

# Stanford

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## Hannah Valentine

Professor of Medicine (Cardiovascular) at SUMC  
Medicine - Cardiovascular Medicine

### CONTACT INFORMATION

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### Bio

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#### ACADEMIC APPOINTMENTS

- Professor - Med Center Line, Medicine - Cardiovascular Medicine

#### ADMINISTRATIVE APPOINTMENTS

- Senior Associate Dean for Diversity and Faculty Development, School of Medicine, (2005- present)
- President, Western State Affiliation, American Heart Association, (2004-2005)

#### PROFESSIONAL EDUCATION

- MBBS, St Georges Hosp/London Univ, UK , Medicine (MD equivalent) (1978)
- MRCP, London University, London, UK , Internal Medicine (1982)
- Registrar, Hammersmith Hospital, London, UK , Cardiology Fellow (1984)
- Fellow, Stanford University , Cardiology (1986)
- MD, London University, London, UK , Cardiology (PhD equivalent) (1988)

### Research & Scholarship

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#### CURRENT RESEARCH AND SCHOLARLY INTERESTS

Prior to my expanded administrative role, my lab focused on understanding the mechanism mediating acute and chronic allograft failure, in particular on the role of microvascular injury in acute allograft failure and the mechanisms of mediating transplant coronary artery disease.

1. Role of microvascular injury in acute allograft failure. We observed decreased cardiac allograft function in patients to be significantly associated with loss of microvascular cell surface markers, consistent with altered biology of the vascular endothelium or injury, and with up-regulation of cytokines such as IL-6, IL-10, TGF- $\beta$ , and TNF- $\alpha$ . Decreased cardiac allograft function, in particular diastolic dysfunction, was highly predictive of allograft vascular disease and poor outcome in long-term patients. To further characterize cellular and molecular mechanisms we developed quantitative methods to monitor allograft function and correlate it with cytokine expression in a rat heterotopic transplant model. We developed echocardiographic markers of systolic and diastolic function and found decreasing systolic and diastolic function highly correlated with up-regulation of IL-6 expression.

2. Mechanisms mediating allograft dysfunction. We observed the major risk factors for transplant atherosclerosis in patients to be metabolic (hyperglycemia, hypertriglyceridemia, and low HDL). To further study cellular and molecular mechanisms mediating this process, we recapitulated metabolic abnormalities in the rat heart transplant model and confirmed rapid development of transplant atherosclerosis.

My current focus is on clinical and translational research, expanding on my earlier laboratory-based research on the mechanisms of allograft failure and vasculopathy. I study the role of sub-clinical cytomegalovirus infection in the development of cardiac allograft vasculopathy (CAV), and the effect of antiviral agents in preventing CAV, work that has been supported by a program project grant from NIH. Translating my earlier work on gene expression profiling, I conduct clinical trials on the application of this technology for non-invasive diagnosis of transplant rejection. This work, recently published in the *New England Journal of Medicine*, showed that peripheral blood leukocyte gene expression can be used safely for monitoring rejection in heart transplant recipients, with a substantial decrease in the number of endomyocardial biopsies performed. On going studies in this area will include application of the technology to diagnose CAV; monitor level of immunosuppression in a patient to guide therapy; and individualization of immunosuppression. My current research, in collaboration with bio-X faculty, uses the new technologies of whole genome scans, to detect the appearance of donor DNA in the recipient's blood as a novel, non-invasive marker of allograft damage due to acute rejection. Ongoing studies include confirmation studies of the utility, and then external validation in a randomized controlled trial.

## CLINICAL TRIALS

- Angiotensin Converting Enzyme (ACE) Inhibition and Cardiac Allograft Vasculopathy, Not Recruiting
- Clinical Trial of Pioglitazone for Prevention of Cardiac Allograft Vasculopathy After Heart Transplantation, Not Recruiting

## Publications

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### PUBLICATIONS

- **An Integrated Career Coaching and Time Banking System Promoting Flexibility, Wellness, and Success: A Pilot Program at Stanford University School of Medicine** *Academic Medicine*  
Fassiotto, M., Simard, C., Sandborg, C., Valentine, H., Raymond, J.  
2018
- **Transdisciplinary translational science and the case of preterm birth** *JOURNAL OF PERINATOLOGY*  
Stevenson, D. K., Shaw, G. M., Wise, P. H., Norton, M. E., Druzin, M. L., Valentine, H. A., McFarland, D. A.  
2013; 33 (4): 251-258
- **Proliferation signal inhibitors and post-transplant malignancies in heart transplantation: practical clinical management questions** *CLINICAL TRANSPLANTATION*  
Epailly, E., Albanell, J., Andreassen, A., Bara, C., Campistol, J. M., Delgado, J. F., Eisen, H., Fiane, A. E., Mohacsi, P., Schubert, S., Sebbag, L., Turazza, F. M., Valentine, et al  
2011; 25 (5): E475-E486
- **Decisions, Decisions: How Program Diversity Influences Residency Program Choice** *JOURNAL OF THE AMERICAN COLLEGE OF SURGEONS*  
Ku, M. C., Li, Y. E., Prober, C., Valentine, H., Girod, S. C.  
2011; 213 (2): 294-305
- **Impact of Donor-Transmitted Atherosclerosis on Early Cardiac Allograft Vasculopathy: New Findings by Three-Dimensional Intravascular Ultrasound Analysis** *TRANSPLANTATION*  
Yamasaki, M., Sakurai, R., Hirohata, A., Honda, Y., Bonneau, H. N., Luikart, H., Yock, P. G., Fitzgerald, P. J., Yeung, A. C., Valentine, H. A., Fearon, W. F.  
2011; 91 (12): 1406-1411
- **Identification and Classification of Acute Cardiac Rejection by Intra-graft Transcriptional Profiling** *CIRCULATION*  
Holweg, C. T., Potena, L., Luikart, H., Yu, T., Berry, G. J., Cooke, J. P., Valentine, H. A., Mocarski, E. S.  
2011; 123 (20): 2236-U154
- **Universal noninvasive detection of solid organ transplant rejection** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*

- Snyder, T. M., Khush, K. K., Valentine, H. A., Quake, S. R.  
2011; 108 (15): 6229-6234
- **Academic Couples: Implications for Medical School Faculty Recruitment and Retention** *JOURNAL OF THE AMERICAN COLLEGE OF SURGEONS*  
Girod, S., Gilmartin, S. K., Valentine, H., Schiebinger, L.  
2011; 212 (3): 310-319
  - **Differentially Expressed RNA from Public Microarray Data Identifies Serum Protein Biomarkers for Cross-Organ Transplant Rejection and Other Conditions** *PLOS COMPUTATIONAL BIOLOGY*  
Chen, R., Sigdel, T. K., Li, L., Kambham, N., Dudley, J. T., Hsieh, S., Klassen, R. B., Chen, A., Cao, H., Morgan, A. A., Valentine, H. A., Khush, K. K., Sarwal, et al  
2010; 6 (9)
  - **Gene-Expression Profiling for Rejection Surveillance after Cardiac Transplantation** *NEW ENGLAND JOURNAL OF MEDICINE*  
Pham, M. X., Teuteberg, J. J., Kfoury, A. G., Starling, R. C., Deng, M. C., Cappola, T. P., Kao, A., Anderson, A. S., Cotts, W. G., Ewald, G. A., Baran, D. A., Bogaev, R. C., Elashoff, et al  
2010; 362 (20): 1890-1900
  - **Changing trends in infectious disease in heart transplantation** *JOURNAL OF HEART AND LUNG TRANSPLANTATION*  
Haddad, F., Deuse, T., Pham, M., Khazanie, P., Rosso, F., Luikart, H., Valentine, H., Leon, S., Vu, T. A., Hunt, S. A., Oyer, P., Montoya, J. G.  
2010; 29 (3): 306-315
  - **Right Ventricular Dysfunction Predicts Poor Outcome Following Hemodynamically Compromising Rejection** *JOURNAL OF HEART AND LUNG TRANSPLANTATION*  
Haddad, F., Fisher, P., Pham, M., Berry, G., Weisshaar, D., Kuppahally, S., Vrtovec, B., Deuse, T., Virani, S., Fearon, W., Valentine, H., Hunt, S.  
2009; 28 (4): 312-319
  - **New developments in immunosuppressive therapy for heart transplantation** *EXPERT OPINION ON EMERGING DRUGS*  
Khush, K. K., Valentine, H. A.  
2009; 14 (1): 1-21
  - **Twenty-year survivors of heart transplantation at Stanford University** *AMERICAN JOURNAL OF TRANSPLANTATION*  
Deuse, T., Haddad, F., Pham, M., Hunt, S., Valentine, H., BATES, M. J., Mallidi, H. R., Oyer, P. E., Robbins, R. C., Reitz, B. A.  
2008; 8 (9): 1769-1774
  - **Effect of rapamycin therapy on coronary artery physiology early after cardiac transplantation** *AMERICAN HEART JOURNAL*  
Sinha, S. S., Pham, M. X., Vagelos, R. H., Perlroth, M. G., Hunt, S. A., Lee, D. P., Valentine, H. A., Yeung, A. C., Fearon, W. F.  
2008; 155 (5)
  - **Asymmetric dimethylarginine and cardiac allograft vasculopathy progression: Modulation by sirolimus** *TRANSPLANTATION*  
Potena, L., Fearon, W. F., Sydow, K., Holweg, C., Luikart, H., Chin, C., Weisshaar, D., Mocarski, E. S., Lewis, D. B., Valentine, H. A., Cooke, J. P.  
2008; 85 (6): 827-833
  - **Determinants of lumen loss between years 1 and 2 after cardiac transplantation** *TRANSPLANTATION*  
Sakurai, R., Yamasaki, M., Nakamura, M., Hirohata, A., Honda, Y., Bonneau, H. N., Luikart, H., Yock, P. G., Fitzgerald, P. J., Yeung, A. C., Valentine, H. A., Fearon, W. F.  
2007; 84 (9): 1097-1102
  - **Outcome in cardiac recipients of donor hearts with increased left ventricular wall thickness** *AMERICAN JOURNAL OF TRANSPLANTATION*  
Kuppahally, S. S., Valentine, H. A., Weisshaar, D., Parekh, H., Hung, Y. Y., Haddad, F., Fowler, M., Vagelos, R., Perlroth, M. G., Robbins, R. C., Hunt, S. A.  
2007; 7 (10): 2388-2395
  - **Molecular testing for long-term rejection surveillance in heart transplant recipients: Design of the Invasive Monitoring Attenuation Through Gene Expression (IMAGE) trial** *JOURNAL OF HEART AND LUNG TRANSPLANTATION*  
Pham, M. X., Deng, M. C., Kfoury, A. G., Teuteberg, J. J., Starling, R. C., Valentine, H.  
2007; 26 (8): 808-814
  - **Cytomegalovirus-associated allograft rejection in heart transplant patients** *CURRENT OPINION IN INFECTIOUS DISEASES*  
Potena, L., Valentine, H. A.  
2007; 20 (4): 425-431

- **Is there a role for proliferation signal/mTOR inhibitors in the prevention and treatment of de novo malignancies after heart transplantation? Lessons learned from renal transplantation and oncology** *JOURNAL OF HEART AND LUNG TRANSPLANTATION*  
Valantine, H.  
2007; 26 (6): 557-564
- **Frequent occult infection with cytomegalovirus in cardiac transplant recipients despite antiviral prophylaxis** *JOURNAL OF CLINICAL MICROBIOLOGY*  
Potena, L., Holweg, C. T., Vana, M. L., Bashyam, L., Rajamani, J., McCormick, A. L., Cooke, J. P., Valantine, H. A., Mocarski, E. S.  
2007; 45 (6): 1804-1810
- **Changes in coronary anatomy and physiology after heart transplantation** *AMERICAN JOURNAL OF CARDIOLOGY*  
Hirohata, A., Nakamura, M., Waseda, K., Honda, Y., Lee, D. P., Vagelos, R. H., Hunt, S. A., Valantine, H. A., Yock, P. G., Fitzgerald, P. J., Yeung, A. C., Fearon, W. F.  
2007; 99 (11): 1603-1607
- **Interplay between systemic inflammation and markers of insulin resistance in cardiovascular prognosis after heart transplantation** *JOURNAL OF HEART AND LUNG TRANSPLANTATION*  
Biadi, O., Potena, L., Fearon, W. F., Luikart, H. I., Yeung, A., Ferrara, R., Hunt, S. A., Mocarski, E. S., Valantine, H. A.  
2007; 26 (4): 324-330
- **Changes in coronary arterial dimensions early after cardiac transplantation** *TRANSPLANTATION*  
Fearon, W. F., Potena, L., Hirohata, A., Sakurai, R., Yamasaki, M., Luikart, H., Lee, J., Vana, M. L., Cooke, J. P., Mocarski, E. S., Yeung, A. C., Valantine, H. A.  
2007; 83 (6): 700-705
- **Pulmonary nocardiosis in a heart transplant patient: Case report and review of the literature** *JOURNAL OF HEART AND LUNG TRANSPLANTATION*  
Haddad, F., Hunt, S. A., Perlroth, M., Valantine, H., Doyle, R., Montoya, J.  
2007; 26 (1): 93-97
- **Peripheral blood leukocyte counts in cytomegalovirus infected heart transplant patients: Impact of acute disease versus subclinical infection** *TRANSPLANTATION*  
Cooke, M. E., Potena, L., Luikart, H., Valantine, H. A.  
2006; 82 (11): 1419-1424
- **Giant coronary aneurysms in heart transplantation: an unusual presentation of cardiac allograft vasculopathy** *JOURNAL OF HEART AND LUNG TRANSPLANTATION*  
Haddad, F., Perez, M., Fleischmann, D., Valantine, H., Hunt, S. A.  
2006; 25 (11): 1367-1370
- **T-cell immunity to subclinical cytomegalovirus infection reduces cardiac allograft disease** *CIRCULATION*  
Tu, W., Potena, L., Stepick-Biek, P., Liu, L., Dionis, K. Y., Luikart, H., Fearon, W. F., Holmes, T. H., Chin, C., Cooke, J. P., Valantine, H. A., Mocarski, E. S., Lewis, et al  
2006; 114 (15): 1608-1615
- **Acute rejection and cardiac allograft vascular disease is reduced by suppression of subclinical cytomegalovirus infection** *TRANSPLANTATION*  
Potena, L., Holweg, C. T., Chin, C., Luikart, H., Weisshaar, D., Narasimhan, B., Fearon, W. F., Lewis, D. B., Cooke, J. P., Mocarski, E. S., Valantine, H. A.  
2006; 82 (3): 398-405
- **Discordant changes in epicardial and microvascular coronary physiology after cardiac transplantation: Physiologic investigation for transplant arteriopathy II (PITA II) study** *JOURNAL OF HEART AND LUNG TRANSPLANTATION*  
Fearon, W. F., Hirohata, A., Nakamura, M., Luikart, H., Lee, D. P., Vagelos, R. H., Hunt, S. A., Valantine, H. A., Fitzgerald, P. J., Yock, P. G., Yeung, A. C.  
2006; 25 (7): 765-771
- **Wound healing complications with de novo sirolimus versus mycophenolate mofetil-based regimen in cardiac transplant recipients** *AMERICAN JOURNAL OF TRANSPLANTATION*  
Kuppahally, S., Al-Khaldi, A., Weisshaar, D., Valantine, H. A., Oyer, P., Robbins, R. C., Hunt, S. A.  
2006; 6 (5): 986-992
- **Validation of a screening protocol for identifying low-risk candidates with type 1 diabetes mellitus for kidney with or without pancreas transplantation** *35th Annual Meeting of the American-Society-of-Nephrology*  
Ma, I. W., Valantine, H. A., Shibata, A., Waskerwitz, J., Dafoe, D. C., Alfrey, E. J., Tan, J. C., MILLAN, M., Busque, S., Scandling, J. D.  
WILEY-BLACKWELL PUBLISHING, INC.2006: 139-46

- **Recurrence of iron deposition in the cardiac allograft in a patient with non-HFE hemochromatosis** *JOURNAL OF HEART AND LUNG TRANSPLANTATION*  
Kuppahally, S. S., Hunt, S. A., Valentine, H. A., Berry, G. J.  
2006; 25 (1): 144-147
- **Use of the implantable cardioverter-defibrillator in long-term survivors of orthotopic heart transplantation** *HEART RHYTHM*  
Ptaszek, L. M., Wang, P. J., Hunt, S. A., Valentine, H., Perloth, M., Al-Ahmad, A.  
2005; 2 (9): 931-933
- **Induction therapy for pediatric and adult heart transplantation: Comparison between OKT3 and daclizumab** *TRANSPLANTATION*  
Chin, C., Pittson, S., Luikart, H., Bernstein, D., Robbins, R., Reitz, B., Oyer, P., Valentine, H.  
2005; 80 (4): 477-481
- **From clinical trials to clinical practice: An overview of Certican(R) (everolimus) in heart transplantation** *Meeting on Certican in Heart Transplantation*  
Valantine, H., Zuckermann, A.  
ELSEVIER SCIENCE INC.2005: S185-S190
- **Certican (Everolimus) in heart transplantation: from clinical trial to clinical experience. Proceedings of a meeting, Vienna, Austria, September 9, 2004.** *journal of heart and lung transplantation*  
2005; 24 (4): S183-211
- **Prevention of cardiac allograft vasculopathy with Certican(R) (everolimus): The Stanford University experience within the Certican Phase III clinical trial** *Meeting on Certican in Heart Transplantation*  
Valantine, H.  
ELSEVIER SCIENCE INC.2005: S191-S195
- **Cardiac allograft vasculopathy after heart transplantation: Risk factors and management** *JOURNAL OF HEART AND LUNG TRANSPLANTATION*  
Valantine, H.  
2004; 23 (5): S187-S193
- **Glucose intolerance, as reflected by hemoglobin A(1c) level, is associated with the incidence and severity of transplant coronary artery disease** *JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY*  
Kato, T., Chan, M. C., Gao, S. Z., Schroeder, J. S., Yokota, M., Murohara, T., Iwase, M., Noda, A., Hunt, S. A., Valentine, H. A.  
2004; 43 (6): 1034-1041
- **Cytomegalovirus infection impairs the nitric oxide synthase pathway - Role of asymmetric dimethylarginine in transplant arteriosclerosis** *CIRCULATION*  
Weis, M., Kledal, T. N., LIN, K. Y., Panchal, S. N., Gao, S. Z., Valentine, H. A., MocarSKI, E. S., Cooke, J. P.  
2004; 109 (4): 500-505
- **The role of viruses in cardiac allograft vasculopathy** *AMERICAN JOURNAL OF TRANSPLANTATION*  
Valantine, H. A.  
2004; 4 (2): 169-177
- **Analysis of survivors more than 10 years after heart transplantation in the cyclosporine era: Stanford experience** *JOURNAL OF HEART AND LUNG TRANSPLANTATION*  
Shiba, N., Chan, M. C., Kwok, B. W., Valentine, H. A., Robbins, R. C., Hunt, S. A.  
2004; 23 (2): 155-164
- **Longer-term risks associated with 10-year survival after heart transplantation in the cyclosporine era** *JOURNAL OF HEART AND LUNG TRANSPLANTATION*  
Shiba, N., Chan, M. C., Valentine, H. A., Gao, S. Z., Robbins, R. C., Hunt, S. A.  
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- **Cardiac allograft vasculopathy: Central role of endothelial injury leading to transplant "atheroma"** *TRANSPLANTATION*  
Valantine, H. A.  
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- **Post-operative conversion from cyclosporine to tacrolimus in heart transplantation: A single-center experience** *JOURNAL OF HEART AND LUNG TRANSPLANTATION*  
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- **Preferential involvement of larger vessels in a rat model of diabetes induced graft vasculopathy** *JOURNAL OF HEART AND LUNG TRANSPLANTATION*  
Cantin, B., Zhu, D., Wen, P. Z., Panchal, S. N., Gwathmey, J. K., Reaven, G. M., Valantine, H. A.  
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- **Conversion of cyclosporine to tacrolimus for refractory or persistent myocardial rejection** *2nd International Congress on Immunosuppression*  
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- **Mycophenolic acid concentrations in long-term heart transplant patients: relationship with calcineurin antagonists and acute rejection** *CLINICAL TRANSPLANTATION*  
Cantin, B., Giannetti, N., Parekh, H., Panchal, S. N., Kwok, B. W., Najem, R., Woodman, K., Hunt, S. A., Valantine, H. A.  
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- **Reversal of diabetes-induced rat graft transplant coronary artery disease by metformin** *JOURNAL OF HEART AND LUNG TRANSPLANTATION*  
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2002; 21 (6): 637-643
- **Detection of early atherosclerosis with radiolabeled monocyte chemoattractant protein-1 in prediabetic Zucker rats** *43rd Annual Meeting of the Society-for-Pediatric-Radiology*  
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Valantine, H. A., Luikart, H., Doyle, R., Theodore, J., Hunt, S., Oyer, P., Robbins, R., Berry, G., Reitz, B.  
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- **Transplant coronary artery disease - A novel model independent of cellular alloimmune response** *CIRCULATION*  
Cantin, B., Wen, P. Z., Zhu, D. N., Dai, M., Panchal, S. N., Billingham, M. E., Gwathmey, J. K., Valantine, H. A.  
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- **Detection and treatment of coronary artery disease in liver transplant candidates** *LIVER TRANSPLANTATION*  
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- **Mild hyperhomocysteinemia is not associated with cardiac allograft coronary disease** *CLINICAL TRANSPLANTATION*  
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- **Severe tricuspid regurgitation after heart transplantation** *72nd Annual Scientific Session of the American-Heart-Association*  
Chan, M. C., Giannetti, N., Kato, T., Kornbluth, M., Oyer, P., Valantine, H. A., Robbins, R. C., Hunt, S. A.  
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- **Metabolic abnormalities characteristic of dysmetabolic syndrome predict the development of transplant coronary artery disease - A prospective study** *CIRCULATION*  
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- **Impact of type 1 diabetes on microvascular vs. macrovascular involvement with TXCAD: is there a difference in models of the disease?** *journal of heart and lung transplantation*  
Valantine, H., Zhu, D., Wen, P., Panchal, S. N., Dai, X.  
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- **Neoral use in the cardiac transplant recipient** *Conference on Neoral Absorption Profiling: Advances in Neoral Management in the Solid Organ Transplant Recipient*  
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- **Impact of prophylactic immediate posttransplant ganciclovir on development of transplant atherosclerosis - A post hoc analysis of a randomized, placebo-controlled study** *CIRCULATION*  
Valantine, H. A., Gao, S. Z., Menon, S. G., Renlund, D. G., Hunt, S. A., Oyer, P., Stinson, E. B., Brown, B. W., Merigan, T. C., Schroeder, J. S.

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- **Role of CMV in transplant coronary artery disease and survival after heart transplantation.** *Transplant infectious disease*  
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- **Heart transplantation in patients over 54 years of age - Mortality, morbidity and quality of life** *XVIIIth Congress of the European-Society-of-Cardiology*  
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- **Methotrexate or total lymphoid radiation for treatment of persistent or recurrent allograft cellular rejection: A comparative study** *JOURNAL OF HEART AND LUNG TRANSPLANTATION*  
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1997; 16 (2): 179-189
- **Significant reduction in the number of fungal infections after lung-, heart-lung, and heart transplantation using aerosolized amphotericin B prophylaxis** *XVI International Congress of the Transplantation-Society*  
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Ross, H. J., Gullestad, L., Hunt, S. A., TOVEY, D. A., PURYEAR, J. B., McMillan, A., Stinson, E. B., Valantine, H. A.  
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- **Prophylactic ganciclovir treatment reduces fungal as well as cytomegalovirus infections after heart transplantation** *14th Annual Meeting of the American-Society-of-Transplant-Physicians*  
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