Bladder Pathology
An Introduction

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Outline

- Bladder histology
- Terminology issues
- Natural history of TCC
- Papillary vs. flat lesions
- Divergent differentiation in TCC
- TCC variants: why variants?
- Role of urine cytology

Bladder Histology

- Well developed muscularis mucosae in <5%
- Muscularis mucosae bundles may be relatively organised mimicking detrusor
- Tumour within muscularis mucosae (pT1) may be mistaken for detrusor invasion (pT2)
- Little lamina propria at trigone so detrusor close to surface
- Prominent blood vessels mark the level of muscularis mucosae

Bladder Histology (2)

- Detrusor muscle may be interrupted so pT2 may be understaged at TURBT
- Fat often present in lamina propria and Muscularis propria
  - Tumour invading fat in TURBT is not pT3

Terminology Issues

- Superficial TCC
  - Clinicians: CIS, pTa and pT1
- Invasive TCC
  - Pathologists: pT1 at least
  - Clinicians: pT2 at least
- Muscle invasive TCC
  - Clinicians: pT2 at least
- Carcinoma for non-invasive lesions
  - Basis in natural history of urothelial tumours?

Grading Papillary TCC

WHO 1973

\[\text{Papilloma} \rightarrow \text{G1} \rightarrow \text{G2} \rightarrow \text{G3}\]

- Papilloma
  - Rarely recur
  - Normal life expectancy
  - Grade 1: almost normal
  - Grade 3: like carcinoma in situ
### WHO 1973: Problems
- “Carcinoma” for non-invasive tumours
- Large number of tumours end up as G2
- 3 grades of TCC but only 2 Rx options

### Natural History of pTa G1 TCC
- Significant recurrence rate (33%), generally as G1 pTa
- Progression rare
- Normal life expectancy
- “carcinoma” because may recur

### Re-occurrence rather than recurrence?
- Related to persistence of causative factor rather than reflecting aggressive tumour behaviour
- “Recurrences” of low-grade TCC often at different site from primary

### Grading Papillary TCC
- **WHO 1973**
  - Papilloma – G1 – G2– G3
- **WHO/ISUP 2004**
  - Papilloma
  - Papillary urothelial neoplasm of low malignant potential (PUNLMP)
  - Low-grade urothelial carcinoma
  - High-grade urothelial carcinoma

<table>
<thead>
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</thead>
<tbody>
<tr>
<td>Papilloma</td>
<td>Papilloma</td>
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<tr>
<td>Grade 1</td>
<td>PUNLMP</td>
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<tr>
<td>Grade 2</td>
<td>Low-grade</td>
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<tr>
<td>Grade 3</td>
<td>High-grade</td>
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### Natural History of TCC
- **G3 pTa papillary urothelial carcinoma**
  - High recurrence rate (55%), often as invasive (27%).
  - Significant risk of mets/death (25%)
- **pT2 urothelial carcinoma**
  - High risk of mets (50% in 2 years) and death
When is it a cancer?

<table>
<thead>
<tr>
<th>WHO 1973</th>
<th>Papilloma</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Invasive</th>
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<tbody>
<tr>
<td>WHO/ISUP</td>
<td>Papilloma</td>
<td>Low grade</td>
<td>High grade</td>
<td>Invasive</td>
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Pathogenesis of Urothelial Neoplasia
- ? 1 disease
- ? 2 distinct diseases

1 Disease Model
- Benign
- Carcinogenesis
- Grade 1 pTa
- Progression
- Grade 3 pTa
- pT1 – pT2 – mets - death

2 Disease Model
- Benign
- Carcinogenesis
- G1 pTa
- Normal life expectancy
- Benign
- Carcinogenesis
- G3 pTa
- Progression
- pT1 – pT2 – mets - death

Low-grade and high-grade urothelial neoplasms: Two different diseases?
- Processes that might predispose to adverse outcome have already occurred at time of diagnosis
- Analogous to low-grade and high-grade breast carcinoma

Grade Stage Interaction
- Grade 1 pT1 virtually non-existent
- Almost always reclassified as pTa or G2
- pT2 disease: grade irrelevant

LG DCIS → LG carcinoma
HG DCIS → HG carcinoma
**Relationship of Papillary and Flat lesions**

<table>
<thead>
<tr>
<th>Papillary</th>
<th>Flat</th>
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<tbody>
<tr>
<td>Papilloma</td>
<td>Normal urothelium</td>
</tr>
<tr>
<td>PUNLMP</td>
<td>Urothelial hyperplasia</td>
</tr>
<tr>
<td>Low-grade TCC</td>
<td>Urothelial dysplasia</td>
</tr>
<tr>
<td>High-grade TCC</td>
<td>Urothelial CIS</td>
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**Divergent differentiation in TCC**

- Squamous, glandular and/or small cell differentiation
- Common in high-grade TCC
  - Adverse prognosis
  - Small cell carcinoma of bladder often associated with urothelial carcinoma in situ

**TCC variants: Relevance**

- Histological curiosity
  - TCC with lipid rich cells
- Mimics another entity
  - Plasmacytoid TCC
- Relevance in mets
  - TCC with squamous/glandular differentiation
- Predicts prognosis
  - Micropapillary TCC
- Predicts response to therapy
  - Lymphoepithelioma-like TCC

**Role of urine cytology**

**Advantages**

- Non-invasive
- Samples entire surface of bladder and upper tract
- High accuracy in high-grade tumours

**Limitations**

- Degeneration mimics tumour
- Needs experienced cytopathologist
- Cannot localise tumour
  - May be in bladder, ureter, renal pelvis, urethra
- Low accuracy in low-grade lesions