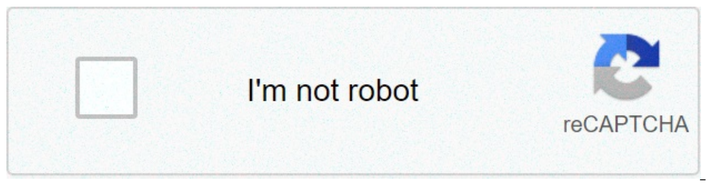

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Microscopic haematuria referral guidelines

The NICE Clinical Knowledge Summaries (CKS) site is only available to users in the UK, Crown Dependencies and British Overseas Territories. CKS content is produced by Clarity Informatics Limited. It is available to users outside the UK via subscription from the Prodigy website. If you believe you are seeing this page in error please contact us. Condition: Non-visible Haematuria Section Author: Jon Rees Review Date: September 2017 Overview Another controversial issue – the management of non-visible haematuria (NVH) in primary care. Non-visible haematuria is now the recommended terminology, replacing phrases such as 'dipstick haematuria' and 'microscopic haematuria'. Some key issues for primary care: When to test for haematuria – screening is not recommended, and much of the difficulty in managing this finding can be avoided if urine is tested for blood only in appropriate circumstances. When to refer patients with NVH to secondary care for further investigation – not all patients with NVH need urological or nephrological assessment – patients with asymptomatic NVH found below the age of 40, with normal renal function, can be managed in primary care – the BAUS / Renal Association guidelines have full detail of this. When to refer patients with NVH via the 2 week wait suspected cancer pathway – this was updated in 2015 in the NICE Referral for Suspected Cancer Guidelines. Remember though that if patients do not meet the 2 week wait criteria, they may still need referral outside of this pathway, according to the BAUS / Renal Association guidelines, which still apply. NICE guidelines should only be used to determine the urgency of referral. Summary of NICE guidance (all haematuria ie including Visible Haematuria), June 2015: Remember that the criteria below ONLY tell you who to refer urgently via a two week wait pathway – many patients who do not meet these criteria will need an urgent urological referral for further investigation. Healthcare Professional Links Guidelines for management of non-visible haematuria in primary care – produced by British Association of Urological Surgeons and the Renal Association in 2009, and still the key document to understand: 'Assessment and management of non-visible haematuria in primary care'. Kelly JD et al. BMJ 2009; 338: a3021. Haematuria – 10 Top Tips for Primary Care, published by MacMillan Cancer Support 2016: NICE guideline (NG12): Suspected cancer: recognition and referral. June 2015. 'Blood in Pee' campaign – information from Cancer Research UK: 'Blood in Pee' campaign – information for patients on NHS Choices: Kelly JD et al. BMJ 2009; 338: a3021 Information for patients BAUS Renal Association The purpose of this guideline is to provide a clinical framework for the diagnosis, evaluation, and follow-up of asymptomatic microhematuria (AMH).MethodsA systematic review of the literature using the MEDLINE database (search dates January 1980 – November 2011) was conducted to identify peer-reviewed publications relevant to the diagnosis, evaluation, and follow-up of asymptomatic microhematuria in adults. The review yielded an evidence base of 192 articles after application of inclusion/exclusion criteria. These publications were used to create the majority of the clinical framework. When sufficient evidence existed, the body of evidence for a particular treatment was assigned a strength rating of A (high), B (moderate), or C (low) and evidence-based statements of Standard, Recommendation, or Option were developed. Additional information is provided as Clinical Principles and Expert Opinion when insufficient evidence existed. See text and algorithm for definitions and detailed diagnostic, evaluation, and follow-up information.Guideline Statements1. Asymptomatic microhematuria (AMH) is defined as three or greater red blood cells (RBC) per high powered field (HPF) 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 Opinion2. The assessment of the asymptomatic microhematuria 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 Principle3. Once benign causes have been ruled out, the presence of asymptomatic microhematuria should prompt a urologic evaluation. Recommendation (Evidence Strength Grade C)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 Principle5. The presence of dysmorphic red blood cells, proteinuria, cellular casts, and/or renal insufficiency, or any other clinical indicator suspicious for renal parenchymal disease warrants concurrent nephrologic workup but does not preclude the need for urologic evaluation. Recommendation (Evidence Strength Grade C)6. Microhematuria 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)7. For the urologic evaluation of asymptomatic microhematuria, a cystoscopy should be performed on all patients aged 35 years and older. Recommendation (Evidence Strength Grade C)8. In patients younger than age 35 years, cystoscopy may be performed at the physician's discretion. Option (Evidence Strength Grade C)9. A 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 Principle10. The initial evaluation for AMH should include a radiologic evaluation. Multi-phasic computed tomography (CT) urography (without and with intravenous (IV) 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)11. For patients with relative or absolute contraindications that preclude use of multi-phasic CT (such as renal insufficiency, contrast allergy, pregnancy), magnetic resonance urography (MRU) (without/with IV contrast) is an acceptable alternative imaging approach. Option (Evidence Strength Grade C)12. For patients with relative or absolute contraindications that preclude use of multiphase CT (such as renal insufficiency, contrast allergy, pregnancy) where collecting system detail is deemed imperative, combining magnetic resonance imaging (MRI) with retrograde pyelograms (RPGs) provides alternative evaluation of the entire upper tracts. Expert Opinion13. For patients with relative or absolute contraindications that preclude use of multiphase 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 ultrasound (US) with retrograde pyelograms (RPGs) provides alternative evaluation of the entire upper tracts. Expert Opinion14. 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 asymptomatic microhematuria patient. Recommendation (Evidence Strength Grade C)15. In patients with persistent microhematuria 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)16. Blue light cystoscopy should not be used in the evaluation of patients with asymptomatic microhematuria. Recommendation (Evidence Strength Grade C)17. If a patient with a history of persistent asymptomatic microhematuria 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 Opinion18. For persistent asymptomatic microhematuria after negative urologic work up, yearly urinalyses should be conducted. Recommendation (Evidence Strength Grade C)19. For persistent or recurrent asymptomatic microhematuria after initial negative urologic work-up, repeat evaluation within three to five years should be considered. Expert Opinion 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 (AMH). The strategies and approaches recommended in this document were derived from evidence-based and consensus-based processes. This document constitutes a clinical strategy and is not intended to be interpreted rigidly. The most effective approach for a particular patient is best determined by the individual clinician and patient. As the science relevant to AMH evolves and improves, the strategies presented here will require amendment to remain consistent with the highest standards of clinical care.MethodologyA systematic review was conducted to identify published articles relevant to the diagnostic yield of mass screening for microhematuria (MH) as well as the work-up and follow-up of adult patients with AMH. Literature searches were performed on English-language publications using the MEDLINE database from January 1980 to November 2011. Data from studies published after the literature search cut-off will be incorporated into the next version of this guideline. Preclinical studies (e.g., animal models), pediatric studies, commentary, and editorials were excluded. Review article references were checked to ensure inclusion of all possibly relevant studies. Multiple reports on the same patient group were carefully examined to ensure inclusion of only non-redundant information. The review yielded an evidence base of 192 articles from which to construct a clinical framework for the diagnosis, work-up, and follow-up of AMH.Quality of Individual Studies and Determination of Evidence Strength. Quality of individual studies that were randomized controlled trials (RCTs), controlled clinical trials (CCTs), or comparative observational studies was assessed using the Cochrane Risk of Bias tool.1 Because there is no widely-agreed upon quality assessment tool for single cohort observational studies, the quality of these studies was not assessed except in the case of diagnostic accuracy studies. Diagnostic accuracy studies were rated using the QUADAS.2-3The categorization of evidence strength is conceptually distinct from the quality of individual studies. Evidence strength refers to the body of evidence available for a particular question and includes consideration of study design, individual study quality, consistency of findings across studies, adequacy of sample sizes, and generalizability of samples, settings, and treatments for the purposes of the guideline. The AUA categorizes body of evidence strength (ES) as Grade A (well-conducted RCTs or exceptionally strong observational studies), Grade B (RCTs with some weaknesses of procedure or generalizability or generally strong observational studies), or Grade C (observational studies that are inconsistent, have small sample sizes, or have other problems that potentially confound interpretation of data).For some clinical issues, there was little or no evidence from which to construct evidence-based statements. Where gaps in the evidence existed, the Panel provides guidance in the form of Clinical Principles or Expert Opinion with consensus achieved using a modified Delphi technique if differences of opinion emerged.4 A Clinical Principle is a statement about a component of clinical care that is widely agreed upon by urologists or other clinicians for which there may or may not be evidence in the medical literature. Expert Opinion refers to a statement, achieved by consensus of the Panel, that is based on members' clinical training, experience, knowledge, and judgment for which there is no evidence. AUA Nomenclature: Linking Statement Type to Evidence Strength. The AUA nomenclature system explicitly links statement type to body of evidence strength and the Panel's judgment regarding the balance between benefits and risks/burdens.5 Standards are directive statements that an action should (benefits outweigh risks/burdens) or should not (risks/burdens outweigh benefits) be undertaken based on Grade A or Grade B evidence. Recommendations are directive statements that an action should (benefits outweigh risks/burdens) or should not (risks/burdens outweigh benefits) be undertaken based on Grade C evidence. Options are non-directive statements that leave the decision to take an action up to the individual clinician and patient because the balance between benefits and risks/burdens appears relatively equal or appears unclear; Options may be supported by Grade A, B, or C evidence.Limitations of the Literature. The Panel proceeded with full awareness of the limitations of the MH literature. These limitations included poorly-defined patient groups, heterogeneous patient groups, or patient groups with limited generalizability; use of different AMH work-up thresholds; use of different AMH work-up protocols; failure to follow all patients; and limited follow-up durations. The completed evidence report may be requested from AUA.Process. The Asymptomatic Microhematuria Panel was created in 2009 by the American Urological Association Education and Research, Inc. (AUA). The Practice Guidelines Committee (PGC) of the AUA selected the Panel Chair and Vice Chair who in turn appointed the additional panel members with specific expertise in this area.The AUA conducted a thorough peer review process. The draft guidelines document was distributed to 59 peer reviewers, of which 30 reviewers provided comments. The panel reviewed and discussed all submitted comments and revised the draft as needed. Once finalized, the guideline was submitted for approval to the PGC, and finally to the AUA Board of Directors for final approval. Funding of the panel was provided by the AUA, although panel members received no remuneration for their work.BackgroundDefinition. For the purpose of this guideline, microhematuria is defined by the presence of three or more red blood cells (RBCs) per high-powered field (HPF)6-8 on microscopic examination of one properly-collected, non-contaminated urinalysis with no evidence of infection for which a combination of microscopic urinalysis and dipstick excludes other abnormalities such as pyuria, bacteriuria, and contaminants. In addition, benign causes, such as menstruation, vigorous exercise, viral illness, trauma, and infection, have been excluded.Literature Limitations and Interpretation. The Panel notes that requiring a single positive urinalysis verified by microscopy is a departure from the 2001 AUA Best Practice Statement on asymptomatic microhematuria in adults,9 which required that two of three properly-collected samples be positive on microscopy. The Panel searched for an evidence base to directly support the selection of one, two, or more positive samples as the threshold for evaluation. Such an evidence base would be comprised of studies that used different numbers of positive samples to trigger an evaluation, conducted thorough evaluations, and followed all patients regularly and over long periods of time to determine the impact of requiring one, two or more positive samples on diagnostic timing, missed diagnoses, and short- and long-term patient outcomes. The existing literature does not contain studies of this type; that is, the literature does not examine the impact of number of positive samples on evaluation yield or patient outcomes.Therefore, the Panel examined the available literature to determine whether it provided indirect support for the use of one or more positive samples to trigger evaluation. This examination led to the conclusion that one positive sample is sufficient to prompt an evaluation for three reasons. First, there is substantial evidence that microhematuria that is caused by a serious underlying condition such as a malignancy can be highly intermittent;10-15 therefore, requiring multiple positive samples may result in an undetermined risk of missing a malignant diagnosis.Second, the existence of this risk is supported by studies that evaluated patients after obtaining one positive sample; urological malignancy rates ranged from 1.0% to 25.8% with most studies detecting malignancies at rates over 2.0%.11-12, 15-29 A meta-analysis of these studies revealed a pooled urinary tract malignancy rate of 3.3% (95% confidence interval: 2.2 to 5.0%). If previously undiagnosed prostate cancers are included in the meta-analysis, then the pooled overall malignancy rate was 3.6% (95% confidence interval: 2.3 to 5.5%). Therefore, working patients up in response to one positive sample resulted in the detection of significant numbers of life-threatening conditions.A comparable analysis of studies that required more than one positive sample before undertaking an evaluation30-41 revealed somewhat lower rates of urinary tract malignancies (1.8% with 95% CI = 1.0 – 3.0%) and all malignancies (1.8% with 95% CI = 1.0 – 3.2%). Whether malignancy detection rates are actually lower in studies that required more than one positive sample, however, is difficult to know given that in a third group of studies it was not clear how many positive samples were required before evaluation.42-59 Meta-analysis of these studies revealed rates of 4.3% for urinary tract malignancies (95% CI: 3.3 to 5.5%) and 4.8% for all malignancies (95% CI: 3.7 to 6.2%). It is likely that this group of studies includes both those that undertook evaluation after one positive sample as well as those that required more than one positive sample before evaluation. The Panel interpreted these data overall to indicate that evaluation in response to a single positive sample was warranted.Third, the Panel notes that diagnoses that may not be life-threatening but that would benefit from active clinical management and/or follow up are frequently revealed during the AMH workup. These diagnoses include medical renal disease, calculous disease, benign prostatic enlargement, and urethral stricture. In studies that evaluated patients after one positive sample, rates of calculous disease ranged from 1.0% to 19.4% with a meta-analyzed rate of 6.0% (95% CI: 3.8 – 9.2%), rates of benign prostatic enlargement ranged from 1.0% to 38.7% with a meta-analyzed rate of 12.9% (95% CI: 6.3 – 24.6%), and rates of urethral stricture ranged from less than 1% to 7.1% with a meta-analyzed rate of 1.4% (95% CI: 0.6 – 3.2%). Overall, the Panel interpreted these data regarding possible underlying malignancies as well as other conditions that would benefit from active clinical management to indicate that a single positive sample constitutes AMH and warrants evaluation.Prevalence. The adult population prevalence of microhematuria varies depending on age, gender, frequency of testing, threshold used to define microhematuria and study group characteristics, such as the presence of risk factors (i.e., past or current smoking). Rates of microhematuria using microscopy and dipstick analyses in over 80,000 individuals that participated in health screenings ranged from 2.4% to 31.1%, with higher rates in males over age 60 years and in men who are current or past smokers.10-15,17,19-20,22-23,25,27-28,60-62 Higher rates are also found in samples that are repeatedly tested.10-13Origins and Causes. The origins of microhematuria are either urologic or nephrologic. The most common urological etiologies are benign prostatic enlargement, infection and urinary calculi. Three sets of studies indicate that only a small proportion of patients with microhematuria will ultimately be diagnosed with a urinary tract malignancy. These studies include the following: Screening studies in which individuals 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. Findings from 17 screening studies revealed an overall urinary tract malignancy rate of approximately 2.6%.10-15,17,19-20,22-23, 25, 27-28, 60-62 Rates in individual studies ranged from 0% to 25.8%, with repeated testing in high-risk individuals (e.g., male smokers aged 60 years or greater) yielding higher rates. Thirty-two studies reported findings from initial work-ups and reported an overall malignancy rate of 4.0%.16, 21, 24,26, 30-32, 34-35, 37, 40-57,59, 63-66Rates in individual studies ranged from 0 to 9.3%. Eight studies reported on AMH patients for whom an initial work-up did not yield a diagnosis and who were referred on for a more detailed work-up; the overall malignancy rate in this group of studies was 2.8%.58, 60, 67-72 For more detailed discussion of these three sets of studies, see Discussion under Guideline Statement 3. The most common risk factors for urinary tract malignancy in AMH patients are listed in Table 1.9Table 1: Common Risk Factors for Urinary Tract Malignancy in Patients with MicrohematuriaMale genderAge (> 35 years)Past or current smokingOccupational or other exposure to chemicals or dyes (benzenes or aromatic amines)Analgesic abuseHistory of gross hematuriaHistory of urologic disorder or diseaseHistory of irritative voiding symptomsHistory of pelvic irradiationHistory of chronic urinary tract infectionHistory of exposure to known carcinogenic agents or chemotherapy such as alkylating agentsHistory of chronic indwelling foreign bodyThe presence of urinary casts, proteins, and/or dysmorphic red blood cells suggests a medical renal etiology for AMH. Nephropathies and nephritis are the most common causes of microhematuria in this category. The processes may be immunological, infectious or drug-induced. The literature on nephrologic findings in AMH patients is not as extensive as the literature on urological malignancies and the finding of renal malignancy is less common than the finding of bladder malignancy.73 However, studies report high rates of nephrologic disease in specialized patient groups, including patients with persistent AMH39, 52, 60, 69, 74-75 and patients referred for a nephrology work up.31, 48, 76-77 It is important to note that in some studies patients ultimately diagnosed with medical renal disease were younger than age 40 years.39, 60Evolution of Imaging Technologies. In the previous version of this document,9 intravenous urography (IVU) 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 had limited sensitivity in detecting small renal masses and could not distinguish solid from cystic masses, resulting in the need for US, CT or MRI to fully characterize lesions. With regard to US, the authors of the 2001 report noted that although it was excellent for detection of renal cysts, it was limited in detection of small solid renal lesions and urothelial carcinoma in the kidney or ureter. For this reason, in patients with risk factors for serious disease states, the authors of the 2001 report recommended the use of CT urography.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. US and IVU generate criteria identifying morphologic changes in the kidneys and collecting system, but while the presence of masses is established with reasonable accuracy, these methods do not provide criteria for tissue characterization. Therefore, the use of these modalities 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 (see discussion under Guideline Statement 10). Both of these issues are avoided with the use of CT urography and MRI urography – two modalities that have been developed and refined during the decade since the publication of the prior document.78 CT urography provides a detailed anatomic depiction of the urinary tract. MR urography, although potentially providing less anatomic detail, has the advantage of avoiding the use of ionizing radiation. Both modalities are superior to IVU and US in sensitivity and specificity for a wide variety of urologic conditions detectable in the AMH patient.78 For these reasons, the Panel emphasizes use of these modalities in the diagnosis sections that follow.It is important to note, however, that the choice of imaging modality is best made by the treating physician who has full knowledge of a particular patient's history and in the context of available resources. In addition, the Panel is fully aware that in patients with contraindications for use of CT and/or MRI, the combination of US with retrograde pyelograms may be the optimal imaging strategy.Diagnosis and Work-UpProper Sample Collection. For most initial evaluations, a random midstream clean-catch collection is sufficient. Patients should be instructed to discard the initial 10 mL of voided urine into the toilet in order to collect the midstream void. If a significant number of squamous cells are present in the sample, then contamination is possible and a repeat specimen collection or catheterization should be considered.Male patients: Mid-stream voided specimens are adequate unless the patient is unable to void. The specimen can be collected into the sterile specimen cup after gently cleaning the urethral meatus with a sterilization towelette. In uncircumcised men it is important to retract the foreskin to avoid contamination.Female patients: A voided midstream specimen should be the primary method unless there are circumstances such as known problems with repeated specimen contamination or a history of difficulty voiding. The patient should be instructed to spread the labia adequately to allow for cleansing of the urethral meatus with a sterilization towelette and to avoid introital contamination.In some patients, catheterization may be necessary in order to obtain an appropriate specimen. This subgroup includes the obese female patient and patients with a non-intact urinary tract, a Foley catheter, a suprapubic catheter, or who use intermittent catheterization. Women with concurrent menstruation should be reevaluated after its cessation or should undergo catheterization to determine if the blood is present in the bladder or only results from vaginal contamination.Specimen: The specimen container should be labeled per institutional protocol and analyzed within standard laboratory regulations. Method of collection, date and time should be included in the labeling.Microscopy Technique. Ten mL aliquots from a freshly voided clean-catch mid-stream urine specimen should be centrifuged in 15 mL tubes at 2,000 revolutions per minute for 10 minutes (or 3,000 revolutions per minute for 5 minutes)79 immediately after collection. The supernatant should be poured off, and the sediment resuspended in 0.3 mL supernatant and/or saline, placed on a microscopic slide (75 mm x 25 mm) and covered with a cover slip (22 mm x 22 mm). At least 10-20 microscopic fields should be examined under 400x magnification. Three or more red blood cells (RBCs) per field is considered a positive specimen.10, 79-81Urine specimens collected immediately after prolonged recumbency (first void in morning) or the first voiding after vigorous physical or sexual activity should not be examined to assess for microhematuria.82-83 It should also be remembered that in dilute urine, usually below an osmolality of 308 mOsm, most RBCs lyse; therefore, the number of RBCs per 400x magnification may be artificially reduced.84The panel emphasizes that a positive dipstick merits microscopic examination of the urinary sediment as described, but does not warrant full evaluation unless this confirms there are three or greater RBC/HPF. If this is not the case but the clinician is suspicious that the findings could reflect true AMH, then repeat microscopic testing may be reasonable after assessing risks of the clinical presentation. Diagnostic and Work-up FrameworkThe guideline statements below are organized to follow and provide the rationale for the accompanying algorithm.Table 2: AUA Nomenclature Linking Statement Type to Evidence StrengthStandard: Directive statement that an action should (benefits outweigh risks/burdens) or should not (risks/burdens outweigh benefits) be taken based on Grade A or B evidenceRecommendation: Directive statement that an action should (benefits outweigh risks/burdens) or should not (risks/burdens outweigh benefits) be taken based on Grade C evidenceOption: Non-directive statement that leaves the decision regarding an action up to the individual clinician and patient because the balance between benefits and risks/burdens appears equal or appears uncertain based on Grade A, B, or C evidenceClinical Principle: a statement about a component of clinical care that is widely agreed upon by urologists or other clinicians for which there may or may not be evidence in the medical literatureExpert Opinion: a statement, achieved by consensus of the Panel, that is based on members' clinical training, experience, knowledge, and judgment for which there is no evidence Asymptomatic microhematuria is a sign, not a diagnosis or health condition. As a result, existing research on the topic is more limited than that available in many topics covered by AUA Guidelines. Nevertheless, 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, 217 there is significant room to improve understanding of this scenario and its management.Furthermore, the panel recognizes that although randomized controlled trials are the gold standard for obtaining evidence to structure care, it is not likely that these will occur broadly on this specific topic based on limited finances and resources to consider related questions when other pressing and more compelling clinical issues are likely to attract these resources. Thus, high quality reporting of single institution or collaborative experiences or registry studies may be the hallmark of future reports. If that is the case, 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 Table 3). The ability to stratify evaluation strategies based on the probability of an underlying serious condition for patients with specific characteristics is currently compromised by the lack of this type of basic information.Table 3. Information To Be Reported in Future AMH StudiesDetailed patient inclusion/exclusion criteriaDetailed patient demographics, including age, gender, race/ethnicity, occupation, and smoking statusPatient past medical and surgical history relevant to conditions associated with AMH, including renal or urological disease, trauma or instrumentation, anticoagulation medication useAMH Diagnosis Methods & FindingsInitial diagnosis methods (e.g., dipstick, microscopy) and findingsWhether dipstick or microscopy was repeated prior to diagnostic workupType of dipstick, use of automation, methods for and findings of microscopic examination, including results of urine specific gravity and proteinWorkup Methods & FindingsDescription of all workup methods, including laboratory tests, cytology, urine markers, cystoscopy, and imagingFindings from all workup methodsReport 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 & FindingsDescription of follow-up protocols in AMH patients with negative findings on initial workup, including periodicity of repeat urinalysesDescription of repeat evaluation methods and trigger for repeat evaluationFindings from repeat evaluationEtiology. Disease-related causes of AMH are well described, but there is little understanding of the underlying cause in patients with an initial negative evaluation. Identification of a marker or other method to define a benign cause could lead to improved risk stratification, especially in the patient with persistent AMH following an initial evaluation.Evaluation Techniques. A growing body of work exists regarding the risk of imaging and contrast agents necessary for characterization of patients with AMH. The panel determined that the benefit of identifying significant pathology outweighs the risk of the evaluation. Nevertheless, there is significant need for even safer contrast agents, or preferably to identify accurate imaging techniques that would not require contrast agents. Recognizing this may be difficult, it is still appealing to identify even a screening evaluation technique that would potentially allow low risk patients to forego contrast agents (i.e. ultrasound). This would ideally also avoid or decrease the dose of ionizing radiation. In lieu of such innovations, there is need for identification of strategies or agents that can limit the risk of contrast agents from both a toxicity and allergic reaction standpoint.With the potential that it might allow avoidance of ionizing radiation and avoids traditional contrast agents, MRU is recommended as an alternative to multi-phasic CT for patients at risk. Nevertheless, the role of MRU in this specific patient population is not well defined in the published literature, and merits further evaluation.The risk of cystoscopy is very low, so it is unlikely that any alternative would be identified that would improve upon this technique. Nevertheless, further efforts at improving patient experience regarding discomfort of the examination are worthwhile. Innovative imaging techniques such as blue light cystoscopy, narrow band imaging, or virtual cystoscopy will require substantial research before it is likely that they will become part of the evaluation, and this should include analysis of costs if they are to play a role in the future healthcare environment.The panel feels that emphasis of research for such diagnostic techniques should approach the question with clarity regarding the need for sensitivity compared to specificity. For example, cystoscopy has proven to be exceedingly sensitive in this specific clinical setting (this is not as clearly established in the bladder cancer patient population, probably based on the difference in prevalence of small, difficult to visualize bladder cancers in the underlying populations). The sensitivity is shown to be high regarding AMH evaluation based on the rarity of identification of bladder cancer following an initial negative evaluation. Thus, it would be unlikely to find value of new techniques such as narrow band imaging and blue light cystoscopy in the evaluation of AMH if their appeal is based on being more sensitive than cystoscopy. Nevertheless, it is possible that emerging technologies may be able to improve upon the specificity of cystoscopy in order to avoid unnecessary biopsies or further investigations.Infectious risk of cystoscopy is low, and the Best Practice Policy Statement on Urologic Surgery Antimicrobial Prophylaxis (2008)117 specifically recommends against routine use of antibiotics for routine cystoscopy. With the recognition that antibiotic resistance is rapidly increasing, the potential for overuse of antibiotics in urological practices to be a contributing factor in subsequent multidrug resistance merits further investigation.Natural history. The panel recognizes that there is almost no published information to guide the decision regarding follow-up after a negative evaluation for AMH. It is recognized that it is uncommon for patients to present in the future with significant findings that appear to have been missed by initial evaluation, but medical, socioeconomic, anxiety, and legal implications create need for this scenario to be further considered.Economic considerations. With the high prevalence of AMH in the population in an era of increasing resource constraints, it would be naïve to ignore economic considerations in future investigations. Most patients who present with this condition have no underlying significant abnormality, so limiting financial expenditures on evaluations of those individuals is particularly appealing. Nevertheless, it is imperative not to allow this to lead to inadequate investigation in the patients who have serious underlying causes, so efforts towards improved risk stratification or triage strategies that allow some patients with AMH to avoid full investigation merit careful consideration. This might involve investigation of urine or serum based tests that could have a high enough sensitivity that a negative test might avert unnecessary invasive and radiological evaluation. Currently, the available literature does not allow evidence-based risk stratification.

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