The Royal College of Pathologists
Pathology: the science behind the cure

Tissue Pathways for Urological Pathology

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General Introduction

1. Staffing and workload

Urological histopathology is a major element of most histopathology departments' workload. Pathologists reporting urological specimens will either be generalists with an interest in uropathology or subspecialists in uropathology. In either circumstance, there must be enough pathologists to provide cover and to conform to the Royal College of Pathologists' guidance on staffing and workload levels.[1]

Pathologists reporting urological pathology should participate in an appropriate external quality assessment (EQA) scheme. Lead pathologists or those whose work consists predominantly of urological pathology should participate in the National Urological and web-based Prostate Biopsy EQA schemes. The web-based prostate biopsy EQA may also be used to maintain and assess competence. Nominated pathways for referral of difficult cases for expert opinions should be in place. Histopathology laboratories should have a lead pathologist for each of the main cancers with responsibility for liaising with relevant local and clinical multidisciplinary teams (MDTs), and ensuring that the relevant specimens are examined, sampled and reported appropriately and in a consistent and timely fashion. Cancer centres and units should be supported by laboratories accredited with Clinical Pathology Accreditation (UK) Ltd and staffed in accordance with the recommendations of the Royal College of Pathologists and the Association of Clinical Pathologists.

Workload may vary considerably according to the nature of the specimens received. Pathologists undertaking a significant amount of oncology work will be able to report fewer requests per year than a pathologist dealing primarily with non-neoplastic specimens. The cancer datasets for reporting tumours are used in the system of standard setting, data collection, audit and feedback for those involved in caring for these patients.[2]

2. Laboratory facilities

The full range of routine laboratory facilities is needed, including access to immunohistochemistry and electron microscopy (EM), which may be off-site. The laboratory should be staffed, equipped and managed in a way that maintains safe and efficient throughput to a high standard.

3. Specimen submission and dissection

Most specimens are received in the laboratory in formalin as routine diagnostic or therapeutic specimens according to standard procedures. Full patient details, clinical consultant, date of procedure and type of specimen must be provided. The indication for the biopsy should be stated. Relevant patient history and clinical findings must be described on the form accompanying the specimen. Details of previous histology should be mentioned, particularly if there is a history of dysplasia or carcinoma.

Each specimen container should be labelled with the patient's details and the site of the biopsy. Formalin should cover the specimen entirely to ensure proper fixation. No interference with the specimen should be allowed unless agreed, prior to receipt in the histopathology laboratory. The following guidelines should be observed in selecting and submitting tissue for microscopic study:

- Small biopsies that will fit in one cassette are generally submitted in total. Diagnostic biopsies of larger size may need to be entirely submitted, but there are exceptions. See organ-specific instructions for sampling.
- Excisional biopsies containing a tumour should be blocked to show margins. India ink (or equivalent) can be used to mark margins. Be careful to ensure than the ink does not spread elsewhere!
- By convention, sections are cut from the *side facing down* in the cassette. If there is any reason to orient the specimen another way, put instructions on the work sheet/form (i.e. 'on edge').

- Tissues must be *thin* (2–3 mm or less than the thickness of the cassette) and must not be crowded into the cassette. Thick or crowded tissue cannot be processed properly and poor sections will result, especially if the tissue contains fat.
- Ensure adequate fixation of large specimens (bladder resections, nephrectomies and prostatectomies) before cutting. Thinner, better anatomically oriented sections will result.

4. Block selection and record

Specimen dimensions are measured in mm. When sampling a specimen, document the site from which each block is taken. Each cassette must have a unique identifying number/letter preferably applied with a microwriter, and the number of pieces of tissue in each cassette recorded. For most specimens no special facilities are required for specimen dissection. Coloured inks for surgical resection margins should be available. Digital photography is the routine now and it is good practice to photograph large specimens so that a permanent record of the macroscopic appearance and location of blocks can be recorded and filed in the patient records. Photography of all large specimens is an invaluable resource for MDT meetings, teaching and research.

Section A: The Kidney And Renal Pelvis

A1. Nephrectomy non-malignant

A1.1 Indications for histology

- Removal of non-functioning kidney (simple nephrectomy) is indicated in patients with an irreversibly damaged kidney because of symptomatic chronic infection, obstruction, calculous disease, ischaemia (atheromatous/non-atheromatous) or severe traumatic injury. It also is indicated to treat severe unilateral parenchymal damage from nephrosclerosis, pyelonephritis, reflux or congenital dysplasia of the kidney.[3] Other indications include failed renal transplant.[4]
- Assessment of primary disease, e.g. pelvi-ureteric junction obstruction, chronic obstructive or reflux uropathy, adult polycystic kidney disease (APCKD) or xanthogranulomatous pyelonephritis (XGP).[5,6]
- Clinical presentation, radiological features and gross appearance of XGP may closely mimic a renal neoplasm making a correct pre-operative diagnosis difficult.
- Staghorn calculus.
- Radiation nephropathy which may be either acute or chronic and related to dose.
- To exclude malignancy (e.g. multilocular cystic lesions, incidental carcinoma in a polycystic kidney, long term dialysis associated cystic lesions).

A1.2 Staffing and workload

(See introduction, page 3.)

- Can be reported by a general pathologist with experience of urological pathology.
- Difficult cystic lesions may be referred for a second opinion.
- Transplant nephrectomies should be reported by a specialist renal transplant pathologist who participates in the National Renal Transplant EQA.

A1.3 Laboratory facilities

- Routine processing for light microscopy (LM).
- Can require both histochemical and immunohistochemical (see below) analysis of background kidney to rule out glomerulonephritis. Very occasional need to extract formalin-fixed, paraffin-embedded material for subsequent electron microscopy (EM) examination.
- Occasionally use of immunohistochemistry to exclude or confirm background renal neoplasia (see below)

A1.4 Specimen dissection

- Treat as for a potential renal malignancy – weigh, measure (length, breadth and depth in mm) and orientate (ureter posterior to vessels and the renal artery enters the hilum partially behind the renal vein but variations occur in 40%).
- The presence or absence of the adrenal gland in the suprarenal fat should be noted and sampled. The presence of lymph nodes near the hilum should also be noted and sampled.
- Identify resection margins of ureter, renal artery and vein. Submission for histology is unnecessary and not cost effective in non-neoplastic kidney diseases.
- Check renal artery for stenosis and take a block to confirm cause if present (atheroma, arterial fibromuscular dysplasia).
- Initial incision should pass through the midline of the kidney in the coronal plane.
- Photograph the bisected kidney if equipment available.
- Use the first cut surface to collect tumour (if present) and kidney tissue for special purposes (EM, imprints, flow cytometry, cytogenetics, tissue culture, snap freezing, etc.).
- Take at least one block of normal residual kidney (for future use if there is any suspicion of underlying glomerulonephritis.[7] If the patient subsequently develops renal impairment, a unilateral kidney biopsy may be contraindicated and archival tissue could be used to identify any aetiology).
- In the absence of any tumour, embed blocks of pelvi-ureteric junction, pelvis and any focal lesions to be taken to include any abnormal area and one from otherwise normal parenchyma.
- In XGP, numerous dilated calyces with yellow–brown calculi are seen. A staghorn calculus may be present. XGP may closely mimic a renal neoplasm.
- For individual cystic lesions, take blocks of solid areas to exclude nests of clear cell carcinoma. For multicystic lesions, take at least one block/cm maximum kidney dimension for thorough sampling to exclude incidental background carcinoma, and for assessment of cysts in congenital disease. For paediatric multicystic conditions, whole mounts may be considered.
- For transplant nephrectomies – blocks should be taken serially (from without in) of the hilar vessels to examine the state of the renal vein and artery. Multiple blocks of cortex and medulla are required for assessment of rejection. SV40 and C4d immunostaining (humoral rejection) are done as appropriate.

A1.5 Sectioning and staining

- Routine processing for LM
- Usually require only one haematoxylin and eosin (H&E) section per block
- May require both histochemical and immunohistochemical analysis of background kidney to rule out glomerulonephritis.
- Renal special set on kidney if indicated by H&E features. These include basement membrane stain (PAS, Jones Silver), fibrous tissue stains (EVG, trichrome) and Congo red[8] (amyloid). The silver stain is also useful for assessing vascular abnormalities
- Access to immunoperoxidase for IgA, IgG, IgM, C3, C4 or C1q.
- Very occasional need to extract formalin-fixed, paraffin-embedded material for subsequent EM examination.
- Occasionally use of immunohistochemistry to exclude or confirm background renal neoplasia (e.g. clear cell lining of cystic lesions) and should include a panel of vimentin, cytokeratin, CK 7, AMACR, CD10, EMA, CD117 (c-kit), RCC antibody or similar.

A1.6 Report content

- Presence or absence of malignancy, background urothelial changes [dysplasia, carcinoma *in situ* (CIS)], type and aetiology of chronic damage.
- XGP is due to renal outflow obstruction (staghorn calculi) in the setting of infection.

- Pattern and size of cysts should be described and features of renal dysplasia looked for (e.g. presence of cartilage). Solid areas and nephron-like elements are absent from cyst walls. In acquired cysts, the inner surface is smooth and there is no communication with the renal pelvis
- Cystic nephroma should be excluded. It is unilateral, solitary and multiloculated with non-communicating cysts sharply demarcated from adjacent kidney by a thick fibrous capsule with a nodular surface. Cysts have flat to hobnail epithelial lining and there is no renal parenchyma within the cysts (so not polycystic disease). The stroma may contain smooth muscle, skeletal muscle, cartilage or resemble ovarian stroma.
- Examine cysts in APCKD for features of malignancy. Micropapillary adenomas are very common in the cyst lining.
- Type and sites of rejection for transplant nephrectomy (description of transplant nephrectomies is not formally part of the Banff '97 classification, and most have had their immunosuppression stopped and demonstrate mixed acute and chronic rejection), any background pathology which might be relevant, e.g. CMV infection, post transplant lymphoproliferative disorder (PTLD).
- Identify cause of renal artery narrowing if present (atheromatous plaque, fibromuscular dysplasia, vasculitis) and the degree of ischaemic parenchymal renal damage.
- Confirm radiation nephropathy if clinically indicated (glomerulosclerosis, fibrinoid necrosis, thickened glomerular capillary walls, fibrinoid necrosis of arterioles and small arteries with variable thrombosis).

A2. Pelvi-ureteric junction (PUJ) specimen

A2.1 Indications for histology

- Primary causes of PUJ obstruction are usually congenital and may be the result of muscle bundle disarray or absence, increased collagen deposition, or abnormal anatomic location of the renal pelvis.[9]
- Secondary causes such as Urothelial carcinoma/transitional cell carcinoma (TCC) or external compression must be excluded.
- Diagnosis of these lesions is histologically problematic and does not affect treatment or prognosis of the patient.

A2.2 Staffing and workload

(See introduction, page 3.)

- Can be reported by a general pathologist with experience of urological pathology.
- Refer problematic cases to the lead urological pathologist.

A2.3 Laboratory facilities

- Routine processing for LM.
- Occasionally use of immunohistochemistry to exclude or confirm urothelial dysplasia, CIS or malignancy.

A2.4 Specimen dissection

- Specimen may be funnel shaped if unopened. The length, diameter at both ends and thickness of the wall are measured, and presence and size of any strictures described.
- Specimen is opened along the long axis. If the specimen has been opened prior to receipt in the laboratory, it may look like a triangular fragment of mucosa.
- Dimensions are measured in mm.
- Mucosal surface is examined for lesions and irregularities in texture.
- Outer surface is examined for mass lesions and fibrosis. Multiple sections taken along the long axis are submitted in one cassette. Submit in total if small sample

A2.5 Sectioning and staining

- Routine processing for LM.
- Usually require only one H&E section per block.
- Histochemical and immunohistochemical stains generally not required.
- Rarely any requirement for EM or molecular investigations.

A2.6 Report content

- Confirmation of pelvi-ureteric obstruction[10] or correlation with the clinical findings.
- Presence or absence of malignancy, background urothelial changes (dysplasia, CIS), type and aetiology of chronic damage.

Section B: The Ureter

B1. Ureteric biopsy

B1.1 Indications for histology

- Recent advances in the field of retrograde ureteroscopy include the development of small calibre fibre-optic endoscopes, improved optics and small calibre instruments enabling biopsy confirmation of previously inaccessible ureteric lesions.
- Abnormal imaging findings – filling defect.
- A number of benign lesions can present with filling defects. These include radiolucent stones, blood clots, sloughed renal papillae, hamartomatous lesions, ureteritis cystica, nephrogenic metaplasia, fibroepithelial polyps, tuberculosis, schistosomiasis, amyloid and endometriosis.[10]
- Evaluation of ureteric injury.
- Therapeutic indications include incision and biopsy of ureteric strictures.
- It is important to obtain an accurate diagnosis so that accurate treatment can be initiated.
- Exclude dysplasia, CIS and malignancy.
- Correlate with aspirated urine/fluid result if taken simultaneously.

B1.2 Staffing and workload

(See introduction, page 3.)

- As routine, can be reported by any pathologist.

B1.3 Laboratory facilities

- Routine processing for LM.
- May require both histochemical and immunohistochemical (CK7/20) analysis.

B1.4 Specimen dissection

- Tiny pieces of tissue (several mm) retrieved using either 'cold' cup forceps or a small diathermy loop are counted, measured, processed intact and examined histologically through three levels.
- Larger specimens (much less common) should be weighed collectively, the number of fragments counted and all tissue embedded.
- Determine the number and size of biopsies (mm). The term ‘multiple’ should be restricted to cases where there are too many to count.
- To avoid loss of smaller endoscopic biopsies during processing, ink with eosin and wrap in filter paper or similar commercial products.
- Embed all fragments in their entirety.
- Embedding fragments in a line facilitates histological assessment.

B1.5 Sectioning and staining

- One H&E section per cassette, at least three levels/serials.
- May require unstained sections between levels, if suspicion of CIS. It may be appropriate to cut additional sections at initial processing if there is a likelihood that these will be required.
- Routine processing for LM.
- Rarely need histochemical stains.
- Can occasionally require immunohistochemical analysis (CK7/20).[11]

B1.6 Report content

- If stricture, confirm benign changes.
- Radiation injury subsequent to treatment for cervical or prostate cancer shows peri-ureteric and submucosal fibrosis with atypical fibroblasts.
- Sclerosing retroperitoneal fibrosis is difficult to confirm and shows non-specific inflammatory changes and occasional granulomatous inflammation.
- Exclude benign tumours, the commonest being transitional cell and inverted papillomas and villous adenomas.
- Endometriosis results in either an intrinsic or extrinsic mass but is histologically similar to typical endometriosis elsewhere.
- Exclude presence or absence of malignancy, background urothelial changes (dysplasia, CIS).[6]
- Uretero-ileal anastomotic sites for ileal conduits show various chronic microscopic changes; cystically dilated intestinal glands, urothelial lined cysts, mucus pools and intestinal epithelial-lined cysts.

B2 Ureteric resection

B2.1 Indications for histology

- Confirm nature of pathology (stricture).
- Confirm other pathologies; congenital anomalies (duplex ureter), ureteritis cystica, nephrogenic metaplasia, endometriosis, sclerosing retroperitoneal fibrosis.
- Exclude dysplasia, CIS and malignancy.

B2.2 Staffing and workload

(See introduction, page 3.)

B2.3 Laboratory facilities

- Routine processing for LM.
- Occasionally use of immunohistochemistry (CK7/20, p53)[11] to exclude or confirm urothelial dysplasia, CIS or malignancy.
- Immunohistochemistry for confirmation of lesions such as nephrogenic metaplasia occasionally required (CK7/20, AMACR).

B2.4 Specimen dissection

- Measure length – usually funnel shaped in PUJ specimens (see above). Place probe to identify ureter.
- Longitudinal sections from pelvic portion and transverse sections from ureter to include distal margin.
- Submit in total if small sample.

B2.5 Sectioning and staining

- One H&E section per cassette, no need for routine unstained levels.
- Histochemical and immunohistochemical stains generally not required.

- Rarely any requirement for EM or molecular investigations.

B2.6 Report content

- Document the presence of ureteric narrowing.
- Note presence of nephrogenic metaplasia, endometriosis, amyloid, ureteritis cystica, sclerosing retroperitoneal fibrosis.
- Comment on dysplasia or CIS particularly if at margins. All carcinomas should be typed, graded and staged as per World Health Organization (WHO).

Section C: The Bladder

C1 Bladder biopsies

C1.1 Indications for histology

- Exclude primary urothelial dysplasia, CIS (G3 Tis) or malignancy.
- Follow up cystoscopy after previous Urothelial carcinoma/TCC or intravesical treatment such as BCG.
- Confirm benign pathology (cystitis, nephrogenic metaplasia, trigonal squamous and keratinising squamous metaplasia, interstitial cystitis, amyloid, malakoplakia or specific infections).
- Radiation cystitis.
- Assessment of cystitis and aetiological factors.

C1.2 Staffing and workload

(See introduction, page 3.)

C1.3 Laboratory facilities

- Routine processing for LM.
- Availability of histochemical stains occasionally used including Congo Red, PAS ± diastase, von Kossa, Ziehl-Neelsen (ZN), Toluidine blue or other mast cell stain.
- Availability of immunohistochemistry for CK20[11,12] and/or other markers (including p53 or CD44)[11] for diagnosis of CIS or incidental papillary lesions.

C1.4 Specimen dissection

- Determine the number and size of biopsies (mm). The term ‘multiple’ should be restricted to cases where there are too many to count.
- To avoid loss of smaller cystoscopic (and cold cup) biopsies during processing, ink (eosin/india) and wrap in filter paper or similar commercial products.
- Larger specimens (much less common) should be weighed collectively, the number of fragments counted and all tissue embedded.
- In the case of multiple biopsies, avoid embedding a large number of fragments in the same cassette, as it may be difficult to keep them properly orientated and at the same level if they are numerous. Embed no more than three in each cassette.
- Embed all fragments in their entirety.
- Embedding fragments in a line facilitates histological assessment.

C1.5 Sectioning and staining

- One H&E section per cassette, at least three levels/serial sections.
- May require unstained sections between levels, if suspicion of CIS. It may be appropriate to cut additional sections at initial processing if there is a likelihood that these will be required.
- Rarely any requirement for EM or molecular investigations.

C1.6 Report content

- The adequacy of the biopsy should be noted, if relevant.
- A separate description for each separately submitted set of biopsies is required unless they all show the same or similar features.
- If adequate details are not provided, this should be stated. Some features (i.e. interstitial cystitis) can only be interpreted with appropriate clinical and cystoscopic findings. Counting mast cells in bladder biopsies is of little pathological or clinical value, although higher numbers are found in interstitial cystitis relative to normal but not relative to other inflammatory conditions. MDT meetings may be helpful with regard to final interpretation.
- Detail presence or absence of urothelial dysplasia/CIS or malignancy.[11,12]
- Detail surface urothelial changes or metaplasia (e.g. squamous, glandular, nephrogenic).
- Squamous metaplasia can arise in the bladder secondary to chronic cystitis, schistosomiasis, diverticulum or non-functioning bladder. If keratinisation is present, this is a risk factor for subsequent development of carcinoma (mostly squamous cell carcinoma) and other complications such as bladder contracture and obstruction.[13]
- Glandular metaplasia of intestinal type may be a risk factor for subsequent adenocarcinoma, so examine carefully for evidence of dysplasia.
- Comment on loss/ulceration or denudation of urothelium where this increases the chances of missing CIS.
- Confirm benign conditions such as amyloid, malakoplakia, collagen polyp, endometriosis and related endocervicosis.
- Presence or absence of inflammation – acute or chronic, follicular, eosinophilic, radiation cystitis or granulomatous post BCG treatment.
- Confirm features of radiation cystitis following treatment for prostate/cervical cancer in particular. Changes can be misinterpreted as neoplastic.
- Need for follow up in the case of specific infections such as viable schistosomal ova and to exclude infectious conditions such as TB.

C2. Partial cystectomy

C2.1 Indications for histology

- Resection of bladder diverticula, cavernous haemangiomas, ulcerative interstitial cystitis, colovesical fistula, vesicovaginal fistula and localized endometriosis of the bladder.
- In the case of diverticulum, stagnation of urine, calculus formation and superimposed infection occur when they reach a large size and require surgery.
- Patient choice, palliation of severe local symptoms, preservation of native bladder function and continence.
- Rule out malignancy.
- Palliation for pain, bleeding or trauma.

C2.2 Staffing and workload

(See introduction, page 3.)

- Can be reported by a general pathologist with experience of urological pathology.

C2.3 Laboratory facilities

- Routine processing for LM.
- May need histochemical stains (ZN, PAS, Congo Red) and occasional use of immunohistochemistry to exclude or confirm background neoplasia.

C2.4 Specimen dissection

- Specimen should be fixed in a volume of formalin that is at least sufficient to cover it.

- Time of fixation should usually be 48 hours after resection, but adequacy of fixation can be estimated fairly reliably by visual inspection. Photographs may be useful. They are required in cases of trauma.
- Ink any relevant margins if there is a possibility of neoplasia.
- Describe the external appearance. Perforations/defects in the wall: record number, site, size, and distance from nearest margin. Look for fistulas and apply probe to confirm. Consider the possibility that the defects are artefactual or iatrogenic.
- Recorded measurements include dimensions of specimen (mm) and maximum dimension of attached fat.
- Record appearance of the mucosa.
- Blocks to confirm gross findings.
- The most common locations of diverticula are the lateral walls. Measure the size in mm and exclude tumour.
- Focal lesions, e.g. ulcer, abscess, stricture, polyp and tumour. Record the presence of any papillary tumour, any ulcerated or inflammatory areas.
- Blocks to include the maximal depth of invasion of any tumour identified, and any close surgical/serosal resection margin.

C2.5 Sectioning and staining

- Routine processing for LM. Usually require only one H&E section per block.
- Deeper levels may be useful if the slide does not show the full face of the block.
- Can require both histochemical and immunohistochemical analysis if neoplasia is detected or to confirm an inflammatory process.

C2.6 Report content

- Partial cystectomy, also known as segmental resection of the bladder, is a surgical method of removing a selected full-thickness portion of the bladder wall. It is being performed less frequently in benign conditions but is used in selected cancer cases (tumours in dome, preservation of bladder function and palliation).
- Describe inflammatory changes and confirm benign pathological changes (fistula, haemangiomas and endometriosis).
- The most common histological findings in a bladder diverticulum are inflammation, granulation tissue, erosion, florid cystitis cystica and glandularis and non-keratinizing squamous metaplasia. The boundary between the lamina propria and the peri-vesical fat in most bladder diverticula is usually readily defined by a band of dense fibrous tissue of variable thickness.
- Report presence or absence of malignancy, background urothelial changes (dysplasia, CIS), type and aetiology of chronic damage. Report, grade, stage and classify any tumour identified.[14]

C3 Cystectomy

C3.1 Indications for histology

- Intractable lower urinary tract symptoms – severe pain, frequency, urgency.[15]
- Rule out malignancy.
- Prophylactic cystectomy for management of keratinising metaplasia.
- Palliation for pain, bleeding, or urinary frequency.
- Trauma.

C3.2 Staffing and workload

(See introduction, page 3.)

- Can be reported by a general pathologist with experience of urological pathology.

C3.3 Laboratory facilities

- Routine processing for LM.
- May need histochemical stains (ZN, PAS, Congo Red) and occasional use of immunohistochemistry to exclude or confirm neoplasia (see below).

C3.4 Specimen dissection

- Specimen should be fixed in a volume of formalin that is at least sufficient to cover it. Some prefer to fix such specimens intact by overdistention with formalin whereas others pin the specimen and cover it with formalin.[16]
- Time of fixation should usually be 48 hours after resection, but adequacy of fixation can be estimated fairly reliably by visual inspection. Photographs may be useful. They are required in cases of trauma.
- Ink any relevant margins if there is a possibility of neoplasia.
- Describe the external appearance. Perforations/defects in the wall: record number, site, size and distance from nearest margin. Consider the possibility that the defects are artefactual or iatrogenic.
- Recorded measurements include dimensions of specimen (mm) and maximum dimension of attached fat.
- Record appearance of the mucosa – note: wash out bladder contents gently with tepid or cold water. Excess washing or hot water may damage the mucosa.
- Blocks to confirm gross findings include ureteric and urethral resection margins.
- Focal lesions, e.g. ulcer, abscess, stricture, polyp and tumour. Record the presence of any papillary tumour, ulcerated or inflammatory areas.
- Blocks to include the maximal depth of invasion of any tumour identified, and any close surgical/serosal resection margin.
- Blocks of prostatic urethra, prostate (including minimum of two blocks from each lateral zone to identify synchronous prostatic adenocarcinoma), its margins and seminal vesicles.

C3.5 Sectioning and staining

- Routine processing for LM. Usually require only one H&E section per block.
- Deeper levels may be useful if the slide does not show the full face of the block.
- Can require both histochemical and immunohistochemical analysis.

C3.6 Report content

- Describe inflammatory changes and confirm benign pathological changes.[17]
- Report presence or absence of malignancy, background urothelial changes (dysplasia, CIS), type and aetiology of chronic damage. Classify, grade and stage any tumour identified.[14]
- Note the presence of submucosal inflammation and oedema, denuded epithelium, ulceration, epithelial and basement membrane thickness, vascular ectasia, fibrosis, and detrusor muscle inflammation and fibrosis.

Section D: The Urethra

D1 Urethral biopsy

D1.1 Indications for histology

- Urethral caruncle, polypoid cystitis, benign stricture, nephrogenic adenoma, prostatic urethral polyp, malakoplakia.[6]
- Urethroscopy may be undertaken in isolation or, more commonly, in tandem with cystoscopy. Small urethral lesions are snared using ‘cold’ cup forceps or resected with a small diathermy loop.

D1.2 Staffing and workload

(See introduction, page 3.)

- Can be reported by a general pathologist with experience of urological pathology.

D1.3 Laboratory facilities

- Routine processing for LM.
- May require both histochemical and immunohistochemical (CK7/20) analysis.

D1.4 Specimen dissection

- Tiny pieces of tissue (several mm) retrieved using either 'cold' cup forceps or a small diathermy loop are counted, measured, processed intact and examined histologically through three levels.

D1.5 Sectioning and staining

- Usually require only one H&E section per block.
- Routine processing for LM.
- Rarely need histochemical stains.
- Can occasionally require immunohistochemical analysis (CK7/20[11]).

D1.6 Report content

- Confirmation of benign pathology, most commonly caruncle or polypoid urethritis both of which may be confused with a papillary neoplasm.[18]
- Be aware of minor changes in the male/female urethra in relation to subepithelial supporting structures.
- If stricture, confirm benign changes.
- Exclude presence or absence of malignancy, background urothelial changes (dysplasia, CIS[6]).

D2 Urethrectomy

D2.1 Indications for histology

- Most urethrectomy resection specimens are for neoplasia as part of a cystectectomy/cystoprostatectomy. Details of previous histology should be available, particularly if there is a history of dysplasia or carcinoma.
- Occasionally isolated urethrectomy is performed. Urethrectomy is performed for a stricture, bladder cancer in continuity with cystoprostatectomy, recurrence of bladder cancer in the urethral stump (secondary urethrectomy) and for primary urethral carcinoma.

D2.2 Staffing and workload

(See introduction, page 3.)

- Can be reported by a general pathologist with experience of urological pathology.

D2.3 Laboratory facilities

- Routine processing for LM.
- May require both histochemical and immunohistochemical (CK7/20) analysis.

D2.4 Specimen dissection

- The specimen may be in several tubular fragments labelled separately or with attached sutures to aid orientation; in the absence of such markers, definitive orientation may not be possible.
- Weigh (g) and measure (mm) each fragment; record the number of fragments.
- Ink the external circumferential radial margin (CRM) comprising adventitial connective tissue.
- Remove the proximal and distal surgical resection limits by taking circumferential transverse sections (rings) from the ends of the appropriate fragments.
- The remaining urethra is serially sectioned transversely throughout its length at 3-mm intervals, and the sections laid out sequentially for examination and photography, if desired.
- Sample any focal lesions, e.g. ulcer (at least one block each). More blocks should be taken from any suspicious lesion, e.g. stricture, warty growth.

D2.5 Sectioning and staining

- Routine processing for LM. Usually require only one H&E section per block.
- Can require both histochemical and immunohistochemical analysis.

D2.6 Report content

- Confirm benign changes such as caruncles, leiomyomas and viral papillomas.
- Record inflammatory changes present and correlate with history (e.g. stricture).
- Record the presence or absence of malignancy,[19] background urothelial changes (dysplasia, CIS).

Section E: The Prostate

Prostate needle core biopsy has been discussed thoroughly within the Dataset for histopathology reports for prostatic carcinoma (2nd edition -October 2009) and does not require further discussion in this document.

E1 Transurethral resection of prostatic chippings (TURP)

E1.1 Indications for histology

- Exclude prostatic or other malignancy (remember TCC, stromal malignancies, phyllodes tumour).
- Confirm nature of pathology (usually benign glandular or stromal hyperplasia).
- Transurethral resection is undertaken for obstructive or irritative lower urinary tract symptoms, not as an alternative diagnostic investigation to detect prostate cancer. However, in patients with prior negative prostatic biopsies, there is a low but definite chance of detecting prostatic cancer on TURP,[20] which increases with abnormal clinical findings on rectal examination (digital rectal examination) or raised prostatic specific antigen (PSA) level. This is due to a subset of cancers arising within the central or anterior (transition) zones, which are less likely to be detected with standard biopsy protocols not specifically targeting these areas. The clinical significance of some smaller volume cancers is not established.

E1.2 Staffing and workload

(See introduction, page 3.)

- Can be reported by a general pathologist with experience of urological pathology. Occasional problematic cases may need intradepartmental opinion and clinicopathological correlation by discussion with the urologist in cases of suspicious foci; rarely referral of the case for a second specialist opinion.

E1.3 Laboratory facilities

- Routine processing for LM.
- Availability of immunohistochemistry for suspicious foci (ideally including antibodies against basal cell markers: first-line high molecular weight cytokeratins – LP34, CK5/6 or 34βE12; second-line p63 or cocktails of both ± positive markers for prostatic carcinoma racemase/P504S/AMACR).[21–23]
- The use of AMACR in routine practice is very useful though some use it in cocktails with basal cell markers. Prostatic intraepithelial neoplasia (PIN) expresses AMACR and this can be helpful diagnostically – note that similar expression is also seen in benign mimics of cancer such as adenosis and nephrogenic metaplasia

E1.4 Specimen dissection

- Weigh the amount of chippings in grammes.
- In general, gross examination of chips for evidence of tumour is largely unrewarding.
- In cases where clinical history specifies a clinical suspicion of carcinoma, post treatment such as radiotherapy, cryotherapy or high-intensity frequency ultrasound (HIFU), embed whole specimen to detect residual carcinoma.
- Prostatic chippings do not require sectioning prior to fixation.
- Embed all of first 12 g in five to six cassettes.[24]
- Sample further chippings – opinions vary as to the optimal amount. Recommend embedding the entire specimen up to 12 g (six blocks) and a further 2 g (one block) for every additional 5 g.[25] Although these additional blocks may detect a higher proportion of tumours, they do not lead to upstaging or upgrading of pT1a tumours if tumour was present in the first six blocks.[26]
- Determining optimum sampling depends on a number of factors, as in any statistical sampling protocol. The site and extent of any tumour determines the percentage of chippings it will be seen in. Submission of all chippings in larger cases may not be cost- or time-effective.[27]

E1.5 Sectioning and staining

- One H&E section per cassette, no need for routine unstained levels as per prostate biopsies.
- Immunohistochemical staining of serial sections from blocks with PIN or atypical small acinar proliferation (ASAP) which are suspicious of carcinoma.
- Rarely any requirement for EM or molecular investigations.

E1.6 Report content

- Detail presence of stromal or glandular hyperplasia/hypertrophy.
- Note absence of invasive prostatic carcinoma, atypical foci suspicious of carcinoma or PIN.
- In cases where ASAP or PIN is seen, embed the rest of the specimen to exclude carcinoma.
- If PIN or ASAP is seen as an isolated finding, consider discussion with clinicians and/or recommend peripheral gland biopsies of residual prostate to exclude carcinoma.
- If an ‘incidental’ carcinoma is found, calculate the number and percentage of chippings involved. Embed and examine any remaining chippings.[25]
- If this is less than 5% (stage T1a, WHO 2004 staging), submission of the remaining tissue may increase the percentage of chippings involved and thus the potential clinical significance of the tumour[6] and also allows more accurate determination of the Gleason grade.[24]
- Where involvement in the initial slides is > 5% (stage T1b, WHO 2004), embedding further sections may not increase the stage, but may influence accurate Gleason grading.[25]

- Incidental low volume stage T1a tumours can become clinically significant and therefore follow-up is advised, e.g. with PSA monitoring, active surveillance or residual gland (saturation) biopsies.[28]

E2 Retropubic radical prostatectomy (enucleation)

E2.1 Indications for histology

As for TURP specimens.

- Exclude prostatic or other malignancy.
- Confirm nature of pathology (usually benign glandular or stromal hyperplasia).
- Retropubic prostatectomy is still occasionally performed for obstructive lower urinary tract symptoms.

E2.2 Staffing and workload

- Can be reported by a general pathologist with experience of urological pathology. Occasional problematic cases may need intradepartmental opinion and clinicopathological correlation by discussion with the urologist in cases of suspicious foci; rarely referral of the case for a second specialist opinion.

E2.3 Laboratory facilities

As above.

E2.4 Specimen dissection

- There are few data on optimum block selection in enucleation specimens, and the best method is treating these similarly to TURP resections.
- Enucleations or prostatectomies are generally restricted to large prostates in patients with lower urinary obstructive symptoms. Such specimens can benefit from incision to allow formalin penetration. Inking of margins is not necessarily useful, even if carcinoma is detected incidentally, because these are not radical resections, and given the multifocality of prostatic cancer, demonstration of negative margins does not necessarily equate with absence of residual disease.
- Weigh gland in grammes (often in several nodular pieces).
- Consider inking margins only where clinical history is suspicious.
- Sample each separate fragment by taking at least one block for each 5 g or three per lobe.

E2.5 Sectioning and staining

- One H&E section per cassette, no need for routine unstained levels as per prostate biopsies.
- Immunohistochemical staining of serial sections from blocks with PIN or ASAP.[22]
- Rarely any requirement for EM or molecular investigations.

E2.6 Report content

- Detail presence of stromal or glandular hyperplasia/hypertrophy.
- Note that some benign entities such as atrophy, adenosis, nephrogenic hyperplasia, basal cell hyperplasia and mesonephric hyperplasia potentially mimic prostatic cancer and may be responsible for misdiagnosis in routine specimens.[6] Immunohistochemistry can be used for confirmation.[21]
- Note absence of invasive prostatic carcinoma, atypical foci suspicious of carcinoma or PIN.
- In cases where ASAP or PIN is seen, embed the rest of the specimen to exclude carcinoma.

- Where carcinoma is found, detail Gleason grading,[29] site and extent of tumour, and status of margins.

Section F: The Penis And Scrotum

F1 Penile biopsy

F1.1 Indications for histology

- The clinical appearance of many benign conditions overlaps with neoplastic and pre-neoplastic lesions, particularly CIS. Therefore biopsy is mandatory to exclude dysplasia and malignancy.
- Confirm benign pathological conditions.
- Rarely Wegener's can present with penile ulceration and may mimic malignancy, requiring biopsy for confirmation.

F1.2 Staffing and workload

(See introduction, page 3.)

- Can be reported by a general pathologist with experience of urological pathology – occasional need for a penile pathologist (supranetwork) or specialist dermatopathology opinion.

F1.3 Laboratory facilities

- Routine processing for LM.
- Occasional need for histochemistry and immunohistochemistry to exclude or confirm neoplasia (see below).

F1.4 Specimen dissection

- Fragments are counted and measured in aggregate. It is important to search the container and the under-surface of its lid to ensure that all fragments of tissue are recovered.
- Larger pieces measured individually. Embed as received, bisect or cut further.
- Punch – bisect if larger than 3 mm and epithelium clearly visible for orientation.
- Ellipse – if narrower than 3 mm, embed as received. If wider, bisect in longitudinal section. Wider/larger lesions are cut in transverse section to include the nearest resection margins. Ink the margins as orientated by the marking sutures.
- Identifiable surface lesions are described and measured, and the macroscopic distance from the closest margin noted.

F1.5 Sectioning and staining

- Usually require three H&E levels per block.
- Routine processing for LM.
- May require both histochemical and immunohistochemical analysis.

F1.6 Report content

- If a cyst, report median raphe cysts (midline in ventral shaft) and mucoid cysts.
- Report benign lesions such as lentiginous melanosis (glans and foreskin), cutaneous verruciform xanthoma (rare – shaft of penis), epithelioid haemangioma, leiomyoma and myointimoma.
- Inflammatory conditions include lichen sclerosus (LS) also known as balanitis xerotica obliterans (BXO)[30] (may occasionally be seen on the shaft), Zoon's balanoposthitis and Fournier's gangrene (necrotizing fasciitis).

- Zoon's balanitis is usually a disease of the glans but may extend onto the foreskin. Zoon's balanoposthitis should not be diagnosed unless the infiltrate is almost exclusively plasma cells and in the absence of necrosis and granulomas.
- Condyloma acuminatum and giant condyloma acuminatum (Buschke–Löwenstein tumour).
- Wegener's can cause penile ulceration often with destructive urethritis (c-ANCA/PR3 positivity).
- Exclude dysplasia/CIS (penile intraepithelial neoplasia) and malignancy. There is no need to distinguish between Bowen's disease and Erythroplasia of Queyrat which are clinically rather than pathologically defined lesions. It is more appropriate to describe as carcinoma in situ with or without warty features. Bowenoid papulosis also shows warty carcinoma in situ but clinically has multiple warty lesions along the shaft. Squamous hyperplasia and pseudoepitheliomatous hyperplasia may be misinterpreted as low grade squamous cell carcinoma. Similarly verrucous carcinoma is frequently underdiagnosed.

F2 Prepuce specimens

F2.1 Indications for histology

- The clinical appearance of many benign conditions overlaps with neoplastic and preneoplastic lesions particularly CIS, therefore biopsy is mandatory to exclude dysplasia and malignancy
- Confirm benign pathology[31] – condyloma, penile cysts and papules, Zoon's balanitis and verruciform xanthoma
- Exclude dysplasia and malignancy

F2.2 Staffing and workload

(See introduction, page 3.)

F2.3 Laboratory facilities

- Routine processing for LM.
- Occasional need of histochemical stains and immunohistochemistry.

F2.4 Specimen dissection

- Measure, inspect and orientate.
- Ideally pin the four corners of the specimen with the mucosa oriented on one side and the skin on the other.
- If there is a history of dysplasia, identify the coronal sulcus and ink the margins (the surgical cut area).
- Fix the specimen overnight in formalin.
- Specimen photography may be necessary.
- Cut serial transverse sections clockwise.
- Include any obvious areas of surface scarring or raised lesions.
- Embed at least two thin sections per block (to aid orientation) in two blocks.

F2.5 Sectioning and staining

- Usually require only one H&E section per block.
- Occasionally need histochemical stains like PAS for fungal infection, or amyloid.
- Although immunohistochemistry to exclude HPV in rare cases may be used, this has no diagnostic or prognostic role in routine practice.

F2.6 Report content

- Comment on any evidence of BXO/LS, Zoon's balanitis (inner foreskin/glans).

- Note recent case reports of granulomatous inflammation with vasculitis in association with the anti-anginal drug nicorandil.[32]
- Report non-specific inflammatory changes in balanoposthitis.
- Mucinous metaplasia is occasionally seen in older patients.
- Exclude sexually-transmitted infections.
- Exclude dysplasia or malignancy particularly with LS/BXO.[30]

F3 Scrotal biopsy

F3.1 Indications for histology

- Biopsy is necessary to confirm benign pathology.
- Removal of suspected cystic lesion or calcified nodule.
- Exclude dysplasia and malignancy.

F3.2 Staffing and workload

(See introduction, page 3.)

- Can be reported by a general pathologist with experience of urological pathology.

F3.3 Laboratory facilities

- Routine processing for LM.
- Occasionally use of histochemistry and immunohistochemistry to exclude or confirm neoplasia (see below).

F3.4 Specimen dissection

- Fragments are counted and measured in aggregate. It is important to search the container and the under-surface of its lid to ensure that all fragments of tissue are recovered.
- Larger pieces are measured individually. Embed as received, bisect or cut further if necessary.
- Punch – bisect if larger than 3 mm and epithelium clearly visible for orientation.
- Ellipse – if narrower than 3 mm, embed as received. If wider, bisect in longitudinal section. Wider/larger lesions are cut in transverse section to include the nearest resection margins. Ink the margins as orientated by the marking sutures.
- Cystic lesions or nodules may require decalcification.
- Identifiable surface lesions are described and measured, and the macroscopic distance from the closest margin noted.

F3.5 Sectioning and staining

- Usually require three H&E levels per block.
- Routine processing for LM.
- Can require both histochemical and immunohistochemical analysis [e.g. Extramammary Paget's disease of scrotal skin is positive with CK7, CAM 5.2, CEA, EMA, PAS, MUC1, MUC5AC and negative for 34βE12 (high molecular weight keratin), CK20 (to exclude pagetoid spread from urothelial tumours), HMB45, Melan-A and S100].[33]

F3.6 Report content

- Non-neoplastic lesions of scrotum include fat necrosis, idiopathic calcinosis (multiple nodules in skin which may arise from keratinous cysts that have lost their lining), massive localized lymphoedema in morbidly obese patients, sclerosing lipogranuloma and post-traumatic spindle cell nodules.
- Lymphoedema of the scrotum is most commonly idiopathic and may have genetic links to syndromes such as Milroy's disease. True lymphoedema following groin and

perineal radiotherapy and in association with Crohn's disease is recognised. Chronic lymphoedema may produce verruciform squamous hyperplasia and there is a rare association with scrotal squamous cell carcinoma.

- Presence or absence of dysplasia, CIS and malignancy. Exclude neoplastic lesions of scrotum such as aggressive angiomyxoma, angiomyofibroblastoma (similar to vulvovaginal angiomyofibroblastoma and spindle cell lipoma), desmoplastic round cell tumour and malignant mesothelioma involving scrotum from the tunica vaginalis/albuginea.
- Extramammary Paget's disease - adenocarcinoma *in situ* of scrotal skin usually not associated with underlying malignancy and has characteristic immunoprofile[33] (see above) and squamous cell carcinoma (occupational exposure) in particular should be excluded. When extramammary Paget's disease is associated with malignancy this is usually apocrine adenocarcinoma in type.

Section G: The Testes

G1 Testicular biopsy

G1.1 Indications for histology

- Assessment of male infertility.
- Variable practice of biopsy at time of contralateral orchidectomy for malignancy,[34] to assess spermatogenesis and the presence of intratubular germ cell neoplasia (ITGCN). This is done particularly in small volume testes in younger males.
- Biopsy of undescended testis to exclude malignancy or ITGCN.
- Biopsy of vestigial remnants such as the appendix epididymis (remnant of mesonephric duct) and the appendix testis (hydatid of Morgagni) which have undergone infarction.

G1.2 Staffing and workload

(See introduction, page 3.)

- Specialised biopsies often uncommon in routine clinical practice.
- Should be reported by a urological pathologist or someone with expertise in assessment of testicular biopsies for infertility, who is participating in specialist urological EQA.
- Close relationship required with urologists and/or fertility clinicians to ensure good clinicopathological correlation.

G1.3 Specimen submission

- Size.
- Number of pieces and orientation.
- Submit all tissue for microscopic evaluation.
- May be fixed in Bouin's or Zenker's medium as opposed to formalin for better nuclear preservation.

G1.4 Specimen dissection

- Careful handling of these specimens is recommended to prevent surface trauma and disruption.
- Recommend wrapping in tissue paper or similar commercial products to prevent loss during processing, as often small samples.
- Embed biopsies from separate testes in different cassettes.

G1.5 Sectioning and staining

- Routine processing for LM.
- At least three H&E sections per biopsy.

- It may be appropriate to cut additional sections at initial processing or keep spares between the levels, if there is a likelihood that these will be required.
- Rarely need histochemical stains for fibrosis, amyloid.
- Occasionally use of immunohistochemistry to exclude or confirm background ITGCN, such as PLAP, CD117 (c-kit) and podoplanin, and nuclear marker OCT3/4.

G1.6 Report content

- The adequacy of the sample should be noted and where artefact or loss impairs interpretation of the biopsy, this should be stated in the report.
- If adequate clinical details are not provided, this should be stated. Clinicopathological meetings help refine interpretation.
- Comment on background atrophy, fibrosis, tubular dilation or changes to sex cord-stromal cells (Leydig cell hyperplasia) and microlithiasis.
- Qualitatively describe spermatogenesis across whole biopsy – often varies between tubules.
- Assess spermatogenesis with a quantitative scoring system[35] (e.g. Johnsen score[36]). However, the need for Johnsen counts now is limited as even the slightest degree of spermatogenic activity allows modern fertilization procedures.
- Comment on presence or absence of any ITGCN.
- Confirm presence of the testicular appendix which is attached to tunica albuginea at the upper testicular pole and may undergo haemorrhagic infarction by twisting on its pedicle.

G2 Orchidectomy non-malignant

G2.1 Indications for histology

- Incidental removal (non-descent, atrophy, hernia repairs).
- Torsion.
- Infection, chronic pain and trauma.
- Granulomatous orchitis. Some cases are associated with urinary tract infections, history of prostatectomy, inguinal hernia repair and trauma.
- Occasionally bilateral orchidectomy for hormonal control of prostate cancer.
- Treat all these specimens as potentially malignant and approach macroscopic cut-up in anticipation of finding an underlying tumour.[34]
- Any incidental tumour should be submitted for regional review to the local testicular germ cell tumour MDT.

G2.2 Staffing and workload

(See introduction, page 3.)

- Can be reported by a general pathologist with experience of urological pathology.
- Refer cases with tumour to the local MDT.

G2.3 Laboratory facilities

- Routine processing for LM.
- Availability of histochemical stains.
- Occasionally use of immunohistochemistry to exclude or confirm background ITGCN such as PLAP, CD117 (c-kit) and podoplanin and nuclear markers OCT3/4.
- Wider immunohistochemical panel for any tumours, including cytokeratin, CD30, AFP, β-hCG, PLAP, CD117, OCT 3/4, CK7, inhibin.[37]

G2.4 Specimen dissection

- Weigh, measure, orientate.
- If any suspicion of a tumour then treat as a potentially malignant testis.
- Embed at least:
  - cord resection margin separately in case of incidental tumour

- base of cord
- hilum including rete and epididymis
- any focal lesions
- two to three random sections of background testis.

G2.5 Sectioning and staining

- One H&E section per cassette, usually one level sufficient.
- Beware hyalinised or atrophic-looking areas with inflammation – possible 'burnt-out' seminoma – take levels and if necessary go back to the specimen and re-embed whole testis to look for residual viable seminoma.
- Granulomatous orchitis shows an irregular rim of lighter-coloured tissue around the periphery and the process seems to extend beyond the testis proper. The cut surface is vaguely nodular, yellowish and hard. It mimics tumour clinically and macroscopically.
- Likewise, before making a diagnosis of epidermoid cyst, exclude mature teratoma by embedding the whole of the lesion and all of the testis (to look for immature teratoma and background ITGCN).

G2.6 Report content

- Comment on the degree of spermatogenesis, any ITGCN, fibrosis or any incidental changes to sex cord stromal cells (Leydig cell hyperplasia or nodules).
- Confirm if cryptorchid.
- Granulomatous orchitis shows a granulomatous inflammatory process with lymphocytes, plasma cells, macrophages, fibroblasts and scattered multinucleated giant cells, but no demonstrable organisms.
- Splenogonadal fusion is a rare congenital malformation in which there is an abnormal connection between the spleen and testes, sometimes mimicking a testicular neoplasm.[38] Histological examination confirms the diagnosis and excludes neoplasia.
- Exclude malignancy – if present, follow protocols for testicular tumours.

G3. Hydrocele

G3.1 Indications for histology

- Inability to distinguish from an inguinal hernia.
- Failure to resolve spontaneously after an appropriate interval of observation.
- Inability to examine testis properly.
- Association of hydrocele with other pathology (e.g. torsion, tumour).
- Pain or discomfort.
- Male infertility.

G3.2 Staffing and workload

(See introduction, page 3.)

- Can be reported by a general pathologist with experience of urological pathology.

G3.3 Laboratory facilities

- Routine processing for LM.
- Use of immunohistochemistry if required.

G3.4 Specimen dissection

- Weigh and measure strips of hydrocele (hydrocelectomy) – usually thickened tunica.
- Note irregular nodules or areas of firmness – submit these for histology.
- Two blocks per specimen adequate if normal appearing.

G3.5 Sectioning and staining

- Usually require only one H&E section per block.
- Routine processing for LM.
- Can require both histochemical and immunohistochemical analysis. May need to exclude mesothelioma in cases with marked mesothelial proliferation. Immunohistochemical panel should include CAM5.2, calretinin, CK5/6, EMA, CK7, HBME1 and BerEP4. The EM findings help secure the diagnosis.
- Histochemistry with Gram, ZN or PAS required if suspicion of infection.

G3.6 Report content

- Confirm benign mesothelial lining and fibrous thickening.
- Presence or absence of malignancy (mesothelial). Hydroceles sometimes seen in association with testicular tumours (10%).
- Most cases idiopathic but may be associated with hernia, trauma, infections (mumps orchitis, filariasis, TB) or tumours.

Section H: The Epididymis And Spermatic Cord

H1 Epididymal biopsy/epididymectomy

H1.1 Indications for histology

- Incidental findings on testicular self-examination or routine physical examination. Failure to transilluminate suggests a solid lesion.
- Often detected incidentally on ultrasound.
- Lump may be painful and require removal.

H1.2 Staffing and workload

(See introduction, page 3.)

- Can be reported by a general pathologist with experience of urological pathology.
- Refer problematic cases to the lead urological pathologist.

H1.3 Laboratory facilities

- Routine processing for LM.
- Occasionally use of immunohistochemistry to exclude or confirm benign tumours (adenomatoid) or malignancy.

H1.4 Specimen dissection

- Specimen consists of a cystic structure which may be multiloculated if a spermatocele.
- Sometimes specimen also contains part of the adjacent normal epididymis (partial epididymectomy).
- Dimensions are measured in millimetres. The fluid is clear in an epididymal cyst and opaque because of the presence of sperm in a spermatocele.
- Outer surface is examined for mass lesions.
- Cyst is bisected and two sections taken to include the epididymis if present.
- If a nodule or mass is present take representative blocks (one per cm).

H1.5 Sectioning and staining

- Routine processing for LM.
- Usually require only one H&E section per block.
- Histochemical and immunohistochemical stains generally not required.
- Rarely any requirement for EM or molecular investigations.

H1.6 Report content

- Microscopic examination reveals a cyst with a fibromuscular wall that is lined by bland cuboidal epithelium.
- Spermatocele results from dilation of an efferent ductule and is lined by a single layer of flattened epithelial cells. The wall is composed of fibromuscular stroma. It may sometimes be difficult to see spermatozoa as they are 'washed' away during specimen processing.
- Note any other lesions (adenomatoid tumour, epididymitis nodosa, hernia sac entrapped epididymis, granulomatous ischaemic lesion, vasculitis and cystadenoma of epididymis).[39]
- Report presence or absence of malignancy.

H2 Vasectomy

H2.1 Indications for histology

- Normally for sterilisation to confirm complete transection.[40]
- Occasionally biopsies of lesions (vasitis nodosum or benign adenomatoid tumour).
- Rarely as part of fertility surgery such as epididymovasotomy.
- Note problems arising from a fairly minor specimen – medicolegal issues of failed vasectomy and subsequent pregnancy.

H2.2 Staffing and workload

(See introduction, page 3.)

- Can be reported by a general pathologist with experience of urological pathology.

H2.3 Laboratory facilities

- Routine processing for LM.

H2.4 Specimen dissection

- Orientate and measure the length and diameter of the vas segment in mm and submit one block of each vas.
- It may be expedient to take two cross-sections from each to obtain a full face section.
- In cases of failed sterilization, block the whole vas (levels may be necessary) to identify possible recanalisation.
- For any other indication (e.g. possible tumour), consider inking margins and embedding the whole lesion depending on size.
- If markedly enlarged soft tissue mass, treat as potential sarcoma; ink margins, sample at least one block/cm diameter and consider taking specimens for freezing or EM if it arrives fresh. Nodular periorchitis involves the tunica, epididymis or spermatic cord and forms a mass lesion.

H2.5 Sectioning and staining

- Routine processing for LM.
- Usually require only one H&E section per block.
- May require levels or re-embedding if the lumen is not clearly visualised.
- Availability of histochemical stains occasionally used including PAS $\pm$ diastase or ZN.
- Very occasionally use of immunohistochemistry for adenomatoid tumour (epithelial marker) or incidental connective tissue lesions.

H2.6 Report content

- Confirm vas deferens and that the full cross-section is seen.
- In failed sterilization, confirm that it is vas and a full cross-section is seen.

- Exclude other associated pathology – sperm granuloma, vasitis nodosa**,** proliferative funiculitis and recanalization.[41]
- Nodular periorchitis is a reactive myofibroblastic proliferation involving the tunica, epididymis or spermatic cord, usually in response to some form of injury or infection. It is known by a variety of names (fibrous pseudotumors, fibromatous periorchitis and nodular periorchitis).
- Exclude malignancy (paratesticular neoplasms). The proliferating ductules of vasitis nodosa may be mistaken for prostatic adenocarcinoma with vascular or perineural invasion of nerves of the spermatic cord.[42]

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