Update on Haematuria and Bladder Cancer

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Declarations

• None
• Recent changes in TWR

• The problem with Microscopic Haematuria

• The myth of the Haematuria clinic

• Update on bladder cancer management
Referral guidelines for suspected cancer

Issued: June 2005  last modified: April 2011
NICE clinical guideline 27
guidance.nice.org.uk/cg27

1.6.4 Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) for bladder cancer if they are:
- aged 45 and over and have:
  - unexplained visible haematuria without urinary tract infection or
  - visible haematuria that persists or recurs after successful treatment of urinary tract infection,
1.8.12 In patients under 50 years of age with microscopic haematuria, the urine should be tested for proteinuria and serum creatinine levels measured. Those with proteinurea or raised serum creatinine should be referred to a renal physician. If there is no proteinuria and serum creatinine is normal, a non-urgent referral to a urologist should be made.

1.8.13 In patients aged 50 years and older who are found to have unexplained microscopic haematuria, an urgent referral should be made.
CLINICAL REVIEW

Assessment and management of non-visible haematuria in primary care

Peter D. F. Saxton, David P. Saxton, Lawrence D. Smalling

What is non-visible haematuria?

Non-visible haematuria refers to the presence of red blood cells in the urine that cannot be detected by the naked eye. This type of haematuria is important to diagnose, as it can be caused by conditions that require medical attention.

Causes of non-visible haematuria

Non-visible haematuria can be caused by a variety of conditions, including:

1. Kidney stones (nephrolithiasis)
2. Bladder infections
3. Prostate problems
4. Urethral strictures
5. Benign prostatic hyperplasia
6. Bladder tumors
7. Kidney tumors
8. Urinary tract infections
9. Infections of the urinary tract
10. Inflammation of the bladder

Management of non-visible haematuria

The management of non-visible haematuria depends on the underlying cause. Treatment may include:

1. Pain management
2. Antibiotics for infections
3. Medications for prostate problems
4. Surgery for tumors or strictures
5. Behavioral changes to reduce the risk of certain conditions
6. Regular check-ups and monitoring

Conclusion

Non-visible haematuria is a common finding in primary care settings. It is important to investigate the underlying cause to ensure appropriate management and prevent complications.
Joint Consensus Statement on the Initial Assessment of Haematuria
Prepared on behalf of the Renal Association and British Association of Urological Surgeons.

Issue date July 2008

Decision algorithm for the investigation and referral of haematuria.
Risk threshold

• ‘The risk of the patient’s symptoms representing a cancer’
• Used Positive predictive value (PPV)
• Clinicians set 5% PPV across all cancers
• Patient representatives wanted 1%
• Settled on 3% - ‘A considerable liberalisation’
1.8.12 In patients under 50 years of age with microscopic haematuria, the urine should be tested for proteinuria and serum creatinine levels measured. Those with proteinurea or raised serum creatinine should be referred to a renal physician. If there is no proteinuria and serum creatinine is normal, a non-urgent referral to a urologist should be made.

1.8.13 In patients aged 50 years and older who are found to have unexplained microscopic haematuria, an urgent referral should be made.
$2 + 2 = 5$
1.8.12 In patients under 50 years of age with microscopic haematuria, the urine should be tested for proteinuria and serum creatinine levels measured. Those with proteinurea or raised serum creatinine should be referred to a renal physician. If there is no proteinuria and serum creatinine is normal, a non-urgent referral to a urologist should be made.

1.8.13 In patients aged 50 years and older who are found to have unexplained microscopic haematuria, an urgent referral should be made.
<table>
<thead>
<tr>
<th>Studies included</th>
<th>Symptom(s)</th>
<th>Patient group</th>
<th>Positive predictive value, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bruyninckx (2003), Collins (2013), Friedlander (2014), Hippisley-Cox (2012),</td>
<td>Haematuria</td>
<td>All patients (N = 70330)</td>
<td>4.43 (2.48-7.79)</td>
</tr>
<tr>
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<td></td>
<td></td>
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</tr>
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<td>4.72 (2.63-8.32)</td>
</tr>
<tr>
<td>Jones (2007, at 3 years)</td>
<td></td>
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</tr>
</tbody>
</table>
But lets look more closely....
The GDG also noted that most of the evidence did not distinguish between visible and non-visible haematuria, but largely grouped these two symptoms together as haematuria. The GDG judged, based on their clinical experience, that most of that evidence was likely to reflect visible haematuria which left them with evidence from one paper about non-visible haematuria.

<table>
<thead>
<tr>
<th>Reference (Year)</th>
<th>Condition Description</th>
<th>Study Population</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Price (2014)</td>
<td>Non-visible haematuria (coded and uncoded data)</td>
<td>Patients 40-59 years</td>
<td>0.79 (0.11-5.6)</td>
</tr>
<tr>
<td>Price (2014)</td>
<td>Non-visible haematuria (coded and uncoded data)</td>
<td>All patients ≥ 60 years</td>
<td>1.6 (1.2-2.1)</td>
</tr>
</tbody>
</table>

5000pts = 7% of the sample
Urine Dipstick

- Sensitivity 0.91 and Specificity 0.99 for MH
- BUT –
  - 16-24% of population have MH
  - 33% of BC patients don’t have any haematuria
How is MH defined by NICE?

• Its not!

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*Trace versus 1+*
- Whilst the sensitivity of urine dipsticks may vary from one manufacturer to another, significant haematuria is considered to be 1+ or greater. Trace haematuria should be considered negative.

*Haemolysed versus non-haemolysed*
- There is no distinction in significance between non-haemolysed and haemolysed dipstick-positive haematuria. 1+ positive for either should be considered of equal significance.

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*c) Persistent a-NVH (in absence of UTI or other transient causes). Persistence is defined as 2 out of 3 dipsticks positive for NVH.*
VH and NVH referrals

Monthly referrals

<table>
<thead>
<tr>
<th>Year</th>
<th>Macroscopic</th>
<th>Microscopic</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1998</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1999</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>2000</td>
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<td>2001</td>
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<td></td>
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<tr>
<td>2002</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2003</td>
<td></td>
<td></td>
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</tbody>
</table>
Change in detection rate

![Graph showing changes in detection rate with categories benign/normal and malignant over a period from December 98 to June 03. The graph indicates fluctuations in detection rates with peaks and troughs.]
• Referrals to Haematuria clinic

  – Was 2/3 Macro, 1/3 Microscopic
  – Now reversed with 2/3 micro
  – 1200/year at RSCH and rising
  – Annual cost to NHS £33M
  – 1/3 of the £100M cost of treating Bladder Ca
The haematuria problem...

74 yo male smoker with frank haematuria

40 year old female N/S incidental finding
Education and debate

Time to abandon testing for microscopic haematuria in adults?
Per-Uno Malmström

Although there is no doubt that macroscopic haematuria is serious, the clinical significance of asymptomatic microscopic haematuria is controversial. Should it still be tested for?

Summary points

- Microhaematuria is poorly predictive of cancers of the urinary tract
- Haemoglobin dipstick testing is not a reliable way of detecting early bladder cancer in patients at high risk
- Microhaematuria is not reliable evidence of a stone in the ureter and may be misleading, as it is often present in other serious conditions that cause acute loin pain
- Testing for microhaematuria is not helpful in evaluating men with lower urinary tract symptoms
If you notice blood in your pee, even if it’s ‘just the once’, tell your doctor.

It could be an early sign of kidney or bladder cancer. Finding it early makes it more treatable, so tell your doctor straight away.

nhs.uk/bloodinpee
Investigations in primary care

No primary care evidence was identified pertaining to the diagnostic accuracy of urine cytology, ultrasound, cystoscopy, blood HCG, urine marker NMP22, and urine marker MCM5 in patients with suspected bladder cancer where the clinical responsibility was retained by primary care.
The haematuria clinic: Fit for purpose?

‘The haematuria clinic is there to detect urological cancer’
Findings at a Haematuria clinic

<table>
<thead>
<tr>
<th>Condition</th>
<th>Incidence %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder cancer (macroscopic haematuria)</td>
<td>19</td>
</tr>
<tr>
<td>UTI</td>
<td>13</td>
</tr>
<tr>
<td>Nephrological Disease</td>
<td>10</td>
</tr>
<tr>
<td>Urinary Calculi</td>
<td>8.4</td>
</tr>
<tr>
<td>Bladder cancer (microscopic haematuria)</td>
<td>5</td>
</tr>
<tr>
<td>Renal Cell Ca</td>
<td>1.9</td>
</tr>
<tr>
<td>Upper tract TCC</td>
<td>0.3</td>
</tr>
<tr>
<td>Primary carcinoma in situ</td>
<td>0.3</td>
</tr>
</tbody>
</table>
The haematuria Clinic: Fit for purpose?

‘Bladder cancer patients present with haematuria’
## Presentation of bladder cancer

<table>
<thead>
<tr>
<th>Symptom</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frank Haematuria</td>
<td>162</td>
<td>67</td>
</tr>
<tr>
<td>Pure LUTS</td>
<td>20</td>
<td>8</td>
</tr>
<tr>
<td>Chance</td>
<td>14</td>
<td>6</td>
</tr>
<tr>
<td>Symptomatic Microscopic Haematuria</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>Symptoms of UTI</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Clear delay in reporting FH</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Gynae bleeding</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Malaise</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Non-specific Sx</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Asymptomatic Microscopic Haematuria</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Incontinence</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Recurrent UTIs</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Anaemia</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>240</td>
<td>100</td>
</tr>
</tbody>
</table>
Are we barking up the wrong tree?

**TABLE 1**

<table>
<thead>
<tr>
<th>Finding</th>
<th>Incidence, %</th>
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<td>5</td>
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<tr>
<td>RCC</td>
<td>1.5</td>
</tr>
<tr>
<td>Upper tract TCC</td>
<td>0.3</td>
</tr>
<tr>
<td>Primary carcinoma <em>in situ</em></td>
<td>0.3</td>
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Incidence of findings in a haematuria clinic [2,3]
## Haematuria Referrals

<table>
<thead>
<tr>
<th></th>
<th>Risk of Bladder cancer</th>
<th>% of pts with bladder Ca</th>
<th>Referral route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macroscopic Haematuria</td>
<td>19%</td>
<td>67%</td>
<td>TWR to one stop haematuria clinic</td>
</tr>
<tr>
<td>Symptomatic Micro. haematuria</td>
<td>5</td>
<td>4%</td>
<td>OPD</td>
</tr>
<tr>
<td>Asymptomatic micro. haematuria</td>
<td>&lt;5%</td>
<td>1%</td>
<td>OPD?</td>
</tr>
</tbody>
</table>
Update on bladder cancer
• NMIBC not ‘superficial’

• NICE Bladder Cancer Guidelines

• BCG shortage

• Centralisation of radical cystectomy
Eliminate the Term “Superficial” Bladder Cancer

Alan M. Nieder and Mark S. Soloway
Department of Urology
University of Miami Miller School of Medicine
Miami, Florida
1.3 Treating non-muscle-invasive bladder cancer

1.3.1 Risk classification in non-muscle-invasive bladder cancer

- Ensure that for people with non-muscle-invasive bladder cancer all of the following are recorded and used to guide discussions, both within multidisciplinary team meetings and with the person, about prognosis and treatment options:
  - recurrence history
  - size and number of cancers
  - histological type, grade, stage and presence (or absence) of flat urothelium, detrusor muscle (muscularis propria), and carcinoma in situ
  - the risk category of the person's cancer
  - predicted risk of recurrence and progression, estimated using a risk prediction tool.

- Low
- Intermediate
- High
1.4 Follow-up after treatment for non-muscle-invasive bladder cancer

Low-risk non-muscle-invasive bladder cancer

1.4.3
Offer people with low-risk non-muscle invasive bladder cancer cystoscopic follow-up 3 months and 12 months after diagnosis.

1.4.4
Do not use urinary biomarkers or cytology in addition to cystoscopy for follow-up after treatment for low-risk bladder cancer.

1.4.5
Discharge to primary care people who have had low-risk non-muscle-invasive bladder cancer and who have no recurrence of the bladder cancer within 12 months.

1.4.6
Do not offer routine urinary cytology or prolonged cystoscopic follow-up after 12 months for people with low-risk non-muscle-invasive bladder cancer.
Centralisation of Bladder Cancer

- Pelvic cancer centre for 1.8 million
- ~80 cystectomies a year
- 2 robotic cystectomies per week
- Improved outcomes – Discharged at D5 cf. D14, ↓ B.Tx