



## Tissue pathways for gynaecological pathology

July 2008

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| <b>Unique document number</b> | G073  |
| <b>Document name</b>          | Tissue pathways for gynaecological pathology  |
| <b>Version number</b>         | 1   |
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| <b>Date active</b>            | July 2008   |
| <b>Date for review</b>        | July 2010   |
| <b>Comments</b>               | <p>In accordance with the College's pre-publications policy, this document was put on The Royal College of Pathologists' website for consultation from 21 May – 20 June 2008. Seventeen pieces of feedback were received and the authors considered them and amended the document accordingly.</p> <p>Please email <a href="mailto:publications@rcpath.org">publications@rcpath.org</a> if you wish to see the responses and comments.</p> <p><b>Professor Carrock Sewell</b><br/><b>Director of Publications</b></p> |

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## **Staffing and workload for a gynaecological pathology service**

- Specimens of gynaecological tissue can be reported by competent general pathologists (including specialist registrars undertaking competency-based training) in an adequately staffed laboratory.
- Unit hospitals may have a pathologist/s with an interest, or specialist experience, in gynaecological pathology who should participate in a relevant External Quality Assessment (EQA) scheme such as the National Gynaecological EQA Scheme.
- In a specialist centre, these cases are reported by a dedicated gynaecological pathologist.
- Specific issues in relation to products of conception are listed in Section H below.

## **A Vulva**

### **1 Vulval epithelial biopsies**

#### **1.1 Staffing and workload**

See introduction above.

#### **1.2 Specimen submission**

- Fresh or fixed material.
- The biopsy will vary according to the size of the lesion, and range in size from small punch biopsies that are up to several millimetres long and 2–4 mm thick, to larger ellipse biopsies of similar size to skin or vulval excisional biopsies. In some institutions, small biopsies may be mounted onto a card.
- Careful handling of these specimens is recommended to prevent surface trauma and disruption or loss of surface epithelium.<sup>1</sup>
- Small lesions such as cysts or papillomas will be submitted intact or in fragments.

#### **1.3 Specimen dissection and block selection**

- It is important to search the container and the under-surface of its lid to ensure that stray fragments of tissue are recovered.
- Fragments – counted and measured in aggregate. Larger pieces measured individually. Embed as received. Larger pieces bisected or cut further.
- Punch – bisected if larger than 3 mm and epithelium clearly visible for orientation.
- Ellipse – if narrower than 3 mm, embedded as received.
- If wider, bisected in longitudinal section.

Wider/larger lesions are cut in transverse section to include the nearest resection margins. The blocks containing the end slices are noted – these will usually be the first and last blocks in the sequence. It may be appropriate to ink the margins as orientated by the clinician with marking sutures or pinned to a cork board. Identifiable surface lesions are described and measured, and the macroscopic distance from the closest margin noted.

#### **1.4 Embedding options**

- All biopsies are properly orientated to provide vertical sections to reduce potential for misidentification of invasion.<sup>2</sup>
- The flat, cut end is embedded downwards to ensure that this surface is cut by the microtome. Intact biopsies are orientated carefully and embedded on edge, with the epithelial surface perpendicular to the face of the block to be cut by the microtome.
- Small biopsies are wrapped, or placed between layers of foam sponge or in mesh bags or wire cages to avert tissue loss during processing.

#### **1.5 Sectioning**

- A single haematoxylin and eosin (H&E) stained section, representing a full face of the block, is adequate for the initial microscopic examination.
- Depending on the appearances, levels may be requested at the discretion of the reporting pathologist. Some laboratories provide three levels as standard for small biopsies.

#### **1.6 Staining**

- H&E.

#### **1.7 Further investigations**

If appropriate, epithelial lesions:

- PAS(D) or Grocott for fungi , silver stains for spirochaetes, Giemsa for Donovan bodies, elastic van Gieson (EVG) for lichen sclerosus.

#### **1.8 Report content**

Vulval intraepithelial neoplasia<sup>3</sup>

- Grades I, II, III
- VIN warty type
- VIN basaloid type
- VIN mixed (warty/basaloid) type
- VIN differentiated type
- Paget's disease
- Assessment of margins
- Assessment of invasion

Non-neoplastic epithelial diseases<sup>4</sup>

- Lichen sclerosus
- Squamous hyperplasia
- Mixed lichen sclerosus and squamous hyperplasia
- Lichen planus

Inflammatory dermatoses.

## **2 Vulval soft tissue excisions**

### **2.1 Specimen submission**

- Fresh or fixed material.
- These specimens are usually submitted in the course of diagnosis or treatment of a vulval mass.
- Larger lesions such as leiomyomas, angiomyxomas or other deep soft tissue lesions may be submitted intact or in fragments.

### **2.2 Specimen dissection and block selection**

- It is important to search the container and the under-surface of its lid to ensure that stray fragments of tissue are recovered.
- If biopsy fragments are very small, they are wrapped in tissue, or placed between layers of foam or in a mesh bag or wire basket to avert tissue loss during processing. The number of fragments or aggregated size is noted.
- The number of pieces received is recorded, as is their size (larger pieces measured individually in three dimensions; measure in aggregate if more than three), shape, colour and texture (fibrous, rubbery, myxoid, mucoid, granular, friable). Embed as received. Larger pieces are bisected or cut further.
- If appropriate, excision margins are inked.
- Excision margins are sampled.
- Myxoid and oedematous areas are sampled to document/identify malignancy.
- Attached tissue is examined and sampled to document infiltration/invasion.

### **2.3 Embedding options**

- If bisected or sliced, the flat, cut end is embedded downwards to ensure that this surface is cut by the microtome.
- Any epithelial surface is orientated perpendicular to the face of the block to be cut by the microtome.

### **2.4 Sectioning**

- Ensure margins are properly faced.
- Small biopsies may require three levels to be cut.
- Levels may be required to elucidate vascular space invasion or involvement of margins.

### **2.5 Staining**

- H&E.

### **2.6 Further investigations**

If appropriate:

- immunohistochemistry: oestrogen and progesterone receptors, SMA, CD34, desmin, h-caldesmon, S100<sup>5</sup>
- possible soft tissue expert opinion.

## **2.7 Report content**

Wide differential diagnosis:

- leiomyoma
- aggressive angiomyxoma
- superficial angiomyxoma
- angiomyofibroblastoma
- cellular angiofibroma
- granular cell tumour
- nodular fasciitis
- postoperative spindle cell nodule
- fibroepithelial polyp
- fibroadenoma
- lipoma
- prepubertal vulval fibroma
- vulval hamartoma
- solitary fibrous tumour
- leiomyosarcoma
- myxoid leiomyosarcoma
- liposarcoma
- synovial sarcoma
- alveolar soft part sarcoma
- epithelioid sarcoma of the vulva
- other sarcomas
- and others.<sup>6</sup>

Report involvement of excision margins and vascular space involvement.

## **3 Vulval cysts**

### **3.1 Specimen submission**

- Fresh or fixed material.
- Small or large cysts may be submitted intact or in fragments.

### **3.2 Specimen dissection and block selection**

- The wall, any solid and/or papillary areas are sampled.
- Contents noted.
- Bisect smaller cysts if appropriate, smallest cysts to be processed intact.

### **3.3 Embedding options**

- A single H&E stained section, representing a full face of the block, is adequate for the initial microscopic examination.
- Depending on the appearances, levels may be requested at the discretion of the reporting pathologist.

- Ensure cyst wall is embedded with the epithelial surface or lining perpendicular to the face of the block to be cut by the microtome.

### 3.4 Staining

- H&E.

### 3.5 Sectioning

- Ensure margins are properly faced.

### 3.6 Further investigations

If appropriate:

- immunohistochemistry, expert opinion.

### 3.7 Report content

- No special issues
- Endometriotic cyst
- Bartholin's gland duct cysts
- Nodular hyperplasia of Bartholin's gland
- Adenoma of Bartholin's gland
- Adenomyoma of Bartholin's gland
- Epidermoid inclusion cyst of the vulva
- Steatocystoma
- Ciliated cyst of the vulva
- Gartner's duct cyst
- Wolffian duct remnant cyst
- Multiple pigmented follicular cysts of the vulva
- Cysts of mammary like glands
- Mucinous cysts of the vulva
- Hydrocoele of the canal of Nuck
- Hidradenoma papilliferum.<sup>7</sup>

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1. Robboy SJ, Kraus FT, Kurman RJ. Gross description, processing and reporting of gynaecologic and obstetric specimens. In: Kurman RJ (ed). *Blaustein's Pathology of the Female Genital Tract (4th edition)*. New York: 2002.
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4. ISSVD classification of vulvar dermatoses 2006. [www.issvd.org](http://www.issvd.org)
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7. Neill SM, Ridley CM. Non-neoplastic pathology of the vulva and related structures. In: Fox H, Wells M (eds). *Haines and Taylor Obstetrical and Gynaecological Pathology (5th edition)*. Churchill Livingstone: 2003.

## **B Vagina**

### **1 Vaginal biopsies**

#### **1.1 Staffing and workload**

- See introduction on page 3.

#### **1.2 Specimen submission**

- Fresh or fixed material.
- Such specimens may originate from symptomatic vaginal lesions, or from incidental lesions that are identified at the time of colposcopy.
- The biopsy will vary according to the size of the lesion, and range in size from small punch biopsies that are up to several millimetres long and 2–4 mm thick, to larger ellipse biopsies of similar size to skin or vulval excisional biopsies.
- In some institutions, small biopsies may be mounted onto a card.
- Careful handling of these specimens is recommended to prevent surface trauma and disruption or loss of surface epithelium.<sup>1</sup>
- It is recommended that such biopsies are handled in a similar manner to vulval biopsies.

#### **1.3 Specimen dissection**

- It is important to search the container and the under-surface of its lid to ensure that stray fragments of tissue are recovered.
- If biopsy fragments are very small, they are wrapped in tissue, or placed between layers of foam or in a mesh bag or wire basket to avert tissue loss during processing. The number of fragments or aggregated size is noted.
- The number of pieces received is recorded, as is their size (maximum dimension if small, or in three dimensions; measure in aggregate if more than three), shape, colour and texture (mucoïd, granular, friable).
- Small punch biopsies <3 mm are processed whole. Larger biopsies >3 mm may need to be bisected perpendicular to the mucosal surface, and both halves are processed. Specimens are wrapped in tissue, placed between layers of foam and in a mesh bag or wire basket.
- If ellipse excisions are submitted, surface lesions may be readily identified, and these are fully described and measured.
- The surgical excision margins of larger vaginal biopsies bearing an obvious lesion are nicked/scored or painted with ink and with different colours of ink if a specimen has been orientated by the clinician, i.e. marked with a suture, or orientated and pinned to a cork board.
- The macroscopic distance from the closest excision margin is measured.
- The specimen is serially transverse sectioned at 2–3 mm slices, perpendicular to the long axis of the ellipse or tissue fragment, and the sections placed in separate cassettes.
- The blocks containing the end slices are noted – these will usually be the first and last blocks in the sequence.
- All of the tissue submitted, including mucoïd fragments, is processed.

## **1.4 Embedding options**

- If bisected or sliced, the flat, cut end is embedded downwards to ensure that this surface is cut by the microtome.
- Intact biopsies are orientated carefully and embedded on edge, with the epithelial surface perpendicular to the face of the block to be cut by the microtome.<sup>2</sup>

## **1.5 Sectioning**

- Small biopsies are handled in the same way as cervical biopsies, i.e. three levels are cut.
- Larger ellipse excisions do not require routine levels; levels are requested if no histological lesion is identified, if invasion needs to be excluded or if a full face, surface epithelium or margins do not appear in the original sections.

## **1.6 Staining**

- H&E.

## **1.7 Further investigations**

- Additional levels may be required.
- Mucin histochemistry (ABPAS) may be helpful to assess glandular lesions. Immunohistochemical marker studies can help to differentiate between metaplastic and neoplastic processes.

## **1.8 Report content**

- The report should incorporate the macroscopic description of the specimen and block designation.
- The pathologist reports all grades of vaginal squamous intra-epithelial neoplasia (VAIN), and invasive lesions of all types are reported and graded.
- National minimum datasets for vaginal carcinomas are not currently available.
- The presence of human papillomavirus-associated features is reported.
- The presence of pathological changes in perilesional vaginal mucosa is described, as are any benign or reactive conditions that might account for/or bear a relationship to the clinical lesions (e.g. in-situ change adjacent to a melanoma).
- The report should also state whether a lesion is completely excised, particularly in the case of larger ellipse excisions, and relate this to known excision margins where specimens have been orientated.
- Where artefact or epithelial loss impairs interpretation of the biopsy, this is stated in the report.

## **2 Vaginal soft tissue excisions**

### **2.1 Specimen submission**

- These specimens are usually submitted in the course of diagnosis or treatment of a vaginal mass.
- Fresh or fixed material.

- Larger lesions such as leiomyomas, angiomyxomas or other deep soft tissue lesions may be submitted intact or in fragments.

## **2.2 Specimen dissection and block selection**

- It is important to search the container and the under-surface of its lid to ensure that stray fragments of tissue are recovered.
- If biopsy fragments are very small, they are wrapped in tissue, or placed between layers of foam or in a mesh bag or wire basket to avert tissue loss during processing. The number of fragments or aggregated size is noted.
- The number of pieces received is recorded, as is their size (larger pieces measured individually in three dimensions; measure in aggregate if more than three), shape, colour and texture (fibrous, rubbery, myxoid, mucoïd, granular, friable). Embed as received. Larger pieces are bisected or cut further.
- If appropriate, excision margins are inked.
- Excision margins are sampled.
- Myxoid and oedematous areas are sampled to document/identify malignancy.
- Attached tissue is examined and sampled to document infiltration/invasion

## **2.3 Embedding options**

- If bisected or sliced, the flat, cut end is embedded downwards to ensure that this surface is cut by the microtome.
- Any epithelial surface is orientated perpendicular to the face of the block to be cut by the microtome.

## **2.4 Staining**

- H&E.

## **2.5 Sectioning**

- A single H&E stained section, representing a full face of the block, is adequate for the initial microscopic examination.
- Ensure margins are properly faced.
- Small biopsies may require three levels to be cut.
- Levels may be required to elucidate vascular space invasion or involvement of margins.

## **2.6 Further investigations**

If appropriate:

- immunohistochemistry: oestrogen and progesterone receptors, SMA, CD34, desmin, h-caldesmon, S100<sup>3</sup>
- possible soft tissue expert opinion.

## **2.7 Report content**

- Wide differential diagnosis:
- Leiomyoma

- Aggressive angiomyxoma
- Superficial angiomyxoma
- Angiomyofibroblastoma
- Cellular angiofibroma
- Nodular fasciitis
- Postoperative spindle cell nodule
- Fibro-epithelial polyps
- Solitary fibrous tumour
- Myofibroblastoma of the lower genital tract
- Leiomyosarcoma
- Myxoid leiomyosarcoma
- Liposarcoma
- Synovial sarcoma
- Alveolar soft parts sarcoma
- Epithelioid sarcoma of the vulva/vagina
- Rhabdomyosarcoma
- Other sarcomas

and others<sup>4</sup>

Report involvement of margins and vascular space involvement.

### **3 Vaginal cysts**

#### **3.1 Specimen submission**

- Fresh or fixed material.
- Small or large cysts may be submitted intact or in fragments.

#### **3.2 Specimen dissection and block selection**

- The wall, any solid and/or papillary areas are sampled.
- Contents noted.
- Bisect smaller cysts if appropriate, smallest cysts to be processed intact.

#### **3.3 Embedding options**

- Ensure cyst wall is embedded with the epithelial surface or lining perpendicular to the face of the block to be cut by the microtome.

#### **3.4 Staining**

- H&E.

### **3.5 Sectioning**

- A single H&E stained section, representing a full face of the block, is adequate for the initial microscopic examination.
- Depending on the appearances, levels may be requested at the discretion of the reporting pathologist.
- Ensure margins are properly faced.

### **3.6 Further investigations**

If appropriate:

- immunohistochemistry, expert opinion.

### **3.7 Report content**

- No special issues
- Diethylstilboestrol related
- Endometriotic cyst
- Epithelial inclusion cyst
- Hymenal cyst
- Mucinous (Gartner's duct) mesonephric cyst
- Paramesonephric<sup>5</sup> cyst.

## **4 Vaginectomy**

### **4.1 Specimen submission**

- Vaginal resections are usually performed for intra-epithelial disease or tumour. Redundant benign tissue may be excised for prolapse or plastic operations. Fresh or fixed material may be received.

### **4.2 Specimen dissection and block selection**

- Describe and measure in three dimensions, giving the maximum thickness of the vaginal wall. Give the distance of the lesion from the closest margins.
- Sample any mass lesions.
- Sample any cyst or soft tissue lesion as above.
- Include the margins and point of maximum thickness/deep margin (margins may be inked).
- Sample any epithelial abnormality.
- For VAIN – the whole of the resection margins are sampled.

### **4.3 Embedding options**

- The sections are embedded cut face down to ensure that the correct surface is cut by the microtome.

#### 4.4 Sectioning

- A single H&E stained section, representing a full face of the block, is adequate for the initial microscopic examination.
- Depending on the appearances, levels may be requested at the discretion of the reporting pathologist.

#### 4.5 Staining

- H&E.

#### 4.6 Further investigations

- Additional levels may be required.
- Mucin histochemistry (AB/PAS+/-D) may be helpful to assess glandular lesions. Immunohistochemical marker studies can be necessary to differentiate between metaplastic and neoplastic processes.
- Immunohistochemistry: oestrogen and progesterone receptors, SMA, CD34, desmin, h-caldesmon, S100.<sup>3</sup>
- Possible soft tissue expert opinion.

#### 4.7 Report content

- As for vaginal biopsies, soft tissue lesions and cysts. See above.
- Any gross lesions are sampled to include the deep resection and nearest radial resection margins.
- Lymphovascular invasion.

### 5 References

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## **C Cervix**

### **1 Cervical biopsy (not otherwise specified) and cervical punch biopsy**

#### **1.1 Staffing and workload**

- See introduction on page 3.

#### **1.2 Specimen submission**

- Fresh or fixed material.
- These are usually colposcopically directed biopsies that may be up to several millimetres long and 2–4 mm thick.
- In some institutions, such biopsies are not mounted onto a card or filter paper,<sup>1</sup> although one study has shown that specimens that were mounted on filter paper before fixation were more likely to be optimally oriented, to have a preserved squamocolumnar junction and to have intact surface epithelium.<sup>2</sup>
- Fixation of small biopsies in eosin-tinted formalin may facilitate their identification and orientation.<sup>2,3</sup>
- Careful handling of these specimens is recommended<sup>3</sup> to prevent surface trauma and disruption or loss of surface epithelium.

#### **1.3 Specimen dissection**

- It is important to search the container and the under-surface of its lid to ensure that stray fragments of tissue are recovered.
- If fragments are very small, they are wrapped, or placed between layers of foam sponge or in mesh bags or wire cages to avert tissue loss during processing. The number of fragments or aggregated size is noted.
- The number of pieces received is recorded, as is their size (maximum dimension if small, or in three dimensions), shape, colour and texture (mucoid, granular, friable).
- If biopsies are >5 mm in dimension, they may be bisected transversely, perpendicular to the mucosal surface, to produce two pieces.
- All of the biopsies, including mucoid fragments, are processed, and small biopsies placed in mesh bags or wire/mesh baskets.

#### **1.4 Embedding options**

- If bisected, the flat, cut end is embedded downwards to ensure that this surface is cut by the microtome.
- Intact biopsies are orientated carefully and embedded on edge, with the epithelial surface perpendicular to the face of the block to be cut by the microtome.

#### **1.5 Sectioning**

- In general, it is recommended that levels of such biopsies are cut.<sup>3,4</sup>
- Although the precise number of levels is not always specified, three levels are recommended.<sup>1</sup>
- Step-serial sectioning is not necessary as a routine.<sup>1</sup>

## 1.6 Staining

- H&E.

## 1.7 Further investigations

- Additional levels may be necessary.
- Mucin histochemistry (AB/PAS+/-D) can be helpful to identify intestinal type differentiation in endocervical glandular elements.
- Immunohistochemical marker studies may be necessary to differentiate between metaplastic and neoplastic changes in endocervical glands, or to assist in the differentiation between atrophy and CIN.<sup>5-9</sup>

## 1.8 Report content

- The report should incorporate the macroscopic description of the specimen, and identify the area/s of the cervix from which the biopsy has originated, i.e. ectocervix, endocervix, transformation zone.
- Where artefact or epithelial loss impairs interpretation of the biopsy, this must be stated in the report.<sup>3</sup>
- The pathologist reports all grades of squamous and/or glandular intra-epithelial neoplasia, and invasive lesions are reported and graded according to national protocols and guidelines.<sup>10</sup>
- It is recommended that koilocytosis and koilocytosis-associated changes are reported, but CIN is mentioned first<sup>3</sup> unless the CIN represents only a minor component of a predominantly koilocytic lesion. The pathologist must be mindful of the cytological report when writing the histology report, and include all pathological lesions (neoplastic and non-neoplastic) that may be associated with, or account for the reported cytological abnormalities.
- When a biopsy fails to reveal the source of the abnormal cells in a smear, it is important to differentiate between a biopsy that is technically adequate but fails to identify a lesion, and a biopsy that is technically inadequate.
- The limitations of punch biopsies in the detection of CIN<sup>11</sup> and particularly high-grade CIN are recognised.<sup>12</sup> If CGIN is identified in a punch biopsy, the report should include a caveat to indicate that the possibility of an invasive component cannot be excluded.<sup>3</sup>

## 2 Cervical cone biopsy and cervical loop biopsy/large loop excision of the transformation zone (LLETZ)

### 2.1 Specimen submission

- Fresh or fixed material.
- Cone/LLETZ/loop biopsies are carried out for women with abnormal smears as part of a 'see and treat' or following a positive punch biopsy, i.e. the biopsy can be either a diagnostic or therapeutic procedure.
- Cone biopsies are performed using a scalpel ('cold knife') but more commonly, large loop diathermy methods are used to the same effect, with the advantage of reduced bleeding, better healing and preservation of cervical anatomy.

- Loop diathermy methods also have the advantage of being performed without a general anaesthetic, as an outpatient procedure.
- A disadvantage of loop diathermy is the artefact at the resection margins that results from electrothermal damage. This may impair histological diagnosis, and also the assessment of resection margins,<sup>13</sup> especially in cases of glandular neoplasia. For this reason, cone biopsy is a preferred procedure for the assessment of glandular lesions of the cervix.

## 2.2 Specimen dissection and block selection

- Intact cone or loop biopsies are roughly conical in shape.
- In some centres, a specific position (usually 12 o'clock) is marked with a suture, or the specimen orientated and pinned to a cork board.
- The specimen may be opened at one end (giving a U-shape), opened at one end and drawn out into a flattened, curved specimen or in some instances submitted as multiple specimens/loops.
- The specimen/s are measured. An intact central loop/cone biopsy is measured in three dimensions (antero-posterior, lateral/lateral and thickness).
- A flat/opened loop biopsy is also measured in three dimensions and care taken to provide a clear statement of exactly what is being measured – the circumference of an opened, flattened loop/cone biopsy is markedly different from that of an intact conical specimen.
- If multiple loop biopsies are submitted, the number of pieces is noted and the smallest and largest measured, maximum dimension if small, or in three dimensions.
- The colour, consistency and presence of any surface lesions are recorded.
- If specific margins have not been indicated, the entire excision margin may be painted with ink to assist with their identification in the histological sections, although this is not usually necessary.
- Pathologists should be aware that opening an intact loop/cone biopsy may result in damage to the surface epithelium.<sup>3</sup> This is not advised. Similarly the os must not be probed.
- Intact central loop/cone biopsies can be sectioned in one of several ways, although there are two preferred, widely used methods. Because the external os in most parous women is transverse and slit-like, loop/cone biopsies can be sliced serially at 2–3 mm intervals,<sup>4,14</sup> from one edge to the other in a sagittal and parasagittal plane (beginning at the 3 or 9 o'clock edge), perpendicular to the transverse axis of the external os. This avoids the problems of interpretation that may arise when dysplastic epithelium arises on the narrow end of a wedge shaped block (if a loop/cone specimen is sectioned radially, see below), and facilitates assessment of tumour volume in small lesions or neoplasms.<sup>15</sup> However, this method does not easily allow direct correlation of CIN with the specific position on a clock face<sup>16</sup> that the radial method of sampling permits.
- The radial method involves the sampling of an intact loop radially, in wedge-shaped slices, according to the hours on a clock face. This is a useful method of sampling if accurate mapping of a lesion is desired,<sup>14</sup> although this is not usually necessary.
- In either case, the slices are submitted in separate, sequentially numbered blocks (corresponding to the hours on a clock face if radial sampling has been carried out, e.g. block 1 = 1 o'clock etc).
- An opened loop biopsy is processed in serial transverse blocks, as are the individual loops if multiple specimens are submitted, in specifically designated cassettes.

- Care is taken to ensure that the correct cut face is placed face down in the cassette. If desired, the opposite cut face can be marked with ink, to ensure that the correct (non-inked) side is embedded downwards to be cut by the microtome.
- Members of the Working Party of The Royal College of Pathologists<sup>3</sup> advocate that each piece of tissue should be placed in a single cassette. Others suggest that if the slices are small, two or three may be placed in one cassette for reasons of convenience and economy.<sup>1,16</sup> **Placing multiple slices in one cassette should be avoided. This practice makes it impossible to measure the horizontal size of any small invasive lesion and compromises accurate staging of such lesions.**
- In all cases, all of the tissue is submitted. The deep radial margin is not trimmed off.

### 2.3 Embedding options

- The sections are embedded cut face down to ensure that the correct surface is cut by the microtome.
- In some centres, for the purpose of expediency, the excision margins of loop biopsies are assessed by embedding the outer (curved) surface of the first and last slices of the loop face down for sectioning, instead of the cut surface. This avoids having to request additional levels to assess these margins.

### 2.4 Sectioning

- A single level from each block is likely to suffice initially.<sup>3,4</sup> Some laboratories provide a 'deeper' as standard along with the index section.
- Deeper levels will be required if there are difficulties in identifying a lesion that might account for the abnormal cells in an antecedent smear.
- One study<sup>17</sup> has shown that examination of a only a single further level is adequate in those specimens where surface epithelium or squamo-columnar junction is missing, or in circumstances where there is a discrepancy between the histological findings and smear.
- If invasive disease is suspected on the basis of the cytological, colposcopic or histological features,<sup>18</sup> further levels are examined.

### 2.5 Staining

- H&E.

### 2.6 Further investigations

- Additional levels may be necessary (see above).
- Histochemistry and immunohistochemistry may also be required (see above).

### 2.7 Report content

- The report should incorporate the macroscopic description of the specimen, and identify the tissue components that are present, i.e. ectocervix, endocervix, transformation zone, isthmus.
- Features that impair interpretation are recorded, e.g. opened loop, fragmentation, surgical/operative trauma, thermal artefact, and pathologists must have access to the cytological report when writing the histology report.
- All grades of squamous and/or glandular intra-epithelial neoplasia are reported<sup>3</sup> and the presence of endocervical crypt involvement recorded in cases of CIN.<sup>1</sup> The

distribution of a lesion is noted if an orientated specimen has been submitted. Any invasive lesions are classified and graded according to national protocols and guidelines.<sup>10</sup>

- If there is significant inflammation, or inflammation associated with specific pathological features, e.g. follicular cervicitis, herpesvirus infection, this is reported. Koilocytosis is also recorded, as are pathological lesions (neoplastic and non-neoplastic) that may be associated with, or account for, the reported cytological abnormalities.
- The report must indicate whether or not the abnormal squamous or glandular epithelium has been completely excised. Fragmentation usually precludes an adequate assessment of the margins. Pathologists should exercise caution in the assessment of excision of a lesion when opened, fragmented or multiple loop biopsies have been submitted.

### **3 Cervical wedge biopsy**

#### **3.1 Specimen submission**

- Fresh or fixed material.
- Wedge biopsies are larger than punch biopsies, but generally smaller than cone/LLETZ biopsies. They are carried out at the time of colposcopy for women with abnormal smears as part of a 'see and treat' therapeutic procedure, and also as a diagnostic procedure as an alternative to a punch biopsy, or to confirm neoplasia before definitive treatment.<sup>4</sup>

#### **3.2 Specimen dissection and block selection**

- Wedge biopsies may be over 10 mm in maximum dimension, and occasionally more than one biopsy is submitted. The maximum size in three dimensions is provided for each biopsy or just give maximum dimension if small.
- The colour, consistency and presence of any surface lesions are recorded.
- The specimen/s is/are cut perpendicular to the transformation zone (this is usually visible macroscopically) or perpendicular to the long axis to ensure that both ectocervical and endocervical edges of the specimen appear in their normal anatomical context in the sections.
- Such specimens are processed in their entirety.

#### **3.3 Embedding options**

- The blocks are embedded cut face down to ensure that the correct surface is cut by the microtome.

#### **3.4 Sectioning**

- A single level from each block is likely to suffice initially.<sup>3,4</sup> Some laboratories provide a 'deeper' as standard along with the index section.
- Deeper levels will be required if there are difficulties in identifying a lesion that might account for the abnormal cells in an antecedent smear.
- One study<sup>17</sup> has shown that examination of only a single further level is adequate in those specimens where surface epithelium or squamo-columnar junction is missing, or in circumstances where there is a discrepancy between the histological findings and

smear. If invasive disease is suspected on the basis of the cytological, colposcopic or histological features<sup>18</sup> further levels are examined.

### **3.5 Staining**

- H&E.

### **3.6 Further investigations**

- Additional levels may be necessary (see above).
- Histochemistry and immunohistochemistry may also be required (see above).

### **3.7 Report content**

- The report should incorporate the macroscopic description of the specimen, and identify the tissue components that are present, i.e. ectocervix, endocervix, transformation zone, isthmus.
- Features that impair interpretation are recorded, e.g. fragmentation, surgical/operative trauma, thermal artefact, and pathologists must have access to the cytological report when writing the histology report.
- All grades of squamous and/or glandular intra-epithelial neoplasia are reported<sup>3</sup> and the presence of endocervical crypt involvement recorded in cases of CIN.<sup>1</sup> The distribution of a lesion is noted if an orientated specimen has been submitted. Any invasive lesions are classified and graded according to national protocols and guidelines.<sup>10</sup>
- If there is significant inflammation, or inflammation associated with specific pathological features, e.g. follicular cervicitis, herpesvirus infection, this is reported. Koilocytosis is also recorded, as are all pathological lesions (neoplastic and non-neoplastic) that may be associated with, or account for, the reported cytological abnormalities.
- The report must indicate whether or not the abnormal squamous or glandular epithelium has been completely excised. Pathologists should exercise caution in the assessment of excision of a lesion when fragmented or multiple biopsies have been submitted.

## **4 Manchester repair**

### **4.1 Specimen submission**

- Manchester repair is performed for uterine prolapse.
- The specimen comprises amputated cervix, usually with one or two triangular pieces of mucosa from the anterior and posterior vaginal walls.

### **4.2 Specimen dissection and block selection**

- The main specimen is measured in three dimensions.
- The length of the attached vaginal mucosa is recorded.
- The surface of the cervix is described, and any lesions on the surface of the cervix or the vaginal mucosa described in full.

- The cervix is sampled according to the recommended protocols for cervical sampling in a non-malignant hysterectomy specimen, i.e. two midline blocks of cervix, one each from the anterior and posterior cervical lips.<sup>14,15</sup>
- Vaginal mucosa is included in continuity with the cervix if possible.

If there is a history of current abnormal smears, this should be processed as a LLETZ (see section C on Cervix, above).

### **4.3 Embedding options**

- Ensure sections are cut at right angles to the epithelial surface.

### **4.4 Sectioning**

- A single H&E stained section, representing a full face of the block, is adequate for the initial microscopic examination.
- Depending on the appearances, levels may be requested at the discretion of the reporting pathologist.

### **4.5 Staining**

- H&E.

### **4.6 Further investigations**

- Any abnormality can be investigated as for cervical biopsies and LLETZ above. Any finding of CIN or CGIN requires the whole of the cervix to be examined as for a LLETZ or cone biopsy, as appropriate.

### **4.7 Report content**

- The report should incorporate the macroscopic description of the specimen.
- Any CIN or CGIN is graded and reported according to the recommendations described above.
- The presence of CIN or CGIN prompts the processing of further blocks as above to exclude a lesion of higher grade or stromal invasion.
- If CIN or CGIN is present, a statement is included to indicate whether or not excision of the lesion is complete because this will influence whether or not follow up smears are carried out as part of the cervical screening programme.

## **5 Endocervical polypectomy**

### **5.1 Specimen submission**

- Most endocervical polyps are identified at the time of smear taking and are removed by avulsion.
- Larger polyps may be removed by excision at the time of colposcopy. Most are benign, smooth surfaced and pedunculated.

### **5.2 Specimen dissection and block selection**

- If submitted as a single polyp, the maximum dimensions are measured.

- If multiple fragments are sent, measure the size of the smallest and largest. Describe the colour and texture (e.g. spongy, solid, mucoid).
- If a single large polyp >5 mm is submitted, bisect the polyp longitudinally parallel to the axis of the stalk, and submit the whole polyp for processing. If the polyp is very large, the polyp halves may need to be cut into smaller pieces and sampled in more than one cassette.
- If multiple fragments are sent, place all of the fragments in a mesh bag or wire/mesh basket for processing.

### **5.3 Embedding options**

- If the polyp has been sliced, the sections are embedded cut face down to ensure that the correct surface is cut by the microtome.

### **5.4 Sectioning**

- A single H&E stained section, representing a full face of the block, is adequate for the initial microscopic examination.
- Depending on the appearances, levels may be requested at the discretion of the reporting pathologist.

### **5.5 Staining**

- H&E.

### **5.6 Further investigations**

- Carcinoma, CIN, CGIN, epithelial hyperplasia, atypical hyperplasia, or stromal neoplasia may require further levels for diagnosis.

### **5.7 Report content**

- The report should incorporate the macroscopic description of the specimen and the anatomical origin of the polyp stated in the report. Endometrial polyps (benign or malignant) can sometimes protrude through the cervix and be mistaken for endocervical polyps; these are reported according to the recommendations for endometrial polyps. Occasionally, prominent Nabothian follicles may be mistaken for endocervical polyps and in such circumstances the possibility of CIN should be excluded.
- The presence of significant inflammation or metaplastic changes is reported in endocervical polyps, and pathologists must look out for cervical cytological reports when writing the histology report, to correlate any low grade smear changes with metaplastic or reactive changes on the surface of inflamed endocervical polyps.

## **6 Endocervical curettage**

### **6.1 Specimen submission**

- Such specimens are submitted to identify the presence of squamous or glandular intra-epithelial neoplasia in the endocervical canal or to assess whether endometrial carcinoma has spread to involve the cervix.<sup>1,16</sup> They are typically scanty and comprise mucus and blood admixed with light grey or brown tissue fragments, usually of small size. Because of this, they are handled with caution.

## 6.2 Specimen dissection and block selection

- The aggregated size (in three dimensions) of the sample is measured after it has been filtered into a mesh bag, and the colour and texture (muroid, spongy, firm) described. The whole sample is processed in a mesh bag or wire/mesh basket to avert the loss of tiny fragments. Filter paper and sponges are avoided because of the possibility of losing tissue fragments becoming entrapped or adherent.

## 6.3 Embedding options

- No specific issues.

## 6.4 Sectioning

- A single H&E stained section, representing a full face of the block, is adequate for the initial microscopic examination.
- Depending on the appearances, levels may be requested at the discretion of the reporting pathologist.

## 6.5 Staining

- H&E.

## 6.6 Report content

- The report should incorporate the macroscopic description of the specimen. The presence of neoplasia (either intra-epithelial neoplasia of glandular or squamous type, or invasive carcinoma) is reported, but classification and grading according to national protocols and guidelines may be hindered by the small volume of material available for examination in such specimens.

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## **D Endometrium**

### **1 Staffing and workload**

- See introduction on page 3.

### **2 Specimen submission**

- Specimens will include: pipelle biopsies, curettings and TCRE (transcervical resection of the endometrium).
- These specimens must be submitted in an adequate volume of fixative to ensure proper fixation; usually this will be 10% formalin, but some centres may utilise Bouin's fixative.
- Pipelle and TCRE specimens will usually float free in the fixative.
- Curettage specimens may be received on filter paper or gauze, depending on the methodology utilised in theatre.
- There may be individual arrangements for particular specimen types. If this includes submission of a fresh/unfixed specimen, there must be a protocol in place to ensure rapid transportation to the laboratory.
- The specimen should be accompanied by a correctly completed request form including patient demographics, name of the clinician, date of procedure, type of specimen and clinical information to include menstrual status (LMP/post-menopausal), history of hormone treatment or previous endometrial surgery, and presence of IUCD, if applicable.
- The specimen container must be labelled with matching patient details and any discrepancy will lead to refusal to process the specimen until corrective action is taken.
- The request form should be labelled if an 'urgent' result is required, with justification for that request, to include a contact/bleep number.
- If audit studies have shown the turnaround time for the laboratory is adequate, an urgent request may be superfluous depending on the proximity of the procedure to the next multidisciplinary team (MDT) meeting.

### **3 Specimen dissection and block selection**

- Describe the volume in a semi-quantitative fashion or weigh:  
Scanty <½ cassette or < 0.5 g  
Moderate >½–1 cassette or 0.5–1.0 g  
Bulky >1 cassette or > 1 g  
Alternatively, an estimate of the volume can be given in ml or by max dimension if small, or measuring three dimensions in mm.
- Small/invisible samples can be filtered or centrifuged and submitted for a cytoblock preparation or embedded in agar.
- Describe and measure in three dimensions (mm) lesions such as polyps.
- Describe the colour and texture of polyps and comment on the presence of necrosis or haemorrhage. It may be necessary to cut large polyps into multiple pieces, identifying the base of the stalk where visible, and examine in separate cassettes. Consider embedding all submitted tissue from polyps.
- Embed and process all the tissue including mucus and blood.
- Depending on the preferred methodology in the laboratory, strain the specimen into, and process in, tissue paper/gauze sachet or wire/mesh basket to prevent tissue loss or cross contamination.

#### 4 Embedding options

- No specific issues.

#### 5 Sectioning

- A single haematoxylin and eosin (H&E) stained section, representing a full face of the block, is adequate for the initial microscopic examination.
- Depending on the appearances, levels may be requested at the discretion of the reporting pathologist.

#### 6 Staining

- H&E.

#### 7 Further investigations

- Special histochemical and immunohistochemical studies will be carried out as appropriate for the H&E findings, e.g. Ziehl-Neelsen stain in a granulomatous condition, Gram for actinomyces spp. PAS(D) or Grocott for fungi. Special studies will not normally be required.

#### 8 Report content<sup>1-3</sup>

- Is the sample adequate or too small to be assessable? A small/tiny specimen may be representative of the endometrial lining and therefore adequate, especially in post-menopausal women. Such cases should be reported in the clinical context. A similarly sized sample in a pre-menopausal woman is inadequate.<sup>2</sup> A specimen may be labelled 'inadequate' in the absence of functional endometrial tissue.
- Normal samples may be reported as:
  - proliferative: early, mid or late
  - secretory: early, mid or late
  - menstrual
  - inactive
  - atrophic.

It is not possible to state whether a sample from a pre-menopausal woman is normal in the absence of an LMP and cycle length.

- If abnormal, the gland morphology, uniformity of development of the epithelium, stroma and vasculature all receive comment.
- Diagnoses include the following:
  - Luteal phase defect
    - atrophy
    - deficient proliferation
    - prolonged proliferation
    - disordered proliferation
    - oestrogen withdrawal bleeding.
  - Ovulatory phase defect
    - coordinated delay
    - dyssynchronous development
    - deficient secretory transformation
    - premature corpus luteum failure
    - delayed/prolonged shedding.

Exogenous hormone/drug effect

- IUCD
- HRT
- oral contraceptive
- Tamoxifen
- GnRH analogues.

With or without abnormal breakdown.

Metaplasias.

Infection/inflammation.

Hyperplasia should be classified as:

- simple
- complex
- atypical.<sup>4</sup>

- It may not be possible to comment on the endometrium in a TCRE specimen because of diathermy artefact.
- Recognition of tangential cutting artefact will prevent over-diagnosis of adenomyosis in TCRE specimens.
- Malignant conditions are covered in the appropriate College cancer dataset.<sup>4</sup>

Polyp

- Type
- Stromal/glandular – comment on
- Mitoses in glands/and or stroma
- Complex hyperplasia
- Atypical hyperplasia
- Carcinoma
- Do not comment on simple hyperplasia
- Adenofibromatous polyp
- Adenomyomatous polyp (non-atypical)
- Atypical polypoid adenomyomatous
- Submucous leiomyoma.

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[www.rcpath.org/publications](http://www.rcpath.org/publications)

## **E Uterus**

### **1 Staffing and workload**

- See introduction on page 3.

### **2 Specimen submission**

Fresh or fixed material.

A hysterectomy may be performed for:

- prolapse (+/- repair)
- fibroids
- adenomyosis
- endometriosis
- dysfunctional uterine bleeding
- tumour (see College cancer dataset)<sup>7</sup>
- persistently abnormal smears ( $\pm$  previous cervical biopsy/LLETZ)
- obstetric causes.

The clinical history is relevant as there are a variety of preoperative treatments such as hormonal manipulation or embolisation which significantly alter the appearance of fibroids. These treatments can give rise to changes which simulate the gross appearances of malignant tumours. Hysteroscopic/transcervical endometrial resection also changes the appearances of the endometrium and myometrium, even with potential for mural perforation.

### **3 Specimen dissection and block selection**

- Orientate the specimen. Identify the anterior and posterior surfaces, cervix, fundus and body, fallopian tubes and other adnexal structures. Typically the peritoneal reflection is lower in the pouch of Douglas in comparison with the anterior peritoneal reflection. Normal ovaries are posterior to the fallopian tubes.
- Identify surgical or traumatic wounds, or serosal abnormalities (adhesions, endometriosis and endosalpingiosis).
- Measure the size of the uterus in three dimensions and give a description of the shape and symmetry. Note any developmental abnormalities (arcuate, bicornuate, didelphys, unicornuate).
- Measure (mm):
  - fundus to cervix
  - cornu to cornu
  - anterior surface of the body to the posterior surface
  - attached vaginal wall in three dimensions.<sup>1,2</sup>
- The weight of the uterus adds little clinically valuable information and can be omitted if desired.<sup>3</sup>
- Laparoscopic specimens may be received in multiple pieces (morcellated). This procedure should not be performed if there is a history of atypical endometrial hyperplasia or gynaecological neoplasia. There should be a previous pipelle or curettage to exclude endometrial abnormality.
- Measurements can be approximated, if appropriate.
- The parts should be identified, orientated if possible and routine blocks taken of the cervical surface, endometrium and any abnormality.

## Dissection

If a cervical lesion is present or suspected, amputate the cervix and dissect the cervix as per the cone biopsy pathway. Do not probe the uterine cavity as this may damage the transformation zone and endocervix.

Probing the uterus may be necessary to identify the orientation of the cavity. However, this may remove diagnostic tissue from the endocervical canal or uterine cavity and is not needed if the uterus is bisected as detailed below.

The uterus may be formally bivalved to expose the uterine cavity. Alternatively, a midline sagittal bisection of the uterus will expose the endometrium and indicate the shape of the uterine cavity. The myometrium can then be examined by multiple parasagittal or horizontal incisions. If the uterus is markedly distorted, for example, by multiple fibroids the plane of bisection can be adjusted to optimally expose the uterine cavity.

Note the nature of the myometrium. Flecks of calcification are often seen in association with blood vessels in the myometrium of older women.

Describe:

- endometrial thickness (atrophic, thickened, cystic)
- endometrial polyps (number, size, ulceration, haemorrhage)
- intrauterine devices (IUD) – type
- adenomyosis (fibroid-like mass with coarse trabecular bands of tissue, small slit-like spaces and brown fluid)
- Caesarian section scars (usually anterior wall below the peritoneal reflection)
- adenomatoid tumours (subserosal, cornual, adnexal)
- uterine perforation
- serosal adhesions (pelvic inflammatory disease, previous surgery)
- endosalpingiosis (one explanation for a gritty serosal surface)
- fibroids:
  - intramural
  - subserosal
  - submucosal
  - number (or an estimate if numerous) and range of sizes
  - nature of boundary (may reflect an infiltrative growth pattern)
  - degenerative changes such as
    - cystic spaces filled with thin serous or mucoid fluid
    - fatty change
    - myxoid areas
    - foci of calcification
    - necrosis
    - red degeneration (common in pregnancy)
    - haemorrhage
- tumours (see College cancer dataset)<sup>7</sup>
- sarcoma
- obstetric
  - removed at delivery or during pregnancy
  - intractable haemorrhage
  - uterine rupture.
  - abnormal placental implantation

- previous Caesarean section
- usually transverse through the lower uterine segment, rarely a vertical classical wound through the uterine body.

### **Block selection**

Sample as follows.

- A representative block of tissue, including the transformation zone, from the anterior and the posterior lip of the cervix.
- The entire transformation zone if there is a recent past history of intraepithelial neoplasia and if the most recent smear was abnormal. Refer to the cone biopsy pathway. The number of blocks taken is related to the cervical anatomy as it is better to have fewer blocks with good representation of the zone rather than more blocks with poor representation.
- Endometrium – anterior and posterior wall ensuring that the full thickness is represented. Ideally this should include the underlying myometrium with serosa at one end of the block and endometrium at the other end.
- Multiple blocks are taken if there is a preoperative diagnosis of simple or complex hyperplasia. Atypical hyperplasia requires the same dissection as for endometrial adenocarcinoma.
- Polyp(s): thoroughly sampled including the base where it abuts the surrounding normal tissue
- Myometrium, including the serosa, if not included with the endometrial blocks.
- Representative fibroids, especially if large (>5 cm) or abnormal – necrosis, myxoid change, poor circumscription. Include the junction of the lesion with the surrounding myometrium. Take one block per 1–2 cm of the maximum diameter, up to four for an otherwise unremarkable fibroid. There is no evidence-based research on the number of blocks to be taken from uterine fibroids.
- Obstetric – numerous blocks of the Caesarean section scar. Retained adherent placental tissue is seen as ragged, haemorrhagic tissue lining the surface of the uterine cavity.
- In placenta previa and placenta accreta, the junction of the placenta and myometrium.
- The edge of a traumatic rupture.

### **4 Embedding options**

- Ensure a vertical section of the endometrium and serosa.

### **5 Sectioning**

- A single haematoxylin (H&E) stained section, representing a full face of the block, is adequate for the initial microscopic examination.
- Depending on the appearances, levels may be requested at the discretion of the reporting pathologist.

### **6 Staining**

- H&E.

### **7 Further investigations**

- CD10, H-caldesmon may be required to differentiate stromal from smooth muscle lesions.

- Progesterone and oestrogen receptors in stromal neoplasia.<sup>4,5</sup>
- BEREp4 negative (or other epithelial marker) and mucin negative for adenomatoid tumour.<sup>6</sup>

## 8 Report content<sup>6</sup>

Ectocervical epithelium, crypts (glandular epithelium) and stroma (see section C on Cervix, above).

Endometrium (phase, cyclical abnormality, hyperplasia, neoplasia – see College cancer dataset,<sup>7</sup> endometrial polyps (see section D on Endometrium, above).

Myometrium (leiomyoma including comment on atypical features, STUMP, adenomyosis, adenomatoid tumour, stromal tumours).

Leiomyoma, smooth muscle tumour of uncertain malignant potential (STUMP). Comment on:

- mitotic activity (normal or abnormal forms) – expressed as count/mm<sup>2</sup>
- necrosis
- infarction
- nuclear atypia/symplastic change
- diffuse/localised
- myxoid change
- margin
- vascular space involvement
- perinodular/hydronic growth pattern
- dissecting growth pattern
- variant types
  - usual
  - cellular
  - epithelioid
  - symplastic
  - myxoid
  - with tubules
  - lipoleiomyoma
  - with lymphoid infiltration
  - diffuse uterine leiomyomatosis
  - dissecting
  - with vascular invasion
  - intravenous leiomyomatosis
  - plexiform tumorlet.

Adenomyosis – comment on:

- extent
- glandular atypia/hyperplasia
- stromal atypia

Stromal tumours: stromal nodule, stromal sarcoma, uterine sarcoma. Comment on:

- mitotic activity (normal or abnormal forms) – expressed as count/mm<sup>2</sup>
- nature of margin (invasive/circumscribed)
- necrosis
- vascular pattern

- if malignant – progesterone receptor status
- serosa.

Endometriosis. Comment on:

- extent
- glandular atypia/hyperplasia
- stromal atypia.

Endosalpingiosis. Comment on:

- epithelial types
- atypia.

Obstetric samples

- Caesarean section scar
- abnormal rupture
- placental implantation

Accreta

Previa

Ectopic implantation

- interstitial
- cornual
- serosal
- cervical.

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[www.rcpath.org/publications](http://www.rcpath.org/publications)

## **F Ovary**

### **1 Staffing and workload**

- See introduction on page 3.

### **2 Specimen submission**

Fresh or fixed material may be sent. Non-neoplastic ovaries are removed as part of a total abdominal hysterectomy and bilateral or unilateral salpingo-oophorectomy (TAH BSO, TAH SO) for uterine, pelvic ovarian or tubal disease. Ovaries, usually with the fallopian tube, are removed without the uterus for pelvic pain (often due to pelvic inflammatory disease or adhesions), cysts, mass lesions, endometriosis and torsion/oedema or to prevent neoplasia in women at risk from heritable genetic disease such as familial ovarian cancer. Wedge biopsies may be used to investigate infertility, polycystic disease or specific clinical findings and cystectomies to investigate clinically benign cysts and to preserve fertility. The fallopian tube is identified, described and measured.

### **3 Specimen dissection and block selection<sup>1,2</sup>**

- Avoid excessive handling of the surface to prevent abrasion of the delicate covering mesothelium.
- Measure in three dimensions and describe any cysts.
- Physiological cysts may measure up to 20 mm in diameter.
- Multiple small subcapsular cysts may indicate polycystic disease.
- Describe the nature of the ovarian surface: any surface papillary or solid projections are noted and measured.
- The ovary is cut transversely (usually at right angles to the long axis), making several parallel cuts to examine the whole organ (important in prophylactic oophorectomy).
- One block is sufficient for a normal ovary.
- Small post-menopausal ovaries are cut longitudinally and half taken.
- The block should include cortex, medulla and hilus. Several blocks may be needed for otherwise normal ovaries larger than 25 mm greatest dimension.
- Cysts with complex internal structures, solid or papillary areas are dealt with as in the College's *Dataset for ovarian cancer*.<sup>3</sup>
- Describe and measure cysts in three dimensions.
- Surface – smooth, roughened or papillary.
- Capsular breach.
- Internal structure – unilocular, multilocular, solid or papillary areas.
- Colour/texture variation – white, whorled, calcified, haemorrhagic, yellow.
- Hair, sebum, bone, teeth, etc. in dermoids. Take blocks from the umbo (Rokitansky's tubercle) and cyst wall.
- Identify residual ovary.
- Cyst contents – watery, serous, mucoid, gelatinous, bloodstained, or chocolate-like.
- Sample thin-walled cysts by rolling up a portion of wall to give a 'Swiss roll' block.

- Block papillary and solid areas to document possible borderline change (see the College's *Dataset for ovarian cancer*). One block per cm of solid or papillary area is recommended for areas under 100 mm and two per 10 mm for larger lesions, but there is no good evidence to support this regime.<sup>4</sup>
- Para-ovarian cysts are treated in the same way.
- Block the whole of wedge biopsies to ensure a vertical section through the cortex, medulla and capsule. Small samples can be bisected along the long axis. Take multiple blocks from larger samples at right angles to the long axis.
- Block the cyst wall, solid, soft or papillary areas in endometriosis to exclude/document atypia, hyperplasia or tumour.<sup>5</sup>
- Block the whole ovary (and fallopian tube) in familial ovarian cancer to identify any microscopic tumours or dysplasia.<sup>6</sup>
- Take a block from yellow areas in fibrous tumours for a fat stain to identify thecomatous areas.

#### 4 Embedding options

- Orientate cyst wall to ensure a vertical section through the epithelial lining, wall and surface.

#### 5 Sectioning

- A single haematoxylin and eosin (H&E) stained section, representing a full face of the block, is adequate for the initial microscopic examination.
- Depending on the appearances, levels may be requested at the discretion of the reporting pathologist.
- Ensure cyst wall blocks are properly faced to visualise the epithelial/stromal interface.

#### 6 Staining

- H&E.
- Oil red O for fat in suspected thecoma.
- Reticulin to identify structure in infarcted/torted ovaries.

#### 7 Further investigations

- Immunohistochemical panel for ovarian tumours.<sup>7</sup>

#### 8 Report content<sup>1</sup>

##### Normal ovary

- It is not necessary to comment on normal features such as antral follicles, corpora albicantes or corpora lutea

##### Pelvic pain

- Small fibrous band(s) may indicate clinically significant surface adhesions
- Larger adhesions
- Inflammation
- Evidence of old/recent bleeding
- Two of three features: organising haemorrhage/endometriotic stroma/endometriotic epithelium to diagnose endometriosis
- Haemorrhagic infarction/torsion

- Oedema (may be massive and simulate neoplasia)
- Ectopic pregnancy – implantation site, trophoblast, fetal parts

#### Infertility

- Presence of primordial follicles
- Signs of previous ovulation such as corpora albicantes/ corpora lutea
- Dysmorphic follicles
- Inflammation
- Capsular thickening/abnormal follicles in polycystic ovaries

#### Cysts

- Functional – follicular (atretic), antral, luteal, corpora albicantes, granulosa lutein, theca lutein, polycystic ovary syndrome.
- Hyperreactio luteinalis
- Pregnancy luteoma
- Cortical inclusion cysts
- Mullerianosis
- Epithelial proliferation, atypia, mitoses
- Epithelial type – serous, mucinous (intestinal or endocervical), endometrioid, transitional, indeterminate<sup>8</sup>
- Haemorrhage, pus

#### With hysterectomy

- Stromal hyperplasia
- Stromal hyperthecosis

#### Enlargement

- Surface papilloma
- Fibromatosis
- Fibroma
- Thecoma
- Luteoma
- Soft tissue tumours not specific to ovary
- See the College's *Dataset for ovarian cancer* and WHO classification<sup>3,8</sup>

#### Familial ovarian carcinoma

- Dysplasia/proliferation of surface
- Report microscopic foci of carcinoma as in the College's *Dataset for ovarian cancer*.

#### Other features:

- Surface adhesions, stromal luteinisation, hyperplasia and any other abnormality.

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## **G Fallopian tube**

### **1 Staffing and workload**

- See introduction on page 3.

### **2 Specimen submission**

Fresh or fixed material

- The tubes (or segments of tube) should be labelled 'Left' and 'Right' by the clinician to enable subsequent exploration of the correct site if necessary.

Fallopian tube biopsies are most commonly excised for sterilisation.

Fallopian tubes may be excised in total for:

- sterilisation
- benign or malignant conditions requiring total abdominal hysterectomy and salpingo-oophorectomy (TAH BSO or TAH SO)
- with an excised ovary
- pelvic inflammatory disease
- cyst
- tumour
- endometriosis
- ectopic pregnancy
- familial ovarian cancer.

### **3 Specimen dissection and block selection<sup>1</sup>**

Biopsy for sterilisation

- Measure the length and diameter of the tube segment in mm.
- One block of each fallopian tube to confirm the organ and full cross-section. It may be more convenient to take two cross-sections from each to obtain a full face section.

Salpingectomy for sterilisation

- Measure the length of the tube in mm. Because of the natural tapering of the diameter, it is unnecessary (and impossible) to give this dimension accurately in a normal organ. Note the presence of fimbriae and any other signs of previous surgery such as a clip.
- Take one block of each fallopian tube to confirm the organ and full cross-section. It may be more convenient to take two cross-sections from each to obtain a full face section.

Failed sterilisation

- Measure the length of the tube in mm. Because of the natural tapering of the diameter, it is unnecessary (and impossible) to give this dimension accurately in a normal organ. Note the presence of fimbriae and any other signs of previous surgery such as a clip.
- Block the whole tube (levels may be necessary) to identify possible recanalisation.
- Where there is gross distortion it may be necessary to take longitudinal blocks.

- If dissection is difficult because of clips, plastic embedding and sectioning may be necessary.<sup>2</sup>

#### Salpingectomy for other reasons

- Record the maximum diameter in mm if dilated.
- Describe any tumour and refer to the College cancer dataset.<sup>3</sup>
- If grossly normal and excised for other organ pathology, make three transverse cuts to examine and take a block of one cross section.
- It may be difficult to identify the fallopian tube stretched over the surface of an ovarian cyst.
- Pelvic inflammatory disease.<sup>4</sup> Take one or two blocks from the dilated portion of a hydro or pyosalpinx. Include one block of non-dilated tube (usually isthmic end), if present, to identify previous or concomitant chronic inflammation/evidence of pelvic inflammatory disease. Sample adhesions to the ovary or other structures.
- Fallopian tube cysts. Describe the nature (unilocular, multilocular, solid or papillary) and contents (watery, serous, mucoid, gelatinous, bloodstained, or chocolate-like.)
- Take one or more blocks of the wall of tubal or paratubal cysts. Most cysts are small and can be blocked in their entirety in one block. Take one block per 10 mm, to include any solid or papillary areas.
- Familial ovarian cancer. Block the whole of both fallopian tubes, including the fimbriae.<sup>5,6</sup>
- In ectopic pregnancy, sample the dilated portion of the tube or implantation site on the surface of the tube. Also sample from the non-dilated portion (usually the isthmic end) to document pre-existing inflammation or structural abnormality. Separate blood clot may contain products and is also sampled.<sup>7</sup>
- With ovarian cancer resections. The fallopian tube may be the site of origin in disseminated intra-abdominal serous carcinoma. Refer to the College cancer dataset. Take blocks of the whole fallopian tube.<sup>8</sup>

#### 4 Embedding options

- Ensure the wall of the tube is orientated at right angles to the plane of section.

#### 5 Sectioning

- A single haematoxylin and eosin (H&E) stained section, representing a full face of the block, is adequate for the initial microscopic examination.
- Depending on the appearances, levels may be requested at the discretion of the reporting pathologist.

#### 6 Staining

- H&E.

#### For pelvic inflammatory disease

- Gram
- PAS(D) or Grocott for fungi
- Ziehl Neelsen.

## 7 Further investigations

- Not usually necessary for benign disease.

## 8 Report content

### Sterilisation

- Confirm fallopian tube
- Confirm full cross-section seen.

### Failed sterilisation

- Confirm fallopian tube
- Confirm full cross section seen
- Identify/document clip or previous surgery
- Block whole tube (levels may be necessary) to identify possible recanalisation.

### Cysts

- Partially solid, papillary, simple unilocular or complex multilocular
- Lining epithelium (serous, endometrioid, transitional, cuboidal, mucinous, mixed, endometriotic, haemorrhagic granulation tissue).

### Pelvic inflammatory disease

- Identify inflammatory cells in acute or sub-acute inflammation
- Identify plical fusion, plasma cells or simplification of plical folds in chronic inflammation.
- Document fusion of plicae to give 'follicular salpingitis'.
- Identify organisms if possible using morphology and special stains
- usually polymicrobial
  - Neisseria gonorrhoea
  - Anaerobic spp.
  - Actinomyces spp.
  - Oxyurius vermicularis/gregorii
  - Chlamydial infection may be deduced from lymphoid follicle formation
  - Mycobacterium tuberculosis
- xanthomatous inflammation
- malakoplakia
- other organisms may require culture and/or microbiological correlation.

### Familial ovarian cancer<sup>5,6</sup>

- Document dysplasia and microscopic tumours (refer to the College cancer dataset).<sup>3</sup>

### Ectopic pregnancy

- Confirm by identifying trophoblast, villi or fetal parts.
- Exclude hydatidiform disease or malignancy.
- Beware of over identifying hydatidiform disease in early gestation.<sup>7</sup>
- Document any pre-existing inflammation or structural abnormality such as tumour, tubal surgery or diverticulum.

With ovarian cancer resections.

- Document dysplasia and microscopic tumours (refer to the College cancer dataset).<sup>3</sup>

Other

- Salpingitis isthmica nodosa
- Endometriosis
- Epithelial metaplasias.

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## H Products of conception

### 1 Staffing and workload

- Specimens of products of conception can be reported by competent general pathologists (including specialist registrars undertaking competency-based training) in an adequately staffed laboratory.
- Unit hospitals may have a pathologist/s with an interest, or specialist expertise, in gynaecological pathology who should participate in the National Gynaecological EQA Scheme.
- In a specialist hospital, these cases are reported by either a specialist gynaecological pathologist or paediatric pathologist.
- There are three specialist centres for the investigation and follow-up of cases of trophoblastic disease (details under point 8).
- Routine light microscopy (LM).
- Access to immunohistochemistry (IHC).
- Access to flow cytometry (FC) and image ploidy analysis.<sup>1</sup>
- A mechanism should be in place to refer material to one of the specialist centres, following a diagnosis of trophoblastic disease; to document the sending of the material and receipt of a report as an audit trail.

### 2 Specimen submission

- Fresh or fixed material.
- Specimens will include:  
products of conception  
retained products of conception  
medical termination of pregnancy.
- Medical termination of pregnancy (MTOP) results in passage of tissue, not evacuation, and consequently specimens are processed as any other endometrial sample (see section D on Endometrium, above).
- Routine suction termination of pregnancy (STOP) will not usually be submitted for histopathological examination unless the obstetrician has observed an abnormality on the ultrasound scan, or at operation, or there are other reasons to suspect a gestational abnormality. This will be exceptional.
- The specimens should be submitted in an adequate volume of fixative (10% formalin) to ensure proper fixation utilising the usual transport mechanism.
- Products may be received confined to a length of stockinette or in the specimen receptacle of a suction device. Blocks may be taken from fresh specimens, but if the specimen is bulky and fixation is required it may be preferable to open the stockinette prior to overnight fixation.
- The correctly labelled specimen must be accompanied by a correctly completed request form with adequate clinical information, including ultrasound appearance, gestational age, history of previous trophoblastic disease, serum hCG (human Chorionic Gonadotrophin) level and time since delivery in cases of post-partum haemorrhage.
- If audit studies have shown the turnaround time for the laboratory is adequate, an 'urgent' request is not necessary unless there is a suspicion of an ectopic pregnancy

and supportive evidence is needed. In such a case, a contact/bleep number should be included on the request form.

### **3 Specimen dissection and block selection**

- Describe the colour, consistency and weigh or estimate the volume of the specimen.
- Comment on whether spongy placental tissue and/or a gestational sac is present.
- Look for vesicles suggestive of trophoblastic disease. Measure (mm) the maximum vesicle diameter.
- Describe the content of any gestational sac.
- Comment on the presence of fetal parts. If identified, measure the foot length of the fetus.
- The placental tissue is often best identified on the sides or bottom of the length of stockinette or suction device receptacle.
- Glistening membranous tissue may contain the implantation site and should be sampled.
- Do not sample fetal tissue.
- If fat is identified macroscopically, it may have originated from the peritoneal cavity due to uterine perforation, and the clinician must be informed immediately.
- Representative sections to include placental tissue/membranes and the implantation site are taken. One block suffices for confirmation of normal products of conception.
- Samples are wrapped, placed between layers of foam or placed in mesh/wire baskets to prevent loss of tissue or contamination of other specimens.
- Further blocks may be required if the initial section has failed to sample products of conception, to confirm an intrauterine pregnancy or if there is a suspicion of trophoblastic disease or malignancy.

### **4 Embedding options**

- No specific issues.

### **5 Sectioning**

- A single haematoxylin and eosin (H&E) stained section, representing a full face of the block, is adequate for the initial microscopic examination.<sup>2,3</sup>

### **6 Staining**

- H&E.

### **7 Further investigations**

- Immunohistochemical studies will be carried out as appropriate for the H&E appearances.
- Extravillous trophoblast (EVT) can be identified with AE1/3, CAM 5.2, hPL (human Placental Lactogen), hCG.
- p57<sup>KIP2</sup> can help in the diagnosis of hydatidiform disease.<sup>1,4,5</sup>
  - syncytiotrophoblast always negative
  - villous cytotrophoblast negative in complete hydatidiform mole

- villous cytotrophoblast positive in partial hydatidiform mole and hydropic abortion.
- Referral to a specialist centre may be required for an expert opinion, flow cytometry or immunohistochemical studies.

## 8 Report content

- Comment on the presence of villi: normal, sclerotic, oedematous.
- If villi are absent, the presence of extravillous trophoblast (EVT) and the implantation site confirm an intrauterine pregnancy.
- Appearances suggesting an ectopic pregnancy must be communicated urgently with the ward and/or clinician.
- A report of normal tissue will be of:
  - products of conception
  - retained products of conception
  - decidua consistent with recent pregnancy
  - gestational endometrium/decidua suggestive of ectopic pregnancy.
- Subinvolution of placental bed vessels can be the cause for post-partum bleeding.
- Gestational trophoblastic disease (GTD) is reported as:
  - complete hydatidiform mole (CHM)
  - partial hydatidiform mole (PHM)
  - choriocarcinoma (CC)
  - placental site trophoblastic tumour (PSTT)
- The diagnosis of GTD will result in referral of the patient to one of three centres for the investigation and treatment of trophoblastic disease: Ninewells Hospital, Dundee, Charing Cross Hospital, London, or the Royal Hallamshire Hospital, Sheffield.

## 9 Specimen disposal

- A standard operating procedure (SOP) should be place which details the method of sensitive disposal of specimens containing fetal parts.<sup>6</sup>

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