BLADDER CANCER: *Presentation, Epidemiology & Risk Factors*

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- ***Cancer Education Day - 2026***

Conflict of Interest Disclosure

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  - No AI was used in the creation of this presentation

Overview

- Bladder Cancer Epidemiology
- Risk Factors
- Presentation & Diagnosis

Epidemiology

- Average age of diagnosis: **73**
- ¾ of cases are in males
- ~12000 new cases per year in Canada[1]
- Relatively stable incidence from 2010-2015. More recent evidence has shown increase
  - 21.8 to 25 new cases/100K pop'n, 2018-2020[2]
- Avg age at diagnosis: 73
- Incidence highest in: NA, Europe, West Asia[3]

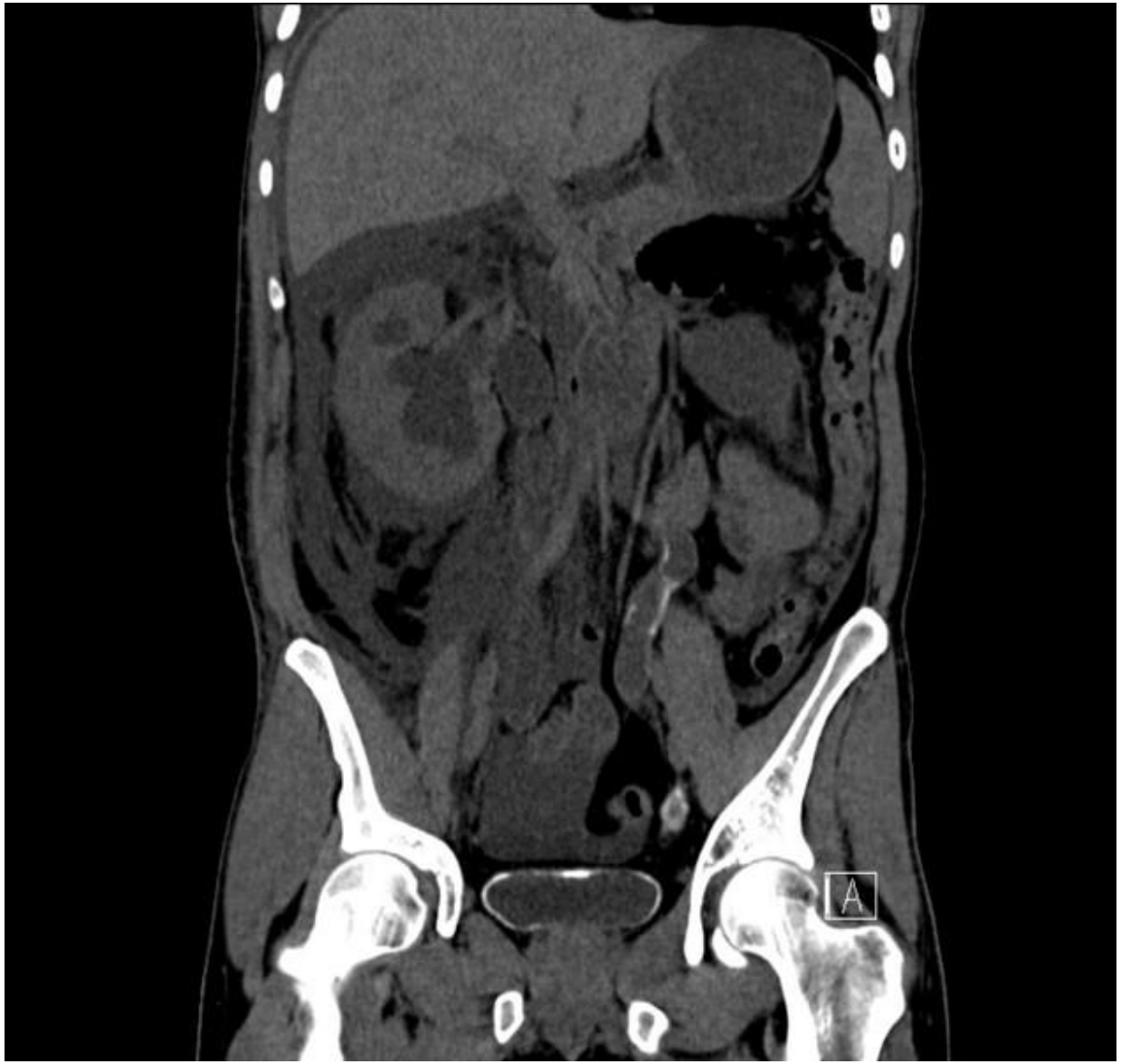
Epidemiology

- A very costly disease to treat…
  - *Most expensive cancer to treat on a per patient basis*[12]
  - High recurrence rate
  - Cystoscopic surveillance
  - Multiple lines of treatment required

Risk Factors

- **Smoking** (2-6x risk)
  - 10 pack years "high risk" threshold[6]
  - 50% of bladder cancers found in current/former smokers[8]
  - More aggressive tumors, worse prognosis[7]
- Organic solvents
  - Benzene, toluene, xylene
- Schistosomiasis
  - *Schistosoma haematobium*
  - Endemic to Africa, Asia, Caribbean, SA
  - ~600 mil people in endemic areas[9]
  - Ova embedded in bladder wall → chronic inflammation → squamous metaplasia → dysplasia → **SCC**

Schistosomiasis – Chronic phase



Risk Factors

- Radiation
  - Latency of 15-30 years
  - 1.5x risk from EBRT for prostate cancer. Lower risk for brachy[11]

Risk Factors

- Genetic/environmental
  - 7% of cases
  - 1st and 2nd degree relatives have increased risk (HR 1.73)[10]
  - **Lynch syndrome** (HNPP)—mismatch repair gene mutation
- **Neurogenic bladder / chronic catheterization**
- Various exposures:
  - Aniline dyes
  - Formaldehyde
  - Phenacetin
  - Cyclophosphamide (**4.5x risk**)

Risk Factors - Vaping

- Increasing use in teens/young adults
  - 2024 (US): 1.63 mil students use e cigarettes, 410k middle school[5]
- No definitive "proof"
- Biomarkers of carcinogens linked to bladder cancer have been identified in urine of e-cigarette users[4]

Presentation & Diagnosis

- Painless gross hematuria (**85%**)
  - 50% with painless gross hematuria have identifyable cause → risk of malignancy **20%**
- Microscopic hematuria (**~100%**)
  - "Dipstick" sensitivity for detecting hematuria reportedly 91-100%. Specificity **65%**
  - Risk of malignancy **2.5-5%**
  - If completely negative workup (cysto, CTU), risk of malignancy among those with persistent MH is **nearly 0** within first 3-5 years

Presentation & Diagnosis

Table 4. AUA Microhematuria Risk Stratification

Low Risk

- Age: Women < 50 years old; Men < 40 years old
- Smoking history: Never or < 10 pack year history
- Urinalysis: 3-10 RBC/HPF

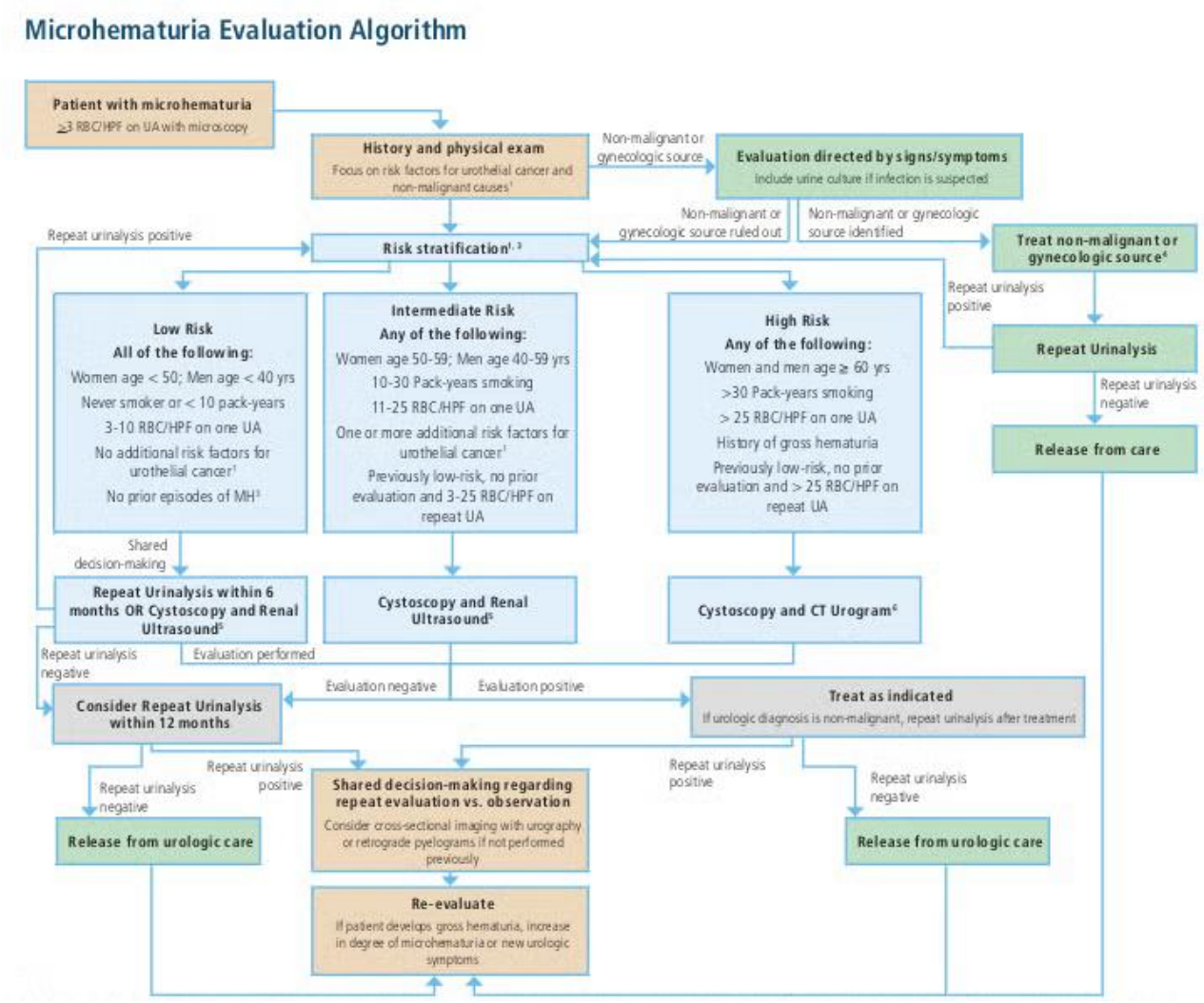
Intermediate Risk

- Age: Women 50-59 years old; Men 40-59 years old
- Smoking history: 10-30 pack year history
- Urinalysis: 11-25 RBC/HPF

High Risk

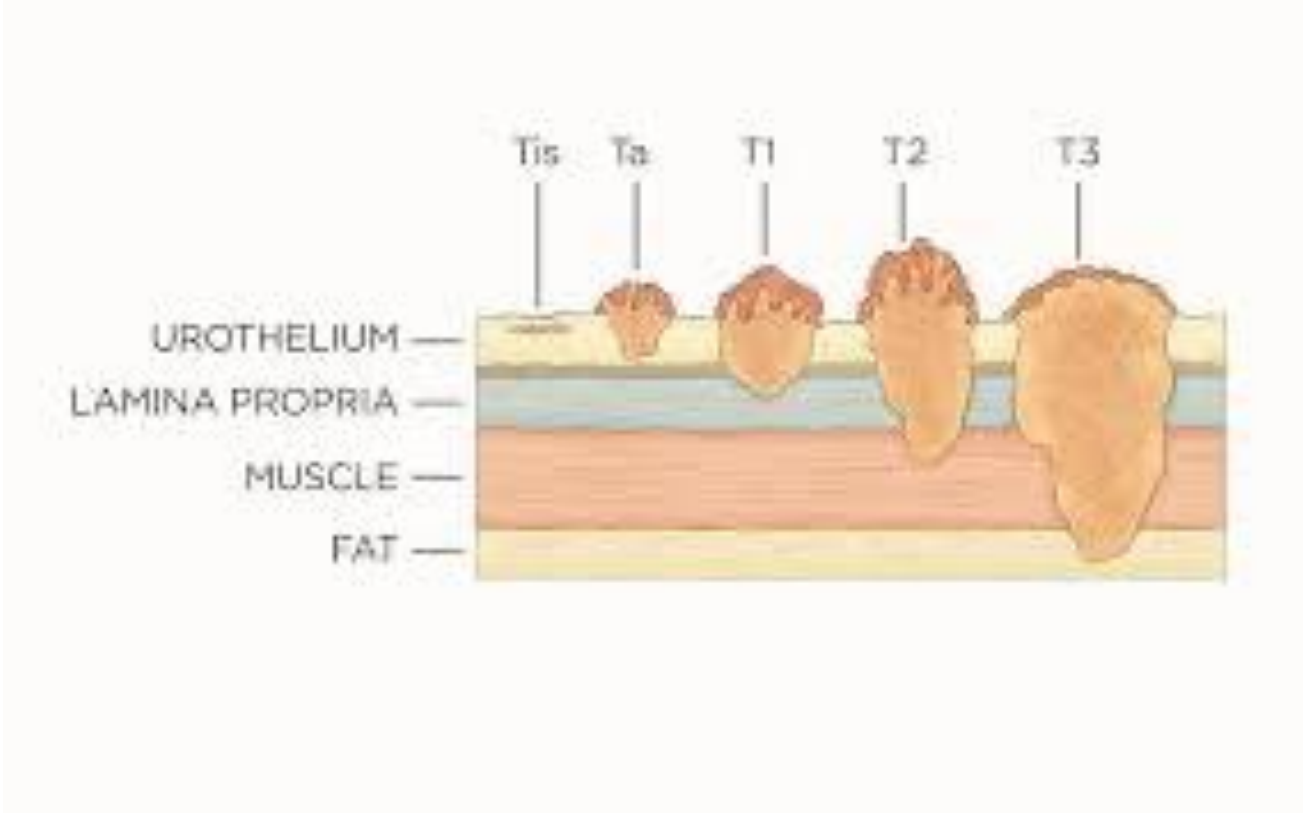
- Age: 60+ years old
- Smoking history: > 30 pack year history
- Urinalysis: > 25 RBC/HPF
- Gross hematuria

Presentation & Diagnosis



Presentation & Diagnosis

- Most bladder CA diagnosed at earlier stages (75%)
  - NMIBC—Ta, T1, CIS
  - Confined to mucosa or submucosa



Presentation & Diagnosis

- Urinary cytology
  - Sensitivity 30-60%
  - Specificity **94-100%**
- Biomarkers
  - *NMP22**
  - *BTA**
  - *UroVysion*
  - *ImmunoCyt*

*POC tests

Presentation & Diagnosis

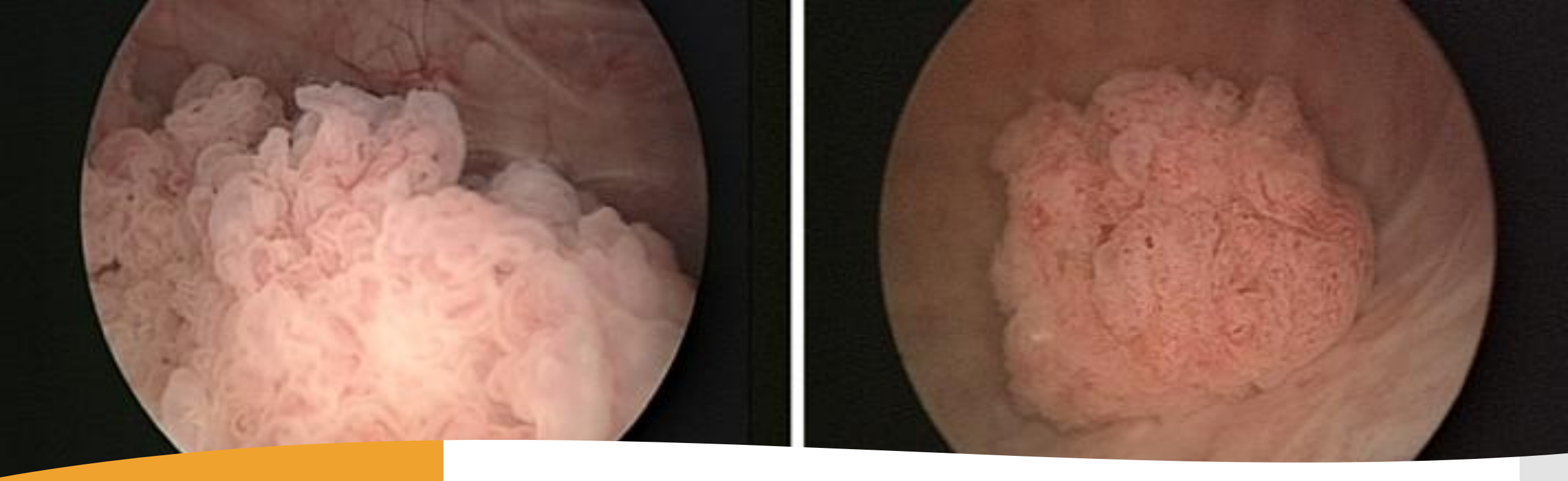
FDA-Approved Urinary Markers	Sensitivity	Specificity	PPV	NPV	Actual Role in Clinical Guidelines
BTA Stat (POC)	40–72	29–96	40–88	38–76.9	--------
BTA TRAK	50–62	68–87	45.4	88.4	--------
NMP22® BladderChek® (POC)	11–85.7	77–100	18.2–100	61.9–93.9	--------
NMP22® Bladder Cancer Test	24–81	49–100	31–100	60–91	---------
UroVysion®	13–100	63–100	21–83	67.9–100	Might serve as a reflex test following unremarkable cystoscopy findings and inconclusive or ambiguous cytology results
ImmunoCyt®	50–85	62–86	26–72	81–93	Might serve as a reflex test following unremarkable cystoscopy findings and inconclusive or ambiguous cytology results

Presentation & Diagnosis

- **Bladder Tumor Antigen Assay (BTA)**
  - Detect human complement factor H-related protein → higher [ ] in bladder CA
  - *BTA Stat* is a qualitative POC assay. Results within 5 minutes
  - Approved by FDA for monitoring only, in conjunction with cystoscopy
  - Initial promise but concerns re: high false positive & low specificity[13]
    - Especially with lower grade tumors (~50-60% sensitivity)[14]
    - False positives up to 2 years limit usefulness[15]
    - Blood in urine samples frequent source of false (+)

Presentation & Diagnosis

- **NMP22**
  - Nuclear matrix proteins over-expressed in urothelial tumours → found in urine after cell apoptosis
  - NMP22 BladderChek (POC) FDA approved for initial diagnosis
  - 58% sensitivity, 88% specificity[16,17]
  - Markedly diminished for NMIBC (as low as 42%)

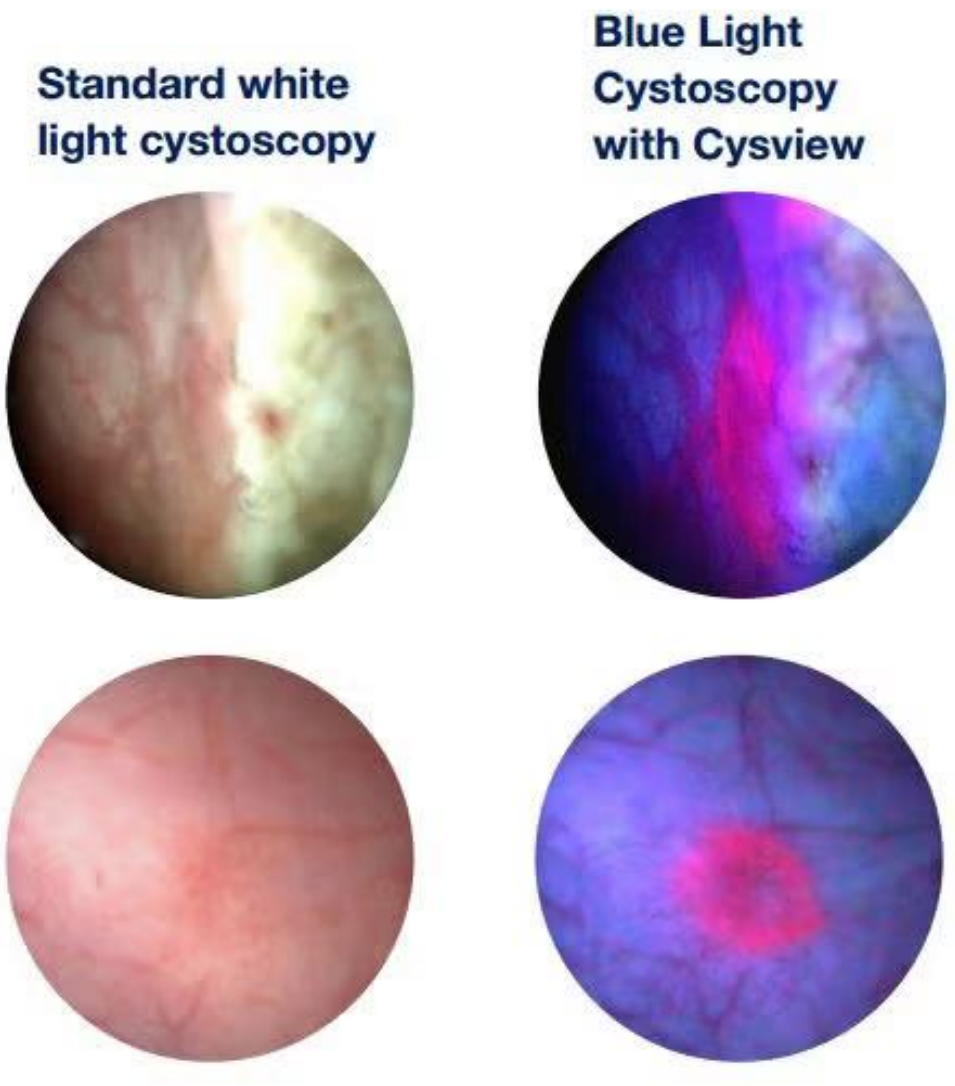


Diagnosis

- Standard white light cystoscopy remains standard, low cost evaluation for patients with gross hematuria
- **No urinary biomarkers have sufficient sensitivity or specificity to replace cystoscopy**

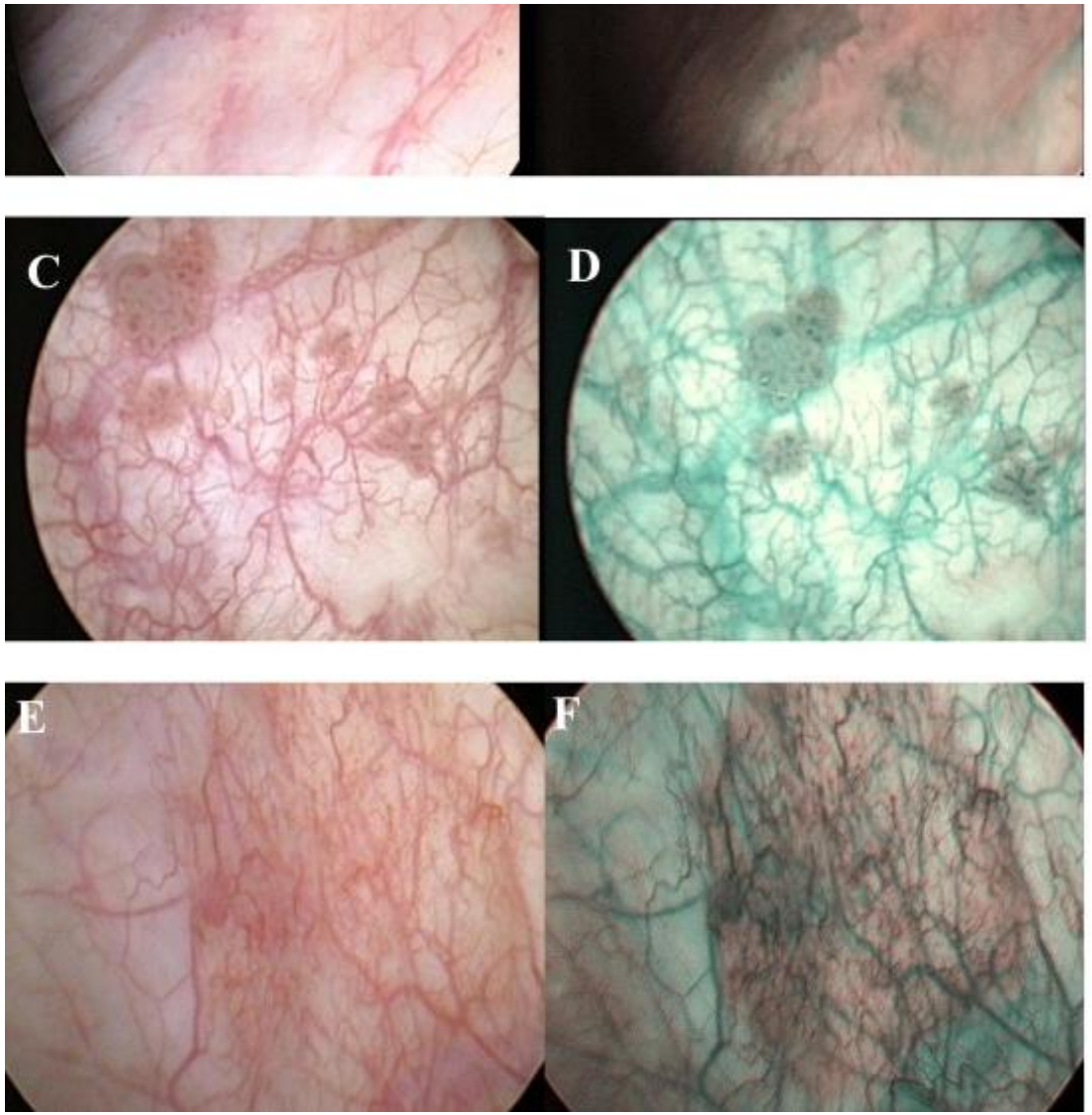
Diagnosis

- **Hexaminolevulinate (HAL) blue light cystoscopy**
  - HAL = photoactive porphyrin that accumulates preferentially in neoplastic tissue
  - Instilled into bladder x1-4h
  - Emits red fluorescence under blue-wavelength light
  - Increased detection rates (15% for Ta, 40% for CIS)[19,20]
  - Decr progression rates & time to progression, but overall onc outcomes unclear[21]
  - Cost-benefit analyses have been positive



Diagnosis

- **Narrow Band Imaging (NBI)**
  - Enhances contrast between mucosal + microvascular surfaces
  - Light of narrow range (blue/415 nm – green/540nm), strongly absorbed by hemoglobin
  - Vascular structures appear dark brown/green against pink or white mucosa
  - Multiple studies have demonstrated improved RFS but mostly in low-risk patients[22,23]



ThankYou!

