

# Heart Biopsies - Antibody Mediated Rejection

## Summary of 2013 Working Formulation for Pathologic Diagnosis of AMR in cardiac transplantation

Grade	Definition	Substrates
pAMR 0	Negative	Histo - IP -
pAMR 1 (H+)	AMR by histology only	Histo + IP -
pAMR 1 (I+)	AMR by IHC or IF only	Histo - IP +
pAMR 2	Pathologic AMR	Histo + IP +
pAMR 3	Severe pathologic AMR	Histo + IP +

**Table 1. Morphologic Criteria for Pathologic Diagnosis of Cardiac Antibody-Mediated Rejection**

Morphologic Criteria <sup>a</sup>	Description
<b>Intravascular activated mononuclear cells</b>	<ol style="list-style-type: none"> <li>Intravascular macrophage accumulation in capillaries and venules that distend and fill vascular lumens.</li> <li>Endothelial cells with large nuclei and expanded cytoplasmic projections that appear to narrow or occlude the lumens.</li> </ol>
<b>Severe antibody mediated rejection</b>	Hemorrhage, interstitial edema, myocyte necrosis, capillary fragmentation, mixed inflammatory infiltrates, endothelial cell pyknosis, and/or karyorrhexis.

2013 ISHLT AMR Working Formulation – Immunoperoxidase (Paraffin) Staining		
Grade	Scoring	Result (Final Interpretation)
<b>C3d/C4d distribution</b>	0: < 10% = negative 1: 10%-50% = focal staining 2: > 50% = multifocal/diffuse	C3d/C4d Positive = multifocal/diffuse staining (2) of weak or greater intensity (>0)
<b>C3d/C4d intensity</b>	0: negative/equivocal 1: faint positive staining 2: strong positive staining	
<b>CD68 distribution</b>	0: < 10% = negative 1: 10%-50% = focal 2: > 50% = multifocal/diffuse	CD68 Positive: >10% (focal/multifocal/diffuse) intravascular macrophage staining

Adapted from Berry G et al. JHLT Dec 2013;32(12):1147-1162

## Criteria for Scoring Immunohistochemistry

Variable	Score	Result
<b>Capillary</b>	0: < 10% = negative	Positive = Distribution 2 with intensity 1 or 2
	1: 10-50% = focal	
<b>C4d Distribution*</b>	2: > 50% = multifocal	Negative = Distribution 0 or 1 with intensity 1 or 2
	diffuse	
<b>Capillary</b>	0: negative/equivocal	(Intensity 2 → Communicate to clinician)
	1: faint +	
<b>C4d Intensity*</b>	2: strong +	
	0: < 10% = negative	Positive = Distribution 1 or 2
<b>Intravascular CD68 Distribution</b>	1: 10-50% = focal	
	2: > 50% = multifocal	
	diffuse	

## Special Notes

- Only interstitial capillaries should be assessed for C4d/CD68 expression

- Only evaluate intact myocardium. Ischemia, healing biopsy sites, scars and Quilty lesions don't count

- IHC is considered positive if either CD4 or CD68 are positive. CD4d is easier to read. CD68 requires expansion/collection in vascular spaces.

- Diffuse pattern 1R type rejectio infiltrate looks very similar to AMR. Post-treatment, may lose C4d but still have histologic changes present.

CD4d

CD4d

Histologic AMR - diffuse pattern