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Pathology: the science behind the cure



BRITISH SOCIETY OF
GASTROENTEROLOGY

Tissue pathways for gastrointestinal and pancreatobiliary pathology

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Introduction

1 Staffing and workload

Gastrointestinal (GI) histopathology is a major element of most histopathology departments' workload. It may be part of a general rota or may be mostly or exclusively reported by specialists. In either circumstance, there must be enough pathologists to provide cover and to conform to The Royal College of Pathologists' (College) guidance on staffing and workload levels.¹

Pathologists reporting GI pathology should participate in the UK national (British Society of Gastroenterology) GI pathology external quality assurance (EQA) scheme or in a local general pathology EQA scheme that includes GI pathology cases. Those whose work consists predominantly of GI pathology should participate in the national GI EQA scheme. If a frozen section or out-of-hours service in GI pathology is offered, this should be provided by those who regularly report GI pathology, and certainly by those whose experience of GI pathology is current or sufficiently recent.²

2 Laboratory facilities

Coloured inks for identifying resection margins should be available. A laboratory whose mucosal biopsy workload is large should be staffed, equipped and managed in a way that maintains prompt throughput. Provision should be made for macroscopic and microscopic photography. Ideally, there should be facilities to process large (wholmount) blocks.

3 Specimen submission

Full details of the patient, clinical consultant, date of procedure and type of specimen should be provided.^{3,4,5} The indication for the surgical/endoscopic/other procedure should be stated. Relevant surgical or endoscopic findings should be supplied, the latter as a description or in the form of the endoscopy report. Details of previous histology should be available, particularly if there is a history of dysplasia or carcinoma. Details of previous treatment are also important.⁵ In some circumstances, interpretation of histology without adequate clinical details is not possible.

Each specimen container should be labelled with patient details and the site of origin of the biopsy or specimen. Formalin should be of adequate volume to cover the specimen entirely and to ensure proper fixation. The specimen should not be disrupted prior to receipt in the histopathology laboratory, unless this has been agreed upon previously.⁶

4 Block selection and record

When sampling a specimen, the site or lesion from which each block is taken should be documented.⁶ Each cassette must have a unique identifying number or letter. A record of the number of pieces of tissue in each cassette is useful, and is particularly important if interpretation might be affected, e.g., lymph nodes. The description should be sufficiently clear that another pathologist can understand the purpose of each block and can identify the site from which it was taken.

5 Dysplasia/neoplasia

- Details of previous diagnoses of dysplasia or neoplasia are useful.^{4,5}
- Columnar (glandular) dysplasia is classified as low grade or high grade.
- Squamous dysplasia is classified as mild, moderate or severe.

- Inflammation and ulceration may cause regenerative epithelial atypia, which can be difficult to distinguish from dysplasia, especially in biopsies. Difficulties are sometimes resolved by examining deeper levels. Immunohistochemistry for p53 and Ki67 is not currently recommended.
- Biopsies that show, or might show, dysplasia are preferably reported by at least two consultants. Interobserver variability for distinguishing low grade dysplasia from non-dysplastic reactive change is higher than for distinguishing high grade from low grade dysplasia.^{7,8}
- The term 'indefinite for dysplasia' may be used if a decision cannot be made as to the presence or absence of dysplasia.^{4,9} Alternatively, the inability to decide can be documented. It may be appropriate to recommend further biopsies.
- Neoplasia should be approached and reported according to the guidelines in the relevant College cancer dataset.¹⁰⁻¹⁴ Neoplasms should be typed, graded and reported according to published guidelines or texts.^{15,16} Staging of resected tumours should follow the UICC (International Union Against Cancer) guidelines.¹⁷

6 Scope of these guidelines

This document is intended as a guide to reasonable practice rather than as a policy statement. It also attempts to provide information that might be useful when dealing with each type of specimen. Where possible, references are given, but it is inevitable that many of the suggestions are based on common UK practice rather than on published evidence, as the latter is often non-existent or sparse. Many laboratories have adopted approaches based on their own experience, evidence, and resources, which may differ from these guidelines but which achieve the same outcome. This document does not aim to change such approaches. In addition, the document is not intended as a replacement for standard textbooks but highlights the principles of handling and reporting non-neoplastic GI and pancreatobiliary histopathology specimens.

A Tissue pathways: gastrointestinal and pancreatic biopsies

A1 General considerations

A1.1 Mucosal biopsy: preparation, dissection and blocks

Fixation

The specimen should be allowed to fix sufficiently before processing. Adequacy of fixation can be estimated by visual inspection if necessary. A biopsy should probably be fixed in formalin for at least six hours and for no more than 3 days, although published evidence for an optimal fixation time is sparse.^{18,19}

Orientation (mucosal *versus* submucosal)

Biopsies may be received free floating in formalin, in which case they will not have been orientated by the endoscopist. Alternatively, biopsies may be received attached to filter paper, cellulose acetate paper or similar, in which case the endoscopist may have attempted to orientate them in terms of mucosal and submucosal aspects. Cellulose acetate strips are suitable for cutting with a microtome, but filter paper is unsuitable.

If mucosal and submucosal aspects of the biopsies can be identified, the biopsies should be orientated as accurately as possible during embedding.⁴

If biopsies are attached in a straight line to a strip that can be embedded on edge, then the entire strip with attached biopsies may be embedded. Assuming that the endoscopist has attempted to place the biopsies submucosal-side down on the strip, this will optimise orientation. If the biopsies are not in a straight line, it may be necessary to remove them from the strip.

Orientation of biopsies from multiple sites (e.g. distal *versus* proximal large bowel)

Biopsies from different parts of the GI tract should be dealt with in such a way that their site of origin is identifiable at microscopy. Possible approaches include multiple specimen pots, cellulose acetate strips, and multi-well cassettes.^{4,20}

1. Biopsies from multiple sites may be received in the same pot. The site of origin of each cannot be determined, unless microscopy distinguishes them (e.g. ileal and colonic mucosa).⁶
2. Biopsies may be in multiple pots, each pot corresponding to a specific site. Each pot should have been labelled with a site of origin. Biopsies from each site can then be placed in a separate cassette (or in a separate well in a multiwell cassette), identified by a unique number or letter. Deduction of the site of origin of each biopsy from the endoscopy report or from other sources is unreliable.
3. Biopsies from multiple sites may have been arranged sequentially on a cellulose acetate strip (or similar). The endoscopist should have marked the strip to allow identification of the proximal/distal end. The meaning of this mark must be agreed in advance. This approach may fail as a result of detachment of biopsies from the strip. It also limits the number of biopsies that can be taken at endoscopy.
4. Biopsies may be received in multi-well cassettes. The well corresponding to each biopsy site must be identified in advance. Several biopsies can be placed in each well. Careful matching of the well contents, embedded tissue and final slide is required to avoid confusion.

5. Precassetted biopsies are sometimes received.

The use of a separate pot for each biopsy site or of multiwelled cassettes will allow accurate mapping of the distribution of changes and allow multiple biopsies to be taken from each site. Local circumstances will influence the approach, but should not allow quality of reporting to be compromised.

Embedding

Embed all fragments or cores in their entirety. Larger (e.g. full thickness) biopsies require orientation and may need slicing before embedding. A method to avoid loss of small biopsy fragments should be used, e.g. insertion of foam pads into the cassette or wrapping of biopsies in a suitable material. It may be better to 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. Embedding fragments in a line facilitates histological assessment.²¹

A1.2 Mucosal biopsy: macroscopic description

Record the number of fragments.⁴ The term 'multiple' should ideally be restricted to cases where there are too many to count or where a precise count is difficult. Record the size of each fragment, or a range of sizes, in millimetres. Record attachment of biopsies to filter paper, cellulose acetate or similar. Describe any other material, foreign bodies, etc.

Discrepancies between the macroscopic description and the number of biopsies in the slide raise the possibility of uncut tissue in the block. Discrepancies between the number of biopsies recorded by the endoscopist and the number received in the laboratory are also worth noting. However, either type of discrepancy could also reflect disruption of biopsies before or during processing.

A1.3 Mucosal biopsy: sections and stains

Minimum stains

Haematoxylin and eosin (H&E). Many laboratories do step sections routinely at two or three levels (e.g. 75 microns apart). We and the authors of several other guidelines favour this approach.^{4,21} However, some laboratories request levels when required, rather than doing them routinely.

Other stains

- Additional deeper levels may be useful, e.g. for orientation, the distinction of reactive epithelial changes from dysplasia, and confirmation of invasive carcinoma.
- If granulomas are present, PAS and Ziehl Neelsen stains may be useful (unless there is an obvious cause).
- In HIV cases with inflamed mucosa, stains for fungi, mycobacteria and protozoa, e.g. PAS, Ziehl Neelsen^{4,22} and Giemsa, are advisable. There is some evidence that these stains provide little additional information, even when inflammation is present, but published studies are few.²³
- A Congo Red stain examined under polarised light helps to confirm or exclude amyloid if this is suspected by the clinician or the pathologist. If amyloid is confirmed, further special stains and immunohistochemistry may be appropriate.²⁴

Immunohistochemistry

Immunohistochemistry for cytomegalovirus (CMV) and/or herpes simplex virus (HSV) is worth considering if these are suspected or if there is ulceration, especially in immunosuppressed patients, e.g. HIV, severe chronic ulcerative colitis, etc.²⁵ However, it is noted that some evidence conflicts with this advice.²³

Additional sections

It may be appropriate to cut additional sections at initial processing if there is a likelihood that these will be required.

A1.4 Mucosal biopsy: report and microscopic description

General

- The adequacy and appropriateness of the sample should be noted, if relevant.
- A separate description should be composed for each separately submitted set of biopsies, unless they all show the same or similar features.
- Many changes can only be interpreted in the light of clinical and endoscopic findings. If adequate details are not provided, this should be noted. Clinicopathological meetings help refine interpretation.

A2 Oesophageal biopsy: additional comments

A2.1 Clinical

Biopsies for diagnosis or follow-up of Barrett's (columnar lined) oesophagus (CLO) should be accompanied by full details of endoscopic findings, the exact site of origin of each set of biopsies, and any history of dysplasia.

A2.2 Sections and stains

Additional stains

Special stains for mucins may be useful, i.e., PAS +/-Diastase (PAS +/- D) and Alcian Blue (AB), often in the form of an ABPAS or ABPASD stain.²⁷ Alcian blue positivity helps to confirm goblet cell (intestinal) metaplasia (although not all Alcian Blue positive cells are goblet cells).²⁶ PAS staining also helps to identify fungi.

Some guidelines recommend PAS and AB if columnar mucosa is seen and other authors favour routine special stains.^{4,27} However, opinions and evidence conflict regarding the value of routine additional stains.^{27,28,29,30} Currently, the approach varies within the UK and there is little evidence to support either approach.^{27,28}

Other special stains

A special stain for Helicobacter may be useful if inflamed gastric-type columnar mucosa is included, but please see preceding paragraph and section A3.1 (additional stains).

A2.3 Report and microscopic description

Indications for biopsy

- Assessment of oesophagitis and its aetiology (e.g. reflux, infection).
- Diagnosis and assessment of Barrett's (columnar lined) oesophagus.
- Exclusion of dysplasia or neoplasia.

Report

If squamous and columnar mucosae are present, it may be helpful to report the appearances of both. It is useful to record severity of inflammation, presence and type of metaplastic epithelium, micro-organisms (particularly fungi) and dysplasia or neoplasia.

- The histology of eosinophilic oesophagitis overlaps with that of reflux oesophagitis. The diagnosis might be considered if numerous eosinophils are seen in the appropriate clinical setting, ideally in a biopsy from the mid-oesophagus. A threshold of >15 eosinophils in at least one high power field [hpf] has been suggested. Other features which lend support include superficial eosinophilic layering / aggregates and eosinophilic microabscesses.^{31,32}
- Diagnosis of intestinal metaplasia requires the presence of goblet cells. There is no need to subclassify intestinal metaplasia as complete or incomplete.
- Barrett's (columnar lined) oesophagus: the British Society of Gastroenterology (BSG) guidelines are recommended.³³

A3 Gastric biopsy: additional comments

A3.1 Sections and stains

Additional stains

A special stain for *Helicobacter pylori*, e.g. Giemsa, Cresyl Fast violet (CFV), should be available. The updated Sydney classification system guidelines suggest that, as a minimum, this stain should be done when there is inflammation in the absence of identifiable *Helicobacter*-like organisms.²² Some authors favour routine stains for *Helicobacter*.²⁷ However, publications conflict regarding the diagnostic value, clinical value and cost effectiveness of performing these stains routinely.^{20,27,28,29,30} Immunohistochemistry for *Helicobacter* is an alternative and may help detect minute numbers of organisms but is expensive and is not done routinely.²⁷

It is recommended, as a minimum, that a *Helicobacter* stain is requested if characteristic inflammation is seen, no *Helicobacter* are apparent, and no clinical test (e.g. CLO) has been performed.^{22,27,29} Currently, some UK laboratories do *Helicobacter* stains routinely and others are variably selective.²⁷

Other stains

Special stains for mucins may help to identify intestinal metaplasia. PAS+/- diastase and Alcian Blue are most often used, i.e. ABPAS or ABDPAS.^{22,27} Routine mucin stains are done in some laboratories but there is some evidence that this approach is not effective.^{27,30}

A3.2 Report and microscopic description

Indications for biopsy

- Diagnosis and assessment of gastritis / ulceration.
- Exclusion of dysplasia/neoplasia.

Report: general comments

- The number of body/fundus-type and antrum/cardia-type biopsies should be noted. Biopsies from different sites should be described separately, unless they are the same or very similar.
- Record chronic inflammation, activity, intestinal metaplasia, atrophy, dysplasia, *Helicobacter* (updated Sydney classification).²²

Report: most common histological categories of gastritis

- *Helicobacter*-associated chronic gastritis.
- Reactive (chemical) gastropathy / gastritis.

- Lymphocytic gastritis (figures vary, e.g. >25 lymphocytes per 100 epithelial cells).^{24,34}
- ‘Granulomatous’ gastritis (exclude Crohn’s disease, Helicobacter, mycobacterial infection, foreign material, crypt rupture, sarcoidosis).^{35,36}

A4 Duodenal/jejunal biopsy: additional comments

A4.1 Sections and stains

Deeper levels may be very useful if villous architecture is difficult to assess in a poorly orientated or small biopsy. Identification of parasites may be assisted by a Giemsa stain.

Immunohistochemistry and Polymerase chain reaction (PCR)

Immunohistochemistry and PCR-based studies may be appropriate in some biopsies with features of coeliac disease, particularly if there is a suspicion of T-cell neoplasia.³⁷

A4.2 Report and microscopic description

Indications for biopsy

- Exclusion of an enteropathy, particularly coeliac disease.
- Assessment of duodenitis or ulceration.
- Exclusion of dysplasia or of primary/secondary neoplasia.

Report

- The number of biopsies should be documented. Multiple biopsies are advisable, and some guidelines recommend at least four biopsies for exclusion of an enteropathy.^{29,38}
- If the biopsies are traumatised or poorly processed to the extent that villous architecture cannot be assessed reliably, this fact should be recorded.
- Note features of an enteropathy, e.g. villous atrophy, increased intraepithelial lymphocytes, distribution of intraepithelial lymphocytes, surface epithelial changes.³⁷
- Giardia and other infections should be sought actively, especially in immunosuppressed patients (e.g. hypogammaglobulinaemia). Giardia are easily missed if they are sparse.³⁹

A5 Ileal biopsy: additional comments

A5.1 Report and microscopic description

Indications for biopsy

- Confirmation that the ileum has been reached. Biopsies are taken for this reason, despite the existence of guidelines stating that they are of no value.²⁹
- Inflammatory bowel disease (IBD) assessment.³
- Characterisation of other inflammatory conditions.
- Exclusion of neoplasia (e.g., abnormal CT appearances, abnormal endoscopy).

Report

Note that native lymphoid tissue may appear polypoid at endoscopy and can be prominent histologically. A diagnosis of ileitis cannot be made easily in the absence of acute inflammation or of other unequivocally abnormal features.⁴⁰

A6 Colorectal biopsy: additional comments

A6.1 Report and microscopic description

Indications for biopsy

- Assessment of altered bowel habit/rectal bleeding.
- Follow up of IBD.
- Exclusion of amyloidosis (rectal biopsy).
- Exclusion or follow up of dysplasia/neoplasia, including Bowel Cancer Screening Programme (BCSP) cases.⁴¹

Report: general comments

For inflammatory conditions, the distribution of changes between biopsies from the same site, and between biopsies from separate sites, should be recorded.³ Ileal and colonic biopsies may be present in the same pot and should be described separately if possible, although their distinction can be very difficult if the mucosa is inflamed.

Assessment: inflammation

Decide whether the mucosa is normal or abnormal. If inflamed, try to categorise as infective type, IBD type or another type. Terms such as 'non-specific chronic colitis/non-specific colitis' should be avoided, especially as a conclusion or diagnosis.^{42,45}

Inflammatory bowel disease

- BSG guidelines are recommended.⁴² Other guidelines are also available.^{3,20,43,44}
- In an initial biopsy, the probability of IBD should be stated. If IBD is definite or probable, it is useful to record the probability that it is ulcerative colitis or Crohn's disease. If neither can be preferred, this should be stated.
- The term 'indeterminate colitis' is not used for biopsy reporting.^{3,43,44,46} The terms 'IBD, type unclassified' or 'IBD, type unknown' can be used if need be.^{24,43,44}
- There is no widely used grading scheme for histological inflammation or activity in IBD but a description of the severity of activity may be helpful.

Comments on other forms of colitis

- Classification as 'collagenous colitis' or 'lymphocytic colitis' is preferable to the term 'microscopic colitis', if this is possible.⁴⁵
- Radiation colitis: an appropriate clinical history is required for interpretation.
- Diversion colitis, diverticular colitis, and graft *versus* host disease: these cannot be diagnosed unless clinical details are forthcoming. They may mimic IBD.⁴⁷
- NSAID-induced colitis and amoebic colitis are worth considering if features do not conform to a recognised pattern.⁴⁷
- Ischaemia and mucosal prolapse should also be considered.

Polyp biopsies/dysplasia/neoplasia

- Polyp biopsies are most often from hyperplastic polyps or adenomas.
- Native lymphoid tissue or mucosal folds may mimic a polyp endoscopically.

- Deeper levels are advised if initial slides show no features of a polyp.
- In the setting of IBD, it is difficult to distinguish an adenoma from IBD-related dysplasia or dysplasia-associated lesion/mass (DALM) using histology alone.²⁴

Hirschsprung's disease

- These specimens are ideally reported in specialist units which receive them on a regular basis. A deep mucosal biopsy should be taken, at least 2 cm above the pectinate line. Fresh tissue may be required. Part or all of the sample can be snap frozen.
- Multiple serial H&E sections from the submucosal aspect towards the mucosal aspect should be examined. Many experts recommend at least 50 sections.
- Guidelines on diagnosis differ, but Hirschsprung's disease (HD) is usually excluded if ganglion cells are seen. HD is very likely if there are no ganglion cells in 50 serial sections. HD is usually diagnosable if, in addition to the absence of ganglion cells, there are abnormal nerve trunks and / or typical cholinergic fibres passing through the muscularis mucosae (acetylcholinesterase histochemistry on frozen tissue / PGP 9.5 immunohistochemistry).⁴⁸

A7 Anal biopsy: additional comments

A7.1 Report and microscopic description

Indications for biopsy

- Diagnosis and assessment of anal intraepithelial neoplasia, wart virus change, and malignancy.

General

- 'Mapping' biopsies from multiple anal and perianal sites may be received. The appearances of the biopsies from each site should be reported separately, unless they are the same.
- The description of squamous epithelium should include a record of wart virus change and dysplasia (the latter classified as AIN 1, AIN 2, or AIN 3).

A8 Ileoanal pouch biopsy: additional comments

A8.1 Report and microscopic description

Indications for biopsy

- Determination of the type of mucosa.
- Assessment of inflammation/pouchitis.
- Exclusion of other inflammatory conditions.
- Exclusion of dysplasia (unusual).
- Prepouch ileal biopsies may also be taken in this setting.

Pouchitis

Adaptive changes, e.g. villous atrophy and inflammation, may occur in a pouch. Diagnosis of 'pouchitis' depends on a combination of clinical, endoscopic and histological findings. Pouch inflammatory scores exist, are required for diagnosis by some centres, and may also

serve as an *aide memoire* to the pathologist.^{24,49,50,51} Accordingly, familiarity with one of these scoring schemes is encouraged. Any comments on the presence of IBD should be cautious. Crohn's disease-like changes, in particular, have other possible causes in this setting.^{49,50}

A9 Ampulla of Vater biopsy: additional comments

A9.1 Report and microscopic description

Indications for biopsy

- Exclusion of neoplasia.
- Characterisation of focal lesions.

Report

The term 'ampulla' may refer to the true ampulla and/or the periampullary duodenal mucosa.¹⁶ There are slight differences between their histology. A report of dysplasia or carcinoma in this area may have profound implications. Histology should be interpreted in the light of clinical/imaging findings and past history. Atypical epithelial changes are not uncommon if there is ulceration, inflammation or a history of intervention. Inflammatory-type polyps are not uncommon and can mimic neoplasia.^{52,53} Double reporting or referral to a specialist pathologist may be appropriate.

A10 Pancreatic biopsy: additional comments

A10.1 Macroscopic description of needle core biopsies: additional considerations

Record the length of each core in millimetres.

A10.2 Sections and stains from needle core biopsies: additional considerations

Production of additional unstained sections at initial processing may be particularly useful for needle core biopsies.

A10.3 Clinical

Pancreatic biopsies should ideally be reported in specialist centres with access to appropriate clinical, imaging and histopathological expertise. Details of the indication(s) for biopsy, imaging, operative findings and previous histology are important, especially if the biopsy was taken to exclude or characterise neoplasia.

A10.4 Sections and stains

Immunohistochemistry

IgG4 may be useful if autoimmune pancreatitis is suspected.⁵⁴ It may be unavailable outside specialist centres. Various stains help characterise pancreatic tumours.^{15,16}

A10.5 Report and microscopic description

Indications for biopsy

- Diagnosis of neoplasia.
- Characterisation of suspected/known neoplasia.

Report

- Chronic pancreatitis can be difficult to distinguish from carcinoma, especially in frozen sections.^{16,55,56,57} Double reporting may be appropriate.
- Autoimmune pancreatitis may mimic carcinoma clinically and radiologically.⁵⁸
- A cautious approach to the interpretation of a needle core biopsy is advised. Unusual tumours and difficult cases are best diagnosed in conjunction with the imaging findings and after discussion at an appropriate multidisciplinary meeting, preferably by a histopathologist who is familiar with pancreatic pathology.⁵⁸

B Tissue pathways: small gastrointestinal resection specimens

B1 Appendicectomy

B1.1 Preparation, dissection and blocks

Sampling

- Serially slice the appendix transversely and bisect the tip longitudinally.²¹
- Sample the surgical margin (base). This section should be identifiable microscopically (e.g. coloured ink/a nick in the relevant section/a section of a different shape/use of a separate cassette, etc).²¹
- Other blocks should include at least one half of the tip and at least one more transverse section, plus representative blocks from focal lesions or abnormal areas.²¹
- Sample the entire appendix if neoplasia is suspected (see below).
- Sample the entire appendix before reporting that it is not inflamed.²⁴

B1.2 Specimen description

Dimensions (millimetres)

Length and diameter of appendix.²¹

Appearances

- External surface: perforation, peritonitis, congestion, abscess, mucin.
- Cut surface: luminal contents, mucin, diverticula, nodules, possible carcinoid (especially at the tip).

B1.3 Report and microscopic description

Indication

- Confirmation or exclusion of acute appendicitis.
- Exclusion of neoplasia.

Report

- Appendicitis: transmural acute inflammation is usually required for diagnosis. Mucosal inflammation (without ulceration) is not universally regarded as sufficient.⁵⁹
- Peritonitis without transmural inflammation may reflect extra-appendiceal pathology.²¹ In this situation, the entire appendix should be sampled to exclude appendicitis.²⁴
- The possibility of Crohn's disease may be raised, e.g. granulomas and transmural chronic inflammation. However, these changes may occur in appendicitis, particularly if treatment has been delayed.^{24,60,61} Ulcerative colitis may also involve the appendix, even in the absence of significant caecal involvement.^{3,24,62}
- The boundaries between hyperplastic polyps, other serrated lesions, and adenomas are currently poorly defined.⁶³ If a large / atypical serrated lesion, dysplasia, or any feature suggestive of carcinoma are seen, sampling of the entire appendix is advised.²⁴ Hyperplastic lesions and adenomas are associated with an increased risk of neoplasia elsewhere in the large bowel, particularly on the right side.^{24,64}

- Record the status of the base (resection margin) if dysplasia or malignancy are present. Report malignancy using appropriate guidelines and texts.^{13,15}

B2 Polyps (gastric and intestinal)

B2.1 Preparation, dissection and blocks

Opening and fixation

Slicing prior to fixation may be required if the polyp is large. This should not interfere with subsequent attempts to orientate the specimen.

Sampling

- If a base (resection margin) can be identified, it should be inked.²¹
- All material should be submitted.
- Small fragments or polyps (e.g., < 5 mm in maximum dimension) can be embedded whole.
- A larger polyp (e.g., > 5 mm in diameter) should be bisected or serially sliced. If the polyp can be orientated, slicing should be in the axial plane. The stalk should be preserved and should be present with the body of the polyp in at least one block. Further details are available in recent guidelines.⁴¹
- If multiple polyps or fragments are received in a single container, identification of separate polyps may be impossible.

B2.2 Macroscopic description

Nature of specimen

Polypectomy/polypoid fragments/nondescript fragments.

Dimensions (millimetres)

Maximum dimension of polyp. Length of stalk and/or diameter of base.

Appearances

External surface: ulcerated/smooth/lobulated/villous/fronded, etc.

Cut surface: cysts, mucus, haemorrhage, necrosis.

B2.3 Sections and stains

Deeper levels

Routine deeper levels are often advised.²¹ Deeper levels help distinguish invasion from gland displacement ('pseudoinvasion').

Immunohistochemistry

May help distinction between various types of non-epithelial polyp, e.g. inflammatory fibroid polyp, neuroma, gastrointestinal stromal tumour.²⁶

B2.4 Report and microscopic description

Indications for polypectomy

- Management of symptoms.
- Characterisation of polyp.

- Documentation of dysplasia and malignancy.
- Bowel cancer screening programme.⁴¹

Adenoma

- Architecture (tubular/villous/tubulovillous). A tubulovillous adenoma should be at least 20% villous. A villous adenoma should be at least 80% villous.^{15,41}
- Degree of dysplasia: low grade or high grade, based on architectural changes supplemented by cytological changes.⁴¹ Refer to 'adenoma with low/high grade dysplasia' rather than 'low grade adenoma/high grade adenoma'.⁴¹
- Record completeness of excision, if possible.
- If carcinoma is present, record precise distance from margin, vascular invasion and differentiation, in particular. Refer to the RCPATH cancer datasets.^{12,13,14}
- Misplaced glands/'pseudoinvasion' can mimic carcinoma. Deeper levels and consultation may help. Occasionally there is no 'correct' answer.⁶⁵

Other polyps

- Inflammatory-type polyps may occur in apparently non-inflamed mucosa.
- Juvenile polyp: expanded lamina propria, variably dilated crypts, often inflamed or ulcerated.⁴⁷ May be difficult to distinguish from an inflammatory polyp.
- Peutz-Jegher polyp: arborising smooth muscle fibres.⁴⁷ May mimic other hamartomatous polyps and mucosal prolapse.⁶⁶

B3 Anal polyps

B3.1 Preparation, dissection and blocks

Sampling

- All tissue from polyps should be embedded if there is any possibility of dysplasia / adenoma. Otherwise, representative blocks may be sufficient.²¹
- Polyps or fragments > 5 mm should be sliced, perpendicular to the mucosal/skin surface.
- Fragments < 5 mm in maximum dimension may be submitted whole.

B3.2 Specimen description

Specimen type

Polypectomy/polypoid fragments/nondescript fragments.

Dimensions (millimetres)

Maximum dimension of each piece, or range of dimensions.

Appearances

Presence of mucosa/skin. Focal changes, e.g. ulceration, haemorrhage, thrombosis.

B3.3 Report and microscopic description

Indications for procedure

- Symptom management.
- Exclusion of dysplasia/neoplasia.

Report

- Haemorrhoids: vascular ectasia, congestion, haemorrhage, thrombosis.
- Mucosal prolapse: crypt angulation, lamina propria smooth muscle fibres, fibrosis, erosion. Can mimic adenocarcinoma.²⁴

B4 Other anal lesions (e.g. fissure, fistula, sinus)

B4.1 Preparation, dissection and blocks

Sampling

- A resection specimen should be sliced in the plane most likely to demonstrate the lesion, and representative blocks of any track/abscess or other focal changes should be taken.²¹
- One block should include skin and any possible opening (punctum), if present.²¹
- One block should include the deep margin and the lesion.
- If multiple fragments are received, representative pieces can be sampled.

B4.2 Specimen description

Dimensions (millimetres)

Specimen dimensions, skin dimensions.

Appearances

Record the presence and appearance of skin/mucosa. Describe tracks and state of adjacent tissue. Note abscesses and the presence of dye.

Report and microscopic description

- Exclude identifiable causes, e.g. Crohn's disease, tuberculosis, pilonidal sinus, hidradenitis, and neoplasia.^{21,24}
- Describe skin/squamous mucosa.
- Note granulomas (which may not be specific for a cause in this setting).
- Describe track/abscess, including contents (e.g. hair shafts).

B5 Doughnut

B5.1 Preparation, dissection and blocks

Sampling

- In some cases, sampling may not be necessary. Distance from the lesion and local preferences will influence the decision to sample or not.²⁹

- If a doughnut is sampled, sutures should be removed and all non-stapled tissue sampled.

B5.2 Specimen description

Dimensions (millimetres)

Approximate diameter and length.

Appearances

Presence of staples/sutures. Focal changes.

B5.3 Report and microscopic description

Indications

A doughnut is usually accompanied by a resection specimen and usually represents the true resection margin. It may represent the entire margin or a part of it (e.g. stomach).

Report

Involvement of doughnut by disease.

B6 Ileostomy/colostomy

B6.1 Preparation, dissection and blocks

Opening and fixation

The stoma and bowel may require opening and further fixation.

Sampling/blocks

Ensure that sections include the mucocutaneous junction and the margin(s). Further representative sections as appropriate.

B6.2 Specimen description

Dimensions (millimetres)

Record the length of skin and of bowel.

Specimen type and appearances

Type of stoma. Note focal lesions.

B6.3 Report and microscopic description

Indications for procedure

- Symptom management.
- Loss of function.
- Inflammatory changes.
- Re-anastomosis.

Report

- The presence of skin should be confirmed.
- Note that ulceration and inflammation are frequently seen near a stoma.
- Features suggestive of IBD, e.g. granulomas and chronic inflammation, should be interpreted cautiously in this setting.

B7 Omentum

B7.1 Preparation, dissection and blocks

Sampling

Serially slice if large. Sample any focal changes. Take representative sections.

B7.2 Specimen description

Specimen type

Omentectomy/fragments of adipose tissue.

Dimensions (millimetres)

Omentum: measure in three dimensions.

Fragments: measure maximum size of each, or a range of sizes.

Appearances

Note nodules/necrotic foci/abscesses/cysts. Record number and size.²¹

B7.3 Report and microscopic description

Indications

- To characterise focal lesions or tumour.
- For technical reasons.
- To reduce tumour burden.

Report

Malignancy in the omentum is usually carcinoma. Elucidation of the site of origin may be assisted by immunohistochemistry. Exclude other causes, e.g. tuberculosis.

C Tissue pathways: large gastrointestinal resection specimens

Preparation, dissection and blocks

Opening and fixation

- A large resection specimen should be received unopened and, ideally, unfixed, so that it can be orientated easily.^{4,5,6} If it cannot be received fresh it should be placed in a sufficient volume of formalin (e.g. 10 times its volume) and sent to the pathology laboratory as soon as possible.⁵
- Ideally, the oesophagus is opened along the anterior border, the stomach along the greater curvature, and the intestine along the antimesenteric border,⁵ all longitudinally, unless there is a focal lesion that would be disrupted as a result.
- Wash out luminal contents gently with tepid or cold water.⁵ Excess washing or hot water may damage the mucosa.
- If the lumen is narrowed or the wall is thickened, it may be easier to make serial transverse slices before further fixation, especially in the intestine. If this is done, it is preferable to leave the specimen intact while it is fixing.
- Serial transverse slicing (before or after fixation) may facilitate the examination of focal abnormalities of the wall, e.g. diverticula, endometriosis.²¹
- Infarcted tissue may be friable and thin-walled and unsuitable for opening.
- Ink any relevant margins if there is a possibility of neoplasia. It should be noted that ink may spread into tissue, particularly if the specimen is not dry. Reliance on ink to identify margins should take account of this possibility. Inks made up in gelatine may be more reliable.
- The specimen should be pinned to a corkboard or stabilised in another way²¹ and fixed in a volume of formalin that is at least sufficient to cover it.
- Fixation for 48 hours after opening is generally recommended, but adequacy of fixation can be estimated fairly reliably by visual inspection.^{5,21}
- Photographs may be useful, particularly for inflammatory bowel disease or for later discussion at meetings.^{5,21} Routine photography has been recommended by some authors, but is not widely practised.^{4,5,6} Photographs are often required in cases of trauma, but this requirement may vary within the UK. Non-digital photographs cannot be manipulated later and may be preferable, if this is feasible.
- Ideally, the pathologist responsible for the macroscopic description and processing should also report the histology.⁵

Sections and stains

Deeper levels/trim

May be useful if the slide appears not to represent full face of block.

Special stains/immunohistochemistry

Please refer to section A1.3.

C1 Oesophagectomy/gastrectomy for non-neoplastic disease

C1.1 Preparation, dissection and blocks

Sampling: margins

- Proximal and distal resection margins: these can be sampled parallel or perpendicular to the margin, depending on the site and nature of the lesion. Perpendicular blocks allow the distance from the lesion to be determined. There is often no published evidence to support sampling of the margins of resection specimens.
- If sutures are present at the margin, they should be removed before sampling.
- If staples are present along the margin, the stapled tissue should be detached. The stapled tissue cannot be sampled properly.

Sampling: lesions

Representative samples of focal lesions, e.g. ulcer, abscess, fistula. More blocks should be taken from any suspicious lesion. At least one block should show the relationship with the circumferential margin/serosal surface if this might be relevant. Longitudinal blocks may help show the relationship with oesophagus/stomach proximal to and distal to the lesion. If no lesion is seen, take at least two random blocks from the specimen.

Sampling: adherent organs

Sample to show any connection, e.g. fistula, diverticulum. A large (wholmount) block may be appropriate and may help to show the anatomical relationships more clearly if this is relevant. It may be appropriate to sample the resection margins of any adherent organ.

Sampling: lymph nodes

Take representative lymph nodes.²¹ If neoplasia is suspected, retrieve all regional nodes. A bisected or serially sliced node should not share a cassette with another node if neoplasia is suspected. The number of nodes and pieces in each cassette should be recorded.

C1.2 Specimen description

Specimen type

Oesophagectomy/total gastrectomy/distal gastrectomy, etc.

Dimensions of specimen (millimetres)

Lengths of oesophagus, greater curve of stomach, lesser curve of stomach and duodenum.⁴ Maximum diameters or range of diameters, if appropriate. Maximum dimension of attached fat.

External surface

- Diffuse changes, e.g. peritonitis, congestion: describe extent and appearance.
- Perforations/defects in wall: record number, site, size, and distance from nearer margin. Consider the possibility that the defects are artefactual or iatrogenic.
- Focal lesions, e.g. stricture, haemorrhage, puckering: record site, size and distance from nearest margin.

Opened stomach/oesophagus/duodenum

- Focal lesions, e.g. ulcer, abscess, stricture, polyp, diverticula and tumour: record appearance, site, size, and, if relevant, relationship with serosal surface/ margins.^{4,21}

- Record appearance of oesophageal, gastric and duodenal mucosa.

C1.3 Report and microscopic description

Indications for surgery

These include stricture, obesity, peptic ulceration, abscess, trauma and perforation.

Report

- Record appearances of oesophagus, stomach and duodenum.
- Note ulceration, inflammation, abscess, fibrosis, granulomas, foreign bodies, etc.
- Describe polyps.
- Record lymph node histology.
- A resection performed for cancer may show no macroscopic tumour but should nevertheless be treated as a cancer resection specimen.^{11,12}

C2 Intestinal resections: general considerations

C2.1 Preparation, dissection and blocks

Sampling: margins

- Proximal and distal resection margins: can be sampled parallel or perpendicular to the margin, depending on the site and type of the lesion. Perpendicular blocks allow the distance from the lesion to be determined. Mesenteric margins may be relevant in some cases.
- In some circumstances, there is no evidence that sampling of margins is of value.²⁹ In other situations (e.g. Crohn's disease) the evidence conflicts.^{5,67,68} However, pathologists may sample margins for various reasons, including clinical demands.²¹
- If sutures are present at the margin, they should be removed before sampling.
- If staples are present along the margin, the stapled tissue should be detached. The stapled tissue cannot be sampled properly.
- Sometimes the proximal and distal margins are attached to one another on receipt, in which case they should be detached carefully from one another.

Sampling: lesions

- In general it is convenient to sample sequentially (i.e. from proximal to distal⁵ or distal to proximal). A careful block record is advised.
- Longitudinal blocks (perpendicular to mucosal folds) are usually preferable to transverse.²¹
- Sample focal lesions, e.g. infarcts, perforations, strictures and abscesses, according to their size and number.²¹
- Diffuse abnormalities, e.g. erythema, loss of folds and inflammatory polyposis, are ideally sampled at intervals of 100 mm or less.²¹
- If no macroscopic lesion is present, at least two blocks are advised, depending on specimen size and indication. If there is a risk of dysplasia, e.g. IBD, and no macroscopic lesion is seen, samples at intervals of 100 mm or less are advised.^{5,21}
- Samples of macroscopically normal bowel may be informative, e.g. Crohn's disease.²¹

- Blocks of the junction between normal and abnormal bowel may be helpful, e.g. ulcerated mucosa.²¹
- Mucosal nodules, polyps or irregular areas that might represent dysplasia should be thoroughly sampled, especially if the risk is high, e.g. in IBD.²¹
- Sampling should demonstrate the deepest extent of macroscopic changes and the relationship of a lesion with the serosal surface and any nearby margins, if these are likely to be relevant.

Sampling: adherent organs

Sample to show any connection, e.g. fistula, diverticulum. A large (wholmount) block may be useful if a clearer picture of complex anatomical relationships is needed, e.g., if there are fistulas. Sampling of the resection margins of adherent organs may be appropriate.

Sampling: lymph nodes

Representative lymph nodes are advised,²¹ as they may show pathological changes which are absent from, or less obvious in, the alimentary tract.²¹ If neoplasia is suspected, retrieve all regional nodes.¹⁴ In general, a bisected or serially sliced node should not share a cassette with another node, especially if neoplasia is suspected. The number of nodes and pieces in each cassette should be recorded.

Sampling: appendix and ileocaecal junction

The tip and body of the appendix should be sampled. A block of the ileocaecal junction may be useful, particularly in cases of inflammatory bowel disease.

Sampling: mesentery

It may be useful to take a block of mesentery, in a plane likely to demonstrate blood vessels. This is particularly useful in cases of ischaemia or suspected ischaemia.²¹

C2.2 Macroscopic description

Specimen type

Small bowel resection/right hemicolectomy/subtotal colectomy/total colectomy/sigmoid colectomy/anterior resection, etc.²¹

Dimensions of specimen (millimetres)

Length of ileum, appendix, colon, rectum and anal canal. Maximum diameter or range of diameters, if appropriate. Site of peritoneal reflection (if present).

Bowel: external surface

- Perforations/defects in wall: record number, location, size and distance from margin. Consider the possibility that these are artefactual/iatrogenic.
- Other focal serosal changes, e.g. puckering, adhesions and strictures: record their appearance, size, and location.
- Note fat wrapping, exudate, congestion and pneumatosis (thin walled cysts or bubbles).²⁴
- Look for evidence of trauma, e.g. perforation. A photograph may be required for legal cases.
- Note adhesions to bowel or to other organs.
- Note Meckel's diverticulum. This is usually located on the antimesenteric border.⁵⁹

- Record presence of any staples.

Opened bowel

- Note luminal contents, e.g. blood, foreign material.
- Note diffuse mucosal changes, e.g. erythema, cobblestoning, loss of mucosal folds, pseudomembranes. Record appearance, extent and relationship with nearer margin.
- Note evidence of trauma, e.g. perforation, foreign object, and take photograph again if appropriate.
- Focal mucosal lesions, e.g. nodules, ulcers, haemorrhage, polyps: record number, size, appearance, distance from nearer margin and the state of the adjacent wall/circumferential margin/serosal surface.²¹
- Stricture, fibrosis, diaphragms: number, location, length, degree of narrowing of lumen, distance from nearer margin.
- Diverticula: record approximate number, perforation, abscess.²¹
- Ischaemia: note the length of the affected segment(s) and distance from resection margins. Seek possible underlying lesions, e.g. adhesion, diverticular disease, tumour.
- Obstructive colitis occurs at a variable distance proximal to an obstructing lesion.^{17,26} The latter may remain *in situ* in the patient.
- Volvulus: has usually already been corrected surgically. Signs of ischaemia may be seen.²¹
- Diversion proctocolitis: may show diffuse mucosal erythema, haemorrhage, nodularity, granularity and flattening. A history is needed.^{69,70}
- Fistula/abscess: record location and relationship with external surface/attached organ.
- Appendix: describe external and cut surfaces, or appendix stump.
- Attached organs: describe appearance, relationship with bowel and presence of fistula, diverticulum, abscess or tumour.
- Mesentery: note haemorrhage, fat necrosis, cystic change, tumour, etc.

C2.3 Report and microscopic description

Proximal and distal margins

Record all abnormalities at margins (if sampled), particularly ischaemia. If there is an abnormality close to a margin, the approximate distance from the margin should be recorded.

Lymph nodes

Record histology, especially specific features such as granulomas.

Appendix

Describe histology, including involvement by IBD and incidental lesions.

Mesenteric vessels

Note thrombosis, vasculitis, atheroma, abnormalities of wall, etc.

Diverticula

Confirm diverticula. Record complications, e.g. peridiverticular fibrosis, abscess, perforation. Crohn's-like changes can occur. Note diverticular colitis, which may mimic IBD (especially ulcerative colitis).⁷¹

Meckel's diverticulum

Describe lining: small intestinal/gastric/pancreatic, etc.^{21,26} Note complications, e.g. ulceration.

Volvulus

Note associated ischaemia, perforation, melanosis and fibrosis.

Diversion proctocolitis

Can only be diagnosed if clinical history is known. May mimic IBD.^{59,69,70} Granulomas can occur.⁵⁹ Inflammation is more severe if there is a history of ulcerative colitis.^{59,69}

Motility disorders

Exclude other common causes of symptoms. Assess myenteric and submucosal ganglion cells, myenteric plexus, muscularis propria/muscularis mucosae, vasculature. Special stains and immunohistochemistry depend on local expert. Possible myopathies and neuropathies should be referred to a specialist pathologist.

C3 Ischaemic colitis/enteritis: additional comments

C3.1 Report and microscopic description

Indications for surgery

- Removal of non-viable tissue.
- Management of symptoms.

Considerations

The cause of the ischaemia may be already be known and supplied. Occasionally, pathological examination reveals the cause, e.g. vasculitis.⁵⁹ Ischaemic changes may be superimposed on other conditions, e.g. IBD, diverticular disease, neoplasia, obstructing lesion. They may even precede some conditions (e.g. IBD).⁷²

Report

- Evidence of acute ischaemia (e.g. haemorrhage, necrosis, atrophic crypts) and chronic ischaemia (e.g. fibrosis).²⁴
- Severity and depth of acute ischaemic changes/infarction (e.g. mucosal, transmural).
- The most important item in the pathology report in cases of acute ischaemia is viability of resection margins.

C4 Vascular malformation/angiodysplasia: additional comments

C4.1 Preparation, dissection and blocks

Opening and fixation

If the specimen is received fresh, it may be possible to inject the vasculature with a contrast medium, e.g. barium sulphate, prior to opening. It can then be distended with formalin, fixed and X-rayed.⁵⁹ However, the specimen is usually received fixed.

Sampling

Sample areas of erythema, haemorrhage, mucosal flattening and discoloration, because macroscopic changes of angiodysplasia may be focal or subtle.⁵⁹

C4.2 Report and microscopic description

Indications for surgery

- Gastrointestinal haemorrhage or its consequences (e.g. anaemia).
- Imaging may have suggested angiodysplasia.

Report

- Histology may confirm the diagnosis and help exclude other causes of bleeding.
- Describe vascular abnormalities. Note depth and extent of vascular changes.
- Record evidence of ischaemia.
- Other lesions may be associated with angiodysplastic changes, especially diverticula. Secondary 'angiodysplasia' is more common than primary vascular anomalies.⁷³

C5 Inflammatory bowel disease (colorectal): additional comments

C5.1 Macroscopic description

Opened bowel

Consider whether the changes favour ulcerative colitis (e.g., continuous disease, proximal sparing, etc.) or Crohn's disease (e.g., segmental disease, cobblestoning, strictures, fat wrapping, etc.). Treated chronic disease may fail to conform to classical patterns.⁷⁴

C5.2 Report and microscopic description

Indications for surgery

- Refractory or severe disease.
- Dysplasia/carcinoma.

Report

- Chronic inflammation: record extent and distribution and whether mucosa-centred or transmural.
- Active inflammation (cryptitis, crypt abscesses): record extent and severity.
- Ulcers: record type and depth (layer affected, including superficial or deep half of muscularis propria).

- Granulomas: note whether necrotising or non-necrotising, and request ZN stain if appropriate.
- CMV inclusions may be present. Consider immunohistochemistry.^{23,25}

Classification of IBD

- Crohn's disease (patchy involvement, fissuring, granulomas, transmural chronic inflammation, etc).^{21,59}
- Ulcerative colitis (diffuse involvement, abnormal mucosal architecture, mucosa-predominant, etc).^{21,59}
- IBD which cannot be further classified. If the term 'indeterminate' colitis is used, it should be confined to resection specimens with definite IBD in which a diagnosis of either ulcerative colitis or Crohn's disease cannot be made.^{43,75} It should not be used to mean 'colitis, cause unknown'.^{3,75,76} Unfortunately, this term has different meanings for different pathologists and clinicians, may cause confusion, and is probably overused.^{24,43} The term 'IBD, type unknown' or 'IBD, type unclassified' may be preferable.⁴³ This is a difficult area of diagnosis, which requires full clinicopathological discussion. Assessment may benefit from the input of more than one pathologist.^{3,76,77}
- Classification of type depends not only on histology but also on macroscopic appearances and clinical findings.

C6 Small bowel resection for stricture/IBD: additional comments

C6.1 Report and microscopic description

Indications for surgery

- Symptoms.
- Obstruction. Identification of cause.
- Removal of non-viable bowel.

Considerations

A small bowel stricture might be due to ischaemia, IBD, drugs, infection, radiation, endometriosis, previous surgery, neoplasia or other causes.^{21,24}

Report

- Record and describe ulceration, inflammation, fibrosis and granulomas.
- Seek evidence of inflammatory bowel disease (Crohn's).
- Look for evidence of trauma, ischaemia, endometriosis (glands, stroma, and haemorrhage), radiation damage (needs appropriate history), NSAID-induced enteritis (including diaphragms) or specific infections.

C7 Intussusception: additional comments

C7.1 Preparation, dissection and blocks

Sampling

Apex of intussusception, including possible causative lesion. Demonstrate intussusception if possible.

C7.2 Macroscopic description

Dimensions (millimetres)

Length of intussusception; distance of apex from distal resection margin; distance of neck from proximal margin; diameter of lumen.

Opened bowel

- Type of intussusception, i.e. ileoileal/ileocolic/colocolic.⁷⁸
- Record the appearance of the mucosa; state of underlying wall; ischaemia.²¹
- Look for a causative lesion, e.g. foreign body, polyp, diverticulum, duplication, various tumours, ileal lymphoid hyperplasia, appendix.^{26,59,78} In children, a cause is often not found.⁵⁹

D Tissue pathways: pancreatobiliary resection specimens

D1 Bile duct resection

D1.1 Preparation, dissection and blocks

Opening and fixation

It may be useful to ink the proximal and distal margins and the external surface if neoplasia is suspected.^{21,24}

Minimum sampling

- One approach is to take the proximal/distal resection margin *en face* (parallel) and then take sequential transverse slices as far as the other resection margin, especially if there is any suggestion of neoplasia.^{24,21} If there is a lesion close to a margin, serial perpendicular (radial) sections of this margin may be more informative.
- Focal lesions: take at least one block, which should show the depth of the lesion and its distance from the external surface.
- Gall bladder: if no focal lesion is present, treat as routine cholecystectomy. If a lesion is seen, take multiple sections.
- All lymph nodes should be taken.²⁴

D1.2 Specimen description

Specimen type

Specify what is included, e.g. common hepatic duct, cystic duct, common bile duct, etc.²¹ The surgeon may be able to assist if orientation is difficult.²⁴

Dimensions of specimen (millimetres)

Length of each portion (e.g. common hepatic duct) and total length. Maximum diameter or range of diameters, if appropriate. Dimensions of attached organs/tissue.

Appearances

Record any focal lesions (e.g., strictures, perforation, nodules) and their site, size, and relationship with margins. Note cysts or cystic dilatations.²⁴

D1.3 Report and microscopic description

Indications for surgery

- Management of symptoms.
- Choledochal cyst.²⁴
- Abnormal imaging.
- Exclusion of neoplasia.

Report

Record features suggestive of sclerosing cholangitis or autoimmune cholangitis. Inflammatory epithelial atypia can be severe, especially proximal to an obstruction or after stent insertion. Deeply located glands can mimic neoplasia and *vice versa*.¹⁶

D2 Cholecystectomy for non-neoplastic disease

D2.1 Preparation, dissection and blocks

Opening and fixation

Open longitudinally,^{24,21} avoiding disruption of the cystic duct margin and gall bladder bed margin. Ink gall bladder bed margin if neoplasia is suspected.²¹

Sampling

- Cystic duct margin *en face*.^{24,21} This may be located adjacent to a clip. Ensure that it is identifiable after processing (e.g. histologically distinct section / inked section / section in separate cassette).
- Cystic duct lymph node.^{24,21} This is often present, but may be small.
- At least one block each of neck, body and any focal lesion.²⁴
- Attached organ, to characterise relationship with gall bladder.
- Polyps/lesions suspicious of neoplasia: sample thoroughly.²¹

D2.2 Specimen description

Dimensions of specimen (millimetres)

Length and maximum diameter.²¹ Dimensions of any attached organs.

Appearances

- Record whether intact, opened or fragmented on receipt.²¹
- Note perforations/defects in wall, serosal haemorrhage, etc.^{24,21}
- Contents: note stones (number, type, range of sizes), bile and mucus.^{24,21}
- Record mucosal changes, e.g. cholesterosis, ulcer, polyp.^{24,21}
- Note abscess, fistula and diverticulum. Record site, size, and relationship with external surface /attached organ.
- Polyp/tumour: describe and record site, size, depth and relationship with external surface/resection margin.²¹

D2.3 Report and microscopic description

Indications for surgery

- Management of symptoms.
- Characterisation of lesions seen on imaging.

Report

- Chronic cholecystitis/acute cholecystitis/features of both.²¹
- Rokitansky Aschoff sinuses can mimic neoplasia.^{16,24}
- Describe attached tissue, e.g. liver.
- If dysplasia is found, extra blocks are required to exclude higher grade dysplasia/malignancy.¹⁶ Dysplasia is classified as low grade or high grade. Involvement of the resection margin should be recorded, especially if dysplasia is high grade.¹⁶

- Carcinoma: record type, stage,¹⁷ vascular invasion, perineurial invasion, involvement of serosal surface and resection margins.²¹

D3 Pancreatic resection for non-neoplastic disease

D3.1 Preparation, dissection and blocks

Opening and fixation

Ink resection margins and other external surfaces if neoplasia is suspected.^{10,24} Slice the pancreas and open the bowel to ensure fixation.

Sampling

- Resection margins of bile duct, small bowel, and pancreas.^{10,24}
- All focal lesions. At least two representative blocks of pancreas if no focal lesion, depending on clinical indication. Usually, more blocks are required,²¹ and are particularly important if neoplasia is suspected or if findings do not correlate with imaging. Large blocks may be useful, e.g., to delineate tumour from fibrosis.
- All peripancreatic lymph nodes, especially if neoplasia is a possibility.
- If there is a bile duct lesion, serial sequential bile duct blocks are advisable.
- All margins and surfaces if a suspicious lesion is seen.^{10,24}
- Ampulla of Vater with adjacent pancreas.

D3.2 Specimen description

Specimen type

Pylorus-preserving pancreatoduodenectomy (PPPD)/Whipple's resection (partial gastrectomy also included)/distal pancreatectomy, etc.

Dimensions of specimen (millimetres)

Pancreas in three dimensions. Extrapancreatic bile duct length. Bowel length.¹⁰

Appearances

Pancreas: note fibrosis, calcification, fat necrosis, haemorrhage.²¹ Focal lesions (nodules, cysts, abscesses): record location, size, and relationship with margins. Small bowel: note congestion, strictures, nodules and mucosal changes.

D3.3 Sections and stains

Immunohistochemistry

IgG4 may be useful for supporting a diagnosis of autoimmune pancreatitis. Diagnosis is based on imaging, clinical, serological and pathological findings.⁵⁴

D3.4 Report and microscopic description

Indications for surgery

- Mostly for resection of a tumour or suspected tumour (e.g. suspicious imaging findings).
- To control symptoms or relieve duct obstruction.

Report

- Features of chronic pancreatitis, e.g. chronic inflammation, fibrosis, atrophy. These changes can mimic neoplasia.^{16,24,57,58} Consider autoimmune pancreatitis.
- Note ectopic or heterotopic tissue.
- Neoplasms: refer to the College dataset and others.^{10,13,14,15,16}

D4 Pancreatic resection: necrosectomy

D4.1 Preparation, dissection and blocks

Sampling

Take at least two blocks and sample any focal changes.²¹

D4.2 Specimen description

Specimen type

Fragments of pancreas/nondescript fragments/semiliquid material.^{24,21}

Dimensions of specimen (millimetres)

Number and size of fragments/range of sizes/maximum aggregate dimension.²¹

Appearances

Fat necrosis, congestion, haemorrhage.²¹

D4.3 Report and microscopic description

Indications

Removal of necrotic tissue, usually in the setting of acute pancreatitis.^{24,21}

Histology

Acute inflammation, necrosis, haemorrhage.^{16,24,21} Exclude tumour.

D5 Pancreatic resection: cysts

D5.1 Preparation, dissection and blocks

Opening and fixation

Ink external surfaces, especially if suspicious or focal lesions are present.²¹

Minimum sampling

One block per 10 mm diameter, especially if neoplasia suspected.²¹ Sample any focal changes, nodules or more solid areas.²¹

D5.2 Specimen description

Specimen type

Intact cyst/opened cyst/fragments.

Dimensions of specimen (millimetres)

Diameter/maximum dimension of cyst.²¹ Size of attached pancreas/other tissue.

Appearances

- External surface: e.g. smooth/nodular/lobulated.²¹
- Contents of cyst: mucoid/serous/haemorrhagic.²¹
- Lining: smooth/papillary areas/nodules/haemorrhage.
- Wall: consistency, nodules, calcification.
- Attached pancreas: fibrosis, calcification, abscess, relationship with cyst.

D5.3 Sections and stains

Additional stains

Mucin stains and immunohistochemistry may help characterise lining.²⁴ Deeper levels if slide appears not to represent full face of block.

D5.4 Report and microscopic description

Indications for surgery

- Exclusion of neoplasia.
- Management of symptoms.

Report

- Describe lining epithelium: absent (? pseudocyst)/flat/cuboidal/squamous/columnar (mucinous/ciliated)/papillary/dysplastic.
- Look for microorganisms (e.g. Echinococcus in a hydatid cyst)
- Underlying stroma: fibrous/ovarian-type/pancreatic tissue/invasive tumour.
- A wide variety of cysts may occur.^{16,24}

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