

Original Article

Recommendations for processing cardiovascular surgical pathology specimens: a consensus statement from the Standards and Definitions Committee of the Society for Cardiovascular Pathology and the Association for European Cardiovascular Pathology

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Abstract

With the advent of molecular subclassification of diseases, much consideration should be given to the proper processing of cardiovascular surgical pathology specimens to maximize patient care. Such specimens include endomyocardial biopsies, cardiac myectomy specimens, cardiac apical core segments, resected cardiac valves, pericardial biopsies, resected segments of aorta, cardiac tumors, vascular stents, vascular grafts, cardiac devices, resected veins, arterial biopsies including temporal artery biopsies and hearts removed during cardiac transplantation. In this report, the Standards and Definitions Committee of the Society for Cardiovascular Pathology and the Association for European Cardiovascular Pathology present consensus guidelines for the gross description, sectioning, processing, and staining of these

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specimens. This report is presented to aid pathologists, pathology assistants, and clinicians in maximizing the diagnostic utility of cardiovascular surgical pathology specimens for enhanced patient care. © 2012 Elsevier Inc. All rights reserved.

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1. Introduction

In recent years, there has been an explosion of new information relating to the molecular basis of human cardiovascular diseases. This new information is being utilized to derive molecular subclassifications for these diseases. Now more than probably ever before, there is a need for systematic procedures for the handling and processing of cardiovascular pathology specimens to maximize patient care, enable molecular/pathologic correlations, and facilitate the acquisition of novel molecular and pathologic data. The handling of cardiovascular surgical pathology specimens in general has never been formally addressed by an international consensus committee, and thus, current practices may vary considerably between institutions and even between pathologists at the same institution. The manner in which cardiovascular surgical pathology specimens are handled by pathologists and clinicians can directly impact patient care.

The Standards and Definitions Committee of the Society for Cardiovascular Pathology and the Association for European Cardiovascular Pathology have put forth these guidelines, to offer guidance in regard to the gross description, sectioning, processing, and staining of cardiovascular surgical pathology specimens. These guidelines represent an overall consensus of the members of the committee. These guidelines should be viewed as recommendations and not as mandatory requirements. It is understood that local and regional laws, standards of care, and fiscal constraints may result in a particular institution justly working up cardiovascular surgical pathology specimens with different protocols than suggested here.

2. Methods

At the 2008 annual meeting of the Society for Cardiovascular Pathology, which was held in conjunction with the annual meeting of the United States and Canadian Academy of Pathology, an open invitation was extended to all attendees to join the Standards and Definitions Committee. Committee membership was extended as well to the members of the Association for European Cardiovascular Pathology. This multi-institutional committee membership identified the types of specimens routinely encountered by cardiovascular surgical pathology services and constructed consensus guidelines for the gross description, sectioning, processing, and staining of such tissue. For this report, consensus is defined as being the majority of the membership of the committee and may not necessarily in all cases indicate a unanimous opinion. The opinions put

forth here do not necessarily represent the opinions of all members of the Society for Cardiovascular Pathology or the Association for European Cardiovascular Pathology. Areas with significant dissenting opinion within the committee are indicated in the text. For the consensus opinions, an emphasis was placed on incorporating the results of relevant published peer-reviewed literature.

3. Specimen recommendations

3.1. General recommendations for tissue distribution

In the interest of patient care, the committee recommends that cardiovascular tissue that is removed from a living person be sent to the pathology department in the institution before disbursement for special molecular and/or proteomic studies and research protocols. The committee acknowledges the importance of both such special studies and research protocols and recommends that the pathologist should coordinate these activities. The pathologist should ensure that such tissue distribution does not prevent clinically relevant pathologic diagnoses from being rendered. For diagnostic studies, the pathologist should coordinate the distribution of tissue for these studies and ensure accurate documentation of the results of these studies in the patient's medical record. The committee also recommends cooperation and communication between the clinical services obtaining the specimens and pathologists evaluating the specimens, as well as referral of specimens to Level 3 cardiovascular pathology services in selected cases [1].

3.2. Native endomyocardial biopsies

3.2.1. Rationale

The use of ventricular endomyocardial biopsies (EMBx) for diagnostic purposes was popularized after the development of the Caves bioptome in the 1970s, an improvement on the Konno–Sakakibara bioptome, invented in the 1960s [2,3]. Despite the initial enthusiasm for the procedure and the low complication rate, it was soon realized that EMBx was not a useful diagnostic test for many patients with heart failure [4]. In recent times, this technique has again gained widespread acceptance by cardiologists for evaluating patients with specific cardiac clinical presentations [5]. It is now established that EMBx can be used to make specific diagnoses in a variety of disease states and can generate a histomorphologic picture in cases in which a specific diagnosis cannot be rendered. While right ventricular EMBx is most common, left ventricular EMBx may also be performed. Tables reporting these diagnoses and descriptions have been described elsewhere [6,7]. A document from

the Society for Cardiovascular Pathology and the Association for European Cardiovascular Pathology specifically addressing the utility of EMBx is currently in preparation.

3.2.2. Gross description and processing

In advance of the biopsy procedure, the cardiologist should consider the reason for performing the biopsy and have the tissue processed appropriately. There are four separate uses for EMBx tissue. Myocardium should always be collected for light microscopy and, in certain clinical situations, may also be taken for electron microscopy (EM), immunofluorescence (IF), or for viral nucleic acid studies [5]. One potential method to distribute tissue for the proper studies is summarized in Table 1. Alternatively, since the complete clinical picture is often still evolving at the time of biopsy, it is also frequently helpful to routinely freeze one piece of myocardium for potential IF or nucleic acid studies. The frozen piece can later be reprocessed for permanent section if needed.

For light microscopy, an adequate specimen for diagnostic interpretation usually consists of three or more pieces of endomyocardium, each measuring at least 1–2 mm³; although a minimum of five or more pieces of endomyocardium may be required in some situations [6,8]. These cardiac tissues are generally red-tan and unoriented. Specimens for light microscopy evaluation should be carefully placed in room temperature 10% buffered formalin [7]. EM, IF, and nucleic acid studies can be accomplished with a single piece of myocardium for each study. The one exception is to increase the number of pieces for EM evaluation of anthracycline toxicity [9]. Tissue for EM should be placed in glutaraldehyde fixative; tissue for IF should be frozen in Optimal Cutting Temperature compound or placed in Zeus solution, and tissue for viral nuclei acid studies should be frozen or placed in RNAlater RNA stabilizing solution. Reporting of the gross description should indicate the number of pieces, their sizes, and their allocation for each study.

Table 1
A typical distribution of EMBx tissues for processing based on clinical scenarios

Clinical scenario	LM	EM	IF	NuAc
New-onset heart failure <3 months	+	+		+
Heart failure >3-month duration	+	+		
Heart failure with DCM	+	+		
Heart failure associated with anthracycline use	+	+		
Heart failure associated with RCM	+	+	+	
Suspected cardiac tumors	+	+		
Cardiomyopathy in children	+	+		+
Heart failure associated with HCM	+	+		
Suspected ARVD/C	+			
Plasma cell dyscrasia and cardiac symptoms	+	+	+	

LM, light microscopy; NuAc, viral nucleic acid studies; DCM, dilated cardiomyopathy; RCM, restrictive cardiomyopathy; HCM, hypertrophic cardiomyopathy; ARVD/C, arrhythmogenic right ventricular dysplasia/cardiomyopathy.

Specimens for light microscopy should be placed in their entirety in a tissue bag or equivalent and submitted for standard histologic processing. Due to the small size of the specimen, it can be processed in a short period of time and is amenable to same-day interpretation. Frozen sections should be avoided at institutions that do not routinely evaluate EMBx in this manner. If different biopsy pieces are submitted separately, as may occur in evaluation of arrhythmogenic right ventricular cardiomyopathy, or other segmental disorders [10], then the pieces should be submitted for processing in separate cassettes.

Specimens taken for EM should be processed to generate thick sections at which time the pathologist can determine if EM will add additional information to the case. If tissue was not originally submitted for EM processing and EM is desired, formalin-fixed tissue can be processed for EM, or paraffin-embedded tissue can be reprocessed for EM. Tissue taken for IF can be held and used when appropriate. IF can be useful for subtyping amyloid deposits and in the determination of cardiac nonamyloidotic immunoglobulin deposition disease [11,12].

When viral myocarditis is suspected, tissue may be frozen or placed in RNAlater and then sent to a laboratory that has expertise in viral genome detection by assessment of nucleic acids [13]. While the histologic assessment and subclassification of myocarditis by EMBx have been shown to predict patient outcome [14,15], the prognostic significance of viral genome detection in EMBx specimens is currently controversial, with potentially contradictory results being recently reported [16–18]. The committee recognizes the need for further studies to clarify the value of viral genome detection in patients with myocarditis and recent-onset dilated cardiomyopathy.

3.2.3. Sections and stains

Various protocols for staining and sectioning EMBx tissue are currently followed at different institutions. These methods are specialized to the needs and workflow of a given institution, and no one protocol is appropriate for all institutions. One consensus of this committee is that multiple sections (three or more) should be stained with hematoxylin and eosin (H&E) at different levels through biopsy. For diseases that have a patchy distribution (sarcoidosis, myocarditis, etc.), even further sectioning can be performed if the entity is not seen on the initial slides. Intervening sections between H&E stains should be used for histochemical or immunohistochemical staining. The most common histochemical and immunohistochemical stains that are used are listed in Table 2. Using 8- μ m thick sections can enhance the sensitivity of Congo red staining for amyloid.

Other specialized stains can be obtained when evaluating amyloidosis, myocarditis, or granulomatous diseases. Kappa, lambda, and transthyretin (prealbumin) immunolabeling can be performed when amyloid is seen on the cardiac biopsy. Brown and Hopps, Gomori methenamine

Table 2
One typical panel of slides for the workup of an EMBx

Slide	Stain	Indication
1	H&E	
2	Collagen stain (Masson trichrome, Azan–Mallory, or Sirius red)	Fibrosis
3	Elastic stain (Movat pentachrome, VVG)	Endocardial fibroelastosis
4	H&E	
5	Lymphocyte marker (CD3, CD8)	Myocarditis
6	Macrophage marker (CD68)	Myocarditis/ myocyte injury
7	H&E	
8	Glycogen stain (PAS)	Glycogen storage disease
9	Amyloid stain (Congo red, thioflavin T, methyl violet, modified sulfated Alcian blue)	Amyloid deposition
10	Iron stain (Prussian blue)	Hemochromatosis
11	H&E	

Non-H&E slides can be held as unstained slides and stained when appropriate. The number of slides generated and the types of stains used may vary according to the institution.

silver (GMS), Warthin–Starry, Gram, Fite, and Ziehl–Neelsen stains can be used in the presence of inflammation or granulomas to identify infectious organisms. A modified Gomori trichrome stain may be used to assess for mitochondrial cardiomyopathy. For EMBx of cardiac tumors, see Section 3.6.

3.3. Heart transplant biopsies

3.3.1. Rationale

EMBx is a mainstay of surveillance for cardiac rejection after transplantation. Despite newer blood-based methods, the cardiac biopsy remains the gold standard of rejection and is an essential part of the care of transplant patients [19,20]. For consistency of reporting between institutions, the International Society of Heart and Lung Transplantation (ISHLT) developed a rejection scoring system in 1990 that was revised in 2005 [21,22].

3.3.2. Gross description

Endomyocardium may be taken for both light microscopy and IF. For light microscopy, an adequate specimen for diagnostic interpretation is defined in the ISHLT working formulation as at least three pieces, but preferably four or more pieces, of endomyocardium, with myocardium representing at least half of each tissue fragment [21]. These cardiac tissues should appear mostly red-tan and will be unoriented. The cardiologist should be aware that tissue fragments that are white may represent endocardial scarring from prior biopsies, and friable tissues may represent thrombus, neither of which is sufficient for evaluation. Specimens for light microscopy evaluation can be carefully placed in room temperature buffered formalin [7]. When IF is to be performed, a single piece of myocardium should be frozen or placed in Zeus or Michel's solution. Reporting of

the gross description should indicate the number of pieces, their sizes, and their disbursement for each study.

3.3.3. Processing

Specimens for light microscopy should be placed in their entirety in a tissue bag or equivalent and submitted for standard histologic processing. Due to the small size of the specimen, it can be processed in a short period of time and is amenable to same day interpretation. Tissue taken for IF is used to assess for C4d and/or C3d staining, which may indicate the presence of humoral/antibody-mediated rejection [23]. Processing of transplant EMBx is variable between institutions, and IF may be routinely performed with every case or only in specific clinical situations.

3.3.4. Sections and stains

H&E staining should be performed on at least three levels of myocardium from the biopsy tissue and graded according to ISHLT criteria [21]. No special stains are routinely obtained on these tissues; however, they can be obtained to assist in diagnosing antibody-mediated rejection or in discerning Quilty lesions [23–25]. In the assessment of antibody-mediated rejection, tissue collected for IF can be stained for complement split products such as C4d and/or C3d, along with positive and negative controls, and paraffin-embedded tissue can be assessed by immunohistochemistry for C4d and the macrophage marker CD68 [22,26].

3.4. Ventricular myectomy specimens

3.4.1. Rationale

Myectomy specimens are taken from the left ventricular septum to relieve outflow obstruction. Traditionally, these specimens are taken from patients with hypertrophic cardiomyopathy, although additional reasons for this resection include age-related angulation of the ventricular septum, sigmoid septum, and discrete subaortic stenosis [27,28]. While these specimens are removed primarily for structural reasons to improve left ventricular outflow, they may be utilized to diagnose cardiac disorders [29,30].

3.4.2. Gross description

Myectomy tissue is variable in size depending on the age of the patient and the degree of outflow tract obstruction. In one study, the range of specimen weights was between 0.2 and 17.7 g [30]. This tissue is usually fragmented, red-tan myocardium with a pearly white overlying endocardium. The endocardium can be extremely thick in some cases. Tissue is generally not orientated.

3.4.3. Processing

The tissue should be cut to fit into a minimum number of cassettes and submitted for light microscopy. Standard overnight histologic processing should be performed. A single piece of tissue may be placed in glutaraldehyde fixative and held for EM. Since septal myectomy specimens

may contain amyloid, which will need to be subtyped [29], institutions equipped for IF may freeze one piece to facilitate amyloid subtyping. There is no indication to process the tissue for viral nucleic acid studies.

3.4.4. Sections and stains

A single H&E-stained slide should be generated for each block. A Masson's trichrome, Azan–Mallory, or Sirius red stain should be obtained to document the degree of fibrosis and a Verhoeff–Van Gieson (VVG) or Movat pentachrome stain can be obtained to evaluate endocardial fibrosis. Phosphotungstic acid hematoxylin is useful for identifying myocyte disarray [31]. In patients over the age of 65 years, a modified sulfated Alcian blue, thioflavin T or Congo red stain should be ordered to determine the presence of amyloid [29]. Additional stains can be ordered as needed if warranted by the findings on the H&E-stained slides.

3.5. Apical core segments

3.5.1. Rationale

Apical cores of ventricular myocardium are obtained at the time of ventricular assist device (VAD) placement. With the advent of smaller and simpler VADs, their use as either a bridge to transplantation or as destination therapy in heart failure patients is increasing [32]. Apical core tissue is removed when a device cannula is placed in the ventricular apex. While this material is not taken specifically for diagnostic purposes, useful information can be obtained from pathologic evaluation [11,33–36].

3.5.2. Gross description

Apical core tissue is generally 2×2×1 cm in size or less. Depending on the institution, the tissue may be in a single piece or fragmented. Tissue is mostly red-tan myocardium and attached yellow adipose of the epicardium. Obvious scarring may be noted as white streaks through the tissue. Tissue may or may not be orientable. If it is orientable, it should be cut to maintain an endocardial-to-epicardial orientation when evaluated by light microscopy.

3.5.3. Processing

Tissue is typically only processed for light microscopy, unless the patient has a clinical history that would warrant a need for EM. Formalin fixation with standard overnight histologic processing should be performed. Since apical core specimens may contain amyloid, which will need to be subtyped [11], institutions equipped for IF may freeze one piece to facilitate amyloid subtyping. As discussed above for EMBx, viral nucleic acid studies may be considered in special situations [37].

3.5.4. Sections and stains

A single H&E-stained slide should be generated for each block. A Masson's trichrome, Azan–Mallory, or Sirius red stain should be obtained on at least one block to document

the degree of fibrosis, a measure variably useful in the clinical setting [34,38,39]. Additional stains can be ordered as needed if warranted by H&E findings as detailed above for native EMBx.

3.6. Hearts

3.6.1. Rationale

The most common indications for heart transplantation in the adult are end-stage ischemic heart disease and cardiomyopathies [40–42]. Referral to a center and/or pathologist with expertise in processing surgically resected hearts should be considered [1,40]. The approach to the examination of the heart should be guided by the clinical history. In cases of congenital heart diseases, it is advisable to review the clinical diagnosis and preoperative imaging studies with the cardiologist before dissection of the formalin-fixed specimen. A detailed approach to the dissection of congenital heart diseases is beyond the scope of this report, and the readers are referred to previous excellent publications [43,44]. In cases of complex congenital heart disease, referral to a center with expertise in this area should be considered. A protocol for the examination of hearts at autopsy in cases of sudden cardiac death has been reported by members of the Association for European Cardiovascular Pathology, and some of these guidelines can be applied to surgically resected hearts [45].

3.6.2. Gross description

It is helpful to photograph both the intact and sectioned heart. The fresh heart weight is taken prior to fixation and dissection; the heart weight after formalin fixation may also be recorded. Note the presence of any attached devices, leads, bypass grafts, or prosthetic valves. Describe the general shape (conical, globular) and consistency (firm, flabby) of the heart. Check the epicardium for adhesions, petechiae, scars, or any changes secondary to surgery. Describe the amount and distribution of epicardial fat. All four cardiac valves should be visible from the base of the heart with most of the atria missing in surgically resected hearts. In cases of total artificial heart implantation, the atria and atrioventricular valves of the recipient heart are not resected and thus will not be included in the specimen. Examine the valves for thickening, calcifications and any other abnormalities (refer to section under native valves). Measure the circumferences of each valve in centimeters.

Identify the ostia of the coronary arteries. Describe the course of the epicardial coronary arteries. If the coronary arteries are not calcified, start with the left main artery and serially section the left anterior descending artery and the remaining left circumflex artery as far as possible. Then examine the right coronary artery distally to the posterior descending artery. Examine the lumen for thrombi and acute plaque changes. Document the location and percentage of narrowing. If stents are present, describe their location. Evaluation of X-ray images of stented vessels is helpful to

determine stent location, adequateness of deployment and presence of damage to the stent. If there are bypass grafts, they should be dissected prior to the native coronary vessels. Describe anastomotic site patency and location as well as luminal stenosis and calcifications in the wall. If the coronary arteries are calcified, dissect the arteries free from the heart in toto or in partial segments and decalcify before cross-sectioning. If metal stents are present, section the artery close to the stent and inspect the lumen.

Examine the atrial cuffs and any atrial appendages, taking note of any endocardial lesions or adherent thrombi. The ventricles can be sectioned using a number of standard approaches [46]. In general, and particularly for ischemic heart disease, serial transverse sections at 1-cm intervals from the apex to about 2 cm below the atrioventricular valves will allow for the greatest surface area to be examined. However, in the setting of cardiomyopathies, a four-chamber section can offer a convenient alternative approach to assess global changes in chamber dimensions and/or wall structure in a single cut. Note the chamber sizes (normal, small, dilated) and check the endocardium for fibrosis or thrombi. Measure the thickness of the interventricular septum and free wall of both ventricles (do not include trabeculations). Inspect the papillary muscles (normal, hypertrophied, fibrotic) and attached chordae. Describe the gross appearance of the myocardium and look for areas of infarction, scars, hemorrhages, or fatty replacement. Note the extent (transmural, subendocardial), size, location (apical, basal, anterior, lateral, posterior) and appearance (color, consistency) of infarcts and scars.

3.6.3. Processing

It is recommended to submit a minimum of 8–10 sections from the left ventricle including the interventricular septum and at least two sections from the right ventricle. For patients with ischemic heart disease, it is often helpful to submit a complete cross-section of the heart to map the ischemic distribution. For patients with cardiomyopathies, it is often most helpful to sample both apical and basal segments from the major compass directions: anterior, lateral, posterior, and septal. It is also recommended to submit representative sections from both atria, any valve lesions, and representative sections of native coronary arteries and grafts, including the sites of most significant luminal stenosis and any areas containing thrombi. The aortic root may also be sampled to exclude aortic disease. This sampling approach represents a consensus of the committee. A minority opinion in the committee represented a more minimalist approach, submitting three blocks of left ventricle/interventricular septum and one to two blocks of right ventricle with additional sectioning if warranted by the initial histologic findings.

Traditionally, histologic examination of coronary stents required plastic embedding and sectioning, which very few laboratories are capable of doing. If histologic examination of a stent is desired, the segment of artery containing the

stent can be sent to institutions performing this procedure. In most routine cases, the stented artery may be opened longitudinally and the stent examined for the presence of thrombus. The stent itself may also be opened longitudinally with scissors, and any luminal material can then be submitted for routine histologic analysis. Recently, a novel and innovative procedure for electrically dissolving metal stents in formalin-fixed arterial segments has been reported [47].

Examination of the atrioventricular node is also possible if needed. This may be done by removing a rectangular block of tissue bordered by the opening of the coronary sinus in the right atrium posteriorly, the membranous interventricular septum anteriorly, approximately 1–1.5 cm of interatrial septum superiorly and 2 cm of interventricular septum below the insertion of the septal leaflet of the tricuspid valve. This block is then serially sectioned in the coronal plane and can be submitted in four to five cassettes [46].

In cases of idiopathic cardiomyopathy, a small piece of left ventricular myocardium is fixed in glutaraldehyde for EM and put on hold until light microscopy is performed. Tissue from the ventricles can also be frozen for IF and molecular nucleic acid studies. Donor tissues may also be submitted and may consist of donor atria, aorta, pulmonary artery, and EMBx.

3.6.4. Sections and stains

A single H&E-stained slide should be generated for each block. Order a connective tissue stain (trichrome, Azan–Mallory, Movat, or Sirius red) on representative sections of myocardium to assess for collagen deposition. Additional stains can be ordered as needed if warranted by H&E findings as described above for native EMBx.

3.7. Cardiac tumors

3.7.1. Rationale

Cardiac tumors or neoplasms can be divided into primary or secondary. While metastatic lesions are much more common than primary cardiac tumors, most of the surgical specimens entail resections of primary tumors. The two most common benign primary cardiac tumors are myxomas and papillary fibroelastomas [48–49]. Malignant primary tumors include sarcomas, pericardial mesothelioma, and primary lymphomas. Primary cardiac sarcomas are classified similar to soft tissue sarcomas, although about a quarter of these tumors are unclassifiable and will be designated as undifferentiated sarcomas [50–55]. Surgical resection of cardiac tumors varies from open biopsy to complete resection and palliative debulking procedures.

3.7.2. Gross description

Gross evaluation with adequate documentation of the resected mass is of vital importance for the evaluation of cardiac tumors. Measure the tumor in three dimensions and weigh it. Describe the presence of epicardium, endocardium,

or myocardium or any identifiable normal structure, such as interatrial septum or valve. Ink the resection margins and document the distance of the tumor from the margins. Note gross features of the tumor including color, consistency, shape, surface (smooth, rough, or villous), type of growth, and presence of pedicle. Cut sections should be inspected for hemorrhage, necrosis, calcifications, or cystic degeneration.

3.7.3. Processing

At least one section per centimeter of the tumor is submitted. Sample areas that exhibit variation in gross appearance and include areas of necrosis. Document involvement of adjacent normal structures. Closest margins are taken perpendicular to the tumor to assess the distance and adequacy of resection. If there is adequate tissue and malignancy is suspected, portions of the tumor can be snap frozen for molecular analysis and sampled for EM. A portion may be placed in cell culture media for karyotype analysis.

3.7.4. Sections and stains

A single H&E-stained slide should be generated for each block. An Alcian–periodic acid-Schiff stain (PAS) may be helpful in cases of cardiac myxoma, and an elastic stain may be helpful in cases of papillary fibroelastoma. Immunohistochemistry is often helpful. In contrast to organizing thrombi, by immunohistochemistry cardiac myxomas are often diffusely positive for calretinin [56]. Immunohistochemical stains are also used to aid in the classification of cardiac sarcomas, lymphomas, mesothelioma, and metastatic tumors. While a detailed discussion of the use of immunohistochemical stains in the workup of malignant tumors is beyond the scope of this report, useful immunostains include, but are not limited to, vimentin, cytokeratin, epithelial membrane antigen, calretinin, desmin, S100, smooth muscle actin, CD34, CD31, CD45, CD3, and CD20.

3.8. Papillary muscle

3.8.1. Rationale

The most important cause of papillary muscle dysfunction is myocardial ischemia [57]. Rupture of papillary muscle as a complication of acute myocardial infarction results in abrupt onset of severe mitral regurgitation and congestive heart failure. Rarely, papillary muscle avulsion has been reported as a consequence of blunt chest trauma. Distortion of the normal spatial relations of the papillary muscles may also be seen in left ventricular dilatation and hypertrophic cardiomyopathy and can result in mitral regurgitation. In some instances, mitral valve mobility is restricted by anomalous direct insertion of the papillary muscle to the leaflet or via shortened chordae.

3.8.2. Gross description and processing

The gross specimen usually consists of the papillary muscle tip with attached segment of mitral valve leaflet and

chordae. Measure the size of the papillary muscle and describe the border. Assess for irregularity, roughening, hemorrhages, and presence of fibrin. A torn papillary muscle will have an irregular necrotic shaggy edge. Section the papillary muscle longitudinally and note any fibrosis, pallor, or hemorrhages. Describe the chordae and leaflet. Inspect the mitral subvalvular apparatus for abnormal connection of the chordae or papillary muscle to the mitral valve. Submit a section of the papillary muscle in continuity with the chordae and leaflet.

3.8.3. Sections and stains

An H&E stain should be evaluated. A connective tissue stain (trichrome, Azan–Mallory, Movat, or Sirius red) is used to assess for interstitial and replacement fibrosis. Additional stains can be ordered as needed if warranted by H&E findings, as detailed above for native EMBx.

3.9. Atrial appendages

3.9.1. Rationale

Atrial appendages from either the right or left atrium may be surgically resected from patients with atrial fibrillation or atrial dilation to prevent embolic episodes, or from patients with congenital atrial aneurysms. The routine histology of the atrial myocardium in these patients differs from the ventricular myocardium. The myocardium in resected atrial appendages frequently displays profound myocyte hypertrophy and vacuolization, interstitial fibrosis, and not uncommonly amyloid deposition due to localized atrial natriuretic factor amyloid, which has been reported to be present incidentally in up to 16% of resected atrial appendages [58–60]. While the presence or extent of some of these changes has been correlated with the presence or recurrence of atrial fibrillation, the utility of these pathologic features in terms of predicting patient outcome has not been established. Other diseases such as sarcoidosis or systemic amyloidosis may on rare occasion be diagnosed in resected atrial appendages.

3.9.2. Gross description and processing

The exterior dimensions should be recorded and the interior surface should be carefully examined for the presence of adherent thrombi. One cassette containing myocardium from both the tip and the midsection should be submitted for routine processing and paraffin embedding. For institutions equipped to perform IF, an additional piece may be frozen to facilitate subclassification of amyloid deposits in patients with systemic amyloidosis.

3.9.3. Stains and sections

A single H&E-stained slide should be evaluated. Congo red stain may be obtained to assess for the presence of amyloid and Masson trichrome, Azan–Mallory, Movat, or Sirius red stain may be obtained to assess for interstitial fibrosis.

3.10. Pericardial biopsies/resections

3.10.1. Rationale

Parietal pericardium may be removed as a diagnostic biopsy particularly in cases of suspected purulent, tuberculous or malignant pericarditis, or as a partial or radical pericardiectomy in cases of constrictive pericarditis [61–63].

3.10.2. Gross description and processing

The number, size and thickness of the specimens should be noted. The degree of calcification and fibrosis should be assessed as well as the presence of purulent exudates and fibrin. If purulent infective pericarditis is suspected, sterile portions should be sent for culture. The specimen should be sectioned perpendicular to the mesothelial surfaces, and the sections should be processed on their cut sides to allow for evaluation of the full thickness of the pericardium. Small biopsies should be processed in their entirety. For larger resections, at least two cassettes each with at least two tissue sections should be submitted for routine processing and paraffin embedding. Calcified specimens will require decalcification prior to processing. In selected cases, consideration should be given to saving material for nucleic acid studies for detection of mycobacteria or other infectious agents.

3.10.3. Stains and sections

H&E stains should be evaluated along with appropriate stains for microorganisms as indicated by the tissue histology and clinical history. Iron stain can be used to assess for asbestos bodies. Immunohistochemical stains are useful in evaluating inflammatory cell infiltrates and assessing for malignancy.

3.11. Aortic resections

3.11.1. Rationale

Segments of aorta are typically resected during the surgical repair of an aortic aneurysm, an aortic dissection, or a congenital anomaly such as coarctation. Such aortic resection specimens may contain diagnostic pathologic features that impact patient care, such as infectious or noninfectious aortitis [64–66], or may show features suggesting an inherited connective tissue disease [67]. Less commonly, segments of aorta may be surgically removed due to the presence of a neoplasm [68]. Thus, all resected aortic segments should be evaluated histologically.

3.11.2. Gross description and processing

The number, size, and thickness of the specimens should be indicated. The specimen should be evaluated for evidence of dissection. The specimen should be sectioned perpendicular to the luminal surface, and the sections should be processed on their cut sides to allow for evaluation of the full thickness of the aortic wall. For

initial screening, it is recommended to evaluate six sections of aortic wall, which may be submitted in a total of two cassettes [65]. If either the gross appearance of the specimen or the initial histologic slides raises concern for aortitis, then 5–10 additional blocks of tissue, if available, should be submitted to allow for more thorough characterization of the inflammatory infiltrate, which may vary greatly from block to block. The tissue should undergo routine processing and paraffin embedding.

3.11.3. Stains and sections

H&E stains should be evaluated. Elastic, trichrome (or Azan–Mallory or Sirius red), Movat and Alcian–PAS stains are helpful to identify areas of degeneration, elastic fiber fragmentation, scarring, and accumulation of proteoglycans and mucopolysaccharides. In cases of aortitis, immunohistochemical staining for IgG4 along with IgG or CD138 can help reveal involvement by IgG4-related systemic disease [69]. In cases of infectious purulent/mycotic aortitis, histochemical stains for bacteria and fungi are helpful. However, in cases of lymphoplasmacytic aortitis, histochemical stains and immunostains for spirochetes may be used, but are seldom, if ever, positive. Sarcomas and other neoplasms are worked up as discussed for cardiac tumors in Section 3.6.

3.12. Temporal artery biopsies

3.12.1. Rationale

Superficial temporal arteries are routinely biopsied to evaluate for vasculitis, particularly giant cell arteritis [70]. Since this disorder affects arteries in a discontinuous fashion with skip lesions [71,72], it is essential to extensively sample cross-sections of the specimen. Evaluation of only a single section can result in a false-negative diagnosis [73]. Although classified as medium-sized arteries, the superficial temporal artery is small enough to pose difficulty with tissue orientation if it is sectioned prior to processing. Thus, sectioning and embedding of the artery are typically performed by the histotechnologist after routine processing.

3.12.2. Gross description and processing

The length and width of the artery segment should be noted. The intact artery should be placed in a bag in a tissue cassette and subjected to routine processing and paraffin embedding. The log sheet should clearly indicate that the specimen is a temporal artery that requires cross-sections to be made and embedded as “rings.” Use of a special colored cassette for temporal artery biopsies is helpful to ensure that the technical staff will realize how to process the specimen. After processing, the artery is retrieved and serially sectioned at 1- to 2-mm intervals. The pieces should be carefully embedded as cross-sections to allow for evaluation of each entire cross-section. All of the artery cross-sections can be embedded in the same paraffin block.

3.12.3. Stains and sections

Multiple H&E-stained slides should be evaluated. For each 1-mm cross-section of artery, it is recommended that a minimum of five levels (slides) be obtained, which may be serial sections or step sections. Each slide may contain a ribbon of 8 sections, to allow for the evaluation of 40 sections per artery cross-section. In borderline cases with inflammation limited to the adventitia, additional levels should be considered. In addition, an elastic stain should be evaluated to assess for fragmentation of the internal elastic lamina. Immunohistochemical stains for CD68 and CD3 are helpful to delineate subtle involvement of the arterial wall by inflammation [74,75]. Temporal arteries may be involved by systemic amyloidosis, which can mimic the clinical presentation of giant cell arteritis [76]. If amyloid is suspected on the H&E stain, an amyloid stain such as Congo red should be assessed.

3.13. Medium-sized artery resections

3.13.1. Rationale

Medium-sized arteries throughout the body may be resected for various reasons including traumatic injury, aneurysms, pseudoaneurysms, dissections, infection, and, on occasion, as a diagnostic sampling during bypass graft placement. All of these specimens should be evaluated histologically to evaluate for clinically relevant conditions particularly vasculitis. Medium-sized arteries may also be removed as part of larger resections such as amputations of the lower or upper extremities or visceral organ resections. While description of the artery processing in these latter situations is beyond the scope of this report, isolated medium-sized artery resections may be processed as indicated below.

3.13.2. Gross description and processing

The shape and dimensions of the specimen should be noted. The specimen should be cut into cross-sections 1–2 mm thick, and the sections should be placed on their cut sides in cassettes. The tissue is fixed in 10% buffered formalin and subjected to routine processing and paraffin embedding. If the specimen is calcified, it should be fixed in formalin and then decalcified prior to sectioning. These specimens are typically small and should be entirely submitted for histologic analysis, usually in one to three cassettes. While cross-sections are considered the standard approach to examine resected arteries, if there is concern for fibromuscular dysplasia, particularly in renal arteries, then consideration should be given to submitting the arteries longitudinally [77].

3.13.3. Stains and sections

H&E and elastic stains should be evaluated. For H&E stains, multiple levels, at least three, are recommended. Immunohistochemical stains for CD3 and CD68 are helpful to characterize and quantify any inflammatory infiltrates.

Trichrome, Azan–Mallory, or Sirius red stains help to delineate scarring in the vessel wall.

3.14. Other artery biopsies

3.14.1. Rationale

Small biopsies of large and medium-sized arteries other than the superficial temporal arteries are occasionally obtained to assess for vascular disease, particularly vasculitis.

3.14.2. Gross description and processing

These arterial biopsies will often be small unoriented fragments of tissue. Such specimens should be placed in small bags in cassettes, fixed in 10% buffered formalin and submitted for routine processing and paraffin embedding. If a tubular section of artery is obtained, then the specimen should be described and processed as detailed above for temporal artery biopsies.

3.14.3. Stains and sections

H&E and elastic stains should be evaluated. For H&E stains, multiple levels, at least three, are recommended. Immunohistochemical stains for CD3 and CD68 are helpful to characterize and quantify any inflammatory infiltrates.

3.15. Endarterectomy specimens

3.15.1. Rationale

Endarterectomy is performed largely as a therapeutic procedure to remove atherosclerotic plaque or excessive intimal hyperplasia. While, on rare occasion, these specimens yield unexpected clinically relevant pathologic information, this is by far the exception. Histologic assessment of these specimens will therefore be largely dictated by regional clinical and legal expectations, with some institutions assessing all of these specimens histologically, and other institutions forgoing histologic analysis.

3.15.2. Gross description

The dimensions and shape of the specimen should be noted, as well as the presence of calcification and thrombus. If a completely intact tubular-shaped specimen is received, then an estimate of the degree of stenosis should be noted. However, frequently, these specimens are not completely intact, and the degree of stenosis cannot be accurately determined.

3.15.3. Processing

The specimen should be fixed in 10% buffered formalin and then decalcified. The specimen should be sectioned in cross-sections, cutting perpendicular to the luminal axis for tubular specimens. The cross-sections should be placed on their cut sides in the cassette and then undergo routine processing and paraffin embedding. One cassette with three to four cross-sections is usually sufficient.

3.15.4. Stains and sections

An H&E stain should be evaluated. If there are concerns for infection, stains for microorganisms should be obtained. Immunohistochemical stains for CD3 and CD68 may be utilized to characterize and quantify any inflammatory infiltrates. Elastic stain may be helpful to identify the presence of tunica media.

3.16. Veins

3.16.1. Rationale

Veins are most commonly resected for dilation (varix), thrombosis and infection [78].

3.16.2. Gross description and processing

The length and diameter of the segment(s) of vein are recorded. Take note of uniformity or irregularity of wall diameter, tortuosity, and dilatation. Check the lumen for thrombus, purulent exudates, or the presence of valves. Representative cross-sections can be submitted in one cassette.

3.16.3. Sections and stains

A single H&E-stained slide should be generated for each block. Connective tissue stain (Movat or elastic) may be requested to confirm the nature of the vessel and to assess the integrity of the wall. Stains for microorganisms (Gram, PAS, GMS, Ziehl-Neelsen) are performed in cases of septic phlebitis.

3.17. Vascular grafts and stents

3.17.1. Rationale

Vascular grafts can be classified into biological or synthetic grafts. The most commonly used biological graft is an autograft taken from the saphenous vein or internal mammary artery. Widely used synthetic grafts are made from polyethylene terephthalate (PET; Dacron) and polytetrafluoroethylene (PTFE; Gore-Tex) [79]. Synthetic grafts are used in aortic and large diameter peripheral arterial bypass surgeries. Dacron is a type of polyester that is manufactured in either woven or knitted form. It often has a crimped pattern for greater flexibility. It may be straight tubular, branched, or bifurcated. PTFE is made from fluorocarbon polymer sheets and has a smooth surface. It is available in a variety of sizes and wall thickness. Some are externally supported with rings to avoid compression and kinking. They are preferred for hemodialysis access and construction of extra-anatomic bypasses. Conditions leading to vascular graft removal include graft occlusion or stenosis, infection, thrombosis, and anastomotic true or false aneurysm formation.

Endoluminal stent grafts are composed of PET or PTFE mounted on expandable metallic stents. These are delivered via the iliac arteries to exclude blood flow through the aneurysm sac in the thoracoabdominal aorta. The top of the

proximal segment of the stent may be uncovered. Barbs are usually present at the proximal and distal ends that attach to the artery wall to prevent stent migration. Endografts can be custom-made with fenestrations or side branches. Fenestrations are holes in the endograft that can be aligned with visceral arteries for deployment of stent grafts into the branch vessels. Removal of stents is due to conversion from endovascular to open repair or stent failure including graft migration, kinking, component separation, infection, and perigraft leakage resulting from an incomplete seal between the graft and aorta at attachment sites [80].

3.17.2. Gross description

Grafts and stents should be examined for integrity of the wall, stenosis or thrombosis of the lumen. The soft tissue around the graft may be included in the specimen and should be sampled. In infected grafts or stents, cultures are ideally obtained by the clinical team preoperatively or intraoperatively from blood, wound, sinus tract or perigraft fluid. Explanted stent grafts are examined grossly for evidence of structural graft failure such as fabric tears, fractures, kinks, or collapse. Evaluation of X-ray images of stented vessels is helpful to determine stent location, adequateness of deployment, and presence of damage to the stent.

3.17.3. Processing

Synthetic vascular grafts can be sectioned easily with surgical blade and submitted for microscopic evaluation along with its luminal contents and soft tissue. Document any structural defects found in the endografts by gross photography and/or radiography. Stented medium-sized arteries can be processed as described in Section 3.5 for stents in coronary arteries of surgically resected hearts.

3.17.4. Sections and stains

A single H&E-stained slide should be generated for each block. Special stains for microorganisms can be requested to demonstrate infection. Connective tissue stains (Movat, elastic) will help differentiate true from false aneurysms.

3.18. Blood clots

3.18.1. Rationale

Blood clots located inside cardiac chambers or blood vessels (thrombi and emboli) may be removed as either part of an open procedure or by catheter embolectomy. Blood clots outside cardiac chambers and blood vessels (hematomas) may also be evacuated surgically. Blood clots in general and thrombi in particular should be evaluated to assess for organization as an indication of the age of the clot and to exclude infection and embolic neoplasm. Clinicians also on occasion request verification if a thrombus is a platelet-rich thrombus, so-called “white clot,” consistent with heparin-induced thrombocytopenia [81].

3.18.2. Gross description and processing

The dimensions of the blood clot should be noted, and the presence of any vascular structures should be determined. A single cassette of tissue should be fixed in 10% buffered formalin and subjected to routine tissue processing with paraffin embedding.

3.18.3. Stains and sections

An H&E stain should be evaluated. If there are concerns for infection, stains for microorganisms should be obtained.

3.19. Native cardiac valves

3.19.1. Rationale

Diseased native cardiac valves may manifest dysfunctional states (stenosis and regurgitation) or show evidence of adherent vegetations, both infective and noninfective.

Valves that are surgically excised are studied for a number of reasons:

- To document the indications for surgery.
- To correlate pathology with the preoperative diagnosis, hemodynamics, echocardiography, angiography, and the suspected complications.
- To document or exclude infective endocarditis.
- To assess the morphologic changes to the valvular tissue caused by disease and correlate these findings to the natural history, surgical risk, postoperative prognosis, and association with systemic disease.
- To validate new diagnostic imaging techniques.
- To assess the validity and consequences of a given valvular surgery for current and future patients.
- To establish the etiology and pathobiology of the valvular disease.

Dysfunctional cardiac valves result from either structural abnormalities or their abnormal function. Valves that are stenotic almost always have some anatomic abnormality, usually fibrosis or calcification. In contrast, purely regurgitant valves do not always have anatomic abnormalities present with the excised specimen. In regurgitation, the abnormality may be related to the valve or to the surrounding supporting structures.

3.19.2. Gross description

Gross examination with adequate documentation of normal and abnormal findings is of vital importance for the evaluation of native valve tissue. Valves may be received fresh from the operating room or in formalin. They should be carefully examined for the presence of thrombus or vegetation. If a thrombotic lesion is noted, then sampling part of the valve lesion for microbiological culture analysis should be considered. It is important not to contaminate the specimen. For cultures, a piece of the thrombus or vegetation is recommended. Swabs are not useful. Material can also be submitted for molecular studies to identify potential

microorganisms, particularly in cases of culture negative endocarditis [82].

Only after infection has been considered should the valve be manipulated. All the tissues from the container must be assessed as the valve pieces may be accompanied by pieces of aorta or other cardiac structures. Photographs of the inflow and outflow surfaces are helpful to document the gross appearance. Excised valve cusps or leaflets may be received in their entirety, but with the increasing incidence of valve repair rather than replacement, only portions of valves are commonly submitted for pathologic analysis.

The dimensions of the specimens should be recorded. In atrioventricular valves the leaflets, commissures, chords, attached papillary muscle and any annular tissue should be examined for thickening, fusion, irregular edges, defects, and calcification. Semilunar valves should be examined for the cusp number, presence of raphe, fusion of commissures, calcification, and defects or irregularities including fenestrations and perforations. An X-ray is useful to visualize the calcification. Submitting tissue in fixative for ultrastructural examination is recommended for storage disease evaluation.

Tricuspid valves and pulmonary valves are usually removed for infective endocarditis, congenital heart disease or carcinoid syndrome. Cultures should be done for cases with visible or suspected infection. Sectioning is recommended for carcinoid valve disease.

Mitral valves may be removed for stenosis due to rheumatic or postinflammatory valvular disease, infection, or storage disease. Valves removed for mitral regurgitation may be macroscopically normal if the underlying cause is ischemic regurgitation or due to ventricular dilatation of any cause. Regurgitant valves may show myxomatous degeneration, rheumatic scarring, a calcified annulus, ruptured chordae, or ruptured papillary muscles. Chordae should be carefully examined for thrombi or pointed ends suggesting spontaneous rupture. The chords may also become tangled if ruptured. Papillary muscles should be bisected and evaluated for signs of ischemia (such as mottling, discoloration, or a white scar) as well as attached thrombus. With the advent of valve repair, smaller specimens are being submitted to pathology. Even a small fragment of valve leaflet or a chord may still provide confirmation of myxomatous degeneration or postinflammatory changes.

Aortic valve cusps should be examined for cusp number, the presence of fusion and the degree of calcification. Distinguishing an acquired bicuspid from a congenitally bicuspid valve is most likely accomplished by careful assessment of the gross morphology. Valve circumference and size are useful. In an acquired fusion of the cusps (postinflammatory), one of the valve pieces would be twice the size of the other. The free edge of the valve is usually indented with fusion in contrast to a straight horizontal with a congenitally bicuspid valve. In a congenitally bicuspid valve, the region of failed cusp separation is called a raphe, and this ridge extends from the base of the cusps at the aortic

wall toward, but not involving, the free margin of the valve cusps. In contrast, the frequently fibrocalcific ridge identified in acquired cusp fusion would extend all the way to the free margin of the cusp.

Regurgitant aortic valves may be grossly normal if the pathologic process is due to the disease of the surrounding aorta. Often, the only abnormality noted is a rolled and/or thickened free cusp edge. If severe, the valve may become soft and stretched. Furthermore, evaluation of heart valves for perforating or fibrotic defects from old injury or infection is important. Commissural fusion and scarring should always be evaluated.

After gross examination, if the valve is calcified, the entire specimen should be decalcified prior to sectioning.

3.19.3. Processing

Sectioning is still debatable for many valves, but the trend has been to section most valves, if not all of them. Thus, it is the consensus opinion of the Committee that the representative sections of resected valves be submitted for light microscopy. In most cases, sections should be made perpendicular to the line of closure. A horizontal section through a raphe or commissure yields two “v” shaped pieces. Special elastic stain of this area can help determine if a valve is an acquired postinflammatory bicuspid valve or a congenitally bicuspid valve. Standard overnight histologic processing should be performed.

3.19.4. Stains and sections

A single H&E-stained slide should be generated for each block. A Masson trichrome, Azan–Mallory, or Sirius red stain should be obtained to document the degree of fibrosis and a VVG elastic stain, Movat pentachrome stain, and/or Alcian–PAS stain can be obtained to characterize the size and composition of fibrous onlays, the degree of ground substance accumulation, and the degree of underlying native valve destruction. The elastic stain may also be useful to help determine if a valve is an acquired postinflammatory bicuspid valve or a congenitally bicuspid valve. If one obtains a horizontal section through the raphe or commissure, the two “v” shaped pieces may be stained with the elastic stain. Following the elastic layers helps determine whether the area is fused from two cusps or represents a single cusp.

A Gram stain should always be accompanied by a silver stain. These stains should be done on valves with thrombi and in areas of valve surface erosion. With treatment, Gram-positive bacteria stain variably purple and then Gram-negative before losing their Gram staining all together. Silver stains will still show the bacteria cell wall and are also essential for detecting fungi. Giemsa, Ziehl Neelson/acid-fast bacilli, and PAS stains are also useful stains for detection of various organisms. In carcinoid syndrome, immunostains for muscle specific actin or smooth muscle actin are useful to delineate and characterize the fibromuscular plaques.

3.20. Prosthetic heart valves

3.20.1. Rationale

Prosthetic heart valves are commonly surgically removed for dysfunction that has an anatomic cause within the specimen submitted for pathologic evaluation, such as calcification, cuspal tears, thrombosis, endocarditis, or material failure. Occasionally, the valve itself may be normal, but removal was necessitated for other indications such as sterile paravalvular leak. Knowledge of the indication for removal usually can be gleaned from the medical record and can be helpful for proper pathologic evaluation and triage of tissue.

3.20.2. Gross description

The type of valve should be noted as bioprosthetic or mechanical. Bioprosthetic valves will typically be fabricated from either porcine aortic valves or bovine pericardium. Mechanical valves generally have either a tilting disk (either single or bileaflet) or ball-and-cage configuration. Published algorithms [83] are available for proper identification of prosthetic valves; the operative notes from the implantation or explantation may also be helpful. It is recommended to photograph prosthetic valves prior to manipulation. Bioprosthetic valves can also be radiographed to allow for evaluation of the degree of calcification. If there is a clinical question of infective endocarditis or if vegetations are noted grossly, this material may be sent for microbiologic culture.

Measure the external diameter of the sewing ring, and note any tissue overgrowth onto the sewing ring or valve cusps. Note any irregularities of the valve cusps. For mechanical valves, this includes any asymmetry, notches, cracks, or abrasions. For bioprosthetic valves, this includes any calcification, tears, or perforations of the cusps. Examine the bioprosthetic cusps carefully near the commissures, as tears in these areas are not always obvious. Describe in detail (size, location, color, consistency) any tissue overgrowth onto the cusps, vegetations, or thrombi on the device, and note if any of these are associated with underlying valve destruction. Describe the calcific deposits of bioprosthetic valves, their location, and their relationship to cuspal tears or abrasions, if any. Gently evaluate the ability of the cusps to fully open and fully close, and note if these are impaired by host material or pathology intrinsic to the cusps.

3.20.3. Processing

Histologic sections of the exterior sewing ring and adherent material should be submitted for all valves. Sections of the bioprosthetic valve cusps should also be submitted. Any thrombus, vegetation or tissue overgrowth should be submitted if not already captured in the above sections. The mechanical cusps or ball are not sectioned.

3.20.4. Stains and sections

Routine H&E stains are used for general morphologic evaluation of the sections of the sewing ring, cusps, and any

associated host material. Porcine aortic valve cusps will have the usual trilaminar valvular architecture, while bovine pericardial cusps will be uniformly dense fibrous tissue; this distinction can help if the type of valve was not definitively identified grossly. Gram and methenamine silver stains are used to evaluate for infectious endocarditis [84].

3.21. Mechanical circulatory support devices

3.21.1. Rationale

VADs and total artificial hearts may be used to provide mechanical circulatory support or replacement, respectively, for patients with congestive heart failure. They are typically removed around the time of heart transplantation, but may be explanted for device dysfunction or in the event of recovery of myocardial function. These devices can be used for left ventricular, right ventricular or biventricular support. There are many different types of mechanical circulatory devices being used throughout the world for a variety of indications, ranging from temporary devices that can be percutaneously implanted for support over a time frame of days, to permanent devices that have been designed for years of function. While it is beyond the scope of this work to detail all of these myriad devices, they do share enough common features to allow for an overall algorithm for their evaluation. In addition, all of the devices may suffer similar complications, such as thrombosis, hemorrhage, infection, structural failure, positioning issues, and adverse device–patient interactions [85].

3.21.2. Gross description and processing

Photographs focusing on the pathologic features and the relationship of the device to the native heart and other host tissues should be taken. The manufacturer and type of VAD should be determined and can easily be ascertained from the clinical or operative notes if there is uncertainty. The VADs in general will have an inflow cannula with or without an inflow valve, a pump (pulsatile, or axial, or centrifugal), an outflow cannula with or without an outflow valve, and a driveline. Many of the devices can be at least partially disassembled by unscrewing the various components to evaluate for intradevice pathology and described along the direction of flow. If the inflow cannula is received with a surgically resected heart, its location should be noted along with possible impingement on native heart structures and integrity of the surgical anastomosis. The inflow cannula should be evaluated for thrombosis, vegetations, kinking, or structural failure. Pulsatile pumps will have either a mechanical or bioprosthetic valve between the inflow cannula and pump, which should be evaluated for structural deterioration, thrombosis, or vegetations if possible. The pump itself may or may not be amenable to opening, but one can often look into the flow chamber using a bright light or an endoscopic instrument borrowed from a clinical department at the end of a working day. The pump should be evaluated primarily for the presence of thrombus. The

serial number of the pump should be noted. Similar to the inflow valve and cannula, the outflow valve and cannula should be evaluated for thrombosis, vegetations, kinking, structural failure, and anastomosis, if present. Because the driveline is a common route of device infection, any adherent tissue to the driveline should be scrutinized for signs of necrosis, hemorrhage, or abscess formation, and cultures can be taken if clinically indicated. Microscopic sections should be taken of thrombus or vegetation, and of the driveline if there is gross evidence or clinical suspicion of infection. Many devices can be returned to the manufacturer after pathologic analysis.

3.21.3. Stains and sections

Routine H&E stains are used for general morphologic evaluation of any suspicious lesions. Gram and methenamine silver stains are used to evaluate for infection, if necessary.

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