors for urinary tract malignancy include male gender, age >35 years, past or current smoking, occupational or other exposure to chemicals or dyes (e.g., benzenes, aromatic amines) and analgesic abuse in addition to a history of gross hematuria, urologic disorder or disease, irritative voiding symptoms, pelvic irradiation, chronic urinary tract infection, exposure to known carcinogenic agents or chemotherapy, such as alkylating agents, and a chronic indwelling foreign body.²

Evolution of Imaging Technologies

In the previous version of this document,² intravenous urography was acknowledged as a mainstay imaging modality for evaluation of the urinary tract because of its widespread availability. The prior document noted, however, that IVU has limited sensitivity in detecting small renal masses and cannot distinguish solid from cystic masses, resulting in the need for ultrasound, computed tomography or magnetic resonance imaging to fully characterize lesions.

A decade later, this Panel approached the issue of appropriate evaluation of the AMH patient with the goal of identifying the imaging strategy that creates maximum diagnostic certainty without the need for additional imaging procedures in order to minimize patient burden and the possibility of missed diagnoses.

The use of US and IVU does not exclude the need for additional imaging studies. In addition, the sensitivities and specificities of US and IVU are such that the possibility of missed diagnoses is significant.^{3,4} Both of these issues are avoided with the use of CT urography and magnetic resonance urography — two modalities that have been developed and refined during the decade since the publication of the prior document.

1. AMH is defined as three or greater RBCs per high powered field on a properly collected urinary specimen in the absence of an obvious benign cause. A positive dipstick does not define AMH, and evaluation should be based solely on findings from microscopic examination of urinary sediment and not on a dipstick reading. A positive dipstick reading merits microscopic examination to confirm or refute the diagnosis of AMH. Expert Opinion

Patients who have a positive dipstick test but a negative specimen on microscopy should have three additional repeat tests. If at least one of the repeat tests is positive on microscopy, then work-up should be undertaken. If all three specimens are negative on microscopy, then the patient may be released from care.

2. The assessment of the AMH patient should include a careful history, physical examination and laboratory examination to rule out benign causes of AMH such as infection, menstruation, vigorous exercise, medical renal disease, viral illness, trauma or recent urological procedures. Clinical Principle

Laboratory tests may be necessary to confirm these diagnoses in order to avoid the incorrect attribution of AMH to an unconfirmed diagnosis, thereby missing an important alternative diagnosis, such as malignancy. Of particular importance is the use of urine culture to confirm infection, preferably before making the diagnosis and treating with antibiotics, but especially in patients with persistent AMH after one or more courses of antibiotic treatment.

3. Once benign causes have been ruled out, the presence of AMH should prompt a urologic evaluation. Recommendation (Evidence Strength: Grade C)

A small percentage of individuals diagnosed with AMH will ultimately be determined to have a urinary tract malignancy. Three sets of studies support this statement: screening studies in which individ-

uals without known health conditions were diagnosed with AMH and worked up; initial work-up studies in which patients who had AMH diagnosed incidentally during a medical encounter, such as a check-up, were worked up; and further work-up studies in which AMH patients not diagnosed during an initial work-up process were referred on for a specialized work-up.

In addition, other conditions that would benefit from active clinical management were frequently diagnosed. The Panel interprets these data to indicate that the frequency of underlying conditions that may be life-threatening or benefit from intervention and/or management is sufficient to warrant evaluation.

The Panel notes that there is a critical knowledge base gap regarding AMH. Distinguishing among patient subgroups for the purpose of differential work-up protocols is accompanied by high levels of uncertainty due to the absence of stratified information regarding the diagnostic yield associated with AMH in patients who have been thoroughly worked up and carefully followed for long periods of time. The Panel notes that the benefit of detecting and treating a life-threatening urinary tract malignancy or other condition that would benefit from intervention or management outweighs the risks/burdens associated with a urologic evaluation.

4. At the initial evaluation, an estimate of renal function should be obtained (may include calculated eGRF, creatinine and BUN) because intrinsic renal disease may have implications for renal-related risk during the evaluation and management of patients with AMH. Clinical Principle

Renal dysfunction increases the risk of contrast or gadolinium radiologic studies and needs to be considered in the selection of these diagnostic procedures. If procedures are considered for the treatment of urologic diseases that may result in a reduction in renal function, then the implications of this reduction may be more pronounced for patients who have baseline abnormal renal function. Concurrent nephrologic evaluation and a clear understanding of nephrologic factors should be considered in the patient with either urinary abnormalities suggestive of nephrologic disorders or in the patient with abnormal renal function.

5. The presence of dysmorphic RBCs, proteinuria, cellular casts and/or renal insufficiency or any other clinical indicator suspicious for renal parenchymal disease warrants concurrent nephrologic work-up but does not preclude the need for urologic evaluation. Recommendation (Evidence Strength: Grade C)

Although the presence of dysmorphic RBCs suggests a glomerular process, this finding does not

exclude the potential for urologic processes. In addition, the presence of proteinuria or renal insufficiency should prompt evaluation for nephrologic diseases in the MH patient regardless of RBC morphology findings.

6. MH that occurs in patients who are taking anti-coagulants requires urologic evaluation and nephrologic evaluation regardless of the type or level of anti-coagulation therapy. Recommendation (Evidence Strength: Grade C)

Work-up for urinary tract and nephrologic abnormalities is indicated in patients on any anti-coagulation therapy. The evidence strength for this statement is Grade C because it is based on one small comparative observational study.⁵ The Panel notes that it should not be assumed that other groups of patients with a known potential cause of AMH, such as those with a chronic indwelling catheter or those using intermittent catheterization, do not need evaluation. At the judgment of the treating clinician, these patients may also require work-up to rule out other causes of AMH.

7. For the urologic evaluation of AMH, cystoscopy should be performed on all patients aged 35 years and older. Recommendation (Evidence Strength: Grade C)

Seventeen screening studies report on diagnostic findings for approximately 3,762 AMH individuals;^{6–22} 98 individuals were diagnosed with a urinary tract malignancy for an overall rate of 2.6%. Among the 98 individuals, 95 individuals (97%) were older than age 35 years. Among the 409 patients diagnosed with a urinary tract malignancy in the initial and further work-up studies, 406 (99.3%) were older than age 35 years. The Panel interprets these data to indicate that cystoscopy should be performed in individuals aged 35 years and older.

8. In patients younger than age 35 years, cystoscopy may be performed at the physician's discretion. Option (Evidence Strength: Grade C)

The probability of a urinary tract malignancy in patients younger than age 35 years is extremely low. In younger patients, the physician should be guided by the results of the history and physical and other clinical indicators to determine whether a cystoscopy is in the best interest of the patient.

9. Cystoscopy should be performed on all patients who present with risk factors for urinary tract malignancies (e.g., irritative voiding symptoms, current or past tobacco use, chemical exposures), regardless of age. Clinical Principle

Accepted risk factors for significant underlying urinary tract disease include current or past tobacco use, history of pelvic irradiation, alkylating chemotherapeutic agents such as cyclophosphamide and

exposure to occupational hazards such as dyes, benzenes and aromatic amines.

10. The initial evaluation for AMH should include a radiologic evaluation. Multi-phasic CTU (without and with intravenous contrast), including sufficient phases to evaluate the renal parenchyma to rule out a renal mass and an excretory phase to evaluate the urothelium of the upper tracts, is the imaging procedure of choice because it has the highest sensitivity and specificity for imaging the upper tracts. Recommendation (Evidence Strength: Grade C)

The ideal radiologic evaluation for AMH would present minimal risk while providing sufficient diagnostic information in a single imaging session to identify disorders requiring treatment and/or follow-up or referral and ruling out rare but serious diseases without the need for repeat scans or additional studies. This imaging strategy maximizes certainty for the clinician and the patient regarding potential causal factors for AMH in a timely manner and provides all data for a fully informed treatment plan. The literature indicates that less than 1% of AMH patients who had negative findings after a thorough work-up manifested a serious disease state during 14 years of follow-up,²³ reinforcing the importance of completing an initial work-up that provides maximal diagnostic certainty. CTU meets these criteria; other imaging strategies (i.e., US in combination with IV pyelograms) do not meet these criteria.²⁴ Furthermore, the American College of Radiology gave CTU its highest rating for appropriateness in the work-up of hematuria patients and notes that the scan must include use of high-resolution imaging during the excretory phase.²⁵

Multi-phasic CTU with and without contrast had the most consistent and highest sensitivities and specificities for detecting lesions of the renal parenchyma and the upper tracts. The multi-detector CT scan appears to offer optimal imaging information.²⁴

The use of iodinated contrast is a well-known cause of acute renal failure, especially in patients with impaired renal function.^{26–28} The risks of severe contrast reactions using American College of Radiology criteria, however, are extremely low. For some reported options that may reduce contrast nephropathy risk, such as N-acetyl cysteine administration, a nephrologist may be helpful in weighing options and identifying measures that may mitigate the risks as well as in providing input that may help with imaging modality selection.

Ultimately, the choice of the imaging strategy for a particular patient is best made by the treating clinician with full knowledge of that patient's history and preferences and the resources available in the clinical context. The Panel's priority in selecting the optimal imaging strategy of multi-phasic CTU

was to maximize diagnostic certainty and the opportunity for prompt clinical action if warranted, minimize the patient burden associated with anxiety regarding an uncertain diagnosis and the need to obtain additional tests and minimize the risk of missing serious disease states. The Panel is aware, however, that US, either alone or in combination with IVU, is widely-used in clinical practice and is recommended by other guidelines.²⁹ The use of US alone or in combination with IVU is an alternative but less optimal option for imaging because these techniques do not reliably produce diagnostic certainty.

The Panel interprets the available data to indicate that the use of US with or without IVU presents significant risks for missed diagnoses. Although serious findings are rare in the AMH patient, and particularly in younger AMH patients and those without risk factors, they have been reported, and their presence requires a prompt clinical response. Therefore, the Panel judges that use of these modalities is an alternative but less optimal imaging strategy.

11. For patients with relative or absolute contraindications that preclude use of multi-phasic CT (such as renal insufficiency, contrast allergy, pregnancy), MRU (without/with IV contrast) is an acceptable alternative imaging approach. Option (Evidence Strength: Grade C)

There appears to be variability in access to high quality MRU technology and a lack of standardization of protocols. Although MRU appears to provide high sensitivity/specificity imaging of the renal parenchyma, its role in visualizing collecting system detail is indeterminate.^{30–32}

Nevertheless, MRU can provide relative diagnostic certainty regarding some underlying causes of AMH. For example, its accuracy in identifying renal obstructions is similar to CTU.^{33–35} With gadolinium enhancement, sensitivity for upper tract malignancies has been reported to be as high as 80%.³⁶ The risk of contrast reaction to gadolinium (nephrogenic systemic fibrosis) in patients with renal insufficiency is uncertain but may be severe and irreversible in some patients. If there is abnormal renal function, then a nephrologist may be helpful to assess the risk from gadolinium.

The Panel judged that the use of MRU is an alternative imaging strategy that can provide relatively high diagnostic certainty in patients who cannot undergo CTU. As with all imaging decisions, this decision is best made by the individual physician who is fully informed regarding a particular patient's history and associated clinical conditions as well as available imaging resources.

12. For patients with relative or absolute contraindications that preclude use of multi-

phase CT (such as renal insufficiency, contrast allergy, pregnancy) where collecting system detail is deemed imperative, combining MRI with retrograde pyelograms (RPGs) provides alternative evaluation of the entire upper tracts. Expert Opinion

RPGs, also referred to as retrograde pyeloureterograms for coding purposes, are a safe way to evaluate the entire urothelium for filling defects, obstructions or irregularities in the patient who is not a candidate for CTU or MRU. Although invasive, RPGs allow confirmation of the radiologic diagnosis while also confirming the need for uretero-renaloscopy or upper tract sampling. The combination of RPGs with MRI can provide an adequate upper tract evaluation for the purpose of clinical decision-making in the patient who cannot tolerate CTU or MRU.

Ultimately, decisions regarding imaging strategy in high-risk patients are best made by the treating clinician who has detailed knowledge regarding a given patient's history and current circumstances as well as the availability of imaging options in the clinical setting. In some circumstances, non-contrast CT or renal US in combination with RPGs may provide sufficient information to guide clinical care and may be the best choices in patients with compromised renal function who also have contraindications to MRI (e.g., a pacemaker). In general, the Panel does not advocate the routine use of RPGs, but in the special circumstances described above, their use may be appropriate.

13. For patients with relative or absolute contraindications that preclude use of multi-phasic CT (such as renal insufficiency, contrast allergy) and MRI (presence of metal in the body) where collecting system detail is deemed imperative, combining non-contrast CT or renal US with RPGs provides alternative evaluation of the entire upper tracts. Expert Opinion

The Panel notes that non-contrast CT will provide more information and create greater diagnostic certainty than will US. For certain patients, such as the pregnant female, however, only US in combination with RPGs should be used.

The pregnant female AMH patient requires special consideration. The majority of AMH cases among pregnant women are associated with non-life threatening conditions, and less than 5% are associated with malignancy. Further, the incidence of AMH in pregnant and non-pregnant women is similar (approximately 4%).³⁷ Given that malignancies in this low-risk group (typically < 40 years of age) are rare, the Panel recommends use of MRU, MRI with RPGs or US to screen for major renal lesions with a full work-up after delivery once gynecological bleeding and persistent infection have been ruled out.

14. The use of urine cytology and urine markers (NMP22®, BTA stat® and UroVysion® FISH) is NOT recommended as a part of the routine evaluation of the AMH patient. Recommendation (Evidence Strength: Grade C)

The literature on urine cytology and urine markers indicates that these tests lack sufficient clinical reliability to be used in the routine evaluation of the AMH patient. Multiple studies report sensitivity and/or specificity values for urine cytology.^{17,38–41} Sensitivity values range from 0% to 100%; specificity values range from 62.5% to 100%. For NMP22®, sensitivities range from 6.0% to 100% and specificities range from 62% to 92%. Only two studies report on BTA stat®,^{41,42} and only specificities could be calculated (69% and 73%, respectively) because no malignancies were detected in the samples. Three studies report UroVysion® FISH^{17,40,41} sensitivities ranging from 61% to 100% and specificities ranging from 71.4% to 93%. Overall, the Panel interprets these data to indicate that these tests are inappropriate for routine use in AMH patients because the burden of emotional stress that could result from a false positive test and the risks of unnecessary diagnostic procedures (e.g., biopsies) outweighs the potential benefits to the patient.

15. In patients with persistent MH following a negative work-up or those with other risk factors for carcinoma *in situ* (e.g., irritative voiding symptoms, current or past tobacco use, chemical exposures), cytology may be useful. Option (Evidence Strength: Grade C)

Although urine cytology exhibits inadequate reliability as a clinical indicator for malignancy when used as a single test, it can be useful in the context of the high-risk patient in conjunction with other findings suggestive of malignancy. Available data suggest that although cytology is likely to result in a false negative finding, it is unlikely to produce a false positive finding. The decision to incorporate cytology as part of the AMH work-up is best made by the treating physician who has knowledge of the patient's history, physical findings and other clinical information. It should be emphasized, however, that a negative cytology finding does not preclude a full work-up.

16. Blue light cystoscopy should NOT be used in the evaluation of patients with AMH. Recommendation (Evidence Strength: Grade C)

Blue light cystoscopy is a form of fluorescence cystoscopy in which a photosensitizing compound is instilled in the bladder where it binds preferentially with neoplastic cells and emits visible fluorescence under blue-violet illumination.⁴³

Hexyl aminolevinate, as well as the associated blue light equipment, is FDA-approved for evaluation of patients with suspicion of papillary bladder

cancer. In addition, the available studies demonstrate improved sensitivity and somewhat reduced specificity for blue light cystoscopy compared with white light cystoscopy; with lower specificity, there is an increased risk of unnecessary biopsy. In the absence of any studies in patients being evaluated for MH, and in light of the known risks, the panel concludes that the risks and burdens of using blue-light cystoscopy in the initial evaluation of patients with MH outweigh the benefits.

17. If a patient with a history of persistent AMH has two consecutive negative annual urinalyses (one per year for two years from the time of initial evaluation or beyond), then no further urinalyses for the purpose of evaluation of AMH are necessary. Expert Opinion

If the urinalysis is negative for two consecutive years, then the risk of urologic or nephrologic disease may be no greater than that of the general population. For example, a group of MH positive patients in whom no disease was found after work-up (e.g., film of the kidneys, ureters and bladder, ultrasound, cystoscopy, IVU) were followed for four years; the probability of discovering a malignancy during the follow-up period was less than 1% in patients aged younger than 90 years.⁴⁴ In addition, a cohort of 234 MH positive male patients aged ≥ 50 years of age at initial testing that underwent a complete evaluation (e.g., cytology, IVU or CT, cystoscopy) and in whom no bladder cancers were detected were followed for 14 years.²³ These data indicate that the overwhelming majority of patients who undergo a thorough initial work-up without positive findings will remain cancer-free.

18. For persistent AMH after negative urologic work-up, yearly urinalyses should be conducted. Recommendation (Evidence Strength: Grade C)

The benefits of annual urinalyses in patients with a negative initial evaluation include early diagnosis of a developing, non-visualized urologic disorder. The risks/burdens of urinalyses are minimal. Data indicate that although the majority of pathologic conditions are captured on a thorough initial work-up, a small proportion of AMH patients have disease states that are not initially detected but progress over time and are identified on later evaluations.^{45,46}

In addition to malignant findings, patients who undergo an initial negative evaluation for AMH may also be at risk for other non-malignant disease processes⁴⁷ (e.g., urolithiasis; obstructive uropathy, such as strictures; infectious processes, such as tuberculosis; medical renal disease, such as glomerular nephropathy).

Patients most in need of yearly testing are those in the higher risk population for development of

subsequent disease discussed previously. Follow-up of these high-risk patients is even more important because MH may precede the diagnosis of bladder cancer by many years.^{6–9,22}

19. For persistent or recurrent AMH after initial negative urologic work-up, repeat evaluation within three to five years should be considered. *Expert Opinion*

The likelihood of finding significant urologic diagnoses on subsequent work-up, particularly urologic cancers, appears to be related to the risk factors within the population being studied. More cancers were found in studies of patients referred for initial work-up of MH (as opposed to those detected by screening), populations of older patients and populations with a higher proportion of male patients.

Changes in the clinical scenario, such as a substantial increase in the degree of MH, the detection of dysmorphic RBCs with concomitant hypertension and/or proteinuria, the development of gross hematuria, pain or other new symptoms, may warrant earlier re-evaluation and/or referral to other practitioners, such as nephrologists. The threshold for re-evaluation should take into account patient risk factors for urologic pathologic conditions, such as malignancy, as well as the fact that patients who previously had a thorough initial work-up with negative findings are likely to remain cancer-free.²³

Patients with causes of AMH that persist and may not require intervention, such as those with enlarged prostate and friable surface vessels, or those with Randall's plaques and non-obstructing stones, present a special challenge since malignant causes of AMH may be masked by the presence of these other entities. The Panel suggests that these patients undergo annual urinalysis and that clinicians use judgment and knowledge of risk factors to decide when and whether to perform a re-evaluation.

FUTURE STUDIES

AMH is a sign, not a diagnosis or health condition. This is one of the most common clinical scenarios physicians face, and based on the existence of widespread screening in the absence of evidence to support its role,⁴⁸ there is significant room to improve understanding of this scenario and its management.

High quality reporting of single institution or collaborative experiences or registry studies may be the hallmark of future reports given the unlikelihood that randomized controlled trials will occur broadly on this topic. It is imperative that authors publish robust information regarding baseline characteristics of the populations reported, evaluation strategies utilized and long term surveillance protocols in place (see [Appendix](#)).

Conflict Of Interest Disclosures

All panel members completed COI disclosures. Relationships that have expired (more than one year old) since the panel's initial meeting, are listed. Those marked with (C) indicate that compensation was received; relationships designated by (U) indicate no compensation was received.

Consultant/Advisor: **Rodney Davis**, Corrections Corp of America (C); **J. Stephen Jones**, Cook (C), GSK, (C), Pfizer (C), Predictive Biosciences (C), GTX (C)(expired), Amgen (C)(expired); **Andrew Charles Peterson**, American Medical Systems Inc. (C); **Daniel Ari Barocas**, Bayer (C), Dendreon (C), GE Healthcare (C), Ferring, (C)(expired); Janssen (C); **Erik P. Castle**, Baxter (C)(expired)

Meeting Participant or Lecturer: **J. Stephen Jones**, Endocare (C), Abbott (C), Pfizer (C), GSK (C)(expired); **Raymond J. Leveillee**, Applied Medical (C), Cook Urological (C), Intuitive (C); **Andrew Charles Peterson**, American Medical Systems Inc.(C); **Erik P. Castle**, Intuitive Surgical (C);

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Disclaimer

This document was written by the Asymptomatic Microhematuria Guidelines Panel of the American Urological Association Education and Research, Inc., which was created in 2009. The Practice Guidelines Committee (PGC) of the AUA selected the panel chair. Panel members were selected by the chair. Membership of the panel included urologists and other clinicians with specific expertise on this disorder. The mission of the committee was to develop recommendations that are analysis-based or consensus-based, depending on Panel processes and available data, for optimal clinical practices in the diagnosis and treatment of asymptomatic microhematuria.

Funding of the committee was provided by the AUA. Committee members received no remuneration for their work. Each member of the committee provides an ongoing conflict of interest disclosure to the AUA.

While these guidelines do not necessarily establish the standard of care, AUA seeks to recommend and to encourage compliance by practitioners with current best practices related to the condition being treated. As medical knowledge expands and technol-

ogy advances, the guidelines will change. Today, these evidence-based guideline statements represent not absolute mandates but provisional proposals for treatment under the specific conditions described in each document. For all these reasons, the guidelines do not pre-empt physician judgment in individual cases.

Treating physicians must take into account variations in resources, and patient tolerances, needs, and preferences. Conformance with any clinical guideline does not guarantee a successful outcome. The guideline text may include information or recommendations about certain drug uses ('off label') that are not approved by the Food and Drug Administration, or about medications or substances not subject to the FDA approval process. AUA urges strict compliance with all government regulations and protocols for prescription and use of these substances. The physician is encouraged to carefully follow all available prescribing information about indications, contraindications, precautions and warnings. These guidelines are not intended to provide legal advice about use and misuse of these substances.

Although guidelines are intended to encourage best practices and potentially encompass available technologies with sufficient data as of close of the literature review, they are necessarily time-limited. Guidelines cannot include evaluation of all data on emerging technologies or management, including those that are FDA-approved, which may immediately come to represent accepted clinical practices.

For this reason, the AUA does not regard technologies or management which are too new to be addressed by these guidelines as necessarily experimental or investigational.

APPENDIX

Information to be reported in future AMH studies

Patient Information	Detailed patient inclusion/exclusion criteria Detailed patient demographics, including age, gender, race/ethnicity, occupation, and smoking status Patient past medical and surgical history relevant to conditions associated with AMH, including renal or urological disease, trauma or instrumentation, anticoagulation medication use
AMH Diagnosis Methods & Findings	Initial diagnosis methods (e.g., dipstick, microscopy) and findings Whether dipstick or microscopy was repeated prior to diagnostic work-up Type of dipstick, use of automation, methods for and findings of microscopic examination, including results of urine specific gravity and protein
Work-up Methods & Findings	Description of all work-up methods, including laboratory tests, cytology, urine markers, cystoscopy, and imaging Findings from all work-up methods Report of findings for patients overall as well as for clinically important subgroups (i.e., males, smokers, older patients, patients with other risk factors)
Follow-Up Methods & Findings	Description of follow-up protocols in AMH patients with negative findings on initial work-up, including periodicity of repeat urinalyses Description of repeat evaluation methods and trigger for repeat evaluation Findings from repeat evaluation

REFERENCES

- Faraday M, Hubbard H, Kosiak B et al: Staying at the Cutting Edge: a review and analysis of evidence reporting and grading: the recommendations of the American Urological Association. *Brit J Urol* 2009; **104**: 294.
- Grossfeld GD, Litwin MS, Wolf JS et al: Evaluation of asymptomatic microscopic hematuria in adults: the American Urological Association best practice policy—part I: definition, detection, prevalence, and etiology. *Urology* 2001; **57**: 599.
- Sutton JM: Evaluation of hematuria in adults. *JAMA* 1990; **263**: 2475.
- Copley JB: Isolated asymptomatic hematuria in the adult. *Am J Med Sci* 1986; **291**: 101.
- Culclasure TF, Bray VJ and Hasbargen JA: The significance of hematuria in the anticoagulated patient. *Arch Intern Med* 1994; **154**: 649.
- Messing EM, Young TB, Hunt VB et al: The significance of asymptomatic microhematuria in men 50 or more years old: findings of a home screening study using urinary dipsticks. *J Urol* 1987; **137**: 919.
- Messing EM, Young TB, Hunt VB et al: Urinary tract cancers found by homescreening with hematuria dipsticks in healthy men over 50 years of age. *Cancer* 1989; **64**: 2361.
- Messing EM, Young TB, Hunt VB et al: Home screening for hematuria: results of a multiclinic study. *J Urol* 1992; **148**: 289.
- Messing EM, Young TB, Hunt VB et al: Hematuria home screening: repeat testing results. *J Urol* 1995; **154**: 57.
- Britton JP, Dowell AC and Whelan P: Dipstick haematuria and bladder cancer in men over 60: results of a community study. *BMJ* 1989; **299**: 1010.
- Britton JP, Dowell AC, Whelan P et al: A community study of bladder cancer screening by the detection of occult urinary bleeding. *J Urol* 1992; **148**: 788.
- Emamian SA, Nielsen MB and Pedersen JF: Can dipstick screening for hematuria identify individuals with structural renal abnormalities? A sonographic evaluation. *Scand J Urol Nephrol* 1996; **30**: 25.
- Haug K, Bakke A, Daae LN et al: Screening for hematuria, glucosuria and proteinuria in people aged 55–64. Technical, clinical and cost-benefit experience from a pilot study. *Scand J Prim Health Care* 1985; **3**: 31.
- Hedelin H, Jonsson K, Salomonsson K et al: Screening for bladder tumours in men aged 60–70 years with a bladder tumour marker (UBC) and dipstick-detected haematuria using both white-light and fluorescence cystoscopy. *Scand J Urol Nephrol* 2006; **40**: 26.
- Murakami S, Igarashi T, Hara S et al: Strategies for asymptomatic microscopic hematuria: a prospective study of 1,034 patients. *J Urol* 1990; **144**: 99.
- Ritchie CD, Bevan EA and Collier SJ: Importance of occult haematuria found at screening. *Br Med J (Clin Res Ed)* 1986; **292**: 681.
- Steiner H, Bergmeister M, Verdorfer I et al: Early results of bladder-cancer screening in a high-risk population of heavy smokers. *Brit J Urol* 2008; **102**: 291.

18. Suzuki Y, Sasagawa I, Abe Y et al: Indication of cystoscopy in patients with asymptomatic microscopic haematuria. *Scand J Urol Nephrol* 2000; **34**: 51.
19. Thompson IM: The evaluation of microscopic hematuria: a population-based study. *J Urol* 1987; **138**: 1189.
20. Topham PS, Jethwa A, Watkins M et al: The value of urine screening in a young adult population. *Fam Pract* 2004; **21**: 18.
21. Yamagata K, Takahashi H, Tomida C et al: Prognosis of asymptomatic hematuria and/or proteinuria in men. *Nephron* 2002; **91**: 34.
22. Hiatt RA and Ordonez JD: Dipstick urinalysis screening, asymptomatic microhematuria, and subsequent urological cancers in a population-based sample. *Cancer Epidemiol Biomarkers Prev* 1994; **3**: 439.
23. Madeb R, Golijanin D, Knopf J et al: Long-term outcome of patients with a negative work-up for asymptomatic microhematuria. *Urology* 2010; **75**: 20.
24. Silverman S, Leyendecker J and Amis E: What is the current role of CT urography and MR urography in the evaluation of the urinary tract? *Radiology* 2009; **250**: 309.
25. Ramchandani P, Kisler T, Francis IR et al: Expert panel on urologic imaging, ACR Appropriateness Criteria® hematuria. American College of Radiology (ACR) 2008; 5.
26. Turney JH: Acute renal failure—a dangerous condition. *JAMA* 1996; **275**: 1516.
27. Morcos SK, Thomsen HS and Webb JA: Contrast-media-induced nephrotoxicity: a consensus report. Contrast Media Safety Committee, European Society of Urogenital Radiology (ESUR). *Eur Radiol* 1999; **9**: 1602.
28. Mehran R and Nikolsky E: Contrast-induced nephropathy: definition, epidemiology, and patients at risk. *Kidney Int Suppl* 2006; **S11**.
29. Wollin T, Laroche B and Psooy K: Canadian guidelines for the management of asymptomatic microscopic hematuria in adults. *Can Urol Assoc J* 2009; **3**: 77.
30. Kawashima A, Glockner JF and King BF Jr.: CT urography and MR urography. *Radiol Clin North Am* 2003; **41**: 945.
31. Chahal R, Taylor K, Eardley I et al: Patients at high risk for upper tract urothelial cancer: Evaluation of hydrophosphorus using high resolution magnetic resonance urography. *J Urol* 2005; **174**: 478.
32. Leyendecker J, Barnes C and Zagoria, R: MR urography: Techniques and clinical applications. *RadioGraphs* 2008; **28**: 23.
33. Nikken JJ and Krestin GP: MRI of the kidney—state of the art. *Eur Radiol* 2007; **17**: 2780.
34. Regan F, Kuszyk B, Bohlman M et al: Acute 1. ureteric calculus obstruction: unenhanced spiral CT versus HASTE MR urography and abdominal radiograph. *Br J Radiol* 2005; **78**: 506.
35. Sudah M, Vanninen R, Partanen K et al: MR urography in evaluation of acute flank pain: T2-weighted sequences and gadolinium enhanced three-dimensional FLASH compared with urography. *AJR* 2001; **176**: 105.
36. Takahashi N, Glockner JF, Hartman RP et al: Gadolinium enhanced magnetic resonance urography for upper urinary tract malignancy. *J Urol* 2010; **183**: 1330.
37. Stehman-Breen CO, Levine RJ, Qian C et al: Increased risk of preeclampsia among nulliparous pregnant women with idiopathic hematuria. *Am J Obstet Gynecol* 2002; **187**: 703.
38. Chahal R, Gogoi N and Sundaram: Is it necessary to perform urine cytology in screening patients with haematuria? *Eur Urol* 2001; **39**: 283.
39. Grossman HB, Messing E, Soloway M et al: Detection of bladder cancer using a point-of-care proteomic assay. *JAMA* 2005; **293**: 810.
40. Sarosdy MF, Kahn PR, Ziffer MD et al: Use of a 1. multitarget fluorescence in situ hybridization assay to diagnose bladder cancer in patients with hematuria. *J Urol* 2006; **176**: 44.
41. Quek P, Chin CM and Lim PH: The role of BTA stat in clinical practice. *Ann Acad Med Singapore* 2002; **31**: 212.
42. Landman J, Chang Y, Kavalier E et al: Sensitivity and specificity of NMP-22, telomerase, and BTA in the detection of human bladder cancer. *Urology* 1998; **52**: 398.
43. Jichlinski P: Photodynamic applications in superficial bladder cancer: facts and hopes+ACE. *J Environ Pathol Toxicol Oncol* 2006; **25**: 441.
44. Edwards TJ, Dickinson AJ, Gosling J et al: Patient-specific risk of undetected malignant disease after investigation for haematuria, based on a 4-year follow-up. *Brit J Urol* 2011; **107**: 247.
45. Yasumasu T, Koikawa Y, Uozumi J et al: Clinical study of asymptomatic microscopic haematuria. *Int Urol Nephrol* 1994; **26**: 1.
46. Davides KC, King LM and Jacobs D: Management of microscopic hematuria: twenty-year experience with 150 cases in a community hospital. *Urology* 1986; **28**: 453.
47. Jaffe JS, Ginsberg PC, Gill R et al: A new diagnostic algorithm for the evaluation of microscopic hematuria. *Urology* 2001; **57**: 889.
48. Chou R and Dana T: Screening adults for bladder cancer: a review of the evidence for the U.S. preventive services task force. *Ann Intern Med* 2010; **153**: 461.