THIS MONTH'S FOCUS:
PEDIATRICS

IN THE SPOTLIGHT: The Road to Washington DC via an English Country Estate…

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One of my first responsibilities as Programme Chair for the 2016 ISHLT Annual Meeting was to choose a programme committee that reflected the professional diversity, geography, gender and specialist skills of the ISHLT membership. Now 4 months into this role, I appreciate why careful selection of this group of individuals was so important.

In mid-July the committee of 35 people came together at a secluded historical location outside London to develop the final invited content for the 42 symposia and 3 plenary sessions to be held in Washington DC next year. The dedication of the group to this task, from pre-meeting preparation to enthusiastic teamwork on site, was tremendous to behold and illustrates why ISHLT thrives through the commitment of its volunteers. Our energies during the meeting were kept focused on the tasks in hand by the efficient support and experience of the ISHLT staff.

I am very fortunate to be working with a fantastic group of people on the programme committee and am very confident that the content generated for our 2016 Annual Meeting is topical, innovative and relevant to the educational needs of all our members. We are now working on producing the preliminary program so that all the content can be shared with ISHLT members in the near future. The next major stage of our preparations is to launch the *call for abstracts* and encourage you all to submit your very best scientific and clinical research to the meeting and share it with your colleagues from around the world in the spoken and poster sessions.

Disclosure statement: The author has no conflict of interest to disclose.

The First 100 Days: Presidential Address to the ISHLT

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It is appropriate that this report of the 1st 100 days as ISHLT President is focused on change and transition. Before focusing on the year ahead, I would like to congratulate Andreas Zuckerman and the program committee on the outstanding 35th annual program in Nice. The content and presentations were excellent and the venue was exceptional. Nice was nice!!!

While it will be a tough act to follow, particularly the Presidential presentation with the Hamburg ballet, Andrew Fisher and the program committee are up to the task. This year's program committee met in the Ashridge House, UK and assembled an extraordinary series of symposia and plenary sessions that I am sure you will enjoy. Andy highlighted much of this year's meeting content in this month's Links, and we hope you find it enticing and innovative. Importantly, we look forward to your abstract submissions, as they are the heart and soul of our annual meeting. With new and exciting advances in our field of heart and lung failure, management and treatment, we look forward to the presentations in 2016. While we won't disclose this year's plans for the Presidential address, in the spirit of last year's performance, we were thinking that past presidents and board members should perform a similar dance in similar attire. You won't want to miss it. We look forward to seeing you in Washington, DC.

As hopefully all of you know, we have initiated strategic planning for our society. Many of you have already completed the survey and have been contacted by your council leadership for input into the future direction of our society. I cannot understate the importance of membership input into the strategic plan. ISHLT has evolved considerably from its origin as a group of like-minded heart transplant colleagues who met in San Francisco 34 years ago. Our evolution has encountered many controversial subjects, such as the addition of lung transplantation both to our name and our focus. Over the years we have matured into a truly multidisciplinary, international society focused on the care of patients with end-stage heart and lung failure. Areas of mechanical circulatory support, both short- and long-term, and pulmonary hypertension are now tremendous areas of growth in our society. Similarly, we have expanded from a North American, Australian and Western European society into a truly international society with further growth in Asia, South America and the Middle East. Unlike many medical societies, we are growing in membership and in our societal role in respect to meeting both our patient's and members' needs. Going forward, we need to better understand and position the society to meet our members' needs; your input is vital. Please make every effort to participate if your council calls for input. I personally welcome any direct input that you might have. Our society's future is dependent on this change and transition, therefore your input and engagement are vital to its success. Thank you for your assistance in making our society better.

Finally, I wanted to provide a brief note on personal change. After 31 years at Duke, I have embarked on a new venture directing the Cardiovascular Institute at Florida Hospital in Orlando. I am writing this report while waiting for movers and internet /phone installers. If I am a little less prompt in my

responses to emails and correspondence, please accept my apologies. Like our society, this venture will require exploring new roads and undertaking new challenges. The joy will be in the journey. I look forward to "hearing" from you and understanding how our society can better address your needs. I could not be more thrilled in taking on this journey with all of you.

Disclosure statement: The author has no conflicts of interest to disclose

STRATEGIC PLANNING UPDATE

A big THANK YOU to everyone who completed the Strategic Planning Survey. We received responses from 404 members whose specialties, ages, and geographic locations were very representative of the membership as a whole. We're off to a great start, but we would still like to hear from the rest of you! For those of you who did not participate in the survey but would like to provide input into the strategic planning process, you may do so by sending an email to president@ishlt.org or by communicating with your Council Chair. During the month of July, each of the Council Chairs will be facilitating discussions with their Council members regarding the future direction of ISHLT. Some will do this via surveys, others via conference calls, others via discussions in the online community. The Strategic Planning Task Force encourages you to be PROACTIVE in this process. Take the initiative to give us YOUR input into the future of YOUR Society.

Call for Abstracts: ISHLT 36th Annual Meeting and Scientific Sessions

The Abstract Submission System is now live on the ISHLT website at http://ishlt.org/meetings/abstracts.asp. The deadline for receipt of abstracts is **November 3, 2015 at 11:59 PM EST**.

NEW THIS YEAR: the Main Menu page of the Abstract Submission Site offers three different link options for submitting an abstract:

1. **New Abstract Submission**
   Use this link to submit an abstract in one of the following 12 main categories:

   - Basic Science (BSI)
   - Economics, Ethics, Public Policy (EEP)
   - Heart Failure – Adult (HF)
   - Heart Transplantation – Adult (HTX)
   - Infectious Diseases (ID)
   - Lung Transplantation – Adult (LTX)
   - Mechanical Circulatory Support – Adult (MCS)
   - Nursing, Health Science, Allied Health (NHSAH)
   - Pathology (PATH)
   - Pediatrics (PEDS)
   - Pharmacy & Pharmacology (PHARM)
   - Pulmonary Hypertension (PH)

2. **New Junior Faculty Clinical Case Reports (JFCCR) Submission** (for Junior Faculty <7 years out of training only)
   Use this link to submit an abstract in one of the following 6 CASE sub-categories:

   - Infectious Diseases
   - Heart Failure/Transplantation
   - Lung Failure/Transplantation
   - Mechanical Circulatory Support
   - Pediatrics
   - Pulmonary Hypertension

3. **New Late Breaking Clinical Science (LBCS) Submission**
   Use this link to submit an abstract in the Late Breaking Clinical Science category.

Detailed instructions for submitting an abstract in any of these categories are available on the submission site and in the 2016 Call for Abstracts brochure which can be downloaded via the following links:

- ISHLT 2016 Call for Abstracts PDF Brochure
- ISHLT 2016 Call for Abstracts Flipbook (great for Android users)

We look forward to receiving your best science submissions!

Management of Allosensitization in the Pediatric Heart Transplant Candidate

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Health care providers have been trying to unlock the secret to managing highly sensitized patients prior to transplantation since the significance of a donor-specific crossmatch was recognized by Patel and Terasaki in 1969.The majority of discussion and practice has focused on avoidance of sensitizing agents and desensitization therapy. Use of cryopreserved homografts in staged single ventricle palliation continues to produce highly sensitized patients. It seems like "failed Fontan physiology" and "single ventricle pump dysfunction" account for just as many transplant evaluations as end-stage cardiomyopathy. Blood product transfusions may not be as bad as was once thought. Intravenous immunoglobulin (IVIg), rituximab, plasmapheresis, and bortezomib have all shown promise as desensitizing agents, butlack consistent and lasting results, perhaps because the inciting antigens remain in place (i.e. homograft) before, and possibly after transplantation. With the growing numbers of "failed" Fontan patients coming to transplantation and our increased abilities to detect HLA and non-HLA antibodies, now seems like the right time to shift our focus to new areas of investigation.

To start, it would be imprudent to give up on current strategies that have shown promise in diminishing or eliminating antibodies. Further breakthroughs may not come in what we use, but when we use it. Proteasome inhibitors offer the most targeted therapy against antibody production by inducing apoptosis of the plasma cell. We commonly exhaust all other treatment options prior to use due to concern for potentially serious side effects like peripheral neuropathy, opportunistic infections, and cytopenias. To date the limited reports in children show only minimal and transient adverse drug effects (ADE). Critically ill children may be more at risk for ADEs given that they have a greater risk for infection and less tolerance of associated cytopenias. The key to success with proteasome inhibition may lie in the timing of administration. The potential for "true" desensitization with bortezomib as a first-line agent was recently shown in adult renal transplant recipients. Also, second generation proteasome inhibitors are currently being studied and appear to be effective with less ADEs. Pediatric studies are needed to evaluate primary desensitization using bortezomib-based protocols.

The question then arises regarding antibody-specific desensitization. Use of a ventricular assist device (VAD) is seen as a potentially sensitizing event, possibly due to blood products administered during implantation or secondary to the materials that comprise the device. Is an antibody clinically relevant if it is against a non-biologic material? Should we even bother with desensitization? How can we tell the difference? In fact, VAD-related antibodies infrequently result in a positive crossmatch

and may occur less with non-pulsatile devices. Despite an increasing knowledge base on antibody generation, we still cannot predict which antibody will lead to a positive crossmatch. But do we need to be as aggressive in eliminating an uncommon antibody like A31 compared to an extremely common antibody like A2? It may not be clinically beneficial to the patient to receive prolonged immunotherapy on the off chance that a potential donor carries a rare HLA allele. Also, when a candidate shows only a few antibodies of weak to moderate mean fluorescence intensity (MFI) and a negative virtual crossmatch, how do we know which will result in a memory response and should potentially be avoided? Improved abilities to predict not only which will result in a positive crossmatch but which will result in antibody-mediated rejection in the first 2-4 weeks due to memory response will be an important area of understanding as we move forward.

This leads directly into the third point of discussion: is it better at times to avoid desensitization therapy and increased waitlist time by simply transplanting a patient across a positive crossmatch? Data exist that shows both decreased cost and resource utilization, as well as improved survival in highly sensitized patients transplanted with the first acceptable organ. We have even seen similar early survival when transplanted across a positive crossmatch, albeit with higher rates of early rejection. While a negative crossmatch remains ideal, transplanting across a positive crossmatch may actually be favorable, in the right patient.

Allosensitization will likely remain a source of frustration for years to come. There are many questions but few answers. Until bioengineered HLA-specific grafts become reality, we must continue to increase our understanding of HLA antibody production, relevance, and optimal pre-transplant desensitization strategies.

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From Clinical to Pathological: The Evolution of Diagnostics in Antibody Mediated Rejection

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Antibody mediated rejection (AMR) has mystified the transplant community for many years and continues to generate discussion and controversy. AMR occurs when an antibody targets donor endothelium, which sets the stage for an immunological assault by activation of complement and other mechanisms. While this entity was first described in the 1980s, the transplant community continues to refine and develop a universal definition of AMR. Much of this work has been done through the International Society of Heart and Lung Transplant (ISHLT), with the first cardiac working group formulating a definition in 1990 with further development and expansion in 2004. The 2004 definition focused on pathological findings and graft dysfunction in the presence of a donor specific antibody (DSA). Over the subsequent years the definition and focus has moved away from clinical sequelae towards a purely pathological diagnosis where graft dysfunction and DSA are no longer part of the definition. This last modification published in 2013 combines both the histological and immunopathological (IP) features seen on biopsy to define pathological AMR (pAMR). This approach to AMR diagnosis is reflective of the criteria set forth for cellular rejection with no requirement for clinical symptoms or additional diagnostics. The important histological features include: capillary injury with swollen endothelial cells, intravascular capillary macrophages, interstitial edema and hemorrhage. The IP features rely on either immunohistochemistry staining on paraffin embedded samples or immunofluorosence staining of frozen samples to identify markers of complement deposition and the presence of intravascular macrophages. Complement deposition is predominantly detected by C4d staining with a positive stain defined as >50% of the capillaries staining positive. Macrophages located within the capillary beds are identified by CD68 staining and a positive stain occurs when >10% of the capillaries are involved.

A number of pitfalls may occur during the interpretation of the biopsy samples making the diagnosis of AMR difficult. Early in the post-transplant period some of the histological and immunological findings may be present secondary to ischemic damage existing at the time of transplant or secondary to post-operative management. In addition, while C4d staining may be considered the hallmark of AMR, false positive results can occur after treatment with intravenous immunoglobulins, rituximab or reflecting a non-specific inflammatory reaction and therefore the biopsy may be uninterpretable. These examples highlight the importance of a strong pathology team, good internal positive and negative controls and excellent communication between the clinical and pathological team in order to guide the diagnosis of pAMR.

Since the new guidelines for AMR diagnosis there are now five different categories that a biopsy sample can be labeled with including pAMR 0 (negative for histological and IP studies), pAMR1(h) (histological findings present/IP negative), pAMR1 (I) (IP positive-either C4d or CD68 and histology negative), pAMR2 (histology and IP positive) and pAMR3 (severe pAMR with advanced histological

features and positive IP). In pediatrics it is unclear what the relationship is between these various pathological categories and clinical outcomes. To date, and association between pAMR 3 and worse cardiovascular outcomes in children has been identified but unlike in adults the significance of subclinical AMR remains unclear.

These categories, while helpful in further categorizing the pathological features of AMR, leave a number of questions for those approaching a patient with a new biopsy finding of pAMR. What are the future implications of asymptomatic AMR? Which categories of pAMR require treatment? Which categories of pAMR affect long-term outcomes? What treatment is indicated for which pAMR category? Do the findings in the adult literature parallel what we would expect in the pediatric patients? All of is further complicated by the evolving field of antibody detection with its own complexities including the use of various thresholds to define significant donor specific antibodies, various detection systems, the unclear role of non-HLA antibodies and reporting of newer HLA antibodies, such as DQ. How to integrate the biopsy findings with the antibody results has become somewhat of an art with room for further scientific guidance.

While there have been a number of adult papers that have started to address some of these questions there is little literature in pediatrics to provide direction. However, this new diagnostic standard for AMR provides a starting point for collaborative efforts to tackle these important questions in pediatrics and shed light on this complex topic.

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Treatment of Antibody Mediated Rejection in Pediatric Heart Transplantation

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Since the beginning of pediatric heart transplantation three decades ago, improved understanding of transplant immunology combined with more effective and less toxic immunosuppressive medications have led to lower rates of cellular rejection and excellent short-term outcomes. However, antibody mediated rejection (AMR) remains an important obstacle to long-term graft survival. Indeed, AMR is being diagnosed more often in pediatric heart transplant recipients, in part due to improved diagnostic tools and criteria, but also as a result of a growing pool of high-risk transplant candidates, particularly those sensitized to potential donor HLA antigens from previous surgeries to repair congenital heart disease and/or mechanical support requirements. As such, AMR and its treatment is becoming an increasingly important research focus. And while advanced technology to detect and elucidate the pathophysiology of antibody-mediated graft injury has certainly offered a number of new therapeutic targets for a growing armamentarium of AMR-specific therapies, there are a few pillars of anti-rejection treatment which cannot be forgotten.

Plasmapheresis, whereby proteins (including HLA antibodies) are indiscriminately removed from plasma, has been described as a method to prevent hyperacute rejection in solid organ transplant recipients since the early 1970s. Today, plasmapheresis remains the cornerstone of treatment for acute AMR with graft dysfunction, where the primary goal is rapid reduction in circulating donor-specific antibody (DSA) levels in order to halt ongoing myocardial damage. Immunoadsorption (using antibody-binding protein columns) is another option for antibody removal, although less commonly used in pediatrics. Unfortunately, these modalities typically provide only short-term reduction in circulating DSA levels, and must be used in conjunction with other treatments.

Several other traditional therapies remain mainstays for treatment of AMR. **Corticosteroids** provide powerful non-specific immunosuppressive effect by altering the function and distribution of all types of immunologically active cells, and remain first-line treatment for both cellular and antibody mediated rejection. The immunomodulatory effects of **intravenous immunoglobulin (IVIg)** are not as well understood, but theories include "neutralization" of damaging antibody activity by alteration of Fc receptor binding, disruption of antigen presentation, and inhibition of the membrane attack complex. In AMR, IVIg also serves to replenish depleted "good" antibodies and to down-regulate rebound DSA production after plasmapheresis. Finally, the T-cell depleting agent **anti-thymocyte globulin (ATG)**, can also be used to treat hemodynamically significant AMR, as T-cells are required for antibody activation.

More recently, several AMR-specific treatments have been used to target different points in the pathway from DSA production all the way to antibody mediated cellular injury. **Rituximab** is an anti-CD20 monoclonal antibody which targets and destroys B cells, the precursors of antibody producing

cells. While rituximab has been available and tried as an AMR treatment for many years, rituximab alone has not been shown to sufficiently lower antibody levels or reduce rates of graft loss related to AMR. **Bortezomib** is a proteasome inhibitor which is FDA approved for treatment of multiple myeloma, a plasma cell cancer. Proteosome inhibition interferes with the cell cycle at specific mitotic checkpoints and ultimately results in destruction of plasma cells, where DSAs are manufactured. There is growing clinical experience with Bortezomib as treatment for AMR in pediatric heart transplant recipients with initially promising results, although few formal studies exist. **Eculizumab**, a humanized anti-C5 monoclonal antibody, acts at the final step in antibody mediated cellular injury by blocking terminal complement activation. Eculizumab can act quickly to block antibody mediated graft injury even while antibody levels are high, potentially protecting the graft from injury while giving other therapies directed at lowering antibody levels time to work.

Several novel biological therapies are now being considered in adult and other solid organ transplant recipients which may hold promise for future AMR treatment in pediatric heart recipients. A **C1-inhibitor** is in the early phases of clinical trials and may work synergistically with Eculizumab to block complement mediated cell damage. **Belatacept** selectively binds to CD86/CD80 on antigen presenting cells and works primarily to block T-cell activation, but also acts to indirectly inhibit antibody production. Finally, several **second generation proteasome inhibitors** are under development for cancer treatments, which may prove useful in AMR as well.

Of course, large-scale randomized clinical trials of these therapies are not routinely being performed in children, and we must therefore rely on data from adult or smaller pediatric studies (often in other organ transplants) to guide our practice. Based on the information we have so far, no single therapy alone is adequate to treat AMR, while the perfect combination remains elusive. It is also important to remember that long-term risks of these new immunosuppressive agents are not well-documented, particularly in children, and we must remain attentive even as we become more comfortable prescribing these medications to our young patients. Finally, our ultimate goal for research and drug development should focus not only on treatment, but also on prevention of AMR and its sequelae.

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You, Abstracts, ISHLT and JHLT: How You Improved the Impact Factor

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The ISHLT is a multidisciplinary and professional organization dedicated to improving the care of patients with advanced heart and lung disease through transplantation, mechanical support and innovative therapies via research, education and advocacy. The force behind this dedication is of the members, by the members and for the members. We are the members and because of us and our dedication to our patients, *The Journal of Heart and Lung Transplantation* is today **first** in the category of Transplantation, **third** in the category of all Surgical Journals and **ninth** in Cardiovascular. We should be proud. You should be proud. This great feat has started with you, still starts with you and will continue to start with you. It ultimately begins with the submissions of your abstracts. Today, begins abstract season for the upcoming 36th Annual ISHLT Meeting in Washington, DC. The season will remain open for 92 days and closes on November 3, 2015. From an English Country Estate, all is ready, the game is afoot. Start submitting your abstracts today.

Lest we forget, it's because of you and under the tutelage of our illustrious Editor-in-Chief, Mandeep Mehra, our *Journal* has risen to the occasion. Instead of resting on our peak Impact Factor of 6.650, we will reach for another summit. Our most recent efforts putting us on the right tract (see figure) over the last five years have included:

1. Nimble review decisions with a target of 21 days to first decision
2. Rapid publications on-line, now within 48 hours of acceptance and 3 months or less in the print edition
3. Development of a strong reviewer base across members with a target for high quality reviews and editorial decisions
4. Diversification of the JHLT into "End Stage Heart and Lung Disease" with special emphasis on Mechanical Circulatory support and Pulmonary Hypertension
5. Launching of new features including State of Art Reviews, Perspectives, Research Correspondences
6. Provision of unlimited online supplementary materials, Audio Slides, Virtual Histology
7. Creation of digital interface with IPAD application
8. Renewed and vigorous involvement of young editors and investigators
9. Evolution of a Social Media office to start in 2015 targeting an interface with Facebook, Twitter, Instagram and online blogs

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The Inimitable Mandeep Mehra

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The one who has been steering us along has been none other than our very own Dr Mandeep Mehra. Who is Mandeep Mehra? Mandeep is not unlike Thomas Jefferson. He is our behind the scenes and in front of the scenes ISHLT leader. But unlike Jefferson, he does not sit quietly and is not a poor public speaker. Mandeep is a gifted public speaker, is our Editor-in-Chief of The Journal of Heart and Lung Transplantation and today serves as Medical Director of the Brigham and Women's Hospital Heart and Vascular Center and Executive Director of the Collaborative Center for Advanced Heart Disease. He is Professor of Medicine at Harvard Medical School. Prior to joining the Brigham, he served as the Dr Herbert Berger Endowed Professor of Medicine and Head of Cardiology and Assistant Dean for Clinical Services at the University of Maryland, School of Medicine. Dr Mehra has authored over 500 book chapters, manuscripts, editorials and abstracts focusing on all aspects of advanced heart failure and cardiac transplantation, treatment modalities, medical therapies and alternatives to transplantation. His specific research interests in heart transplantation include: post-transplant coronary arterial disease (use of intravascular ultrasound and angioscopy), newer immunosuppressive therapies to improve heart transplant outcomes (particularly in minority populations), and bringing genomic and proteomic science from the bench to the bedside (in an effort to avoid the morbidity of endomyocardial biopsies). In the field of heart failure, his research has focused on the role of novel percutaneous cardiac support devices and serum markers to guide diagnosis and therapy. One important area of his focus is in developing International Guidelines for care of the heart transplant candidate and process enhancement for improving performance measure adherence in heart failure. More recently, he has focused on bench research to understand the effects of cigarette smoke on the transplanted heart coronary vasculature and its interaction with the development of nephropathy in the presence of immunosuppression.

Finally, Dr. Mehra is a Past-President treasurer of the ISHLT, served as the 2004 Program Chairman for the ISHLT Annual Scientific Meeting and as a Board member. Mandeep we owe you a debt of gratitude for your efforts and guidance.

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Thomas Jefferson and His Accomplishments

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The more I read about Thomas Jefferson, the smarter he gets. We can spend nearly a lifetime learning the views or trying to learn the views of Jefferson on everything. There are literally thousands of his letters he penned. Above all, Jefferson is second to none in terms of American Character and Patriotism and yet he is the American Sphinx. This fact is easily supported by Dumas Malone, 1892 – 1986, who spent his life studying Jefferson, read over 60,000 correspondences written by him, poured over the letters exchanged between two of the most brilliant Presidents (John Adams and Jefferson) and above all completed a 6-volume magnificent compendium on Jefferson. Yet despite all of this focus on Jefferson, Dumas state he never got the understand him, "*he eluded me*."

Jefferson remains uniquely relevant to us today and can be found across the landscape of America. He is on our currency, on Mount Rushmore, on the names of streets, schools, counties and cities. There is the Jefferson Memorial in Washington, DC and Monticello in Charlottesville, Va. Not unlike Washington, Jefferson is with us everywhere. But unlike Washington, he is one of the most controversial figures in American History, and unlike Washington, there a prodigious amount of written material left by Jefferson for us to examine especially thousands of letters, there's not much to read from by Washington. Most unlike Washington, Jefferson was a chronic debtor, he spent lavishly well above his means. Washington was a consummate businessman and had no debts.

Jefferson was the writer of the Declaration of Independence, pioneered the ideas on religious freedom, he was a biologist, botanist, political philosopher, anthropologist, archaeologist, architect, musician, inventor, a student of natural science and probably the only person in North America than could do the higher order calculus required to follow Newton's arguments in the *Principia Mathematica*. He studied sociology and political theory. He learned ancient and modern languages including; Greek, Latin, Italian, French, German and Anglo-Saxon. He was a Member of the House of Burgesses, delegate to the Continental Congress, Governor, President of the American Philosophical Society, Minister to France, Diplomat, Secretary of State, Vice-President and President of the United States, He authored *A Summary View of the Rights of British America*, wrote the Northwest Ordinance and was responsible for doubling the size of America with the Louisiana Purchase. He was a Statesman and obviously the most accomplished of all American Presidents.

Jefferson was an eternal optimist and very proud of the United States and its revolutionary accomplishments. Yet he was constantly troubled by slavery and education in American. Also, and unfortunately he did not think too highly of women. For that matter what was meant behind those inalienable rights, "that all men are created equal?" What about women, slaves and Native Americans Indians? Jefferson was full of paradoxes. But does anyone in history live up to his or her own ideals? Do as I say and not as I do therefore carries more meaning, everywhere.

Among his paradoxes he lived luxuriously but favored the simplicity of a yeoman farmer. He lived beyond his means and died in debt. In an effort to pay off his debts, the sale of his massive collection of expensive books became the foundation of the Library of Congress. His passion for learning was more suited for those of leisure rather than independent farmers. He hated slavery but preserved it and kept slaves of his own. A man of principle, he violated his own principles. On one hand, he was a visionary expansionist and realized his vision with the Louisiana Purchase, but it violated his own constitutional prerogative. He attacked the Barbary pirates with the Navy built by Adams that Jefferson fought against. The embargo against Britain in 1807 created hardships on New England.

One of the most enduring aspects of Jefferson character was his behind the scenes meddling and most of all, his mastery as a “dinner table” politician. He avoided confrontation and hated public speaking. He gave only two speeches during his eight years as President. However his gift was in his pen and yet he was behind the scenes of all ideas. Over dinner he solved many controversies.

Today, Americans from every political persuasion find inspiration from the words of Thomas Jefferson. Conservatives find great inspiration in his opposition to taxes and big government, his backing of States rights, his advocacy of individual freedom, his belief in natural rights deriving from God. Liberals, including Franklin Delano Roosevelt, embraced Jefferson as the inspirational founder of his Democratic Party and pushed for the creation of the Jefferson memorial. Roosevelt enlisted Jefferson’s commitment to freedom, liberty, self-government in the precarious struggle against the tyranny of fascist Germany and fascist Japan during World War II. Modern liberals find inspiration in Jefferson’s opposition to special privilege, his campaign against superstition and ignorance, his crusade for religious and intellectual freedom, and his support of the common people against the wealthy and special interest.

Some of Jefferson’s detractors want to banish him from the Pantheon of American heroes. Some critics believe he was an Anglo-Saxon imperialist, slave-holder who physically and sexually exploited his slaves. An opponent to positive government and a dangerous advocate of violence justified in the name of freedom. Nevertheless, historians argue that Jefferson was a classical liberal concerned with individual rights and a classical republican concerned with people’s duties and virtues.

The debates about Jefferson are essentially the debates about the meaning of America. His principles guideposts for our lives. The efforts to understand the real Thomas Jefferson sharply aligns with our quest to discover the real America itself. He is an eloquent champion of political principles and a visionary thinker who often expressed his ideas with near perfect rhetoric and with some degree of abstraction lending itself and inviting opposing interpretations. It is easy to read what you want to believe in his writings.

Again, his obvious shortcoming is his myopic view on women, slavery and Indians, yet these are the actual groups who are inspired by Jefferson’s legacy to help them secure their individual rights and freedom at a time away from the times of Thomas Jefferson who was a man of times. Although, he avoided action on the problem with slavery, he did take action on the problem with education.

Jefferson was a staunch advocate for education and education for all. As a result of his own personal success he championed that an ideal society should be through meritocracy of talent and ability, not aristocracy of birth and privilege. He promoted the cause of upward mobility, the result was his founding of the University of Virginia in 1819.

Finally, incessant education and inquiry to any new intellectual development were his passions. He was the most intellectual President. In 1962, when John F Kennedy invited a group of Noble Prize winners to the White House, he remarked "*this is the most extraordinary collection of talent and human knowledge that has ever been gathered at the White House with the possible exception of when Thomas Jefferson dined alone."* No other President, including Abraham Lincoln is as much remembered for his words as is Thomas Jefferson.

Jefferson supplied his own epitaph for his tombstone: *Here was buried Thomas Jefferson, Author of the Declaration of American Independence of the Statute of Virginia for religious freedom and Father of the University of Virginia.*

Disclosure statement: The author has no conflicts of interest to disclose.

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Old Hickory to Young Hickory and the Manifest Destiny

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Despite receiving very little education, Andrew Jackson was revered as a self-made frontiersman and a champion of the common people. He was born very poor in a log cabin in South Carolina on March 15, 1767. He earned the nickname "**Old Hickory**" by those he commanded because he was strong and tough like a hickory tree. He was loved by his soldiers and the American people. Unaware of the peace treaty signed to end the War of 1812, Jackson led troops in a decisive battle against the British at the Battle of New Orleans on January 8, 1815 which transformed him into America's greatest living national hero. From that point on, it was assumed he would one day be President.

He lost the controversial 1824 Presidential election to John Quincy Adams by the dubious "corrupt bargain" between Henry Clay and Adams. Jackson had won the popular vote and saw himself as the people's choice. When Clay was named Secretary of State, the "fierce fighter" Jackson was determined to topple the old "Eastern Establishment." Jackson stated, "*Did the Presidency belong to the privileged few, as it had almost de facto from the beginning, or did it belong to a much wider America*?" In 1828, four times as many voters as ever before voted with Jackson defeating Adams by a landslide with more than two-thirds electoral votes to become the first President outside the Aristocracies of Virginia and Boston west of the Allegheny Mountains. As seventh President, he promised to turn over government to the common man. Jackson was sworn in at "the People's Inaugural." For the first time, the White House was opened to public, after all, it was built by and for the American people. Thousands of ordinary Americans swarmed in to celebrate their hero. Many spittoons were installed by Jackson in the once elegant East Room. Although Jackson would later become known as "King Andrew I" by his political enemies, he handily won reelection in 1832 against Henry Clay.

His legacy was tarnished however by the "forced" Native American Indian Removal Act of Five Civilized Tribes to present day Oklahoma now popularly referred to as the "**Trail of Tears**." Was he a genocidal racist or a man of the people? Either way, as President, Jackson used his powers to strengthen the national government and improve the lives of ordinary Americans. He tenaciously opposed those who thought that individual states could nullify laws they didn't like. He fought against the Bank of the United States which he believed favored the rich. His most enduring quote in this regard was, "*There are no necessary evils in government. Its evils exist only in its abuses*." He dismissed nearly 2000 government employees in an effort to eradicate a "corrupt bureaucracy." When challenged by congress Jackson responded that a president was not responsible to the Senate, but solely to the American people. He insisted, "*The people are the sovereign power, the officers are their agents*."

After he recognized the Republic of Texas in 1836 he left office as popular as ever. Jackson retired to Hermitage and died on June 8, 1945. He obviously had dropsy either due to heart failure, but

more likely to renal failure. "*Gasping for breath…I am swollen from my legs to my abdomen and in bandages to my hips. My whole system a jelly. You can run a finger half an inch into the liver and the impression will last for minutes?"* However, an article published in JAMA 1999:282:569-571 suggested he experienced mercury and lead poisoning through the therapeutic use of calomel (mercury chloride) and sugar of lead (lead acetate) from measurements of hair samples. It should be noted that two musket lead bullets remained lodged in his left shoulder and left lung which were considered contributors to the high lead levels identified by a recent analysis of his hair samples.

Martin Van Buren of Kinderhook, New York, unlike previous Presidents, was of Dutch rather than British ancestry. He was born on December 5, 1782 after the Declaration of Independence, therefore he was the first President born as an American subject. Van Buren started his long and influential career in politics as a New York state senator, then US senator and later governor of New York. He was an ardent supporter of Jackson in the 1828 presidential election and was named Secretary of State. In 1832, he was elected Vice President under Jackson. As Jackson's hand-picked successor, Van Buren defeated William Henry Harrison in 1836 to become the eighth President. He was the last Vice President elected to succeed the President under whom he served until George H W Bush was elected following Ronald Reagan in 1988. Van Buren was such a clever politician that he was referred to as "**The Little Magician**", "**The Red Fox of Kinderhook**" and "**The Flying Dutchman**." Shortly after he took office in 1837, his clever skills could not save America from a major financial panic causing banks and businesses to fail which resulted in severe economic depression. He established an independent treasury system to ensure solvency of the federal government but refused to help states and business with federal funds. "*The less government interferes with private pursuits the better for general prosperity*." Many blamed him for not doing more, and because he opposed the spread of slavery, he refused to annex Texas which further added to his unpopularity. He served just one term and lost to William Henry Harrison in 1840. Therefore, he was not an "OK" President. As an aside the term O.K. is said to have come from one of Van Buren's nicknames, "Old Kinderhook." However, he tried unsuccessfully for the presidency two more times. He died in Kinderhook on July 24, 1862 following pneumonia of asthmatic suffocation or congestive heart failure.

Although the Whig party deceptively portrayed William Henry Harrison as "the log-cabin and hard cider candidate" during his Presidential campaign, he was actually born in Berkeley, Virginia on February 9, 1773 as heir to one of the oldest and most distinguished families in America. His father, Benjamin Harrison, was a signer of the Declaration of Independence and his grandson, also named Benjamin Harrison, was elected 23rd President of the United States in 1888. William Henry (the only President to attend medical school) attended medical school but disliked it and decided to pursue a military career. He became governor of the newly formed Indiana Territory. He negotiated treaties with Native Americans opening up about three million acres of wilderness for American settlers. Shawnee leader Tecumseh combined all Indian tribes from Florida to Canada along the banks of the Tippecanoe River in Northwestern Indiana to resist further encroachments of the white people. Harrison led American forces against Tecumseh in the Battle of Tippecanoe in 1811. However, his most successful victory came at the Battle of Thames in 1813 (present-day Ontario) where he soundly defeated the combined British and Indian forces. Among the slain was his archrival Tecumseh. It was this war hero and rough "log cabin" frontiersman appearance that Harrison used with his running mate, John Tyler, to tour the country attracting huge crowds chanting "**Tippecanoe**

and Tyler Too." Because of this, Harrison was nicknamed "**Old Tippecanoe**." He was the first Presidential candidate to actively campaign for office. Running purely on his past record and his popularity, he defeated a beleaguered Van Buren and became the 9th President of the US. He was the first President from the Whig Party. After delivering an exceptionally long inaugural speech in a downpour, he died of pneumonia on April 4, 1841 one month after his inauguration, making his term the shortest of any President in history. He was the first president to die in office and his death set a new precedent for the orderly transfer of power to the vice president. Also, his funeral set the standard of funerals for presidents to come. The type of president William Henry Harrison would have made will never be known, but his quote provided a glimpse of what would have been, "*The only legitimate right to govern is an express grant of power from the governed."*

John Tyler was born in Charles City County, Virginia on March 29, 1790. He descended from wealthy Virginia planters of tobacco. Tyler served with distinction in both houses of the Virginia legislature, as a two-term Governor and in both houses of congress before becoming the nation's first unelected President. He was thus known as "**His Accidency**" because he became President almost by accident. Tyler was a staunch supporter of state's rights, defected from the Democratic Party and joined the Whigs in protest of President Jackson's expansive use of federal power. The Whigs chose Tyler as **Old Tippecanoe's** running mate to balance the ticket and win the South. They never expected him to become President one month into Harrison's term. Among the highlights of Tyler's Presidency were a trade mission to China, the annexation of Texas and the admission of Florida to statehood. After his Presidency, he was elected to the Confederate House of Representatives during the Civil War and considered a traitor by the US government when he died in Richmond, Virginia on January 18, 1862. His notable quote, "...*I can never consent to being dictated to*..."

The **"Dark Horse"** the nickname given to James K Polk because he was the first unexpected candidate nominated for President. Born near today's Pineville, North Carolina on November 7, 1795, he became a Tennessee lawyer and with the help of Jackson, became Speaker of the House in 1835 then Governor of Tennessee from 1839 - 1841. He was relatively unknown when he unexpectedly won the Democratic Party's Presidential nomination. But was this unexpected? Recall Andrew Jackson's hand-picked successor, Van Buren. In 1844, the 77 year-old Old Hickory summoned Polk to an emergency conference at Jackson's estate, the Hermitage. From Polk's diary, General Jackson regretted the fatal error which Van Buren committed, that is Van Buren came out publicly against immediate action on the annexation of Texas. Polk wrote, "Jackson thinks the candidate…should be an annexation man and reside in the Southwest; and he openly expresses that I would be the most available man." This appeared to be a controlled plan by Old Hickory who mentored Polk who was latter dubbed "**Young Hickory.**" Another fact, Jackson's controlled lingered on from his hugely popular hero reign from 1812 through his Presidency from 1829-1837 which extended beyond. Jackson was so admired he continued to receive write in votes for president after his retirement and death. But Old Hickory and Young Hickory can be traced back to none other Jefferson's grand vision of westward expansion.

In any event, Polk defeated the Whig nomination, Henry Clay, to become the 11th President and the youngest to date at age 49 in 1844. Polk claimed America had a "manifest destiny" to expand across the continent. As President, he oversaw the annexation of Oregon south of the 49th parallel by the

Oregon Treaty of 1846 with Britain. However, as a result of the Mexican-American War in 1846 and the Guadalupe-Hidalgo Treaty of 1848, the Texas border was established at the Rio Grande followed by purchase of lands encompassing California and Nevada, and parts of Arizona, New Mexico and Utah.

During Polk's administration, the first US postage stamps were issued and gold was discovered in California in 1848. Most importantly, he fulfilled all his campaign pledges including lowering the national tariff, establishing an independent treasury and promising to serve only one term. Polk was an extremely hard and dedicated worker who frequently pushed himself to exhaustion and rarely took a vacation. After he left office in 1849 to retire, he died of cholera just over three months later on June 15, 1849. It was believed he contracted cholera in New Orleans while on a goodwill tour of the South after leaving the White House.

In less than 75 years since the Declaration of Independence much of the shape of mainland America was near completion. While Jefferson did not support a strong Federal Government and preferred westward expansion, his powerful followers Old and Young Hickory wielded their executive powers to realize Jefferson's vision. A Jeffersonian America of the people, by the people and for the people.

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