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# Evaluating Haematuria: Ultrasonography And The Day Case Diagnostic Service

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## Summary

*Haematuria may herald the presence of sinister underlying disease, notably malignancy of the urinary tract. Applying the conventional management pathway involving numerous clinic visits and referrals, waiting list for imaging studies of the upper tract, diagnostic cystoscopy and then therapeutic endoscopy in different venues often leads to substantial delay in diagnosis and appropriate intervention. A rapid access haematuria clinic is therefore advocated. The day case haematuria diagnostic service combining diagnostic imaging and flexible cystoscopy has proven to be highly effective. In this connection, transabdominal ultrasonography has been employed increasingly as the primary imaging modality. (HK Pract 1998;20:615-623)*

## 摘要

血尿可能是潛在嚴重疾病，特別是泌尿道惡性腫瘤的訊號。傳統處理包括多次門診診治、轉介專科、等候上泌尿道造影和診斷性膀胱鏡檢查以及治療性內窺鏡等等，常造成診斷和治療的延誤。血尿檢查診所提供診斷性造影和膀胱纖維內窺鏡檢查，快捷而有效，值得提倡。使用經腹超聲波作為初步影像學檢查的方法也逐漸有所增加。

## Introduction

Haematuria of any degree should never be ignored and in adults, it should be regarded as a symptom of urologic malignancy

until proven otherwise.<sup>1</sup> Mariani and associates, in their evaluation of 1000 consecutive patients, revealed life threatening lesions in 9.1%.<sup>2</sup> The series included 691 patients with microscopic haematuria and 309 with gross haematuria of which life

threatening lesions were found in 3.9% and 20.7%, respectively ( $P < 0.001$ ). It is obvious that the chances of identifying significant pathology is much higher with gross haematuria.

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## Differential diagnosis of haematuria

Haematuria may reflect either renal or urological disease. Haematuria of renal origin is frequently associated with casts in the urine and is almost always associated with significant proteinuria. Even significant haematuria of urologic origin does not elevate the protein concentration in the urine into the 100-300 mg/dl range or the 2+ to 3+ range on dipstick, and proteinuria of this magnitude almost always indicates glomerular disease (Table 1).<sup>3</sup>

Erythrocytes arising from glomerular disease are typically dysmorphic and show a wide range of morphologic alterations. Red blood cell (RBC) morphology is more easily determined through phase contrast microscopy, but with practice this can be accomplished with a conventional light microscope.<sup>4</sup>

## Refined urinalysis

Fracchia and associates evaluated whether a comprehensive

and refined urinalysis utilizing qualitative, quantitative, chemical and urine sediment parameters might aid in identifying those patients who had a significant urologic cause for their microhaematuria in contrast to those patients who appeared to have 'pure' renal, i.e. medical bleeding.<sup>5</sup> The studied patients submitted a first morning urine specimen for the refined urine diagnostic assay. This examination, performed by a cytopathologist, was both qualitative (such as RBC morphology, sediment casts, and urine chemistry) and quantitative (such as cell count/10 high power field, protein in mg/dl). They noted that the presence of dysmorphic urinary red blood cells and RBC casts was strongly suggestive of renal parenchymal bleeding. Overall, 43 of 44 subjects (98%) with dysmorphic RBCs and RBC casts failed to demonstrate any significant urological lesion.

However, in this series of 100 patients, the refined urinalysis alone did not identify any of the three renal tumours. It was suggested that refined urinalysis needed to be combined with selective upper tract imaging. Taken together, the sole presence of dysmorphic RBCs and RBC casts by refined urinalysis and

a negative upper tract evaluation strongly suggests a non-urologic cause of haematuria.

## Dipstick tests and microscopic haematuria

The sensitivity of urinary dipsticks in identifying haematuria, defined as more than three RBCs per high power microscopic field of centrifuged sediments, is over 90%. On the other hand, in comparison with microscopy, the specificity of the dipstick for haematuria is somewhat lower, reflecting a higher false positive rate with the dipstick.<sup>6</sup> The efficacy of haematuria screening with the dipstick to identify patients with significant urologic disease is somewhat controversial. In older adults, one study from the Mayo clinic consisting of 2000 patients with asymptomatic haematuria showed that only 0.5% had a urologic malignancy and only 1.8% developed other serious urologic diseases within 3 years after identification of the haematuria.<sup>7</sup> However, Messing *et al* found that 26% of asymptomatic men over 50 years old who had a positive dipstick reading for haematuria in a home screening study were subsequently found to have

**Table 1: Differential diagnosis aided by microscopy and urinalysis**

Origin	Examples	Typical microscopy and urinalysis		
		RBC*	RBC Casts	Proteinuria
Glomerular	IgA nephropathy, glomerulonephritis	Dysmorphic	May be present	Significant
Non-glomerular surgical	Tumours, urolithiasis	Isomorphic	Absent	Minimal

\* RBC = red blood cell

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significant urologic pathology, including 5% to 15% who had unsuspected bladder cancer.<sup>8-9</sup> Furthermore, repeat dipstick screening 9 months later in men over 50 whose dipstick urinalysis was initially negative identified an additional 1.8% with significant urologic pathology, including 0.8% with superficial bladder cancer.<sup>10</sup>

Obviously, the age of the study population, the completeness of the subsequent urologic evaluation, and the definition of significant disease all influence the benefit of dipstick screening for haematuria in asymptomatic patients. It does appear, however, that dipstick screening for haematuria is most effective in men over 50 and could be done annually to detect bladder cancer in a superficial stage before invasion occurs.

### Asymptomatic microscopic haematuria: selection for investigation?

The implications of a widespread use of urine analysis with dipsticks in health screening clinics and in routine clinical practice have resulted in an increased urological referrals from family physicians for advice about investigating patients with asymptomatic microscopic haematuria. Opinion is divided as to who needs referral and how extensively they should be evaluated. Some authorities recommended the investigation of anyone with microscopic haematuria, irrespective of age, sex or whether associated with any symptoms.<sup>11-13</sup>

On the other hand, Sultana *et al* were of the opinion that careful selection was necessary to be able to better use the available facilities and increase the diagnostic yield giving priority to those patients with a greater risk of having an underlying urologic malignancy.<sup>14</sup> They studied the difficult but important subject of how microscopic haematuria, and in particular asymptomatic microscopic haematuria, should be investigated, by describing the results obtained from 381 patients investigated for microscopic haematuria over a period of one year. No malignancy was found in any patient under 50 years of age ( $n = 131$ ); while in patients aged over 50 years, the overall incidence of malignancy was 7.5% (19/250). During the same period, 233 patients were referred with gross haematuria. In these patients, those aged under 50 years had a 10% incidence of malignancy (6/60), while in those aged over 50 years the incidence was 34.5% (60/173). They concluded that the investigation of older patients with microscopic haematuria (and all those with gross haematuria) was well justified, as malignancy would be found in a significant proportion even if they were asymptomatic. The benefit of a full urologic investigation of younger patients with microscopic haematuria was debatable.

The authors' preference is that the initial diagnostic approach to asymptomatic microhaematuria of patients includes renal ultrasound, x-ray of kidneys, ureter and bladder (KUB) and flexible cystoscopy, acknowledging that a rare, small and non-obstructing renal pelvis or ureteral tumour might be missed. Little in sensitivity and specificity with regards to tumour detection is

sacrificed with this strategy. This view is shared by other authors.<sup>15-16</sup> For patients over 40 years old, more extensive investigation may be warranted. This entails an upper tract imaging (e.g. ultrasonography) and lower tract endoscopy, to be followed by an alternative imaging (e.g. intravenous urography) and cytology if there is persistent microhaematuria. After a negative urologic work-up, patients under 40 years old with asymptomatic microhaematuria should be referred for a nephrological opinion, particularly if they have persistent proteinuria or hypertension.<sup>17</sup> Twenty-four hours urinary protein level, creatinine clearance and serum C3/C4 complement levels can be carried out by the family physician and will enable more selective referral of those with abnormal results.

### Upper tract imaging: which modality to choose?

In upper tract imaging, ultrasonography (USG) is safer and cheaper than intravenous urography (IVU).<sup>15</sup> It is well recognized that a proportion of small renal cell carcinoma are undetected by IVU, even with the addition of tomography, and that USG is superior for imaging parenchymal renal masses.<sup>18-20</sup> Conversely, IVU more readily detects upper tract transitional cell carcinoma (TCC), which is poorly detected by USG unless it is associated with upper tract dilatation. Overall, parenchymal renal tumours represents 80 to 90% of primary upper tract malignancies in adults. (Table 2)

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**Table 2: Comparing ultrasonography and intravenous urography**

	Ultrasonography	Urography
Cost	cheap	slightly more expensive
Preparation	minimal, full bladder essential	light bowel preparation required
Availability	can be performed in clinic, or in ward using portable machines	radiology suite
Prior to imaging	good quality KUB	serum creatinine
Additional information	color Doppler	tomography
Irradiation	nil	yes
Allergy	nil	small risk
Superior for detecting	<ul style="list-style-type: none"> <li>- renal parenchymal lesion</li> <li>- bladder tumour and stone</li> <li>- differentiating cystic/solid lesion</li> </ul>	<ul style="list-style-type: none"> <li>- calculi and upper tract urothelial tumour</li> <li>- qualitative renal function assessment</li> <li>- road-mapping endourological procedures</li> </ul>
Inferior for detecting	<ul style="list-style-type: none"> <li>- ureteric stone without obstruction</li> <li>- small upper tract TCC*</li> </ul>	<ul style="list-style-type: none"> <li>- small (&lt; 2.5 cm) renal lesion</li> <li>- bladder lesion</li> </ul>

\* TCC = Transitional cell carcinoma

We compared the efficacy of USG and IVU by conducting a prospective study on 146 consecutive patients presenting with painless gross haematuria.<sup>21</sup> Forty seven genitourinary malignancies (32%) were detected, of which 72% were carcinoma of the bladder. The sensitivity and specificity of USG and IVU were comparable for the upper tract; but in the lower tract evaluation, sensitivity was significantly higher for USG (96%) compared with IVU (50%) ( $p < 0.05$ ); while the specificities were similar.

The series was updated to include 468 patients from 1992 to 1997 with very similar findings regarding incidence of pathologies and accuracy of imaging modalities (unpublished data). We concluded that USG is more sensitive than IVU for diagnosing urologic malignancies in patients presenting with painless

haematuria, where carcinoma of the bladder is the commonest pathology. Its utilization as the initial screening investigation is recommended. Patients diagnosed to be suffering from carcinoma of bladder by ultrasound should be scheduled promptly for therapeutic endoscopy.

### Rapid access clinic: to minimize delay

Patients tend to report haematuria to their family physicians fairly quickly. Stower reported that the median delay was one week.<sup>22</sup> The merits of a rapid haematuria diagnostic service in a tertiary referral centre are therefore two-fold. It aims to encourage immediate referral, and to offer early investigation.<sup>23</sup> Definitive treatment can then be scheduled on a priority basis once diagnosis is confirmed.

Britton reviewed the effectiveness of the haematuria clinic and considered that an 'open access haematuria clinic' to be the ideal system where referral is by phone and all investigations, including urine microscopy, urine cytology, intravenous urography and flexible cystoscopy, are performed at one visit (Table 3). This system will require considerable effort of co-operation with the family physician, the patients and most importantly one's radiological colleagues; arrangement with the latter may be the limiting factor. Lynch reported his experience of such an open access clinic in the investigation of 395 patients and commented that it was efficient and easily run.<sup>24</sup>

In fact, as early as in 1990, Plail predicted that integrated, single visit haematuria clinics might soon be

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common place.<sup>25</sup> His prediction was based on the increasing accuracy of ultrasonography and availability of outpatient flexible cystoscopy examination. However, while there were a number of reports on the efficacy of haematuria clinics, IVU remained to be the primary imaging modality.<sup>26-27</sup>

We recently reported the efficacy of a Day Case Diagnostic Service employing ultrasonography and flexible cystoscopy in the evaluation of patients presenting with painless gross haematuria.<sup>28</sup> While we emphasized direct access from the Accident and Emergency Department to our Urology clinic appointment system for urgent referrals, we also accepted referrals by fax from family physicians. From July 1994 to June 1997, 312 consecutive patients presenting with painless gross haematuria were studied. They were seen in the next clinic slot (by allowing forced-in quota) for first consultation within one week of referral. This was followed shortly by evaluation in a Day Case Diagnostic Service setting, where ultrasonography and flexible cystoscopy were performed together with other laboratory investigations. Intravenous urography was performed subsequently for possible additional diagnostic information.

Eighty-one urinary malignancies were detected in 78 patients, 51 being carcinoma of bladder, followed by renal cell carcinoma (n = 15). A definitive diagnosis was made in 68 cases and an abnormality was noted in nine other cases after the day case work up. Decision of further

management and listing for surgery, where appropriate, was made in the Day Case Diagnostic Clinic. The day case diagnostic work-up has also led to highly selective computed tomography (CT) with high diagnostic yield; whereas intravenous urography only added important diagnostic information, not available in the earlier work-up in nine patients.<sup>28</sup>

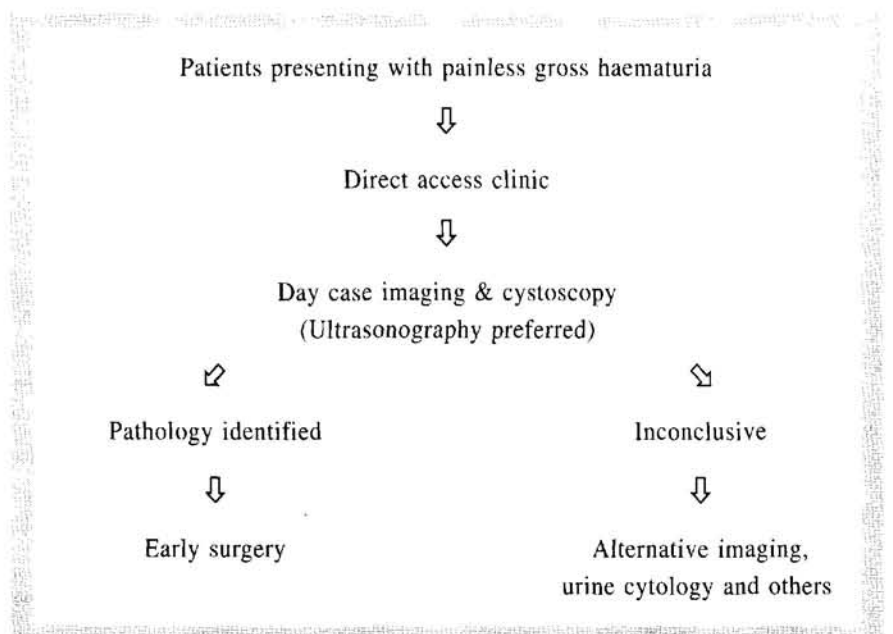
We conclude that the Day Case Diagnostic Service is a feasible arrangement. By combining ultrasonography and flexible cystoscopy, the majority of pathologies were diagnosed and abnormalities detected. Such a service enhances rapid completion of the diagnostic work-up, and operations for surgical conditions can be scheduled promptly. (Figure 1)

**Table 3: Where is the delay?\***

1. Onset of haematuria and consultation	Patient delay
2. Initial consultation with GP and hospital referral	GP delay
3. Hospital referral and attendance at clinic	Hospital delay
4. Attendance at clinic and investigations	Hospital delay
5. Investigations and then review in clinic	Hospital delay
6. Waiting list time for diagnostic cystoscopy	Hospital delay
7. Waiting list time for definitive treatment	Hospital delay

\* Adapted from Britton JP. Review: Effectiveness of Haematuria Clinics (Br J Urol 1993;71: 247-452)

**Figure 1: Optimal management pathway for haematuria**



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## Key messages

1. Haematuria is a worrying symptom which may suggest an underlying urologic malignancy.
2. The family physician can assist in the management by careful evaluation of the patient and initiating appropriate investigations, including proper urinalysis and imaging studies.
3. Ultrasonography together with plain KUB film is the preferred primary imaging modality.
4. If there is reasonable suspicion of an underlying pathology, the family physician should alert the specialist and ensure that there is minimal delay for formal urologic work-up.
5. Referral centres should make every effort to minimize the hospital delay.

Whether the rapid diagnostic service can be converted to substantial improvement in survival outcome cannot be assessed in the current study,<sup>29</sup> but the relief of patients' anxiety is beyond doubt. The impact on clinical service improvement is also tremendous, since we have shown that close co-operation between different specialties leads to achievement of a high quality of service.

The family physician may opt to arrange for imaging studies (ultrasonography or IVU where indicated) while the patient awaits for specialist opinion. Such pre-consultation imaging has also been reported to minimize the delay in diagnosis and would be appreciated especially in busy tertiary referral centres.<sup>30</sup>

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