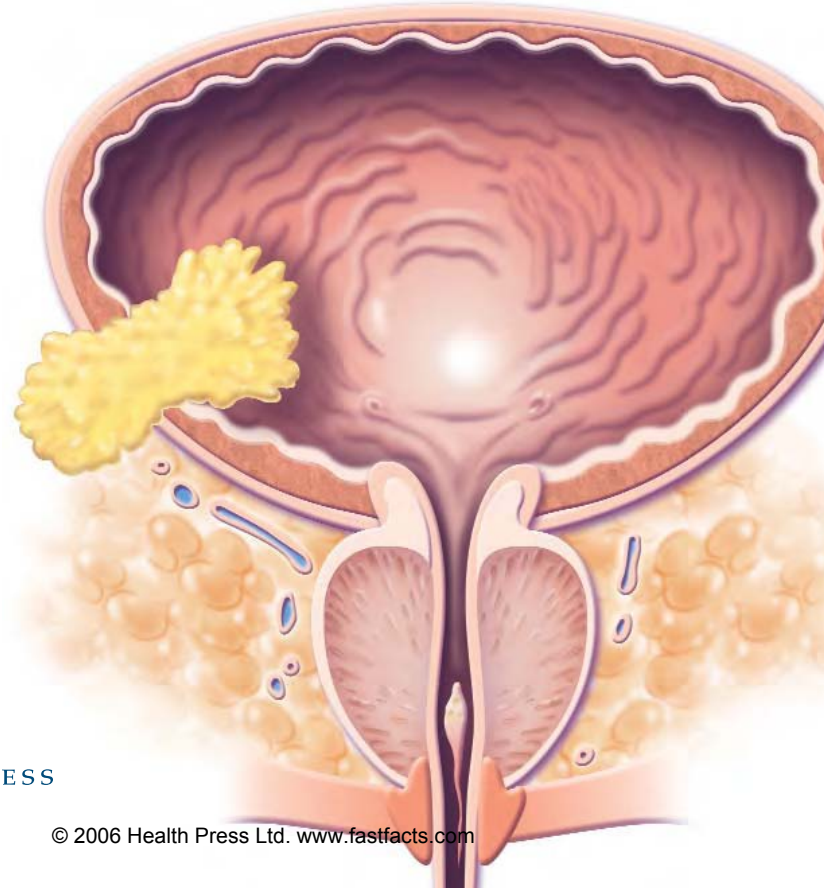
Fast Facts

# Fast Facts: Bladder Cancer

**Derek Raghavan and Michael Bailey**

Second edition



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# Bladder Cancer

**Second edition**

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## Declaration of Independence

This book is as balanced and as practical as we can make it. Ideas for improvement are always welcome: feedback@fastfacts.com

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## Glossary

**AMH:** asymptomatic microscopic hematuria

**Anaplasia:** loss of typical cell characteristics or differentiation that can occur, for example, in rapidly growing malignant tumors

**BCG:** bacillus Calmette–Guérin, a strain of tubercle bacillus that can stimulate an immune response even though it does not cause tuberculosis

**BTA stat test:** bladder tumor antigen test

**BTA TRAK test:** test that quantifies bladder tumor antigen

**CAP:** cyclophosphamide–doxorubicin–cisplatin

**CIS:** carcinoma in situ, a high-grade, flat, non-invasive malignant change in the urothelium; also known as Tis

**CMV:** cisplatin–methotrexate–vinblastine

**CT:** computed tomography

**Cystectomy:** surgical removal of the bladder

**Cystoscopy:** examination of the bladder using a cystoscope

**Dysplasia:** abnormal development of tissues with cellular changes (some of which may connote increased risk of subsequent bladder cancer), including increased nucleus-to-cytoplasm ratio or cellular irregularity, but with normal mitosis

**EORTC:** European Organisation for Research and Treatment of Cancer

**F/FDP:** fibrin/fibrinogen degradation products

**HA/HAase:** hyaluronic acid/hyaluronidase

**HPF:** high-powered field

**IVU:** intravenous urogram

**KUB:** kidneys, ureters and bladder

**MRI:** magnetic resonance imaging

**MVAC:** methotrexate–vinblastine–doxorubicin–cisplatin

**NMP:** nuclear matrix protein

**NMP-22 test:** test for an NMP that is secreted by some bladder tumors

**Primary CIS:** carcinoma in situ in the absence of exophytic tumors

**RBC:** red blood cell

**RTOG:** Radiation Therapy Oncology Group

**Secondary CIS:** carcinoma in situ with associated papillary or solid tumors

**TCC:** transitional cell carcinoma

**TNM:** tumor–nodes–metastases, a staging system

**TURBT:** transurethral resection of a bladder tumor

**UBC:** urinary bladder cancer

**Urography:** radiographic examination of the kidneys, ureters and bladder with contrast medium (see IVU)

**UTI:** urinary tract infection



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## Introduction

Cancer of the urinary bladder (UBC) is a common tumor, and most primary care physicians will see two or three new cases each year. Since many of these patients will have a good prognosis, the number of patients with bladder cancer in the population of every practice will be much larger.

Our aim in this book is to provide the relevant facts regarding bladder cancer clearly and succinctly, so that those caring for these patients can explain their condition and help them through some of the difficult treatment choices they may have to make. It is intended to be a concise guide to clinical practice rather than a comprehensive textbook, although we have tried to include the evidence base for diagnosis and management of UBC together with recent developments in treatment. *Fast Facts – Bladder Cancer* will also be of interest to patients keen to learn more about their condition, and to junior doctors wanting a concise review of bladder cancer.

In this second edition, we have expanded the sections on chemotherapy and radiotherapy, and provided more detail about oncology and palliation. We hope that you will find the book useful.

We thank Mike Sarosdy for his contributions to the first edition, on which this book is based.



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# 1 Epidemiology and etiology

## Incidence

The incidence of bladder cancer has risen over the past 20 years. Currently, around 54 500 new cases of bladder cancer are diagnosed in the USA each year, and 15 000 cases in the UK. Bladder cancer is the fourth most common cancer in men in the USA and the tenth most common in women. It is one of the most frequent causes of cancer death, accounting for about 10 000 deaths annually in the USA and 5000 in the UK.

The incidence of bladder cancer varies among different patient groups. For example, there is a 3:1 male-to-female ratio, though the prevalence among women appears to be rising. The incidence is higher in elderly populations, with a median age at presentation of 60–65 years. No evidence exists for a familial or inherited pattern among any patient group, although occasional family clusters have been recorded. In black people the incidence is lower than in white people; in Asian races it appears to be intermediate. The lifetime risk of developing bladder cancer is:

- 2.8% for white men
- 0.9% for black men
- 1.0% for white women
- 0.6% for black women.

Five-year survival for both black and white people during the period 1986–92 (60% and 82%, respectively) was significantly better than the equivalent rates for 1974–76 (47% and 74%, respectively; $p < 0.05$). It is not really known why there are substantial ethnic differences in incidence and prognosis, although putative factors include differences in diet and nutritional status, differences in gene expression (especially of enzymes that may metabolize carcinogens) and differential access to healthcare.



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## Etiology

A number of factors have been implicated in the development of bladder cancer, including environmental and industrial carcinogens (Table 1.1).

**Cigarette smoking.** Smoking is now recognized as the prime cause of bladder cancer in industrialized countries. Between 60% and 80% of patients with bladder cancer have a history of cigarette smoking; there is a twofold to fivefold increase in the risk of bladder cancer associated with smoking. (Development of cancer lags 10–20 years behind exposure, so current incidence reflects smoking patterns of up to 20–30 years ago.) Smokers have a higher rate of tumor recurrence and a greater proportion of tumors of higher stage and grade than do non-smokers. The correlation between cigarette smoking and cancer is reportedly higher for bladder cancer than for lung cancer.

The prevalence of cigar smoking in patients with bladder cancer has not been well defined.

**Occupational risks.** The strongest association between work and bladder cancer is among aniline dye workers exposed to aromatic amines, with a relatively increased risk of 1.7–8.8. Other occupations with increased risk of urinary bladder cancer (UBC) due to exposure to carcinogens in the workplace are listed in Table 1.2.

TABLE 1.1

**Known bladder carcinogens**

- 2-Naphthylamine
- Benzidine
- 4-Aminobiphenyl
- Dichlorobenzidine
- Orthodianisidine
- Orthotolidine
- Phenacetin
- Chlornaphazine
- Cyclophosphamide



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# 4 Investigations

## History

A thorough history should be obtained from all patients presenting with symptoms suggestive of bladder cancer. The history should cover smoking, possible carcinogen exposure in the workplace, previous bladder tumor resection and any change in bowel habits or stool characteristics. Direct questioning may reveal hematuria for 6–12 months prior to presentation.

## Examination

Physical examination is usually unremarkable in cases of superficial bladder cancer unless acute urinary retention is present with bladder distension. In men, a careful rectal examination should be carried out to exclude prostatic disease such as cancer or benign enlargement, both of which may cause many of the same symptoms as bladder cancer, and to rule out gross extension of bladder cancer. A careful pelvic examination in women is equally important. A thorough nodal examination should be undertaken, including supraclavicular lymph nodes, as well as assessment for hepatic or pulmonary involvement.

## Detailed investigation

**Urinalysis** should begin with dipstick testing for the presence of red blood cells and, if the result is positive, microscopic analysis should be performed for confirmation. The presence of nitrates or leukocytes should prompt urine culture to look for infection.

Several recently developed tests for urinary markers of urothelial malignancy are commercially available, and tests for other urinary markers are still at the laboratory stage. At present, none of the tests alone is sufficiently sensitive to replace cystoscopy in diagnosing or excluding UBC. They may prove useful in dictating the frequency of cystoscopy for recurrence in patients with known



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bladder cancer. Table 4.1 shows the sensitivity and specificity of some of these markers.

**Imaging.** The upper tracts should be imaged in all patients with symptoms suggestive of bladder cancer. In the investigation of hematuria (the commonest presentation of bladder cancer), the imaging can be performed either by intravenous urography (IVU) or by ultrasound plus a plain radiograph of the kidneys, ureters and bladder (KUB). The diagnostic yield from these procedures is equivalent, but ultrasound is better at detecting solid renal masses than IVU, and IVU (Figure 4.1) is better at demonstrating upper-tract urothelial tumors. If one imaging modality yields negative results, and cystoscopy is also normal, the other type of imaging should be carried out.

TABLE 4.1

**Sensitivity and specificity of tests for urinary markers of bladder cancer**

| Test | Sensitivity (%) | Specificity (%) | Comment |
|---|---|---|---|
| Cytology | 49.8 | 96.6 | Readily available |
| BTA stat | 67.7 | 65.8 | False positives with infection/hematuria |
| BTA TRAK | 71.1 | 62.0 | Complex test* |
| NMP22 | 64.3 | 71.2 | Complex test* |
| Telomerase | 74 | 89 | Complex test,* not commercially available |
| HA/HAase | 91 | 86 | Complex test,* not commercially available |
| Immunocyst | 68 | 79 | Complex test* |
| F/FDP | 68 | 86 | No longer commercially available |

* Requires reference laboratory.
BTA, bladder tumor antigen; F/FDP, fibrin/fibrinogen degradation products; HA/HAase, hyaluronic acid/hyaluronidase; NMP, nuclear matrix protein.



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