



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

Tissue pathways for pulmonary pathology

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Produced by	Dr John R Gosney, Royal Liverpool University Hospital (Writing Group Lead) Professor Andrew G Nicholson, Royal Brompton Hospital London Dr Allen R Gibbs, Llandough Hospital Penarth, Glamorgan
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The Royal College of Pathologists
2 Carlton House Terrace
London, SW1Y 5AF
Tel: 020 7451 6700
Fax: 020 7451 6701
Web: www.rcpath.org

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CONTENTS

Bronchial and transbronchial biopsies.....	2
Pulmonary needle biopsies	4
Video-assisted thoracoscopic (VATS) and open pulmonary (surgical lung) biopsies	6
Pleural needle biopsies	9
Thoracoscopic or open pleural biopsies	11
Pulmonary resection for non-neoplastic disease.....	13
Pleural resection for non-neoplastic disease.....	14

TISSUE PATHWAY: BRONCHIAL AND TRANSBRONCHIAL BIOPSIES

1 STAFFING AND WORKLOAD

The lead pathologist responsible for reporting bronchial and transbronchial biopsies should have appropriate expertise in thoracic pathology and participate in a relevant EQA scheme. Cover should be available at an appropriate level during periods of leave, but it is acknowledged that, in most units, only one pathologist will have such specialist expertise.

2 SPECIMEN SUBMISSION

Specimens are immediately placed in formalin.

3 SPECIMEN DISSECTION AND BLOCK SELECTION

All of the specimen is submitted with a brief description of the number and size of fragments.

4 EMBEDDING AND SECTIONING

All fragments are embedded as a group in one block. At least three step sections are prepared, keeping spares at each level for any special stains that might be required. If no abnormalities are identified at any of these levels and tissue remains in the block, further step sections are prepared as features such as granulomas may be scanty within the tissue.

5 STAINING

Haematoxylin and eosin is usually sufficient to identify common pathological changes with other stains on request by the pathologist.

6 FURTHER INVESTIGATIONS

If a neoplasm is present, a diastase-PAS stain for mucin may be useful to identify adenocarcinoma. Immunohistochemistry may be required to classify a tumour precisely and exclude the possibility that it is metastatic. This is at the discretion of the pathologist. For example, the distinction of neuroendocrine tumours, usually small cell carcinoma, from non-neuroendocrine tumours, is aided by the identification of antigens indicative of neuroendocrine differentiation (egCD56, synaptophysin, chromogranin A). The distinction of primary from metastatic adenocarcinoma is aided by the identification of TTF-1 and cytokeratin subclasses, especially 7 and 20.

If pulmonary infection (e.g. tuberculosis, Pneumocystis) is suspected, appropriate stains (e.g. Ziehl-Neelsen, Grocott, PAS) will be necessary. Elastic Van Gieson (EVG) stains are of value if considering a vasculitic process.

7 REPORT CONTENT

The report comments on the adequacy of the specimen (e.g. is there sufficient parenchyma if parenchymal disease is being investigated?), the nature of any morphological changes and provides at least a differential diagnosis of their causes.

A neoplasm is classified according to the World Health Organisation Classification and, if appropriate, an attempt made to grade it as poor, moderately or well differentiated. At the very least, a distinction is made between small cell and non-small cell carcinoma, since this is the most crucial decision in terms of subsequent management.

Transbronchial biopsy is not infrequently uninformative in many diffuse parenchymal lung disorders, in particular the interstitial pneumonias, and pathologists should not be pressured into the diagnosis of such histological patterns when it is not appropriate.

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2. Curley FJ, Johal JS, Burke ME, Fraire AE. Transbronchial lung biopsy: can specimen quality be predicted at the time of biopsy? *Chest* 1998;113:1037-1041.
3. Travis D, Brambilla E, Muller-Hermelink HK, Harris CC. *World Health Organisation Classification of Tumours: tumours of the lung, pleura, thymus and heart*. World Health Organisation. Lyon: IARC Press, 2004.

TISSUE PATHWAY: PULMONARY NEEDLE BIOPSIES

1 STAFFING AND WORKLOAD

The lead pathologist responsible for reporting pulmonary needle biopsies should have appropriate expertise in thoracic pathology and participate in a relevant EQA scheme. Cover should be available at an appropriate level during periods of leave, but it is acknowledged that, in most units, only one pathologist will have such specialist expertise.

2 SPECIMEN SUBMISSION

Specimens are immediately placed in formalin.

3 SPECIMEN DISSECTION AND BLOCK SELECTION

All of the specimen is submitted with a brief description of the size of the core or the fragments into which it sometimes breaks.

4 EMBEDDING AND SECTIONING

The core or fragments are embedded in one block and stepped sections cut.

5 STAINING

Haematoxylin and eosin is usually sufficient to identify common pathological changes with other stains on request by the pathologist.

6 FURTHER INVESTIGATIONS

If a neoplasm is present, a D-PAS stain for mucin may be useful in some carcinomas to identify solid pattern adenocarcinoma. Immunohistochemistry may be required to classify it precisely and exclude the possibility that it is metastatic. This is at the discretion of the pathologist. For example, the distinction of neuroendocrine tumours, usually small cell carcinoma, from non-neuroendocrine tumours, is aided by the identification of antigens indicative of neuroendocrine differentiation (e.g. CD56, synaptophysin, chromogranin A). The distinction of primary from metastatic adenocarcinoma is aided by the identification of TTF-1 and cytokeratin subclasses, especially 7 and 20.

If pulmonary infection (e.g. tuberculosis, Pneumocystis) is suspected, appropriate stains (e.g. Ziehl-Neelsen, Grocott, PAS) will be necessary. Elastic Van Gieson (EVG) stains are of value if considering a vasculitic process.

7 REPORT CONTENT

Pulmonary needle biopsies are usually performed to identify the nature of a pulmonary mass. The report comments on the adequacy of the specimen and the pathological changes present. A comment that non-specific inflammatory changes may represent changes due to obstruction by hitherto unsampled pathology may also be of value.

A neoplasm is classified according to the World Health Organisation Classification and, if appropriate, an attempt made to grade it as poor, moderately or well differentiated. At the very least, a distinction is made between small cell and non-small cell carcinoma, since this is the most crucial decision in terms of subsequent management.

8 REFERENCE

Travis D, Brambilla E, Muller-Hermelink HK, Harris CC. *World Health Organisation Classification of Tumours: tumours of the lung, pleura, thymus and heart*. World Health Organisation. Lyon: IARC Press, 2004.

TISSUE PATHWAY: VIDEO-ASSISTED THORACOSCOPIC (VATS) AND OPEN PULMONARY (SURGICAL LUNG) BIOPSIES

1 STAFFING AND WORKLOAD

The lead pathologist responsible for reporting these biopsies should have appropriate expertise in thoracic pathology and participate in a relevant EQA scheme. Cover should be available at an appropriate level during periods of leave, but it is acknowledged that, in most units, only one pathologist will have such specialist expertise.

2 SPECIMEN SUBMISSION

In the context of non-malignant pulmonary disease, surgical lung biopsies are almost always taken to investigate the cause of diffuse parenchymal lung disease (DPLD), most frequently to differentiate between the patterns of interstitial pneumonias. High resolution computed tomography (HRCT) has removed the need for surgical biopsy in a large proportion of patients who present with DPLDs, but this type of biopsy still plays a significant role in diagnosis in a minority of patients and will remain so, as some DPLDs do not have specific HRCT features and both atypical presentations and abnormal longitudinal behaviour are still encountered. Surgical lung biopsies may also be used in the diagnosis of unexplained pulmonary hypertension, in paediatric lung disease where HRCT is less specific and, occasionally, for patients with neoplasia.

Ideally, biopsy sites are targeted pre-operatively through HRCT correlation, sample sites are multiple, and biopsies of at least 30mm in maximum width are taken to maximise diagnostic yield.

Should infection be suspected, a second, separate specimen is sent fresh and directly for microbiological study. If tissue is in short supply and a staple line is present, then the tissue attached to the staple line, which would otherwise be redundant, can be used.

Ideally, and particularly in paediatric cases, small, separate pieces of tissue are snap frozen and fixed in glutaraldehyde to facilitate additional genetic or ultrastructural investigations if required.

The remaining tissue is ideally gently inflated with formalin *via* a small bore needle, taking care not to over-expand the tissue as this can cause artefact that mimics lymphangiectasia, especially in children. Overinflation also may wash out alveolar contents, for example macrophages that are key to the diagnosis of respiratory bronchiolitis. The specimen is then fixed overnight.

3 SPECIMEN DISSECTION AND BLOCK SELECTION

The specimen will be a wedge of subpleural lung, stapled along the surgical margin. A description includes its dimensions and any parenchymal or pleural abnormalities. The row of staples is cut off (unless already used). The axis of slicing will depend on the volume of tissue, but ideally aim for sections with the largest possible area.

4 EMBEDDING AND SECTIONING

A single section of each slice embedded provides an adequate picture of the extent, distribution and nature of any pathology present.

5 STAINING

Haematoxylin and eosin is usually sufficient for the investigation of diffuse pulmonary disease. A stain to highlight collagen and the pulmonary vasculature is also applied routinely (e.g. Elastic Van Gieson, haematoxylin and Van Gieson, Movat's stain).

6 FURTHER INVESTIGATIONS

If asbestos is suspected as a cause of interstitial fibrosis, thick (25-30 μm) unstained sections or sections stained by the Perls' Prussian Blue method are examined for asbestos bodies. A Perls' stain is also of value in identifying haemosiderosis, both primary and secondary, and distinguishing this pigmentation from that of smokers' macrophages.

If pulmonary infection (e.g. tuberculosis, Pneumocystis) is suspected, appropriate stains (e.g. Ziehl-Neelsen, Grocott, PAS) will be necessary.

Immunohistochemistry is used at the discretion of the pathologist for identification of tumours and some DPLDs, particularly Langerhans cell granulomatosis, in which the characteristic infiltrate will be highlighted by its immunoreactivity for S-100 protein and the CD1a antigen.

Ultrastructure is infrequently used in a diagnostic setting, but is of value when assessing inborn errors of metabolism and some surfactant protein gene mutations.

7 REPORT CONTENT

The report comments on the adequacy of the specimen. In end-stage 'honeycombing' fibrosis, it may be impossible to determine the underlying cause and the specimen should be considered inadequate for diagnosis, although it may still be of value in excluding/identifying diseases such as sarcoidosis and neoplasms. This situation can ideally be avoided in the majority of cases by pre-operative targeting of multiple sites (see above).

For the *idiopathic interstitial pneumonias (IIPs)*, the 2002 American Thoracic Society/European Respiratory Society classification is used. By far the commonest IIP is usual interstitial pneumonia (idiopathic pulmonary fibrosis). This diagnosis should be accompanied by an estimate of activity - that is the prevalence of foci of fibroblastic foci/granulation tissue. For other IIPs, a comment on the extent and pattern of any fibrosis is also made.

Once the pathologist has a diagnosis of a histological pattern, multidisciplinary review should occur, ideally through formal and regular team meetings but, as a minimum, review of imaging and clinical data for individual cases, after which a final clinicopathological diagnosis can be given.

For other DPLDs, the nature, pattern and severity of any pathological changes are described, taking care to assess all anatomic compartments as, for example, collagen vascular disease can present with coexistent interstitial pneumonias and vascular disease. Again, multidisciplinary review should be part of the diagnostic algorithm. If a specific diagnosis cannot be made, a differential diagnosis of the causes of any changes present is given.

In cases where a diagnosis of asbestosis is suspected, controversy remains over how many asbestos bodies are required for diagnosis. Identification of a single asbestos body in the setting of diffuse interstitial fibrosis raises the possibility of asbestosis but, in order to make a firm diagnosis, two asbestos bodies per 1 cm^2 should be identified. Multidisciplinary review of such cases is again recommended.

In the investigation of pulmonary vascular disease, the distribution of changes such as vascular medial muscularization and the presence of fibrinoid vasculosis and of plexiform or angiomatoid lesions is

sought and described. Pathologists should distinguish veno-occlusive disease from those of pulmonary arterial hypertension.

8 REFERENCES

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2. Nicholson AG, Addis BJ, Bharucha H, Clelland CA, Corrin B, Gibbs AR *et al*. Inter-observer variation between pathologists in diffuse parenchymal lung disease. *Thorax* 2004;59:500-505.
3. Pilling JE, Nicholson AG, Wells AW, Hansell DM, du Bois RM, Renzoni EA, *et al*. Multidisciplinary approach to surgical lung biopsy maximises diagnostic yield. *Am J Respir Crit Care Med* 2007;175:A568
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5. Deutsch GH, Young LR, Deterding RR, Fan LL, Dell SD, Bean JA *et al*. Diffuse lung disease in young children: application of a novel classification scheme. *Am J Respir Crit Care Med - in press*.
6. Pietra GG, Capron F, Stewart S, Leone O, Humbert M, Robbins IM *et al*. Pathologic assessment of vasculopathies in pulmonary hypertension. *J Coll Cardiol* 2004;43:25S-32S.
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8. Roggli VL, Pratt PC. Numbers of asbestos bodies on iron-stained tissue sections in relation to asbestos body counts on lung tissue digests. *Hum Pathol*. 1983;14:355-361.
9. Gibbs A, Attanoos RL, Churg A, Weill H. The "Helsinki criteria" for attribution of lung cancer to asbestos exposure: how robust are the criteria? *Arch Pathol Lab Med*. 2007;131:181-183.

TISSUE PATHWAY: PLEURAL NEEDLE BIOPSIES

1 STAFFING AND WORKLOAD

The lead pathologist responsible for reporting these biopsies should have appropriate expertise in thoracic pathology and participate in a relevant EQA scheme. Cover should be available at an appropriate level during periods of leave, but it is acknowledged that, in most units, only one pathologist will have such specialist expertise.

2 SPECIMEN SUBMISSION

Specimens are immediately placed in formalin.

3 SPECIMEN DISSECTION AND BLOCK SELECTION

All of the specimen is submitted with a brief description of the number and size of the fragments.

4 EMBEDDING AND SECTIONING

The fragments are embedded in one block and stepped sections cut through it.

5 STAINING

Haematoxylin and eosin is usually sufficient to identify basic pathological changes with other stains on request by the pathologist.

6 FURTHER INVESTIGATIONS

If a neoplasm is present, the usual distinction to be made is between mesothelioma and metastatic adenocarcinoma, since these are by far the commonest malignant neoplasms at this site. A diastase-PAS stain may therefore be of use. Staining for acidic mucins (Alcian blue +/- hyaluronidase) can also be of value but has largely been superseded by immunohistochemistry. Diagnosis, however, may be impossible with the small amount of tissue usually present in a pleural needle biopsy and further large biopsies may be required, especially for distinguishing reactive from neoplastic infiltrates. The diagnosis of malignant mesothelioma should not be made on a needle biopsy specimen without knowing that the clinical and radiological features are appropriate. Bear in mind also, that other neoplasms occasionally arise in or spread to the pleura.

The distinction between mesothelioma and metastatic adenocarcinoma cannot be made with confidence on morphological grounds alone and immunohistochemistry is mandatory. Because, currently, none of the antigens indicative of mesothelial or glandular differentiation is sufficiently sensitive or specific, a panel is used. This will vary according to the preference of the individual pathologist, but recommended markers of mesothelial differentiation include cytokeratins of classes 5 and 6, calretinin, N-cadherin and thrombomodulin. However, it is emphasised that the specificity and sensitivity for mesothelioma using these antibodies is significantly reduced in poorly differentiated epithelioid neoplasms and in spindle cell tumours, and these data should not be interpreted in isolation of other data. Suitable markers of glandular differentiation include epithelial glycoprotein (BerEp4 antibody), CEA and the CD15 antigen.

Further immunohistochemistry (e.g. TTF-1, cytokeratin subclasses) may be required to further define the nature of metastatic adenocarcinoma.

7 REPORT CONTENT

The report comments on the adequacy of the specimen (some pleural needle biopsies consist largely or even entirely of connective tissue from the chest wall) and describes any pathological changes present. The morphological and immunochemical features of any neoplasm present are described and at least a differential diagnosis provided. The diagnosis of mesothelioma has serious medicolegal implications and is made with due care, especially on a small biopsy.

Should only a tentative or equivocal diagnosis be possible, it may be appropriate to suggest recourse to thoracoscopic or open pleural biopsy.

8 REFERENCES

1. Ordóñez NG. The immunohistochemical diagnosis of epithelial mesothelioma. *Human Pathology* 1999;30:313-323.
2. Miettinen M, Sarlomo-Rikala M. Expression of calretinin, thrombomodulin, keratin 5, and mesothelin in lung carcinomas of different types: an immunohistochemical analysis of 596 tumors in comparison with epithelioid mesotheliomas of the pleura. *Am Surg Pathol* 2003;27:150-158.
3. Galateau-Salle F and International Mesothelioma Panel. *Pathology of malignant mesothelioma*. London: Springer, 2006.

TISSUE PATHWAY: THORACOSCOPIC OR OPEN PLEURAL BIOPSIES

1 STAFFING AND WORKLOAD

The lead pathologist responsible for reporting these biopsies should have appropriate expertise in thoracic pathology and participate in a relevant EQA scheme. Cover should be available at an appropriate level during periods of leave, but it is acknowledged that, in most units, only one pathologist will have such specialist expertise.

2 SPECIMEN SUBMISSION

Should infection be suspected, submission of a second, separate specimen for microbiological study is encouraged. This is submitted fresh, the specimen for histopathology being immediately placed in an adequate volume of formalin. Ideally, a small amount of tissue is snap frozen and also fixed in glutaraldehyde as additional genetic (e.g. for the diagnosis of primitive neuroectodermal tumour (PNET) and synovial sarcoma) or ultrastructural (some sarcomas and mesothelioma) investigations may be required.

3 SPECIMEN DISSECTION AND BLOCK SELECTION

All of the specimen is submitted with a brief description of its size and appearance; pleura infiltrated by a neoplasm is often conspicuously nodular.

4 EMBEDDING AND SECTIONING

A single section through each block is usually adequate to reveal the nature of any pathology present.

5 STAINING

Haematoxylin and eosin is usually sufficient to identify basic pathological changes with other stains on request by the pathologist.

6 FURTHER INVESTIGATIONS

If a neoplasm is present, the usual distinction to be made is between mesothelioma and metastatic adenocarcinoma, since these are by far the commonest malignant neoplasms at this site, although other, rarer neoplasms do occasionally arise in or spread to the pleura.

The distinction between mesothelioma and metastatic adenocarcinoma cannot be made with confidence on morphological grounds alone, and immunohistochemistry is mandatory. Because, currently, none of the antigens indicative of mesothelial or glandular differentiation is sufficiently sensitive or specific, a panel is used. This will vary according to the preference of the individual pathologist, but recommended markers of mesothelial differentiation include cytokeratins of classes 5 and 6, calretinin, N-cadherin and thrombomodulin. However, it is emphasised that the specificity and sensitivity for mesothelioma using these antibodies is significantly reduced in poorly differentiated epithelioid neoplasms and in spindle cell tumours, and these data should not be interpreted in isolation of other data. Suitable markers of glandular differentiation include epithelial glycoprotein (BerEp4 antibody), CEA and the CD15 antigen.

Further immunohistochemistry (e.g. TTF-1, cytokeratin subclasses) may be required to further define the nature of metastatic adenocarcinoma. A broader panel of antibodies is required to distinguish mesothelioma from sarcomas (primary and metastatic), as well as sometimes sending tissue for genetic analysis (e.g. X:18 translocation for synovial sarcoma).

For the distinction of reactive from neoplastic epithelioid infiltrates, staining for desmin and EMA may be helpful, although diagnosis remains primarily morphological. This is also true of distinguishing desmoplastic mesothelioma from fibrosis, although cytokeratin staining may be of value.

7 REPORT CONTENT

The report describes any pathological changes present.

The morphological and immunochemical features of any neoplasm are described and at least a differential diagnosis provided. The diagnosis of mesothelioma has serious medicolegal implications and is made with due care. Referral for expert opinion is considered in difficult cases. It should be acknowledged that mesothelioma may be present only focally, especially in a fibrotic pleura, such that its absence from even a generous biopsy by no means excludes the diagnosis.

8 REFERENCES

1. Ordonez NG. The immunohistochemical diagnosis of epithelial mesothelioma. *Hum Pathol* 1999;30:313-323.
2. Miettinen M, Sarlomo-Rikala M. Expression of calretinin, thrombomodulin, keratin 5, and mesothelin in lung carcinomas of different types: an immunohistochemical analysis of 596 tumors in comparison with epithelioid mesotheliomas of the pleura. *Am J Surg Pathol* 2003;27:150-158.
3. Cury PM, Butcher DN, Corrin B, Nicholson AG. The use of histological and immunohistochemical markers to distinguish pleural malignant mesothelioma and in situ mesothelioma from reactive mesothelial hyperplasia and reactive pleural fibrosis. *J Pathol.* 1999;189:251-257.
4. Attanoos RL, Griffin A, Gibbs AR. The use of immunohistochemistry in distinguishing reactive from neoplastic mesothelium. A novel use for desmin and comparative evaluation with epithelial membrane antigen, p53, platelet-derived growth factor-receptor, P-glycoprotein and Bcl-2 *Histopathology* 2003;43:231-238.
5. Churg A, Colby TV, Cagle P, Corson J, Gibbs AR, Gilks B *et al.* The separation of benign and malignant mesothelial proliferations. *Am J Surg Pathol* 2000;24:1183-1200.
6. Galateau-Salle F and International Mesothelioma Panel. *Pathology of malignant mesothelioma.* London: Springer, 2006.

TISSUE PATHWAY: PULMONARY RESECTION FOR NON-NEOPLASTIC DISEASE

1 STAFFING AND WORKLOAD

The lead pathologist responsible for reporting these resection specimens should have appropriate expertise in thoracic pathology and participate in a relevant EQA scheme. Cover should be available at an appropriate level during periods of leave, but it is acknowledged that, in most units, only one pathologist will have such specialist expertise.

2 SPECIMEN SUBMISSION

Should infection be suspected, submission of a second, separate specimen for microbiological study is encouraged. This is submitted fresh, the specimen for histopathology being immediately placed in an adequate volume of formalin. If possible, distension with formalin *via* an airway is desirable to aid rapid fixation.

3 SPECIMEN DISSECTION AND BLOCK SELECTION

The specimen will be a wedge, lobe or whole lung. A full description is made including the nature and extent of any pathological changes evident on macroscopic examination. In paediatric cases, typically with lung cysts, the bronchial anatomy is closely examined and any abnormality noted. Photography of the specimen is recommended during cut-up. Blocks are selected as appropriate at the discretion of the pathologist.

4 EMBEDDING AND SECTIONING

A single section from each block is sufficient to provide an adequate picture of the extent, distribution and nature of any pathology present.

5 STAINING

Haematoxylin and eosin is usually sufficient to reveal the nature of the pathology.

6 FURTHER INVESTIGATIONS

If pulmonary infection (e.g. persistent consolidation, cavitating masses) is suspected, further appropriate stains (e.g. Gram, Ziehl-Neelsen, Grocott, PAS) will be necessary. Elastic Van Gieson (EVG) staining is undertaken if a vasculitis is suspected.

7 REPORT CONTENT

The report describes any pathological changes present and their cause, if appropriate. The cause of any infective pathology is pursued as far as possible by appropriate staining, bearing in mind that microbiological examination is generally more sensitive than histopathology as a means of identifying the organism(s) responsible. Cysts are classified according to current terminology.

8 REFERENCE

Langston C. New concepts in the pathology of congenital lung malformations. *Semin Pediatr Surg* 2003;12:17-37.

TISSUE PATHWAY: PLEURAL RESECTION FOR NON-NEOPLASTIC DISEASE

1 STAFFING AND WORKLOAD

The lead pathologist responsible for reporting these resection specimens should have appropriate expertise in thoracic pathology and participate in a relevant EQA scheme. Cover should be available at an appropriate level during periods of leave, but it is acknowledged that, in most units, only one pathologist will have such specialist expertise.

2 SPECIMEN SUBMISSION

Should infection be suspected, submission of a second, separate specimen for microbiological study is encouraged. This is submitted fresh, the specimen for histopathology being immediately placed in an adequate volume of formalin.

3 SPECIMEN DISSECTION AND BLOCK SELECTION

Pleural resection (decortication) for non-neoplastic disease is usually performed to relieve respiratory impairment due to compression of the lung by thickened, chronically inflamed or fibrotic pleura, subsequent to inflammation, most often empyema. The specimen will consist of pieces of pleura of varying size that are fully described, noting the consistency of the changes, the presence of any focal pathology, and the presence and nature of any exudate. Blocks are selected as appropriate at the discretion of the pathologist.

4 EMBEDDING AND SECTIONING

A single section from each block is sufficient to provide an adequate picture of the extent, distribution and nature of any pathology present.

5 STAINING

Haematoxylin and eosin is usually sufficient to reveal the nature of the pathology, but further stains will be necessary if, for example, infection is suspected.

6 FURTHER INVESTIGATIONS

If infection is suspected, appropriate stains (e.g. Gram, Ziehl-Neelsen) will be necessary.

7 REPORT CONTENT

The report describes the nature of the pathological changes present, including, for example, whether granulomas are present. The cause of any infective pathology is pursued as far as possible by appropriate staining, bearing in mind that microbiological examination is generally more sensitive than histopathology as a means of identifying the organism(s) responsible. Pleurisy can sometimes complicate mesothelioma or other malignancy that may be masked by reactive inflammation and fibrosis and care should be taken to exclude underlying neoplasia. If there is an atypical mesothelial proliferation, immunostaining for cytokeratins may aid the identification of invasion. Desmoplastic mesothelioma, in particular, may be difficult to distinguish from pleural fibrosis.

8 REFERENCE

Mangano WE, Cagle PT, Churg A, Vollmer RT, Roggli VL. The diagnosis of desmoplastic malignant mesothelioma and its distinction from fibrous pleurisy: a histologic and immunohistochemical analysis of 31 cases including p53 immunostaining. *Am J Clin Pathol* 1998;110:191-199.

Dr John R Gosney

Professor Andrew G Nicholson

Dr Allen R Gibbs

**On behalf of the RCPATH Specialty Advisory Committee on Histopathology
and the Cancer Services Working Group**

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