

# The Journal of Heart and Lung Transplantation

The Official Publication of the International Society for Heart and Lung Transplantation (ISHLT)



## NEWS RELEASE

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### Contact:

Elsevier Newsroom

Tel: +31 20 485 3564

[newsroom@elsevier.com](mailto:newsroom@elsevier.com)

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## ISHLT Finalizes New Nomenclature and Diagnostic Criteria for Antibody-Mediated Rejection in Heart Transplantation

Experts Issue Consensus Statement in *The Journal of Heart and Lung Transplantation*

New York, NY, November 18, 2013 – Antibody-mediated rejection of the transplanted heart is a recognized clinical complication and a major limitation to survival of patients who have undergone heart transplantation. Experts have now developed a new working formulation for the pathologic diagnosis, grading, and reporting of cardiac antibody-mediated rejection. Their consensus statement is published in the December issue of *The Journal of Heart and Lung Transplantation* and is freely available at [www.jhltonline.org](http://www.jhltonline.org).

Heart transplantation is the definitive therapy for eligible patients with end-stage heart failure. However, antibody-mediated rejection (AMR) of a cardiac allograft -- a heart from a genetically non-identical donor -- is a recognized clinical complication in the management of heart transplant patients and can develop more than a year after transplantation has occurred.

Over the past 25 years experts have wrestled to establish practical working definitions to guide the diagnosis, grading, and reporting of AMR. In the initial 1990 International Society for Heart Transplantation (ISHLT) working formulation, “positive immunofluorescence, vasculitis, or severe edema in the absence of cellular infiltrates” were proposed as the key diagnostic hallmarks. This working formulation included the qualified recommendation that “centers routinely performing immunofluorescence should consider staining all endomyocardial biopsy specimens obtained in the first six weeks following transplantation.” More detailed histopathologic features and immunopathologic criteria were proposed in the follow-up 2005 ISHLT revision of nomenclature and diagnostic criteria.

In 2010 the increasing awareness of asymptomatic AMR and its association with accelerated cardiac allograft vasculopathy and increased mortality, together with the need to define a therapeutic strategy, led an international multidisciplinary group to recommend the removal of the clinical and serologic components specified in the 2005 working formulation as requirements for the diagnosis of AMR. The biopsy tissue diagnosis of cardiac AMR has since been established by using agreed reproducible histopathologic and immunopathologic criteria akin to the diagnosis of acute cellular rejection (ACR).

In this statement, members of the Pathology Council of ISHLT led by Gerald J. Berry, MD, Professor of Pathology, Stanford University School of Medicine, and Director, Cardiac and Pulmonary Pathology, Stanford University Hospital and Clinics and Lucile Packard Children's Hospital at Stanford, reports the consensus findings from a series of meetings held between 2010 and 2012 to develop a new working formulation for the pathologic diagnosis, grading, and reporting of cardiac AMR.

"Tremendous progress has been achieved over the last decade in recognizing, diagnosing and grading AMR, but its recognition and diagnosis by histopathology, even among experienced transplant pathologists, is challenging," says Berry. "With the rapid changes that occur in medicine, new and more specific antibodies—or even new technologies—may provide more accurate and reproducible results for the diagnosis of AMR. Until then, there remain numerous challenges and unresolved clinical, immunologic, and pathologic questions. It is our distinct intention and hope that the diagnostic criteria and grading scheme presented in this working formulation will aid in the resolution of these and other issues."

The report covers:

- Histopathologic features of AMR
- Interstitial edema
- Hemorrhage, necrosis, and vascular thrombosis
- Immunopathologic findings in cardiac AMR
- Antibody panels for paraffin immunohistochemistry
- Antibody panels for frozen-tissue immunofluorescence
- Summary of the ISHLT 2012 pAMR biopsy specimen validation study
- Pathologic grading and reporting of cardiac AMR
- Indications, frequency, and follow-up of immunostaining
- Initial and surveillance immunophenotypic studies
- Follow-up of immunophenotypic studies after a positive result
- Surveillance and immunostaining for late-onset AMR
- Mixed ACR and AMR

The Working Group points out that this document reflects the current state of knowledge and experience of transplant pathologists, and also serves as a framework for the organization of future multicenter studies. Areas pinpointed as needing further evaluation include AMR in children and the threshold for therapeutic intervention in patients with "asymptomatic AMR."

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#### **NOTES FOR EDITORS**

"ISHLT Consensus Statement: International Society for Heart and Lung Transplantation 2013 working formulation for the standardization of nomenclature in the pathologic diagnosis of antibody-mediated rejection in heart transplantation," by Gerald J. Berry, MD, Margaret M. Burke, FRCPATH, Claus Andersen, MD, Patrick Bruneval, MD, Marny Fedrigo, MD, PhD, Michael C. Fishbein, MD, Martin Goddard, MD, Elizabeth H. Hammond, MD, Ornella Leone, MD, Charles Marboe, MD, Dylan Miller, MD, Desley Neil, MD, Doris Rassl, MD, Monica P. Revelo, MD, Alexandra Rice, FRCPATH, E. Rene Rodriguez, MD, Susan Stewart, FRCPATH, Carmela D. Tan, MD, Gayle L. Winters, MD, Lori West, MD, Mandeep R. Mehra, MD, and Annalisa Angelini, MD, *The Journal of Heart and Lung Transplantation*, Volume 32, Issue 12 (December 2013), published by Elsevier (doi: <http://10.1016/j.healun.2013.08.011>). The online version, including supplementary data, is freely available at [www.jhltonline.org](http://www.jhltonline.org).

Full text of the article is available to credentialed journalists upon request. Contact the Elsevier Newsroom at [newsroom@elsevier.com](mailto:newsroom@elsevier.com) or +31 20 485 3564. To obtain additional information from the ISHLT regarding "ISHLT Consensus Statement: International Society for Heart and Lung Transplantation 2013

working formulation for the standardization of nomenclature in the pathologic diagnosis of antibody-mediated rejection in heart transplantation,” or to arrange an interview with Gerald J. Berry, MD, please contact *The Journal of Heart and Lung Transplantation* Editorial Office at [jhlteeditor@ishlt.org](mailto:jhlteeditor@ishlt.org).

### **ABOUT THE JOURNAL OF HEART AND LUNG TRANSPLANTATION**

A forum that includes all aspects of pre-clinical and clinical science of the failing heart and lung

The Official Publication of the [International Society for Heart and Lung Transplantation](http://www.jhltonline.org), *The Journal of Heart and Lung Transplantation* ([www.jhltonline.org](http://www.jhltonline.org)) brings readers essential scholarly and timely information in the field of cardiopulmonary transplantation, mechanical and biological support of the failing heart, advanced lung disease (including pulmonary vascular disease), and cell replacement therapy. Importantly, the journal also serves as a medium of communication of pre-clinical sciences in all these rapidly expanding areas.

With an Impact Factor of 5.112, *The Journal of Heart and Lung Transplantation* ([www.jhltonline.org](http://www.jhltonline.org)) is ranked 2nd of 26 journals in the Transplantation category, 19th of 122 journals in the Cardiac and Cardiovascular Systems category, and 5th of 50 journals in the Respiratory System category in the 2012 *Journal Citation Reports*®, published by Thomson Reuters.

### **ABOUT THE INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION (ISHLT)**

The International Society for Heart and Lung Transplantation ([www.ishlt.org](http://www.ishlt.org)) is a multidisciplinary, professional organization dedicated to improving the care of patients with advanced heart or lung disease through transplantation, mechanical support, and innovative therapies via research, education, and advocacy. ISHLT was created in 1981 at a small gathering of about 15 cardiologists and cardiac surgeons. Today, ISHLT has over 2500 members from over 45 countries, representing over 14 different disciplines involved in the management and treatment of end-state heart and lung disease. This multinational, multidisciplinary mix is one of the biggest strengths of the Society. It brings greater breadth and depth to ISHLT's educational offerings and provides an exceptional environment for networking and exchanging information on an informal basis.

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