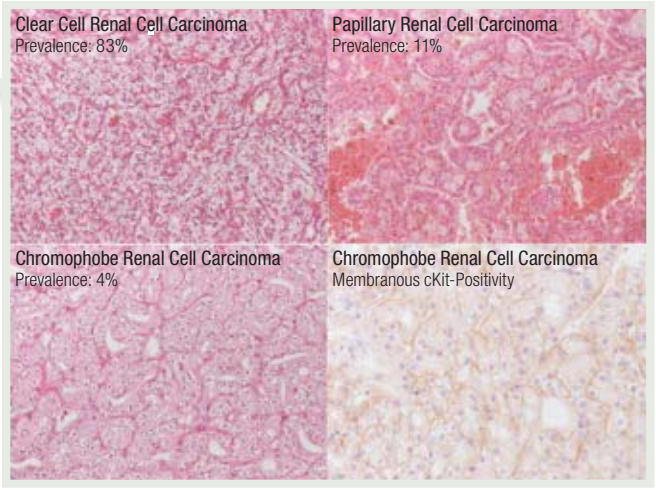
1 Anatomy of the GU tract and histology of GU tumours

Tumours of the kidney

>95% of kidney cancers have a characteristic morphology that can be classified as: clear cell, papillary, chromophobe renal cell carcinoma, and carcinoma of the collecting ducts of Bellini.

Patient outcome varies between histological kidney cancer subtypes and is dependent on the treatment given.

Only a few kidney cancers have an unusual morphology and have been categorised as rare kidney cancer entities, e.g. mucinous tubular and spindle cell carcinoma.



Clinical and Pathological Classification of the Primary Tumour (pT)	
T1	Tumour 7 cm or less in greatest dimension, limited to the kidney
T2	Tumour more than 7 cm in greatest dimension, limited to the kidney
T3	Tumour extends into major veins or perinephric tissues
T4	Tumour invades beyond Gerota fascia

Primary tumour category has a strong prognostic impact.

Histological tumour grade (mostly performed according to Thoenes or Fuhrman) is more subjective and has less prognostic influence.

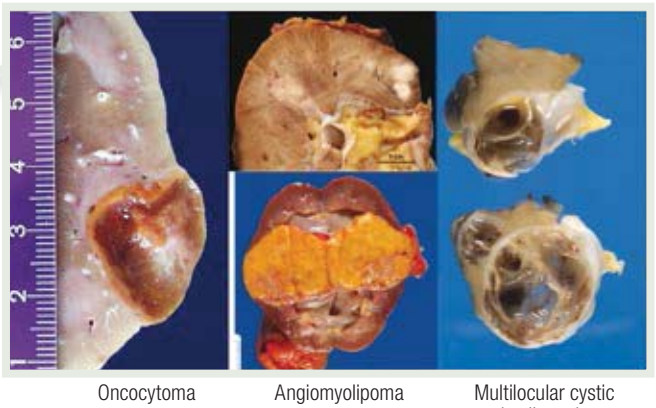
Criteria for a high (unfavourable) grade generally include a large nucleus size, polymorphy of the nuclei, presence of prominent nucleoli, and mitoses.

5%-7% of kidney tumours are benign. Oncocytoma is the most frequent benign tumour. The tumour is well circumscribed, mahogany brown with a central scar.

Angiomyolipomas represent 1% of kidney tumours. They consist of varying proportions of mature fat, thick-walled blood vessels, and smooth muscle.

Multilocular cystic carcinoma is in principle a malignant tumour but is entirely composed of cysts, with very few cancer cells. Metastases have not been reported.

"Benign" renal tumours



Oncocytoma | Angiomyolipoma | Multilocular cystic renal cell carcinoma

REVISION QUESTIONS

1. What are the main subtypes of renal cell carcinoma?
2. What is the best predictor of prognosis in renal cell carcinoma?
3. Which carcinoma has the best prognosis?

Tumours of the urinary system

Urothelium is present in the kidney pelvis, ureters, urinary bladder, and the urethra.

Urothelial neoplasms can occur in all of these organs but >90% are in the urinary bladder.

The normal bladder wall consists of several tissue layers, the distinction of which is critical for bladder cancer staging.

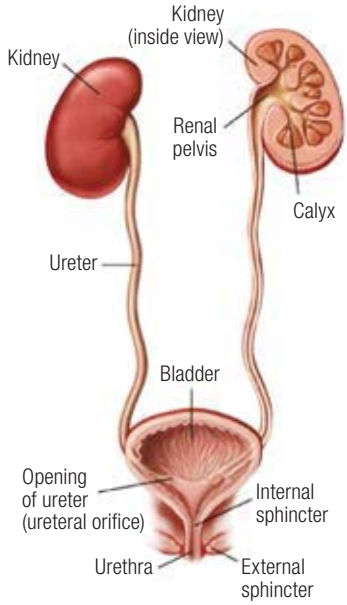
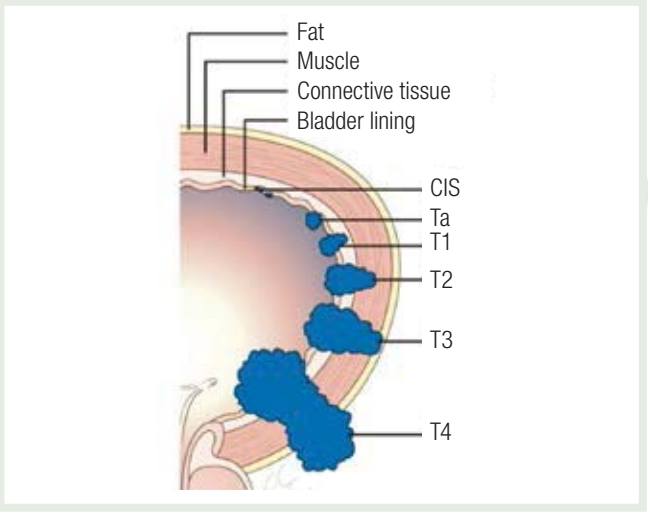


Diagram showing the T stages of bladder cancer



The urothelium covers the inner surface of the bladder. The connective tissue layer between the urothelium and the muscular bladder wall is the lamina propria.

The staging system of urothelial neoplasms is unusual as two non-invasive lesions exist: non-invasive papillary carcinoma (pTa) and carcinoma in situ (pTis).

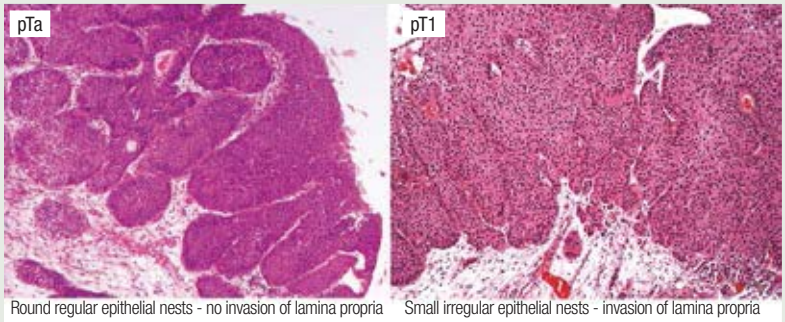
The invasive stages are pT1: invasion of lamina propria; pT2: invasion of muscular wall; pT3: invasion of perivesical fat; pT4: invasion of adjacent organs.

Staging of bladder neoplasms is critical for treatment decisions, but challenging for pathologists.

This is due to the nature of transurethral tumour resection, because it always leads to fragmentation and substantial crush artefacts in the removed tissues.

The distinction between pTa and pT1 tumour can be very challenging and is subject to high interobserver variability.

pTa versus pT1: High Interobserver Variability



Round regular epithelial nests - no invasion of lamina propria

Small irregular epithelial nests - invasion of lamina propria

Author	N pT1	downstaged to pTa
Abel 1988	28	25%
Witjes 1994	120	31%
Tosoni 2001	235	34%

Assessment of interobserver variability of staging pTa and pT1 tumours:
In these studies pT1 tumours were reviewed and the initial diagnosis was downstaged to pTa in 25%-34% of cases.

REVISION QUESTIONS

1. What is the most common site for urothelial cancer?
2. What is the difference between stage pTa and pTis?
3. Which tumour stages are subject to particularly high interobserver variability?

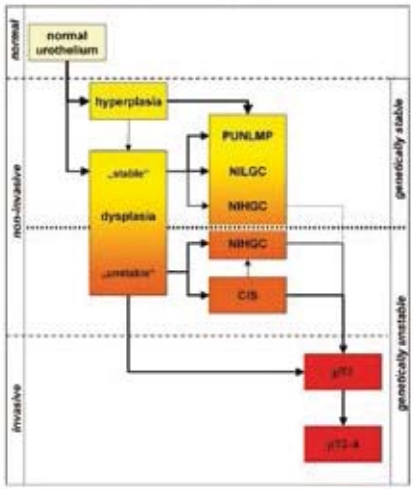
Tumours of the urinary system

Development and progression of urothelial neoplasia occurs through two quite different genetic pathways.

Non-invasive papillary cancers of low/intermediate grade (pTa, G1/2) develop from dysplasia/hyperplasia and almost never progress to invasive cancer.

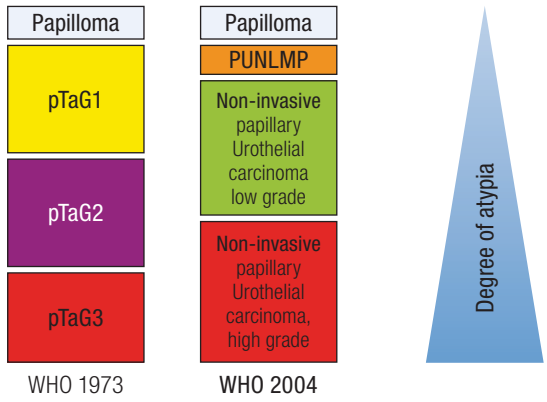
Invasive carcinomas are mostly of high grade and are mainly derived from carcinoma in situ or high-grade non-invasive papillary carcinomas (pTa, G3).

Model of bladder cancer development and progression based on genetic findings



NILGC = non-invasive low-grade carcinoma; NIHGC = non-invasive high-grade carcinoma

Non-invasive papillary tumours



The classification of non-invasive papillary carcinomas is confusing because two "non-congruent" systems are typically used, either alone or in parallel.

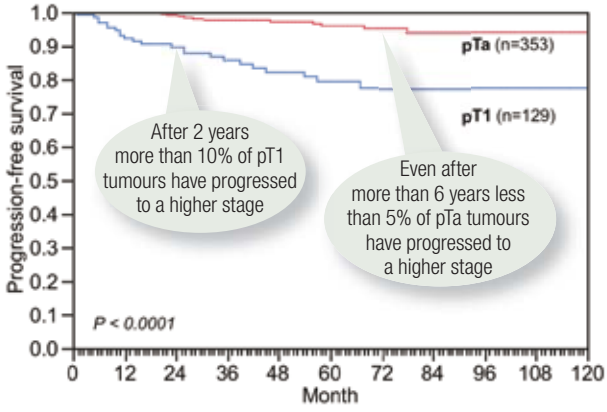
Most clinicians are familiar with the WHO 1973 grading system that classifies non-invasive cancers as pTaG1, pTaG2, or pTaG3.

The WHO 2004 version also includes: papilloma, papillary urothelial neoplasm of low malignant potential (PUNLMP), non-invasive papillary cancer, low grade, and non-invasive bladder cancer, high grade.

The term "superficial bladder cancer" is used for pTa and pT1 tumours.

pTa and pT1 tumours not only represent two different entities at the genetic level, but also have a completely different clinical course.

While pTa tumours rarely progress, pT1 tumours are early stages of highly malignant neoplasms.



REVISION QUESTIONS

1. What are the two main groups of urothelial neoplasms?
2. What is the difference between the WHO 1973 and WHO 2004 classification?
3. Why should the term "superficial bladder cancer" be avoided?

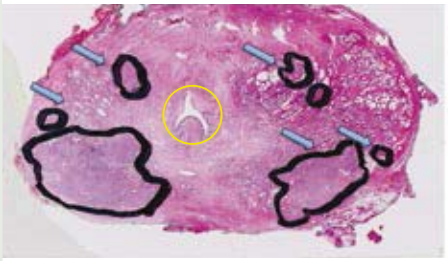
Tumours of the prostate

Prostate cancer is very common. A complete examination of the prostate will reveal cancer in 50% of men at the age of 50 and >75% at the age of 75 years.

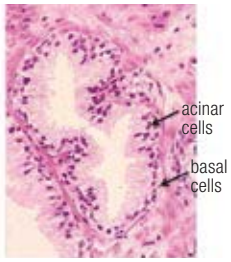
Accordingly, precursor lesions are even more common in the prostate and many patients have more than one spatially separated prostate cancer.

Normal prostate epithelium is characterised by the presence of two cell layers: basal cells and acinar cells.

Prostate cancer is often multifocal
(Whole section through the prostate gland; blue arrow: prostate cancer, yellow circle: urethra)

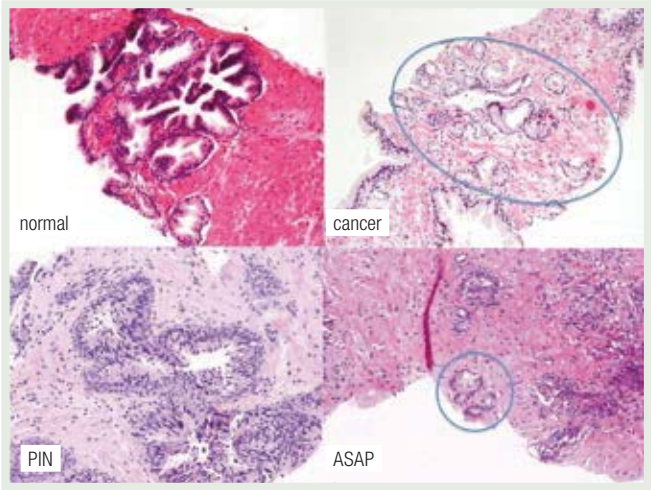


Normal prostate gland



Clinical and Pathological Classification of the Primary Tumour T

T1	Clinically unapparent tumour
T2	Tumour confined within the tumour
T3	Tumour extends through the prostatic capsule
T4	Tumour invades adjacent structures other than seminal vesicles



Prostate biopsy is the only tool for establishing a definitive diagnosis of prostate cancer.

Findings in prostate biopsies include: normal, prostatic intraepithelial neoplasia (PIN), atypical small acinar proliferation (ASAP), and carcinoma.

PIN is the precursor lesion of prostate cancer. ASAP is a diagnostic category that includes all changes that are suspicious for cancer but not unequivocally diagnostic.

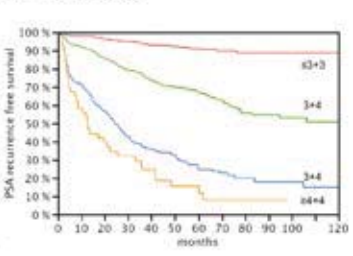
Prostate cancer is entirely composed of atypical cells, while basal cells are completely lost. Gleason grade is the strongest predictor of tumour aggressiveness.

In contrast to all other grading systems, the Gleason grade is purely based on tumour architecture and does not consider any cytological changes.

It distinguishes 5 sets of histological patterns with increasing "dedifferentiation" from 1 to 5.

Gleason grading

PROSTATIC ADENOCARCINOMA
(Histological patterns)



Gleason grade correlates with PSA recurrence-free survival

REVISION QUESTIONS

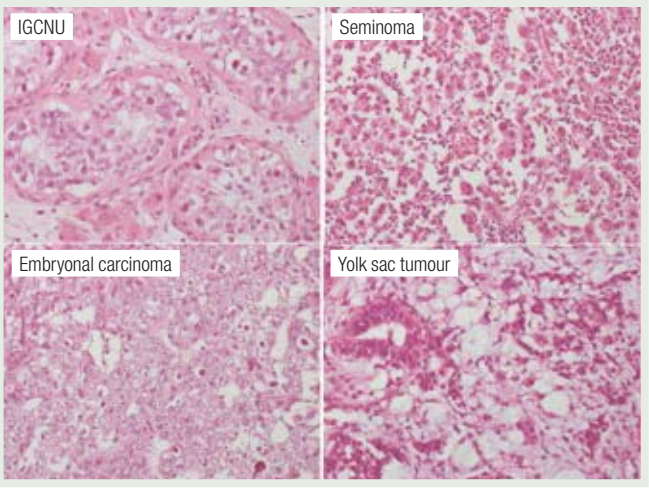
1. What is the precursor lesion of prostate cancer?
2. What is the meaning of "ASAP" and when is this term used?
3. What is the characteristic of Gleason grading?

Tumours of the testis

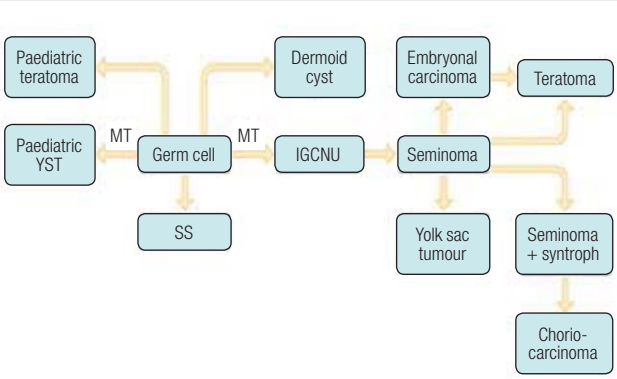
More than 95% of all testicular neoplasias are germ cell tumours. Germ cell tumours mostly occur at young age (highest frequency at the age of 30 years).

More than 90% of these develop through intratubular germ cell neoplasia (IGCNU), which is commonly found in the vicinity of these cancers.

50% of IGCNU progress into invasive germ cell tumours within 5 years.



Model of development of germ cell tumours



YST = Yolk sac tumours; MT = Malignant transformation; SS: Spermatocytic seminoma.

Seminoma is the least differentiated (earliest) development stage of invasive germ cell carcinoma.

About 50% of all testicular germ cell tumours halt at that stage of development and are diagnosed as pure seminomas.

Teratoma in the adult is a "differentiated type" of germ cell tumour having evolved from IGCNU and seminoma. Teratoma in the adult is thus considered malignant.

Tumour stage (pT) is critical for subsequent therapy of testicular tumours.

Most pT2 stages are diagnosed because of vascular invasion.

Regional lymph nodes include the abdominal, paraaortic, preaortic, interaortocaval, precaval, paracaval, retrocaval, and retroaortic nodes.

Clinical and Pathological Classification of the Primary Tumour T	
T1	Tumour limited to testis and epididymis without vascular/ lymphatic invasion
T2	Tumour limited to testis and epididymis with vascular/ lymphatic invasion or tumour extending through tunica albuginea with involvement of tunica vaginalis
T3	Tumour invades spermatic cord
T4	Tumour invades scrotum

REVISION QUESTIONS

1. What is the precursor lesion of most germ cell tumours?
2. What is the typical age of patients with germ cell tumours?
3. Why is a testicular teratoma in an adult considered malignant?

Summary: Anatomy of the GU tract and histology of GU tumours

- The most common kidney cancers are clear cell, papillary, and chromophobe renal cell carcinoma
- Urothelium is present in the renal pelvis, ureters, urinary bladder, and the urethra, but >90% of urothelial neoplasms occur in the urinary bladder
- The staging system of urothelial neoplasms is unusual as two non-invasive lesions exist: pTa and pTis
- There is a high interobserver variability in staging pTa and pT1 tumours
- pTa and pT1 tumours represent two different entities at the genetic level and have a completely different clinical course
- Prostate cancer is very common, >75% of men at the age of 75 years will reveal prostate cancer
- Prostate cancer is graded according to Gleason grading, the strongest predictor of tumour aggressiveness
- More than 95% of all testicular neoplasias are germ cell tumours
- Germ cell tumours mostly occur at young age
- Germ cell tumours include seminoma, embryonal carcinoma, yolk sac tumour, choriocarcinoma, and teratoma

Further Reading

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