



The Royal College of Pathologists

Pathology: the science behind the cure

Histopathology and cytopathology of limited or no clinical value

2nd edition, December 2005

This document was produced by the Working Party on Histopathology and Cytopathology of Limited or No Clinical Value, chaired by Dr Alec Howat. It supersedes the first edition, published in August 2002.

In accordance with the College's publications policy, this document was placed on the Fellows' and Members' area of the College website for consultation from 29 March to 29 April 2005, and again from 31 May to 1 July 2005. Twelve detailed comments were received. The Working Party considered the feedback and amended the document accordingly. Please email publications@rcpath.org if you wish to see the feedback and Dr Howat's responses.

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INTRODUCTION

In January 2001, the *Bulletin* of The Royal College of Pathologists published an article entitled *A Recovery Plan for Histopathology*.¹ This emanated from a meeting of consultant histopathologists in September 2000, in response to the growing concerns regarding histopathology consultant staffing. The article was published as a draft, with the express purpose of encouraging comment and debate through wide consultation with the College membership.

The salient points were:

- relationship between the College and histopathologists
- recruitment and training
- workforce and workloads
- flexible working
- service configuration.

Under the heading of 'Workforce and workloads', the report stated that: "The College should, however, initiate a series of evidence-based multidisciplinary evaluations of investigations of doubtful clinical utility to identify those that make little or no contribution to patient care and welfare. Some diagnoses made traditionally by histology may be made with higher sensitivity and specificity by other methods, thus relieving histopathologists of some of their burden." That was the remit of the Working Group. The first report was published in August 2002.²

COMPOSITION OF THE WORKING GROUP

The Working Group was formed by the SAC on Histopathology. The original Group consisted of six consultant histopathologists working in district general hospitals, namely Alec Howat (Chair), Katie Boyd, Gillian Douce, Margaret Jeffrey, Alastair Lessells and Neil Shepherd. The Group was selected for experience in cytology and gastrointestinal and gynaecological pathology, as well as a broad base of general histopathology. Gillian Douce was not able to continue with this work in preparing the second edition and Glenn McCluggage replaced her.

METHODOLOGY

Each member undertook to review their own working practices and critically examine the clinical usefulness of their histopathology reports. This process was to be backed up by an extensive literature review, identifying evidence-based articles in peer-reviewed journals. Information from local audits would also be used. The end point was an article illustrating areas for further discussion between the histopathologist and clinical team in a multidisciplinary approach.

The 2002 report was published, after a period of consultation as a draft.

This second edition continues to address the original goals, plus an examination of areas not in the first report. In addition, some data generated as a response to the original report (audits, published work, abstracts, etc.) are included.

GENERAL POINTS

The Working Group re-emphasises the following general principles, before looking at specific points.

- 1) It must be stressed that these guidelines should be discussed and agreed at a local level with clinical colleagues. Implementation will vary depending on local circumstances, such as the degree of training, staffing, research interests, etc.

- 2) It should be appreciated that unnecessary biopsies impact on other areas as well as histopathology laboratories; for example, these specimens have to be transported to the laboratory, the reports read and filed, and appropriate letters about them written to general practitioners (GPs) by clinicians.
- 3) The pathology report is often the key factor in accurate patient management and should be appreciated as such.
- 4) Histopathologists should critically review the length and complexity of their reports. A brief comparison of breast cancer reports from a number of neighbouring Trusts by one of us has shown huge variation, with some reports covering less than a single page and others many pages, yet all contain similar data as outlined in the College's minimum datasets for breast cancer.
- 5) The use of standard reports is encouraged, particularly in high-volume specialties such as dermatopathology, gastrointestinal and gynaecological pathology. This will save both secretarial and consultant time.
- 6) The recent College minimum datasets for cancers are welcomed and play a key role in standardisation of reporting. However, the Working Group remain dismayed that, three years on, the report templates still cannot easily be imported into pathology computer systems.³ Histopathologists are left to devise their own systems locally or continue with free text reporting. Published evidence shows that the use of templates improves the quality of information in pathology reports.⁴⁻⁶ A national initiative to solve this problem is again recommended. However, The Royal College of Pathologists has been recently addressing this issue and is in the process of ensuring that electronic minimum dataset reporting will be incorporated into certain commercially available pathology computer systems.
- 7) There are a number of idiosyncrasies leading to increased workloads that occur in almost every laboratory. Publicising these facts might help in their eradication. Historical panels of tinctorial stains, often only performed in solitary departments, should be critically reviewed in the light of superior immunohistochemical methods for diagnosis.
- 8) The major factors causing the huge increase in workload are those associated with specialisation and clinical demand leading to increased work on difficult cases; they are not related to an absolute increase in requests. Reducing the absolute number will have only a marginal impact.
- 9) Histopathologists are asked for an opinion on a specimen that may not necessarily need extensive histology; for some specimens, a gross inspection with a single histology section to act as a record, and for audit purposes, may well suffice.
- 10) Some clinicians appear to feel that an examination is not complete without a biopsy, a good example being a normal upper gastrointestinal (GI) endoscopy. A change in this clinical behaviour pattern will only be achieved by good audit evidence and local discussion within clinical teams.
- 11) When drawing up guidelines, it would be helpful if clinical societies and organisations consult with histopathology colleagues with, ideally, one being on the team making the recommendations.
- 12) The value of each test should be maximised by submission of samples correctly; for example, three sputum specimens should be sent on three different occasions, rather than three at one time.
- 13) Negative sputa and urines are often reported by biomedical scientist (BMS) staff under consultant supervision.⁷ Departments should review their working practices with regard to BMS histology dissection.⁸ It is expected that a BMS role in these areas will be formalised in the near future, and linked to a level of competency indicated by holding of The Institute for Biomedical Science's Advanced Specialist Diploma (Intermediate level) or preceding Certificate in Diagnostic and Interpretive Cytology.

SYSTEMS

i) Cytology

The BSCC are revising their *Code of Practice for Cytology Laboratories* document, which will contain guidance on best practice. In addition, see General point 13 above.

a. Cervical cytology⁹

- i. Routine use of two slides is unnecessary (see point iv below).
- ii. It is usually unnecessary to take a repeat smear at initial colposcopy after referral for an abnormal smear, especially if a biopsy is also performed.¹⁰⁻¹¹
- iii. Screening smears should only be taken as indicated by the NHS Cancer Screening Programme.¹²
- iv. With the implementation of liquid based cytology, there will be a reduction in inadequate smears;¹³ double smears will be eradicated.

b. Respiratory cytology

- i. Sputum samples should be requested in the main by respiratory physicians and only from patients unfit for bronchoscopy.¹⁴⁻¹⁹ After discussion of these guidelines with clinical colleagues, a 60% reduction in sputum samples has been reported.²⁰ Negative sputa are often reported by BMS staff under consultant supervision (see General point 13, above).
- ii. The British Thoracic Society's guidelines recommend biopsy, brushings and washings at bronchoscopy.²¹ The Group feel that, if a tumour is visible, biopsy and brushings should suffice. Washings are unnecessary when the tumour is visible.
- iii. Cytology should not be used to diagnose *Pneumocystis carinii*; a sample for microbiology is more appropriate with a result being available within 24 hours using specific immunofluorescence.

c. Urine cytology

- i. A single cytospin slide is sufficient for diagnosis.²²
- ii. Negative urines are often reported by BMS staff under consultant supervision (see General point 13).
- iii. An unpublished audit from Edinburgh looked at 2256 cases and concluded that urine cytology should not be used in the follow-up of low-grade transitional cell carcinomas (TCC) due to poor sensitivity, and should not be used in patients prior to, or during, intravesical therapy. The authors also noted the extreme rarity of TCC in patients under the age of 50 years and that no patient with a biopsy-proven TCC presented clinically with microscopic haematuria.²³
- iv. The NHS Cancer Registry Office decided to suspend all further work on the National Bladder Cytology Recall Scheme, with effect from 1 June 2003.²⁴ Screening urines should therefore not be encountered.
- v. The practice of sending urine cytology from urodynamic clinics in patients without evidence of haematuria should be discouraged.

d. Pleural fluid

Only a single sample should be assessed when draining effusions related to cardiac failure, unless there is other good evidence of malignancy.

e. Ascitic fluid

Again, only a single sample should be assessed in patients with chronic liver disease.

f. Peritoneal washings and ovarian cyst fluid

See section on gynaecological pathology.

g. General FNA comments

A maximum of four well-prepared slides should be submitted for examination.

h. Breast

Fine-needle aspirations (FNAs) should only be undertaken and reported by those skilled in each area.²⁵

- i. Breast cyst fluid should only be examined if bloodstained or if there is a residual lump after aspiration.
- ii. For those using direct smears from FNAs, a maximum of four well-spread slides is recommended as stated above.

i. Salivary gland and thyroid

FNA cytology of thyroid nodules and of salivary gland lesions has an established role in the initial assessment of patients and in deciding which patients require surgery. However, this is a specialised field and both aspiration and interpretation of the material obtained is best restricted to centres and individuals with special expertise.²⁶

j. Cerebrospinal fluid (CSF)

Cytological examination should only be performed on cases with a suspicion of malignancy,²⁷ or aseptic meningitis; the possibility of multiple sclerosis is not an indication for CSF cytology.

ii) Gastrointestinal pathology

This is the area that has resulted in a significant reduction in workload, if the guidelines are followed after dialogue with clinical colleagues. After the first edition of this publication, many have indicated that a management guideline such as this should be addressed not only to pathologists but to endoscopists. In fact, in concert with The Royal College of Pathologists, the British Society of Gastroenterology is currently constituting a 'management guideline document' to be entitled *The Indications for Biopsy at Gastro-intestinal Endoscopy*, which will be circulated to all BSG members.

Overall, reductions of 18–38% of total biopsy numbers have been reported,^{28–31} after publication of the first edition, with higher percentages for gastric biopsies. Audits have shown that no serious pathology would have been missed by this policy.³² A simple rule of thumb is that biopsies from the upper GI tract should only be taken from endoscopic lesions and not from endoscopically normal mucosa. Whilst some pathologists have stated that an upper GI endoscopy is incomplete without a biopsy (especially for the diagnosis of gastritis and 'carditis'),³³ most UK gastrointestinal pathologists are unconvinced by this argument. There is no good evidence base that shows that such biopsies are useful in the management of individual patients and we fear that the recommendation is more for research than for the provision of useful clinical information. The same applies to most colonoscopies, with the notable exception of an examination for chronic diarrhoea when biopsies of endoscopically normal large bowel are needed for detection of the various forms of microscopic colitis.

a. Oesophagus³⁴

- i. There is no justification for a biopsy from the normal oesophagus.
- ii. Biopsies from patients with reflux oesophagitis are unhelpful; endoscopy is better at assessing reflux than histology. However, if there is considerable ulceration, biopsy may be justified to exclude malignancy.
- iii. Diagnostic and surveillance biopsies for Barrett's oesophagus are reasonable, not least due to the increasing prevalence of the disease and its complicating adenocarcinoma.

- iv. So-called ultra-short segment Barrett's oesophagus (cardia intestinal metaplasia [CIM]), with or without carditis, is a highly prevalent condition and its management is not yet determined. We believe, as do others, that this condition should not be sought as it infers a normal junction, on the one hand, and we currently have no idea of the appropriate management of this condition or its neoplastic risk. However, as with all these recommendations, the decision to undertake biopsies of an endoscopically normal oesophagogastric junction (OGJ) must rest with the local medical community.

b. Stomach³⁵⁻⁴⁵

- i. There is no evidence base that biopsy of the normal stomach gives any useful clinical information that is likely to alter management in the routine setting. It is emphasised that there is always a need to biopsy abnormal areas of the stomach.
- ii. Biopsies should not be done purely to identify *H pylori* (HP); there are equally good alternative and much cheaper tests.³⁶⁻⁴⁰
- iii. There is little evidence that histological grading of 'gastritis', with or without intestinal metaplasia, gives any useful information for the subsequent management and follow-up of individual patients. Indeed, there are two time-honoured, admittedly retrospective, studies that indicate that the demonstration of intestinal metaplasia, particularly of incomplete type, is not of any utility, in the clinical setting, for identifying those patients likely to suffer subsequent gastric cancer.^{41,42} Whilst there is an important role for gastric biopsies for research in this area, we believe that 'routine' biopsies of the endoscopically normal stomach cannot be justified in the current climate because there is no evidence base that the information gleaned alters patient management.
- iv. We agree that there is little or no correlation between endoscopic appearances and the presence or absence of gastritis.^{43,44} Nevertheless, despite this, we reiterate our view that biopsies are unlikely to change management on the basis of such a lack of correlation and there is no evidence base that they do. Once again, we emphasise that any policy on biopsy for the diagnosis of any form of gastritis must be a local one, after discussion with all interested parties. For instance, advocates of routine gastric biopsy have indicated that the evidence of a severe atrophic gastritis, in HP-associated disease, is predictive of gastric cancer risk. We would not deny the evidence for this,⁴⁵ but would question whether such data justify the routine biopsy of all stomachs at endoscopy and whether the demonstration of such a phenotype changes management in any way (assuming the HP gastritis is appropriately treated).

c. Duodenum and small bowel

Biopsy of D2 or beyond remains the gold standard for the diagnosis of coeliac disease as serological tests are neither 100% specific nor sensitive. There are national and international recommendations indicating that four 'good-sized' biopsies are taken from D2 of beyond as the histopathological changes of coeliac disease can be strikingly focal.

d. Colonoscopic biopsies

- i. A colonoscopic examination, with a normal appearance, should only prompt biopsies in the correct clinical setting; that is persistent watery diarrhoea without blood, usually in a middle-aged or elderly (often female) patient, with the express intention of confirming or refuting a diagnosis of microscopic colitis.
- ii. When biopsied, a maximum of five or six biopsies are recommended and, in the correct clinical setting, there is a case for dividing them into two/three from the 'right' side (caecum to distal transverse colon) and two/three from the left in two containers so that only two slides need be examined.⁴⁶ This is because collagenous colitis, in particular, is more likely to be demonstrated in right colonic and transverse colonic biopsies.⁴⁷
- iii. Ileal biopsies purely to demonstrate that the colonoscopist has reached the terminal ileum are not justified (a photograph will suffice for audit and training purposes). Ileal biopsies for the

demonstration of chronic inflammatory bowel disease and other inflammatory conditions are, of course, merited.⁴⁸

iv. Random rectal biopsies with a clinical history of rectal bleeding are not justified.

e. Resection margins

Proximal and distal margins, including doughnuts, should not be examined for a colorectal tumour if it is >3 cm from the margin in question. Resection margins need not be examined in resections for Crohn's disease as there is no evidence that a positive margin is predictive for recurrent disease, although macroscopic active ulcerating disease at a margin may influence subsequent therapy.

iii) Gynaecological pathology

a. Social termination of pregnancy

Specimens should not be sent to the laboratory if foetal parts are visible.

b. Endometrium

Endometrial sampling should not routinely be performed in women with abnormal bleeding under the age of 40 years. Some gynaecologists do not biopsy the endometrium even in women over this age if the transvaginal ultrasound shows a thin endometrium with no focal lesions, and a normal hysteroscopy.

c. 'Normal' uterus for abnormal bleeding

It is rare for a significant abnormality to be found on histology if the gross examination is negative.⁴⁹ A larger audit on this subject is recommended.

d. Uterus for prolapse

If there are no focal lesions, one block from the cervix and one from the endo/ myometrium is all that is required.⁵⁰ Focal lesions should be examined as per protocols.

e. Hysterectomies after previous CIN

Clearly, all the cervix should be sampled if examined soon after diagnosis of CIN. However, when there has been a series of interim negative smears, more limited sampling is appropriate.⁵¹

f. Ovarian cyst fluid⁵²

In up to 76% of cases, no lining cells are present making the test of little use. Fluid sent as well as the ovary is not warranted.

g. Peritoneal washings

This should not be sent for cytology during gynaecological surgery for benign disease.⁵³ However, when there is doubt whether an ovarian mass is benign or malignant, washings must be sent for cytological examination. These samples should be reported in conjunction with the resection specimen.

h. Omental sampling⁵⁴

Based on a ten-year experience of 692 cases, it is recommended that one block is needed if the ovary and omentum are either both benign or both malignant on gross inspection. If the ovary is malignant or borderline on gross inspection or histological examination, and the omentum appears normal, thorough sampling is needed.

iv) General

a. Breast reductions for cosmetic purposes

These can generate a considerable amount of work. Obviously a section from macroscopically abnormal areas is justified. However, the value of random histology is limited. A retrospective audit on 1289 patients showed that, if two random blocks are taken from each breast, 'important diagnoses' were made in 2.1% of cases.⁵⁵ The question remains as to how many blocks are reasonable.

b. Mastectomy specimens after primary chemotherapy

These can involve taking many blocks looking for residual tumour; marking of tumours prior to chemotherapy will aid location of residual tumour and reduce the number of blocks that need to be taken.

c. Skin biopsies

- i. In secondary care, plastic surgeons in many units triage specimens which they send for histopathology. This applies in particular to small (3 mm or less) multiple skin tags. This can be supported.
- ii. In primary care, there is a widespread good practice clinical consensus that general practitioners undertaking minor surgery and general practitioners with a specialist interest in dermatology should submit all tissue removed for histopathological examination. This requirement is often part of local protocols to accredit service provision, as endorsed by the National Institute for Health and Clinical Excellence (NICE) (*Improving Outcomes in Patients with Skin Tumours*), to ensure that any case of skin pre-cancer or cancer is not missed. In view of the low risk, however, it would appear reasonable that small (3 mm or less) multiple skin tags are submitted in one specimen container.
- iii. Reporting of excision margins on benign lesions should be limited to those having clinical relevance for potential recurrence and/or as specifically requested by a local clinician or agreed in local protocols.

d. Orthopaedic and soft tissue

- i. Femoral heads and other articular surfaces removed for known osteoarthritis or inflammatory arthritis arguably need not be submitted for histology unless there is a specific clinical question, such as is there evidence of pre-existing osteonecrosis, sepsis or a radiological abnormality suggestive of a coincidental metabolic bone disease or tumour? In contrast, tissue removed at surgery for revision of a prosthesis does require examination, to differentiate between mechanical loosening and infection.
- ii. In patients with femoral neck fractures, femoral heads should only be examined where there is a suspicion radiologically of a pathological fracture or there is a relevant past history of malignancy.
- iii. All soft tissue lumps and bumps (e.g. ganglia, Morton's neuromas, etc.) do need to be examined because of the risk of missing small juxta-articular synovial sarcomas, epithelioid sarcomas and the like.
- iv. Amputation specimens for non-tumorous reasons such as ischaemia should not be sent to the laboratory for examination.

e. Re-excision of melanomas

This topic remains contentious despite evidence in the UK literature to show that gross inspection, with a single slide from the centre of the previous biopsy site, is all that is needed if the original lesion was fully excised and in the absence of macroscopical disease.⁵⁶⁻⁵⁸ The College's *Minimum Dataset for the Histopathological Reporting of Common Skin Cancers* does not endorse this view,⁵⁹ nor is it a protocol that is followed in many other countries. The debate is more one of how many blocks to take through the scar in addition to complete blocking of the

radial margins.⁶⁰ No firm guidance can therefore be given at present, until further evidence-based information is available.

f. Gallbladders and appendices

These should be examined as significant pathology may be present with normal gross morphology, despite one study suggesting that routine gallbladder histopathology is not indicated.⁶¹

g. Sentinel lymph node

The clinical significance of micro/occult metastases in breast cancer is becoming clearer,⁶²⁻⁶⁴ and will become more so when large clinicopathological studies such as ACOSOG Z10 report.⁶⁵ Published guidance from the NHS Breast Screening Programme is also awaited after the ALMANAC trial reports.⁶⁶ Similar information is awaited from malignant melanoma sentinel lymph node studies.⁶⁷

h. Placenta⁶⁸

There is no justification for examination of the placenta following a normal birth. The clinical scenarios in which placentas should be examined have recently been the subject of an Association of Clinical Pathologists' *Best Practice* document.⁶⁹ In general, only those placentae associated with maternal conditions such as pre-eclampsia or with abnormal live births (prematurity, growth retardation, malformation, etc.) should be examined. Twin placentae should be examined to identify monochorionic placentation that is associated with a very high rate of pre- and post-natal morbidity.

i. Nasal polyps

It is rare to find significant pathology in nasal polyps that are not worrying on clinical grounds or gross inspection,⁷⁰ therefore most should not be submitted for histopathology.

j. Tonsils

These should not be submitted for histopathology unless there is a clinical suspicion of malignancy.

DISCUSSION

It is clear that the areas identified above have resulted in some decrease in work for which there is no or limited clinical value. The topics should be discussed with clinical colleagues in a multidisciplinary manner.

Members are encouraged to use the Discussion Forum of the College website to share information and comments about this report (in the Fellows' and Members' Area of www.rcpath.org – log-in required).

CONCLUSIONS

The Working Group has produced this second edition of the report, confirming and expanding a number of areas that are suggested as being worthy of discussion with local colleagues in order to help with workload management. The issues roughly divide into four:

- specimens being sent for histology without any obvious clinical reason, i.e. ischaemic limbs, placentas from normal pregnancies, etc.
- changing clinical practice, i.e. gastric biopsies for *H. Pylori*, identification of *Pneumocystis carinii*, etc.
- misuse of the service by users, i.e. inappropriate sputum and urine cytology, etc.
- inefficient service provision, i.e. unnecessarily long-winded reports, lack of involvement of BMS for histology dissection, and reporting of certain types of cytology by BMS and advanced practitioners, etc.

It is stressed that any decision regarding limiting clinicians' access to histopathology must be discussed and recorded at local multidisciplinary team meetings.

Undoubtedly, the value of certain histopathology tests will change over time and with further evidence. Again, this report should be interpreted as 'fluid', reflecting the Working Group's views in 2005, and should not be seen as a permanent record.

There is evidence that relatively few departments have attempted to implement these guidelines. Why is this so? Possibilities include ignorance of this report, uncertainty in how to proceed with implementation, a deferential attitude to clinicians and an unwillingness to relinquish 'easy' normal cases.

Finally, there are several areas raised in the report that would value from further audit, for example the value of histology in breast reductions, 'normal' uteri, etc.

ACTION PLAN

The Department of Health has set up a working party to look at 'Workload Management in Pathology'. This report will partly inform that working party and will be instrumental in deciding how, and by what mechanism, to proceed. It has been suggested that Pathology Networks might be the best conduit for implementation of the guidelines.

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