VINCENT’S STUFFING SENSE:

In this issue, we measure our Thanksgiving with insightful contributions that reflect the success and collaboration of the ISHLT. Such reflections include a report from Joshua Mooney, Hannah Copeland and Daniel Kim on the "Associação Brasileira de Transplante de Órgãos (ABTO)/ISHLT Joint Symposium", after which Pablo Pego-Fernandes provides his perspective in "Joint ABTO/ISHLT Symposium on Thoracic Transplantation". Terry Noah, Arlene Davis, Debra Boyer and Elisabeth Dellon harvest anew the gluttony of challenges leaving us with simply humanity and benevolence, "Ethical Issues Surrounding Bridge Strategies to Pediatric Lung Transplant in Cystic Fibrosis: Case Series and Suggested Process Framework", while Diana Kim and Howard J. Eisen's present "Applications of CRISPR-Cas9 Technology in Heart Failure and Transplantation." Christina VanderPluym and Beth Hawkins offer a cornucopia of ideas, "IN THE SPOTLIGHT: The Use of Novel Ventricular Assist Device Smart Phone Application for Outpatient Management in Children." Pamela Combs transcends our care out of the hospital, "Perspective of the VAD Caregiver: The Transition Home." Finally, we sail away to Spain with Javier Carbone's, "A Big Bang in Barcelona: ESOT Congress 2017."

Happy Feasts!

Vincent Valentine, MD
Links Editor-in-Chief
The era of smartphone technology is upon us. Everywhere you turn, from street corners to restaurants, adults and children are glued to their phones for information, entertainment and socialization. Based on data from the Pew Research Center, 77% of Americans own a smartphone as of 2016, up from only 35% smartphone ownership in 2011, with 100% of adults aged 18-29 owning a cell phone [1].

Given the success and popularity of smartphone technology - especially in the adolescent and young adult population - we felt that the crossover of this technology to home monitoring for the complex medical care of outpatient ventricular assist device (VAD) could prove more efficient and effective than traditional modes of communication and monitoring. Management of outpatient VAD- especially in the pediatric population- is a new and evolving field of care [2]. The daily tasks of a VAD patient include; sterile driveline dressing changes, recording pump performance, vital signs, INR measurement and remembering to take medications. All this information must be seamlessly communicated between the VAD patients/families and their care providers on a day-to-day basis [3].

Over the course of the Boston Children’s Hospital Outpatient VAD Program, we have attempted multiple strategies to convey this information in a secure and efficient manner [4]. From these experiences, we identified the key aspects of home monitoring that would streamline outpatient care: (1) fast and easy patient data entry, (2) platform for electronically captured data to be trended and (3) an effective communication modality. Based on the prolific use of smartphones in our pediatric VAD population by both parents and patients, we developed a pediatric focused VAD app with support from the Fast Track Innovations Grant from Boston Children’s Hospital.

**Boston VADkids App**

The Boston VADkids® app has 3 main features related to: education/reference material (device specific- HeartWare HVAD®, HeartWare Inc.®, Framingham, MA), data entry (patient and device specific) and secure communication through texting (text, emoji, and photos).

**Education/Reference Material**

When a patient is discharged on a VAD, the patient and their caregivers participate in intensive education. The enormity of information makes it hard to retain. As such, we uploaded the information
contained in our patient’s home management guide directly to the app, including all the necessary instructions of how to care for the patient on VAD. This is now an easily accessible guide that can be tabbed through by topic, rather than turning pages in a manual.

Since the reference material is so important in case of an emergency, there is a section that is accessible without a log in and password. This will allow first responders or a layperson who might come across a VAD patient in distress, the ability to open the app with critical information about the VAD and how to deal with emergencies as well as our center’s contact information so they can call for more information. All VAD patients wear a medical alert bracelet that directs people to their phone for this information.

Data Entry
The specific fields of entry include: patient weight, temperature, blood pressure, home INR values (measure on point of care home INR machine CoaguCheck XS®, Roche Diagnostics®) and device settings such as operating speed, flow, power consumption and any alarms. Data entry takes less than 5 minutes and can be visualized on a provider dashboard that is reviewed daily by members of the VAD care team. Additional alarms for out-of-range values can be set that will send email alerts to providers to check values. Current initiatives are focused on marrying this data input into hospital electronic medical records.

Communication Modality
We wanted the app to be able to support secure texting between our team and the patient and families. Adolescents wanted a private option of communicating with us. All providers have the ability to view or join the text thread. Parents and adolescents have separate views, so that adolescents can privately ask questions that they might not feel comfortable asking in front of their parents.

Picture Capability
The ability to send photos through secure texting was pivotal for monitoring and assessing the driveline exit site. Taking photos of the driveline and texting it to the care team allows for closer surveillance for infection.

Conclusion:
The VADKids App is the first smartphone app specifically designed for the pediatric VAD recipient with the intended goal to improve our patients’ quality of life by streamline communication with the care team. If you would like more information on using the app at your center, please contact christina.vanderpluym@childrens.harvard.edu.

Disclosure statement: The authors have no conflicts of interest to disclose.

References:


FOCUSING ON BASIC SCIENCE & TRANSLATIONAL RESEARCH:

A Big Bang in Barcelona: ESOT Congress 2017

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The European Society for Organ Transplantation Congress held in Barcelona on September 24-27, helped refine our knowledge of basic science and clinical concepts to improve transplantation in a holistic approach.

One interesting example of this was the session entitled, “The Devil’s Advocate: a moderated controversy in basic science.” During this session, a presentation of a basic science article was followed by a critical discussion with an ‘opponent’ and a general discussion with the audience. The first conference was “New insights in the priming of recipient’s immune system: Donor dendritic cell-derived exosomes promote allograft-targeting immune response” by Adrian Morelli (‘Defender’, Pittsburgh, United States) and Gavin Pettigrew (‘Opponent’, Cambridge, United Kingdom). Following was the “Impact of microbiota on transplantation outcomes: The composition of the microbiota modulates allograft rejection” by Maria Luisa Alegre (Defender, Chicago, United States) and Heinz Zoller (‘Opponent’, Innsbruck, Austria).

Other examples of selected content in Basic Science were: “A CRISPR way to engineer the human genome” by Angelo Lombardo (Milan, Italy), “Genetic, epigenetic and cellular approaches to combat disease and aging” covered by Juan Izpisua (La Jolla, United States) and “hidden sensitization: the memory B cell repertoire” by Oriol Bestard (Barcelona, Spain).

Sun and Basic Science in Zell am See, Salzburg, Austria: Austrotransplant Congress 2017

I had the opportunity to attend this interesting meeting in a lovely place in Austria on October 18-20.

During this congress, Mahr Benedikt (Vienna) discussed natural killer cells targeting mature lymphocytes under inflammatory conditions by missing-self recognition. Resch Thomas (Innsbruck) reviewed Toll-Like Receptor 3 as a novel target for the prevention of ischemia-reperfusion injury in solid organ transplantation.

There was an interesting Basic and Translational Science Session, moderated by Thomas Wekerle (Vienna) and Rupert Oberhuber (Innsbruck). Eller Katrin reviewed the current status of distinct strategies for induction of tolerance in kidney transplantation including recent data and challenges observed during the ONE Study, which is evaluating cellular immunotherapy in solid organ transplantation. Mario Wiletel discussed the induction of tolerance by treatment with IL2/JES6-1 (anti-IL-2 monoclonal antibody) complexes. Nina Pilat-Michalek conversed the potential synergistic action of anti-IL6 with IL2/anti-IL2 complexes to promote transplantation tolerance with participation of regulatory T cells and antigen presenting cells.

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Applications of CRISPR-Cas9 Technology in Heart Failure and Transplantation

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As predicted, CRISPR-Cas9 has taken the field of heart failure and transplantation by storm, and we feel invigorated by recent efforts that will make tremendous impacts in patient care and research [1]. CRISPR-Cas9 is a bacterial-derived technology that takes advantage of a Cas9-induced double-strand DNA break that is then rejoined or replaced through non-homologous end joining, leading to efficient, site-specific DNA editing. As we previously discussed, CRISPR-Cas9 has tremendous implications for the field of heart failure and transplantation. Physicians and scientists must be aligned in their objectives to meet their mutual clinical needs. To this end, some major advances have recently been made.

In Nature, Ma et al. recently reported editing of the MYBPC3 mutation in human preimplantation embryos using CRISPR-Cas9 mediated targeting and repair [2]. This mutation is a dominant mutation that when expressed, causes hypertrophic cardiomyopathy, a leading cause of heart failure and the most common cause of sudden death in young, otherwise healthy adults. A single parent carrying such a dominant mutation has a 50% chance of passing this mutant gene to offspring, and inheritance of such a mutation is not often realized as the heart failure phenotype may not be evident until adulthood. CRISPR-Cas9 modification of human embryos preimplantation led to homozygous, mutation-free embryos without off-target mutations. By treating M-phase oocytes, they were able to prevent development of subsequent mosaic patterns, which could complicate preimplantation genetic diagnosis (Figure 1). This treatment has major implications for the field of heart failure for its ability to completely eradicate genetic causes of heart failure and can be a huge complement to preimplantation genetic diagnosis. As there are genetic causes of dilated cardiomyopathies, these approaches can be extended to patients with these diseases.

In Science, Niu et al. uses CRISPR-Cas9 to inactivate porcine endogenous retroviruses in pigs (PERVs) [3]. During xenotransplantation, the use of porcine organs is complicated by the need to achieve immunologic compatibility and the presence of retroviruses that can infect humans, potentially causing tumorigenesis and immunocompromise. Here, the authors were able to remove PERVs from primary pig fibroblasts. These reprogrammed fibroblasts are then able to produce embryos using somatic cell nuclear transfer, leading to PERV-inactivated, transgenic piglets, of which 15 are still alive and 4-months old as of the report. These pigs represent a source of tissue that may significantly improve xenotransplantation of all organs, including the heart. In particular, this technology bodes well for editing of other immunogenic genes as well as generating hearts that may be less susceptible to immunogenicity.
In the Journal of Immunology, Reyes et al. used CRISPR-Cas9 to generate pigs free of Class I MHC molecules, also known as swine leukocyte antigens (SLA), which play a major role in xenotransplant rejection. These novel pigs may reduce immunity to pig antigens during xenotransplantation, further facilitating the use of pigs as a source of organs such as the heart [4]. Additional studies have also demonstrated the ability to alter murine cardiac genes to both improve [5] and induce [6] cardiac failure.

It is clear that CRISPR-Cas9 will continue to advance its way into heart failure and transplant. In light of these major developments, it is more important than ever for physicians to be wary of the future of gene editing enabled through CRISPR-Cas9, and to continue to investigate its potential for use in current practices, not only in heart failure and transplantation but in all of medicine.

Disclosure statement: The authors have no conflicts of interest to disclose.

References:
FOCUSBING ON PEDIATRICS:

Ethical Issues Surrounding Bridge Strategies to Pediatric Lung Transplant in Cystic Fibrosis: Case Series and Suggested Process Framework

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Although the incidence for pediatric lung transplantation is decreasing worldwide, the need is still present for some pediatric CF patients with end stage lung disease. While these patients await their ‘donor offer’ and are hopeful for the promise of a longer and an improved quality of life, many deteriorate further. Such decline necessitates open discussions regarding the application of advanced life support such as ECMO or consideration for placement of external oxygenators that may allow a patient to be bridged to transplant. Despite initial experience resulting in poor outcomes with ECMO bridging to transplant, recent data suggest that this strategy is appropriate in selected cases [2]. Nonetheless, the technical complexities, involvement of multiple caregivers and disciplines, and potential for fatal complications from ECMO and other life-saving approaches remain extremely high [3]. There is scant information published and there are no established guidelines for the medical team and caregivers to consider in these dire circumstances.

The major ethical challenges associated with bridge strategies to pediatric lung transplantation include: (1) timing and adequacy of informed consent, (2) ethical concerns about unproven and potentially painful, life-prolonging therapies in children and (3) management of end of life care and the high likelihood for the need to withdraw the bridging therapies should transplant no longer be an option. These decisional challenges require consideration for variations in disease comorbidities, family members’ and patients’ level of education, treatment goals, personal values and philosophical outlooks; many of which can change over time. As well, the ethical framework must also account for variation among team members in expertise, experience, values and appraisals of ethical permissibility.

As stewards of responsible decision-making, it is our duty to address end-of-life decisions with unity, concern and compassion. Similar processes are currently evolving at many transplant centers that care primarily for adult recipients. We suggest that pediatric lung transplant centers convene as a community to formulate such a framework applicable to children, since the frequency of transplant is low and the communication issues are complex.
Substantive discussions must be had so that as a group, guidelines may be formulated that delineate processes to inform the care team, patient, and family decisions about options for bridging to transplant and related care concerns. A guideline, as such, would outline approaches to obtaining informed consent, ethical decision making and team communication for pediatric lung transplant candidates. The guidelines would optimally include: (1) a general discussion of bridging methods that discuss ECMO and other transthoracic oxygenator devices with the attending Pulmonologist and Transplant Coordinator at time of consideration for recipient candidacy, and (2) such that at the time of any patient’s acute deterioration, a care conference with Pediatric Pulmonology, Cardiothoracic Surgery, PICU/ECMO teams, PICU nursing and Clinical Ethicist to discuss candidacy for bridging modalities can be held if the technology is thought to be imminently required, including rehabilitation goals for re-activation of listing if the patient needs to be de-activated temporarily and (3) frequently scheduled “check-ins” with the family after bridge support is initiated, allowing team members to realistically reassess goals, anticipate and/or address complications and approach these difficult situations with humanity, sympathy and benevolence.

Disclosure statement: The authors have no conflicts of interest to disclose.

References:
NEWS & ANNOUNCEMENTS:

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**ISHLTConnect Code of Conduct**

We wanted to take the time to remind everyone that there are rules and restrictions for activity on ISHLTConnect. There have been several posts recently that have violated the Code of Conduct for our online community, many of which have been promoting the meetings and events of other societies. If you review the [Code of Conduct](#) you will see that the first item under Rules states that members are not permitted to “post messages about other organizations’ and institutions’ meetings, publications, programs or services on any discussion list, resource library entry, or other area where others might see it”.

We STRONGLY encourage all members to review the [Code of Conduct](#) for further guidelines and restrictions for posts to ISHLTConnect.
SPECIAL INTEREST:

Perspective of the VAD Caregiver: The Transition Home

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"The two most powerful warriors are patience and time." – Leo Tolstoy (1828-1910).

The most dramatic impact of being a caregiver is reflected in one of the waves of the Caregiver Health Effects Study (CHES), which discovered that caregivers are at greater risk of death than those who do not administer care to a significant other (Bookwala, Zdaniuk, Burton, Lind, Jackson, & Schulz, 2004). We often fail in evaluating the perspective of the caregiver of a patient with a VAD regarding preparation to care at home. Exactly what the VAD caregivers perceive of the transitioning experience from hospital-to-home is an area that is neglected of research studies. Therefore, as a nurse researcher, I desired to understand the meaning of the lived experience for caregivers of VAD patients during their transition from hospital to home.

Using Colaizzi’s (1978) method, I had the privilege of interviewing 7 caregivers regarding their experience transitioning a newly implanted VAD patient home. The predominant theme of “power” dominated their experience, by blanketing the influence of: 1) electricity, 2) life, 3) control, 4) change, 5) a spiritual entity and 6) the unknown. Transitioning home from the hospital was associated with a variety of intense emotions. Although the interviews only provided snapshots of the issues and challenges faced by caregivers, these events and feelings were presented as crucial in their telling. VAD teams should consider assisting the caregiver in identifying stress management techniques to prevent a sense of feeling overwhelmed. VAD support groups that enable communication and provide information is recommended for caregivers as well as follow up phone calls with the VAD coordinator. These programs should focus on empowering caregivers and incorporating them as a part of the team as we do the patient.

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References:

Associação Brasileira de Transplante de Órgãos (ABTO)/ISHLT Joint Symposium

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Foz do Iguaçu is one of the New 7 Wonders of Nature. These impressive falls sit in this beautiful international intersection straddling Brazil and Argentina, with Paraguay a stone throw away. A bridge goes down to the valley of the waterfall, called the Devil’s throat. You can walk on the bridge, but bring your poncho because you are guaranteed to get drenched. In addition to beautiful natural wonders, there are unique delights; my favorite being savory breakfast crepes made of tapioca flour and bananas sweetened with cinnamon for breakfast.

What a great place to have a meeting and that’s just what ABTO (Associação Brasileira de Transplante de Órgãos) did! And better yet – they invited ISHLT to hold a joint symposium at this magnificent place on Oct 21, 2017.

Daniel Kim, Joshua Mooney and I, Hannah Copeland, participated in the joint symposium. The symposium was entitled Management Dilemmas and Practical Insights in Thoracic Transplantation and Mechanical Support and, as expected from the long title, discussed heart, lung transplant and mechanical circulatory support topics. Paolo Pego Fernandes discussed donor recipient matching. Daniel Kim moderated the session with Paolo and also spoke on temporary mechanical circulatory support and the treatment of antibody mediated rejection. Joshua Mooney conversed lung transplant rejection and combined heart and lung transplantation. I, Hannah Copeland, discussed thoracic allocation policies and cardiac recovery after mechanical circulatory support implantation. Noedir Antonio Groppo Stolf discussed cardiac allograft vasculopathy.

The joint symposium brought together surgeons, cardiologists, pulmonologists and others from all over Brazil to discuss timely topics and improve the care of heart and lung transplant patients. The joint symposium truly fueled insightful questions to the panelists. Fortunately, as we were the last session in the room, discussions continued long after the last presentation, even as we eventually walked out into the hallway.
Through this intercontinental collaboration, I hope and believe that our Brazilian hosts benefited from us. More importantly, we- Daniel Kim, Joshua Mooney and I- learned about the Brazilian heart and lung transplant system, organ allocation and mechanical circulatory support options in Brazil. We also glimpsed into the challenges and opportunities our southern colleagues work through daily. But above all, we were impressed by their enthusiasm and commitment to bettering the care of their patients. These joint symposia are truly an example of what the founders of ISHLT sought for the society; a society where all people who care for heart and lung transplant patients can come together to freely discuss various topics and learn from one another.

Disclosure statement: The authors have no conflicts of interest to disclose.
Joint ABTO/ISHLT Symposium on Thoracic Transplantation

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The XV ABTO’s meeting took place in Iguassu Falls October 18-21. There were 1350 people attending the meeting and part of these people are professionals that work with heart or lung transplantation. For these people was very special the opportunity to participate of the Joint ABTO/ISHLT Symposium on Thoracic Transplantation. During the 20 October afternoon cardiologists, heart surgeons, lung surgeons, pulmonologists, infectologists and nurses from the Chief Hospitals that performed heart or lung transplantation in Brazil could interact with ISHLT members as Daniel Kim, Hannah Copeland, Joshua Mooney and Alejandro Bertolotti. It was a very fruitful experience, with a lot of ideas that may improve the transplant activity in Brazil and South America.

The program of the Joint ABTO/ISHLT Symposium: Management Dilemmas and Practical Insights in Thoracic Transplantation and Mechanical Support, chaired by Paulo Manuel Pego-Fernandes and Daniel Kim, featured the following talks:

- **The Art of Donor Recipient Matching**
  Paulo Manuel Pêgo-Fernandes, MD, PhD

- **An Approach to the Marginal Heart Donor**
  Juan Alberto Cosquillo Mejia, MD

- **Thoracic Organ Allocation Policies: What Have We Learned?**

- **Beyond Heart Transplantation: Evolving Indications for Mechanical Circulatory Support**
  Hannah Copeland, MD

- **Acute Cardiopulmonary Salvage: The Role of Temporary Mechanical Circulatory Support**

- **Treatment of Antibody Mediated Rejection in Heart Transplantation**
  Daniel Kim, MD

- **How to Manage Pulmonary Hypertension and RV Failure Before and After Heart Transplantation**
  Silvia Ayub, MD

- **What’s New in Lung Transplant Rejection**

- **Combined Heart and Lung Transplantation: Redefining the Indication**
  Joshua Mooney, MD
• **What’s New with Cardiac Allograft Vasculopathy?**
  Noedir Antonio Groppo Stolf, MD, PhD

We hope that this was only the first ABTO/ISHLT Joint Symposium and we will work to do the next at the 2019 ISHLT meeting in Orlando, Florida.

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EDITOR’S CORNER:

The Discovery of Circulation

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As you recall, modern science emerged in the 17th century with the scientific revolution and was largely based on skepticism. This same skepticism motivated Andreas Vesalius, the father of modern anatomy, in the 16th century. Among other things, it was William Harvey who reintroduced the notion of experimentation by basing his theories on human dissections and observations he made himself. Galen had originally introduced experimentation through his research; however, he dissected and observed animals rather than the human body. Also recollected from Galen were his philosophical contributions to medicine involving humoral imbalance, which lasted until Harvey’s discovery of circulation.

Like Andreas Vesalius, William Harvey studied medicine at the University of Padua, where he absorbed the spirit of free inquiry and intellectual independence that characterized Italian universities during the Renaissance. Having a restless and skeptical nature, Harvey was dissatisfied with the old Galenic concept that organs received nutrition by a process of drenching, in which blood ebbs and flows to the organs through large veins originating in the liver, the site at which blood was thought to be manufactured to fill the needs of each outpouring. To test his suspicion, Harvey created a series of ingenious experiments and measurements that demonstrated the heart’s function as a pump, which as he described it in 1628, ensures that “the blood in the animal body moves around in a circle continuously.” Harvey’s discovery of circulation was the product of the curiosity and expansive thought characterizing the Scientific Revolution of the illuminating 17th century, a time when the likes of Galileo, Newton, van Leeuwenhoek, Halley, Descartes, Bacon, Hooke and Bernoulli were tested to establish the basis of modern observational and experimental research.

Before proceeding on with Harvey’s discovery, let’s summarize the current theories of blood flow before he started his work. According to Galen’s theory, after swallowed food entered the stomach it was processed and passed through the “portal vein” into the liver to produce blood. The blood would then exit the liver through large veins into the vena cava. The vena cava came from the heart, which propelled the blood all over the body such that all tissues were drenched with it. It was believed that pneuma, the ethereal stuff, was a vital principle in the air that was constantly inhaled into the lungs then transported to the left side of the heart, the left ventricle. The pneuma was mixed with the blood and delivered to the rest of the body through the arteries, giving the blood a bright red appearance, whereas nutritional blood was believed to be dark. Although it was never understood how the blood returned and passed the flowing blood to the tissues, this concept was accepted and persisted for nearly 1500 years.
This brings us to Harvey, the very talented physician with an outstanding practice that kept growing. When eventually, he became the doctor for royalty and nobility. James I, Charles I and the Lord Chancellor Sir Francis Bacon were among his patients. Around the time of Shakespeare’s death, Harvey was appointed to the Lumleian lectureship for the Royal College of Physicians. For these lectures, he was asked to present new knowledge. It was during this time that he was intent on studying how the heart beats. Years of his work were presented in these Lumleian lectures which comprised the first seven chapters of his book Exercitatio Anatomica de Motu Cordis et Sanguis in Animalibus, Anatomical Studies on the Motion of the Heart and of the Blood in Animals, and as we know it today...de Motu Cordis.

His first observation was the clenching thrusting motion of the heart, systole. He was able to show that blood actually returns to the heart via the “vena cavae” and enters the right atrium. While it returns from the lungs, blood enters the left atrium via the pulmonary veins. From the atria, blood cascades down into the ventricles, then at the very last instant, in the wink of an eye, both atria contract followed immediately by ventricular contraction ejecting blood into the lungs and the rest of the body. As he had written so beautifully, “the atria arouse the somnolent heart.”

But he remained confused about the large quantity of blood drenching the tissues with so little returning. He measured that the human cadaver heart held only 60 cc of water and that it beats 72 times a minute. The result over the course of an hour the heart would pump over 500 lbs of blood. “The only way he can explain all of this blood pumping out of the heart is if it's the same blood, and it keeps coming back. We just can’t make that much.” As an aside, it was Harvey’s teacher, the great professor of anatomy at the University of Padua who had discovered valves in the veins. Fabricius didn’t know what the valves did because blood was traveling to the periphery; therefore, he concluded their function was to slow the blood down. It was Harvey who determined that blood in the arms travels from the periphery to the center, and that the purpose of the valves was to keep blood from regurgitating back. Consequently, he wrote in Chapter Eight of his book:

I ponder often and deeply these matters. For a long time, I turned over in my mind such questions as how much blood is transmitted, how short a time its passage takes, not deeming it possible for food mass to furnish such an abundance of food, unless it somehow got back to the veins from the arteries, and returned to the ventricles. I began to think there had to be some sort of motion as in a circle.

It was in Chapter 14 where he wrote: “It must therefore be concluded that the blood in the animal body moves about in a circle, continuously, and that the action or function of the heart is to accomplish this by pumping. This is the only reason for the motion and the beat of the heart.” By this point, Harvey understood the blood was being carried out through the arteries and back to the heart through the veins. The heart provided the motion by its pumping action, but how did the blood move from the most peripheral arteries into the most peripheral veins? He postulated a passageway between the arteries and the veins. Then 32 years later, Marcello Malphighi showed capillaries carrying blood from the most peripheral end arteries into the end veins.
Harvey was the first physician to use the scientific method and apply the principles of inductive reasoning, yet interestingly uninfluenced by his patient, Sir Francis Bacon. It was Vesalius and Harvey who moved us from the “age of the ear,” where people listen to authority and learned only from authority to the “age of the eye,” where one had to see for oneself and prove to others what you said was true.

Harvey leaves us with his most enduring quote on inductive reasoning, “Nature herself must be our adviser. The path she chalks must be our walk, for as long as we confer with our own eyes, and make our assent from lesser things to higher, we shall be at length received into her closet secrets.”

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