VINCENT’S VALENTINE SENSE:

Spotlight, look, see, medicine, art, World. NHSAH, Movement, ECMO, platoon, brigade, warning, mix, sweep, change, donor, allocation, prepared, preparedness, no show, appointments. Special, interest, ISHLT, travel, scholarship, complex, multidisciplinary, team, communication, lost art, depersonalized medicine, robotic, imprecision. France, physics, motive force, heat, Fourier transformation, Carnot cycle, Carrell, anastomosis, pumps, transplantation, extracorporeal life support, a full circle, propulsion, VAD, ECMO, bridge. In bridge, no trump is an option and nothing trumps success.

Happy Valentine’s Day!

Vincent Valentine, MD
Links Editor-in-Chief

WORD OF THE MONTH:

Perfidious (adjective) - treacherous, disloyal and deceitful
IN THE SPOTLIGHT:

Looking and Seeing: Lessons about Medicine from the World of Art

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I recently read that visitors to the Louvre spend an average of fifteen seconds examining the Mona Lisa. *Fifteen seconds*. I was initially shocked and wondered how this could be enough time to take in the coloration, contouring, shadowing, and meaning of the painting. I have admittedly not yet visited the Louvre, but I assume that the large crowds play a significant role in museum throughput. Nonetheless, the “Mona Lisa fifteen seconds” made me think about the principles of *looking* and *seeing*; concepts that were taught in my college art history classes, but which have also resonated with me as a physician.

The Merriam-Webster dictionary states that to look is to “ascertain by the use of one’s eyes,” while to see is to “perceive by the eye” [1]. While the difference between the two may seem semantic at first, in the world of art, looking and seeing are intrinsically different actions. In *Studies in Iconology: Humanistic Themes in the Art of the Renaissance*, the famed art historian, Erwin Panofsky, delineated a three-pronged approach to understanding and interpreting art; this has more recently been described as “Look, See, Think” [2,3]. When we *look* at a piece of art, our brain recognizes a general motif such as a painting, photograph, or sculpture. This most basic understanding permits us to describe shape, texture, and general content; however, when we *see* a piece of artwork, we begin to apply meaning. For example, we may recognize a group of thirteen people sitting at a dinner table as an image of the Last Supper or a depiction of a bearded man holding a lightning bolt as Zeus. When we *think* about a piece of art, we ponder its deeper meaning and ask questions such as, “who was the artist and why did she depict the subject this way?”

Seeing is equally as pertinent to medicine as it is to art. On the first day of rounds, one of my favorite medical school professors (who also happens to be a professional painter) would routinely ask his team of medical students and house staff what they saw after leaving a patient’s room. Most would accurately describe physical exam findings; however, the group would rarely be able to provide a description of other pertinent findings, such as a bible tucked under the patient’s arm or the content of family photos on the bedside table. In essence, the team *looked* but didn’t see. Appreciation of such details is equally as important as the physical exam itself and allows us to understand the larger context of a patient’s illness and better treat that patient; it is the factor that allows us to move from “the disease a person has” to “the person who has the disease.”
Henry David Thoreau once wrote, “It’s not what you look at that matters, it’s what you see.” In medicine, seeing is an art that makes us better providers.

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

References:
1. https://www.merriam-webster.com
Early Mobilization and ECMO: It Takes an Army

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"Alone we can do so little; together we can do so much." – Helen Keller

If you asked me 8 years ago when I was applying to graduate school to become a physical therapist what patient population I would want to work with, I most likely would have responded with, “The Philadelphia Eagles.” Yet, here I am 8 years later working with the most critically ill population and collaborating with a great team of medical professionals to make the impossible, possible.

At any given day in the Temple University Hospital Respiratory ICU, you can find an army of medical professionals parading medical equipment down the hallway. This army includes: physical therapy, occupational therapy, mobility aide, respiratory therapy, a perfusionist, and of course, a nurse. We have come together as a group to attempt to master early mobilization while on Extracorporeal Membrane Oxygenation (ECMO). While I know many hospitals with progressive transplant programs participate in this type of mobilization, it is something that we often take for granted and/or overlook benefits of for those patients on ECMO as a bridge to lung transplantation. When you really step back and take a moment to think that this machine is oxygenating someone’s body, yet they are able to participate in a therapy program, while bringing a team of medical professionals together for the same cause, it is truly amazing.

Active rehabilitation during ECMO as a bridge to lung transplantation has demonstrated patients to have a shorter post-transplant hospital stay, a shorter post-transplant mechanical ventilation length, shorter ICU stays, and less incidences of post-transplant myopathy [1]. In addition, you may be surprised to learn that mobilizing patients while on ECMO significantly cuts costs hospital-wide. Patients who participated in ambulatory ECMO have shown to have 22% reduction in total hospital cost, 73% reduction in post-transplant ICU cost, and 11% reduction in total cost compared with non-ambulatory ECMO patients [2].

Of course, we must stop to consider the complications and logistics. We must take into account the time it takes, the critically ill level of the patients, and most importantly for physical therapists, the cannula placement. In most studies looking at ambulation while on ECMO, the upper body was the common site of cannulation, which allowed for increased mobility, less weakness, fewer mechanical ventilation days, less sedation, earlier rehabilitation, and shorter ICU stays compared to those with femoral cannulation [3]. Currently at Temple University, we have not initiated ambulating patients with femoral cannulation while on ECMO. Some of the reasons why include: difficulty for patient to go from supine to standing while not impeding the line and concern for safety of line placement with hip flexion and movement. However, a new study has shown it is feasible and safe to deliver early
rehabilitation including standing and ambulation to patients on extracorporeal membranous oxygenation support in those with femoral cannulation sites with veno-arterial extracorporeal membranous oxygenation and veno-venous extracorporeal membranous oxygenation [3]. In this study, the cannulas are secured to the thigh using sutures and adhesive anchors by surgeons, and hip flexion is performed to 90 degrees to test the flow of the cannula prior to mobility by physical therapists. In addition, specialized hospital beds are available that go from supine to standing, allowing patients to avoid hip flexion/sitting to prevent compression or kinking of the femoral cannula. Safety of the patient undoubtedly comes first and the same study showed that 66 patients, out of a sample of 167, with at least one femoral line experienced no major adverse events while mobilizing, including standing and ambulation [3].

According to Wells et al., to achieve a successful early rehabilitation program, a well-trained multidisciplinary team is required to complement the work of the advanced ICU ECMO-trained physical therapist with competent clinical judgement, advanced practical skills, and ability to collaborate [3]. We hope to begin implementing these new findings at Temple University Hospital, as well as continuing our progressive mobilization with patients on ECMO. After all, physical therapists are constantly finding ways to safely and feasibly mobilize our critically ill patients, especially those on ECMO and those waiting for lung transplants. With collaboration of the multidisciplinary teams, it is indeed possible.

In closing, when I stop to think about my daily routine and about the accomplishments our team is able to achieve, this is just one example of how great things can be accomplished when there is collaboration with all members of the medical team and physical therapists. It ultimately creates improved outcomes for patients who are both pre- and post-lung transplantation. I know through this ongoing collaboration we will continue to make progress and improvements in what we are able to provide for our patients; however, it takes an army.

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

References:
Managing immunosuppressant medications can be difficult, even for those with years of experience in the transplant field. Each patient can respond differently to medications for an assortment of reasons, and special considerations need to be made for a variety of factors, such as renal function. Immunosuppressant medications can be affected by other traditional drugs as well as nutrients and herbal supplements. The effect can be an increase or decrease in blood concentration of the medication depending on the drug, nutrient, and/or herbal supplement. For this reason, it is imperative that both pre- and post-transplant patients inform their healthcare providers of all medications and herbal supplements they are using. Below is a chart summarizing common herbal supplements and their effect on various medications used in a transplant recipient.

<table>
<thead>
<tr>
<th>Herbal Supplement or Extract</th>
<th>Drug</th>
<th>Mechanism of Interaction/Therapeutic Consequence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Berberine</td>
<td>Cyclosporine</td>
<td>Inhibits CYP3A4 and intestinal P-gp / Increased bioavailability</td>
</tr>
<tr>
<td>Caffeine/high doses of chocolate</td>
<td>Methylphenidate Sedative-hypnotics Bronchodilators</td>
<td>Increase effect Decrease effect Increase chance of side effects like excitability, nervousness, and rapid heart beat</td>
</tr>
<tr>
<td>Cannabidiol</td>
<td>Cyclosporine</td>
<td>Inhibits hepatic CYP3A4 / Increases bioavailability</td>
</tr>
<tr>
<td>Chamomile</td>
<td>Cyclosporine</td>
<td>Inhibits CYP3A4 / Increases bioavailability</td>
</tr>
<tr>
<td>Cranberry juice</td>
<td>Cyclosporine</td>
<td>Inhibits CYP3A4 / Increases bioavailability (speculative)</td>
</tr>
<tr>
<td>Echinacea</td>
<td>Cyclosporine</td>
<td>Possible inhibitor of CYP / Increases bioavailability (speculative)</td>
</tr>
<tr>
<td>Fish Oil</td>
<td>Cyclosporine</td>
<td>Inhibits CYP2C19, 2D6 and 34A / Increased bioavailability</td>
</tr>
<tr>
<td>Garlic</td>
<td>Anticoagulants &amp; aspirin</td>
<td>Unknown / Increased bleeding</td>
</tr>
<tr>
<td>Herb</td>
<td>Drug Interaction</td>
<td>Interactions</td>
</tr>
<tr>
<td>-------------------------------------------</td>
<td>----------------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Ginger</td>
<td>Cyclosporine (oral only)</td>
<td>Reduces gastrointestinal motility / Decreases bioavailability</td>
</tr>
<tr>
<td>Gingko biloba</td>
<td>Anticoagulants &amp; aspirin</td>
<td>Inhibition of platelet activating factor / Increased bleeding</td>
</tr>
<tr>
<td>Grapefruit juice, and other citrus fruits</td>
<td>Cyclosporine</td>
<td>Increased bioavailability (oral only) / Enhanced immunosuppression or toxicity</td>
</tr>
<tr>
<td></td>
<td>Felodipine</td>
<td>Increased bioavailability / Possible hypotension</td>
</tr>
<tr>
<td></td>
<td>Itraconazole</td>
<td>Decreased bioavailability / Fungal infection</td>
</tr>
<tr>
<td></td>
<td>Warfarin</td>
<td>Decreased warfarin blood concentrations / Risk of thrombosis</td>
</tr>
<tr>
<td></td>
<td>MAO inhibitors</td>
<td>Can cause headache, trouble sleeping, nervousness and hyperactivity</td>
</tr>
<tr>
<td></td>
<td>Benzodiazepines</td>
<td>Additive sedation with benzodiazepines / Oversedation, possible coma</td>
</tr>
<tr>
<td>Liquorice</td>
<td>Cyclosporine (oral only)</td>
<td>Induced P-gp and CYP3A4 / Decreased bioavailability</td>
</tr>
<tr>
<td></td>
<td>Diuretics and/or antiarrythmic agents</td>
<td>Sodium retention and potassium depletion / Hypertension, hypokalemia, and increased risk of arrhythmia</td>
</tr>
<tr>
<td>Mu huang</td>
<td>MAO Inhibitors</td>
<td>Sympathomimetic interaction / Hypertensive crisis</td>
</tr>
<tr>
<td></td>
<td>Antihypertension</td>
<td>Ephedrine alkaloids increase blood pressure / Hypertension</td>
</tr>
<tr>
<td></td>
<td>Theophylline and/or caffeine</td>
<td>Enhanced CNS stimulant effect / Theophylline toxicity</td>
</tr>
<tr>
<td>Pomegranate juice</td>
<td>Cyclosporine</td>
<td>Inhibits intestinal CYP3A / Increased bioavailability</td>
</tr>
<tr>
<td>Quercetin</td>
<td>Cyclosporine (oral only)</td>
<td>Induces CYP3A4 and intestinal P-gp / Decreased bioavailability</td>
</tr>
<tr>
<td>Reseveratroal</td>
<td>Cyclosporine</td>
<td>Inhibits CYP3A4 / Increases bioavailability</td>
</tr>
<tr>
<td>Scutellariae radix</td>
<td>Cyclosporine (oral only)</td>
<td>Induces CYP3A4 and intestinal P-gp / Decreased bioavailability</td>
</tr>
<tr>
<td>Serenoa repens</td>
<td>Cyclosporine</td>
<td>Potent inhibitor of CYP3A4, 2D6, and 2C9 / Increases bioavailability (speculative)</td>
</tr>
</tbody>
</table>
Spices/Condiments (pepper, fennel, dill, Asian ginseng, evening primrose, cat’s claw, feverfew, frankincense)  | Cyclosporine | Inhibits CYP3A4 / Increases bioavailability (speculative)  
---|---|---  
St John’s wort | Cyclosporine  
Indinavir, other protease inhibitors  
Theophylline  
Antidepressants (SSRIs) | Digoxin  
Reduced bioavailability and/or enhanced clearance  
Reduced immunosuppression, possible organ rejection  
Reduced bioavailability / CHF treatment failure  
Reduced bioavailability / HIV treatment failure  
Enhanced clearance / Sub-therapeutic theophylline concentrations  
Inhibition of serotonin reuptake / Serotoninism  
Valerian | Barbiturates  
Prolongs barbiturate sedation / Enhanced sedation  
Wine (red) | Cyclosporine  
Inhibits CYP3A4 / Increases bioavailability (speculative)  
Herbal supplement intake can also have potentially life-threatening complications including increased risk of bleeding, sedating properties, and direct organ (renal, hepatic, and cardiac) toxicities.  
**Herbal Supplements Associated With Hepatotoxicity**  
- Baikal skullcap  
- Chaparral  
- Pyrrolizidine  
- Germander  
- Greater celandine  
- Saw palmetto  
- Noni juice  
- Margosa oil  
- Aloe vera  
- Black cohosh  
- Lipokinetix  
- *Astractylis gummifera*  
- Impila  
- Mistletoe  
- Valerian  
- Senna  
- Pennyroyal  
- Kava  
**Herbal Supplements that May Increase the Risk of Bleeding**  
- High-dose fish oil  
- Garlic  
- Ginkgo biloba  
- Ginseng  
- Feverfew  
- Vitamin E  
- Ginger
Due to the fact that herbal supplements are found over-the-counter, many believe they are harmless and have no repercussions when used. However, as the previous tables show, not all supplements are benign, so it is best that healthcare teams are aware of their patients’ comprehensive medication list.

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

References:

Sweeping Changes to the New Donor Heart Allocation...How Can I Prepare?

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In 2017 there were 3,244 heart transplants performed in the United States according to the Organ Procurement and Transplantation Network (OPTN). Currently there are 3,999 people awaiting heart transplant as of January 29, 2018 per OPTN website. Unfortunately, there are more people waiting for donor hearts than there are organs available. With longer waiting times and increased mortality on the heart transplant waiting list, the Thoracic Organ Transplantation Committee was charged to propose modifications to its current allocation policy. Currently the donor heart allocation is operating on a 3-tier system. Recently it has been announced that heart allocation will go to a 6-tier system.

While there is no definitive set date for the implemented changes, we are anxiously awaiting an announcement with the exact details. It may be of benefit to prepare for what considerations and actions need to be taken for programs affected by these policy modifications.

In order to ensure a seamless transition each center will have to identify what additional measures must be taken to accommodate the new donor heart allocation system.

Program considerations:

- What does this mean for patients?
- How will patients be informed of the change? Ie: via letters, emails, education sessions, etc.
- Patients to sign an acknowledgement that they received the information regarding the change?
- Will UNOS provide standardized letter to inform patients?
- Educate MDs/coordinators of the new change
- Educate interdisciplinary team members
- Educate hospital administration about the changes and how this may affect ICU beds, staffing and other system-wide considerations (if any)
- Educate the quality team about changes in compliance monitoring and frequent audits
- Include allocation change in current education materials to new patients undergoing evaluation

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References:
But They Don’t Always Come to Appointments!

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“But they don’t come to all of their appointments,” is an occasionally heard statement in selection meetings when discussing patient candidacy for VAD implantation. Psychosocial factors, like adherence to medical appointments, form evidence of whether the team typically feels a patient is an “ideal candidate” for VAD therapy. This week, I wondered how much weight should be placed on a patient’s attendance record.

Gravlee et al. (2016) stresses the importance of candidate selection and warns healthcare teams to exercise caution in offering VAD therapy to patients who have a history of appointment non-adherence. Consistently attending clinic appointments is viewed as a strong predictor of how adherent a patient will be to other key aspects of VAD therapy—anti-coagulation, driveline management and follow up medical visits to name a few. In a review of psychosocial factors and its subsequent implications for VAD patient candidacy, it is often noted that the ability to select candidates from these factors can be problematic based on a lack of standardized assessment tools (Grogan et al. 2015). If there is a lack of standardized assessment, is it appropriate to use appointment attendance as a means of compliance? Being one of the few tangible psychosocial factors that can be measured, tracked and quantified, is it a justified and ethical means to determine candidacy in all potential clients?

CASE
A patient was admitted to the Coronary Intensive Care Unit (CICU) for an exacerbation of Heart failure (HF). He was diagnosed with an acute kidney injury and an acute liver injury during his admission to the hospital. The patient had severe bilateral pitting edema to the knees and bilateral pleural effusions on a chest x-ray. The CICU started to optimize his HF medications along with diuretics, but found that they could not support his end organ function without the aid of inotropes. After failing to wean inotropes, a consult was placed both to the transplant team and the VAD team. The patient’s past medical history included Type II Diabetes Mellitus and HIV. Etiology of the HIV was thought to be from a blood transfusion he had during the 1980s. The patient had a strong support system in his wife and children whom he lived with outside the city. His finances were stable. He denied the use of all drugs, tobacco and alcohol. As our team social worker started her assessment of the patient, it was noted from colleagues in the transplant team that the patient had "no showed" numerous medical appointments. During discussion of the patient’s candidacy in our weekly meeting, many colleagues felt that the patient was not a good candidate for transplant due to the severity of
his illness at the time. His VAD candidacy was taking heavy scrutiny because of the multiple missed appointments with transplant. His absenteeism was probing at a metric of compliance for adherence to VAD therapy. But, we believed there to be a better measure of compliance that could be quantified—CD4 counts. In reviewing the patient’s blood work, it was noted that his CD4 counts had been stable for years. Upon talking to the physician following his CD4 counts and managing his antiretroviral therapy, the patient had in our minds demonstrated compliance. Our physician advocated that since the patient had a stable CD4 count and has complied with his current HIV regime, this was a stronger predictor of future compliance with a VAD. His multiple missed appointments stemmed from the family going through financial hardship at the time and making the drive into the urban center multiple times a week was not feasible. The patient, in his mind, chose to attend appointments that were offering therapy to him now instead of a mere glimpse of his future self.

Petty and Bauman (2015) argue that “[psychosocial] evaluation isn’t simply a matter of evaluating compliance history…but rather to ensure that the appropriate resources are available to care for the patient as a whole” (p. 2182-2183). In the context of the case study provided above, if as teams we only quantify compliance as attendance to medical appointments, it could be argued that we are not being judicial in our final decision to offer VAD as a therapy option. Additionally, the authors would contend that circumstances surrounding non-adherence to clinic visits must be explored and the patient needs to be provided with adequate support from the interdisciplinary team to correct/demonstrate compliance. Furthermore, due to the lack of VAD specific psychosocial assessment tools, it is difficult to quantify how much weight should be placed on attendance versus other factors determining outcomes such as income and social support. As VADs become more widely used within the heart failure community, research and predictors such as clinic adherence need to be evaluated to observe if they are indeed an objective measurement of future compliance with VAD therapy.

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

References:

Preparedness

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Although natural disasters have occurred since the beginning of time, they still catch us off guard. Reflecting back on this last year, there were many such catastrophic events including hurricanes, floods and fires. Even if not directly involved in one of these nature events, there may be consequences for those nearby as well.

Some may draw strength and composure from past experience. The positive vibes from the old Girl and Boy Scouts’ motto, "Be Prepared," or the seasoned ICU charge nurses’ catchphrase, “Always Have Plan-B,” may be overshadowed by the hospital unit late-shift recollection of the “night that wouldn’t end.”

It was a busy Friday for the transplant coordinator. Both of her shared-role colleagues were out due to unavoidable schedule changes. Leaving work an hour late, she noticed a news alert on her phone about a fire in the general direction of her home. A quick call to her husband clarified that although he could see some smoke on the horizon, there was not imminent danger at the moment.

Freeway rush hour should have been ending by now, even by Los Angeles standards. Listening to the local radio news feed in the car, she heard and simultaneously saw that her freeway had been closed due to either fire involvement or need to keep clear for emergency vehicle access.

GPS guided her through side streets which were backed up and barely moving. Arriving home at about 9:30 PM, it had taken 2.5 hours to go the 14 miles from the hospital to her house.

As they prepared dinner she and her husband recalled another fire experience from several years ago that they had been called to evacuate from, so they listened for updates on the latest one.

By 10:30 PM, just sitting down to dinner but on-call, she received a donor offer.

After careful data review and discussion with the surgical and medical teams, the donor heart was accepted and the coordinator began to set plans for the case in motion. As those in the transplant world know, many notifications, ongoing clinical and logistical assessments, transportation
arrangements, repeated explanations, updates, problem-solving, and negotiations are just part of the actions that are necessary until the transplant is accomplished.

Thoughts of the family and child who had been waiting for this chance while in-hospital about a year due to his tenuous condition, boosted the determination to ensure success.

Unable to give a firm OR time, the OPO was still placing the other donor organs. Each person on the team to be notified of the case she was booking asked, “What time are we going?” She gave the same, “no set OR time yet/still placing organs,” answer and explanation that she would keep them posted.

The fire was getting worse -- she heard reports of increasing acreage burn and that it was rapidly spreading while giving a tiny percentage of containment. At about that time she noticed that her assigned work phone had shut down. She knew it had been nearing the upgrade time due to battery signs of age, but the thought in her head at this moment was, “Do I really need this to happen right now?! Really?!” She began to give her personal mobile number as back-up contact and contacted the hospital IS Department who resolved the issue enough to get through the rest of the weekend.

Well into Saturday now, the OPO had been granting requests for further donor diagnostic testing, managing the donor, and continuing to complete their offer list. The challenges of the donor hospital for weekend staffing and test access within their system, despite their efforts, were recognized. Meanwhile the teams were growing more impatient and demanding that case timing be set. Finally, a procurement OR time was set for later Saturday evening.

The recipient candidate coordinator began the task of notifying the large number of team members, some of which were frustrated with the delays and expressed this to the coordinator in various ways. The coordinator was planning to leave her house for the hospital to work on the case when the view from their front porch stopped her cold. She phoned a trusted neighbor-friend, an experienced firefighter, and asked for his professional assessment and opinion if he thought her family would be among those forced to evacuate. After a few minutes followed by his explanation of some highly technical terms and predictions, he summarized for the layperson, saying, “At most, we are looking at a voluntary evacuation...but I don’t think it will happen.” Good enough for her. Making sure her family was all set, she took off for work.

The helicopter she had arranged for the procurement surgeon and team to travel to the donor hospital in had just departed. As she sat down to complete some paperwork, check on the recipient candidate and prepare forms for the case, the OPO phoned to inform her that the procurement case was bumped due to an emergency surgery that had to be done in the donor OR. The OPO coordinator was obviously concerned, as evidenced by the sound of her voice, but could do nothing but request the organ teams...just wait.

Re-notifications were begun once again and rather painfully received and completed. Three hours later, it was now early Sunday morning. Everything had been re-arranged...once more. The very busy and experienced procurement surgeon was not pleased with the new timing, resulting in idle
time in the procurement OR break room, but made the most of it when an old colleague showed up from out-of-state to procure one of the other organs, allowing them to catch up on their past and current events.

Fast forward: By around 5:30 AM, the recipient case was successfully accomplished. The child was transported from the OR to the CTICU where he recovered rapidly over the next few days and was discharged home in just a little over a week.

The local fire was beginning to be contained, but would take several days for completion.

When the coordinator looks at the photos of the fire now, she is reminded not only of the stress experienced on that particular weekend, but also how transplant coordinators routinely just assimilate, making the best of difficult situations in order to move forward for the benefit of their patients/patients’ families, while assisting the talented medical teams to accomplish the important end-result of successful transplantation.

In retrospect, the coordinator can’t help but wonder if the stars were somehow aligned those nights described in the story above. The recipient’s father happened to be a firefighter.

Transplant families seem to always make the most of their life challenges. I guess the least we coordinators can do is help them to accomplish their goals.

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

Early Bird Registration Deadline Fast Approaching

Don't miss your chance to Save Big by taking advantage of the $150 Early Bird Discount on registration fees for the ISHLT 38th Annual Meeting and Scientific Sessions in Nice, France this April. Discount ends on February 22. Between February 23 - March 12, registration fees are $150 higher so don't delay, register today!

ISHLT Lifetime Achievement Award: Call for Nominations

The ISHLT Lifetime Achievement Award is bestowed annually by the Board of Directors on an individual whose lifetime body of work has:

a. made a significant contribution toward improving the care of patients with advanced heart or lung disease
b. engaged in pioneering work that improved the care of patients with advanced heart or lung disease OR
c. is representative of outstanding dedication and service to the Society

The awardee will most commonly be a current or former ISHLT member of senior stature within the profession. Non-members who are meritorious may be considered on a case by case basis as long as clear justification is provided concerning why a non-member should be considered.

ISHLT is actively seeking the nomination of those individuals thought to fit the above criteria. All engaged members of the Society are asked to consider submitting a nomination form for those they feel are worthy of this honor. You can access the nomination form using the link below:

https://ishlt.wufoo.com/forms/ishlt-lifetime-achievement-award-nomination-form/

All nomination forms must be submitted by 5:00 PM US Eastern Time, March 1, 2018. Upon its completion, a copy will be automatically sent to megan.barrett@ishlt.org
Spanish Translation of ISHLT Guidelines NOW AVAILABLE!

Based on the 2016 Strategic Plan, ISHLT is working to translate a number of Standards & Guidelines documents into other languages. As part of this ongoing effort, we are pleased to announce that we now have the Spanish translations of two documents available on the JHLT website.


As a member of the International Society of Heart and Lung Transplantation (ISHLT), I was awarded the ISHLT Traveling Scholarship and granted the opportunity to visit Brazil and learn about Chagas cardiomyopathy and heart transplantation from the team at the Heart Institute (InCor), University of São Paulo Medical School. First described by Brazilian physician Dr. Carlos Chagas over 100 years ago, Chagas disease is a fascinating entity that has afflicted 6 million people in Central and South America. Generated by the protozoan parasite Trypanosoma cruzi and predominantly transmitted by the reduviid bug through fecal contact with mucous membranes or breaks in the skin, this disease is credited for 300,000 newly reported cases each year. Approximately 20-30% of infected patients progress to develop cardiac damage and cardiovascular complications including Chagasic cardiomyopathy, the most common and most severe manifestation of this disease process, which is almost always progressive. Other cardiac complications include bradyarrhythmias, ventricular arrhythmias, sudden cardiac death and cardiogenic shock. The growing migrant population from Latin America, where Chagas disease is endemic, has led to a gradually increasing prevalence of Chagas throughout the world with approximately 400,000 patients currently afflicted with T. Cruzi infection in non-endemic countries, predominantly the United States and Europe.

The direct challenges faced in the management of Chagas cardiomyopathy patients include initial trypanocidal therapy, supportive congestive heart failure therapies and ultimately heart transplantation, with pre-transplant optimization of the Chagas infection and post-transplant immunosuppression in conjunction with infection management. The implications of the large number of Chagas infected migrants are becoming more recognized as a world health issue, with recent publications describing care protocols used by experienced medical centers and calling for universal registries to aid in facilitating the international exchange of this knowledge. As such, I sought to thoroughly grasp the facets of this disease process and its effective management, through the progression into and following heart transplantation, and subsequently share this information with the ISHLT community. With high volumes of fifty adult and twenty pediatric heart transplantations in the past year, over 25% of which were indicated for Chagasic cardiomyopathy, Dr. Fernando Bacal and his highly skilled heart transplant team at InCor have a deep familiarity with the longitudinal care of these challenging patients. The variation in treatment options and lack of clinical trial-based standardization in this disease entity also encouraged me to travel to learn from an institution that has utilized their wealth of knowledge and experience to effectively manage their vast Chagas patient cohort over the years.

Upon my arrival at InCor, a 500-bed facility that exclusively treats cardiovascular and pulmonary disorders within the public health system in Brazil, I quickly learned that their team really is a tremendous example of the importance of multi-specialty collaboration for the efficient and efficacious treatment of complex disease processes. During my time at their institution, I was fortunate to work with a number of experts in their respective specialties who have had extensive exposure to Chagas disease patients. To illuminate the intricacies of Chagas disease as well as the infectious processes warranting attention in
Chagas cardiomyopathy patients, I met with Infectious Disease Specialist of Tropical Diseases, Dr. Tânia Mara Varejão Strabelli, who described the classic manifestations of Chagas cardiomyopathy and their implications. One in three patients treated with chronic Chagas cardiomyopathy are noted to develop acute Chagas reinfection during their post-heart transplantation period. Acute Chagas infection in this patient population most commonly presents as myocarditis or cutaneous lesions. Confirmation of the presence of infection is done through biopsy, with all samples examined under direct exam, culture and using the polymerase chain reaction (PCR) method. In the rarer meningoencephalitis, the cerebral spinal fluid does not usually test positive for Chagas present, and therefore, definitive diagnosis must be obtained through brain biopsy. When manifested in the form of myocarditis or cutaneous lesions, patients can successfully be treated with a 2-month course of anti-parasitic benznidazole or nitrofurthiromox, while the more severe reactivation as meningoencephalitis requires a longer 9-month course for resolution.

To further expand on the pathology involved with Chagas cardiomyopathy, concomitant Toxoplasmosis and the implications of immunosuppression and reactivation of Chagas disease post-transplantation, I met with pathologist, Dr. Luiz Alberto Benvenuti, and observed case samples of a variety of clinical challenges. The pathophysiologic progression of Chagas cardiomyopathy involves the hypertrophy of the cardiac sarcomeres in parallel, in contrast with hypertrophy in series noted in dilated cardiomyopathy. The pathognomonic pathologic presentation of Chagas cardiomyopathy is the presence of left ventricular apical wall thinning with inferior wall involvement also noted at times. Lymphohistiocytic infiltration due to myocarditis results in patchy, fine fibrosis throughout the left ventricle, which can provoke ventricular arrhythmias. Another common presentation is the “Chagasic rosary,” noted as white spotty lesions over the coronary arteries with associated fibrosis. An interesting challenge faced in this immunosuppressed patient population is making the distinction between Toxoplasmosis infection and Chagas reactivation. Though the clinical presentation of patients or even the evaluation of samples under gross examination may appear indistinguishable, under microscopic examination, Toxoplasmosis appears as a cyst with a membrane, while Chagas in contrast, has a pseudocyst with no membrane present. This important microscopic characteristic can therefore guide us toward the appropriate management of Toxoplasmosis or Chagas accordingly.

A major challenge in Chagasic cardiomyopathy patients post-heart transplantation is maintaining the balance between adequate immunosuppression to prevent organ rejection and anti-parasitic treatment to limit reactivation of Chagas disease. The Immunology department at InCor plays an integral role in the pre- and post-transplant care of Chagasic cardiomyopathy patients and has formulated their own antibody against T. cruzi to aid in the process. Using paraffin embedded and formalin fixed samples, T. cruzi parasites within myocardial cells or skin histiocytes are found in the amastigote form, while the trypomastigote form can be seen in blood and fluid samples. The definitive diagnosis of Chagas disease is through confirmation of the presence of a parasite. Ultimately, when unable to adequately establish the presence of parasite to confirm reactivation, the decision is understandably made to err on the side of caution and treat patients for active organ rejection. The team at InCor has also discovered that the use of azathioprine in place of mycophenolate for immunosuppression in Chagasic patients post-heart transplantation has decreased the reactivation of latent Chagas disease 6-fold and have therefore incorporated azathioprine as part of their standard immunosuppression regimen for this distinct population.

A notable observation during my visit to Brazil was the stark contrast between the public health system and private hospital system. Being part of the public healthcare system, the team at InCor faces unique and unfortunate challenges in providing heart transplantation to patients in a system with limited
resources. Despite cost limiting the use of ventricular assist devices, implantable cardiac resynchronization, cardioverter defibrillator devices and even certain medications, the InCor team has streamlined their peri-transplant process for patient care with excellent success rates. Adhering to the adage of necessity being the mother of invention, their team has even worked to create their own more cost-effective temporary ventricular assist device, aptly named InCor, to utilize as cardiac support therapy for pre-transplant patients. By incorporating their system-based approach, I truly feel that the heart transplant team in São Paulo has effectively implemented a holistic and inclusive manner in which they provide care to each of their patients.

Overall, I feel very appreciative and honored to have been awarded this once-in-a-lifetime opportunity to learn from those at the forefront in the field managing peri-transplant Chagas cardiomyopathy. As medical care providers around the world, we must be cognizant that our Latin American migrant patients are at risk of having underlying Chagas disease and in turn, be aware of the nuances to look for when evaluating and caring for such patients. I am truly grateful to the ISHLT and Dr. Bacal’s team at InCor for contributing to my education and allowing me to disseminate my gained knowledge to our medical community, and I wholeheartedly encourage my ISHLT colleagues to also try to take advantage of this exceptionally unique scholarship award.

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The Complex, Multidisciplinary Team Involved in Heart and Lung Transplantation

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The management process for heart and lung transplantation is very complex, with transplantation teams comprising heart and lung surgeons, cardiologists, chest physicians, critical care specialists, and other clinical specialties. Many other professionals are involved in the direct care of patients including specialists in infectious diseases, internal medicine, pediatrics, and clinical immunology. Examples of other clinical services include the nephrology department, where the patient undergoes apheresis for desensitization.

Nurses perform specialized tasks related with distinct procedures of transplantation. Transplant nurses also provide specialized nursing care, support, and education for patients and their families throughout the transplant process. Pre- and post-transplantation activities (preparation for surgery and discharge) are relevant.

Transplantation requires a spectrum of laboratory investigations. Laboratory immunology procedures related to thoracic transplantation include HLA typing of donors and recipients and assessment of anti-HLA and other relevant antibodies. Immunochemical assessment of humoral and cellular immunity markers is also performed. The hematology department covers automated hematology, hemostasis, thrombophilia, and anticoagulation therapy as well as transfusion medicine. Biochemical tests include the assessment of immunosuppressive drug levels. The pathology department covers histopathology of allograft rejection including C4d or C3d deposition in heart and lung allografts and more recently, underlying molecular mechanisms involved in allograft rejection. Radiology departments are actively involved in all kinds of imaging techniques.

The complexity of the procedure involves many other professionals and departments such as psychosocial management of transplant candidacy and post-transplant evaluation. Socioeconomic support and social support are covered by social workers.

A series of allied health professionals also play a role. These include clinical laboratory scientists, clinical officers, dental hygienists, dietitians and nutritionists, laboratory technicians, medical interpreters, medical radiation scientists, occupational therapists, paramedics, perfusionists, physical therapists and physiotherapists, recreational therapists, and social workers.

The multidisciplinary nature of transplantation teams is well established in transplant centers for coordination and performance of procedures and protocols.

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The Lost Art of Medical History

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“Hello Mrs. Anderson, I’m Dr. Dilling, one of the pulmonologists on our lung transplant team. It’s great to meet you and your family.”

We have some of the usual introductory chatter and I ask them what they understand about the reason for this referral. I swivel my chair around to the computer consul in the exam room and enter my sign-on password. I click on her name in the patient roster. I turn to her and her family and say, “what we are going to do today is to talk about your medical history and the story of your lung disease. I’m going to be typing on the computer some of the things you tell me while we are talking (because I have to) but I am listening. So... tell me your story”.

I sometimes start my new patient appointments this way. Thankfully, I’m a good typist! (I think that typing was the most important class I took in high school. Back in 1987 I really didn’t even know why I would need the skill but my mother had suggested it for a summer school class.) Yes, conducting my appointments this way adds an element of “impersonality” to the encounter, but I think patients understand why I have to do it. Most have seen other physicians do the same. In these complex appointments, where I have to efficiently collect and document the medical facts and the content of our conversations, I find that it is the only way to accomplish what I need to do in our limited time together – and so that I won’t forget important details, as I might do if I tried to recount everything later in the day.

Electronic medical records have become nearly universal. They are touted as means to make records more understandable, reduce errors in medication ordering, foster communication between care providers, and reduce the paper waste and need for paper record storage. That sounds all good, right? But does the computerized medical record get in the way of the physician-patient relationship?

In some computer record systems, there are sections about social history and family history that are inputted once by a nurse or doctor in a particular hospital. From then on, the computer “auto-populates” these sections in subsequent physicians’ histories. Medications are imported into the note in the same way. How many physicians never double-check these sections? Not to mention the problem that some of the most important patient-physician bonding occurs during the collection of information about the patient’s occupation and family life. How sad to miss those parts!

And how many times have you seen “copy and paste” sections to the notes (which are sometimes not well-updated) and which over time become both monotonous and meaningless.

When René Laennec at the Necker-Enfants Malades Hospital in Paris invented and introduced the stethoscope into the patient encounter, it was actually met with some of the same concerns. Both
physicians and patients saw the tool as an impediment to the important close physical proximity and intimacy of the physical examination. It separated them physically, and (many believed) professionally. Before that time, hearing a heart murmur or adventitious lung sounds was possible only by putting an ear to the chest wall. The stethoscope enhanced the examination and improved the quality of diagnosis. The instrument eventually became intricate to the profession and now symbolizes medicine itself. Similar arguments were made for radiography (first x-rays, and later computed tomography), but their diagnostic prowess allayed such concerns. Some lament that technology and testing has largely supplanted the dying art of physical examination.

Has the electronic medical record – and the computer we use to interface with it – brought with it a wall between our patients and us? I think so, despite its apparent necessity. That said, just yesterday I was starting to see a new consult in my clinic – a young man with a rare cystic lung disease called Birt-Hogg-Dubé syndrome -- when suddenly my computer froze up. I fumbled around and pushed some buttons on the keyboard, but, alas, it remained non-functional. I thought about moving to a different room, but then I saw a blank piece of paper on the shelf. I picked it up and started jotting a few data points on the paper as we talked. I looked him in the eyes as we spoke more than any patient in years. It was a delight! Thankfully, his history was not a deep one and there weren’t as many details as is usual in one of our transplant candidates -- and so it was manageable to translate it all into a note afterwards in the charting room. But the encounter made my week!

We already have robotic surgery. Pocket ultrasound devices have started to replace a stethoscope and other parts of the physical examination. Who knows what’s next, virtual reality (VR) appointments? The impersonalization of medicine will certainly continue into the future. Let’s just all hope for that occasional technological malfunction when we get to do things the old-fashioned way.

Sit down. Look a person in the eye. Get to know them and their family. Let them get to know you. Do a thorough examination. It’s a privilege to get to talk to people so intimately and know people in the way we do. Enjoy!

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Out of France and the Science of Heat to Extracorporeal Support and Transplantation

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Let’s warm things up about our upcoming ISHLT meeting in France by exploring some of the early 19th century ideas about heat. Not so much what heat was thought to be, but instead how heat behaves with the “Laws” it follows. This is important because of the central role heat plays among nature’s many forces, i.e. motive, magnetic or electrical force. Let’s be sure to stay away from all the recent heated topical news in the workplace related to perhaps, the Descent of Man or Men of Power, or more aptly named – Man and His Nature and those “Laws” not followed.

Heat is important because it is ubiquitous. Whenever one force is used to produce another, almost without exception heat will be produced. Heat has important characteristics. Think about electromagnetism exemplifying the interrelationships among forces like a generator. Turning a coil of wire mechanically in a magnetic field interrupts that field giving us electrical current. Is the mechanical force used to turn the coil made use of to produce the electrical force of a current or is the mechanical force converted to electrical force? What about an electric motor that starts with electrical current and ends with the rotating mechanical motion of the armature. Is the electrical force of the current made use of to produce the mechanical rotation or is the electrical force converted to mechanical force? Note, the first posits that mechanical or electrical force is made use of to produce the alternative, then these forces are made use of or used but not used up. Therefore, the initial force is recoverable and can be used again. The latter posits that mechanical or electrical force is converted to electrical or mechanical force respectively, then the initial mechanical or electrical force has been used up and is no longer around.

Early attempts to understand the behavior of heat were proposed by French natural philosophers from the early decades of the 19th century who began to explore the relationship between heat and motive force. In the early 1800s society was keenly aware of the use of heat to obtain motive force, the steam engine. The invention of the steam engine, the most important symbol of the industrial revolution, represented the major shift away from animal power to inanimate power. Falling water was another favorite use of power to turn the wheels of a mill. Pause here if you will about the steam engine and reflect on the ventricular assist devices and other extracorporeal devices and circuits of today. Consider the inefficiencies and efficiencies. Think about heat.

Now let’s turn to the direction of influence on science and technology. The usual direction is from science to technology, theory to application, such as the aftermath of the discovery of electromagnetism. On the other hand, technology precedes science as occurred with the steam engine. Effective steam engines were built well before how they worked was understood. The steam engine set the stage for the birth of thermodynamics. In this instance, science learned a lot more
from the steam engine than the steam engine learned from science. So how did the science of heat come about?

One of the first natural philosophers to consider the behavior of heat from a theoretical as opposed to a practical point of view was the French mathematician Jean-Baptiste Joseph Fourier who is also credited with the discovery of the greenhouse effect – again let’s stay away from politics, men of power and global warming. Because Fourier was born into humble surroundings, this enthusiastic and driven youth with amazing mathematical abilities had natural sympathies for the French Revolution. He survived the Reign of Terror and acquired an important position at the École Polytechnique. Indirectly from the influence on Napoleon, Fourier devoted himself to the study of heat and asked the question, how does heat flow through solid bodies? Can this be described mathematically? Fourier had developed an unconventional aspect on the treatment of heat. It was the introduction of a nonnewtonian element into physics showing the way heat flowed. The Laws Fourier had formulated for the conduction of heat implied that heat flow was not reversible. For the early 19th Century, this was in opposition to the mechanical laws that Newton had formulated to describe how the machinery of nature ran were reversible. Nature’s laws should not be reversible as predicted by Newtonian laws.

Now there was another Frenchmen also fascinated by the theoretical study of heat as it appeared in the steam engine. His name was Nicolas Leonard Sadi Carnot. Unlike Fourier, Carnot came from an important family in France. Carnot completed his studies at the increasingly famous École Polytechnique in Engineering, Mathematics and Science. He developed an important curiosity about heat engines which enabled him to ask an intriguing and fundamental set of questions about the way heat is used to produce motive force. One of his questions was whether there was a maximal amount of motive force that could be obtained using a certain amount of heat. For example, a steam engine puts out a certain amount of heat. Is there a limit to the amount of motive force produced from heat? Were some substances better than others in producing a given amount of motive force. Is coal better than wood?

Those who worked steam engines used trial and error to answer these questions. From experience they can determine if different engines could produce different amounts of force from the same quantity of heat. Carnot focused on the theoretical side of these questions. He knew very little about working on or with steam engines. In his pursuit of these theoretical questions, Carnot discovered something that took years to appreciate. He recognized that if heat were used to produce motive force, then the only way that could occur was when heat from a higher temperature fell to a lower temperature, $\Delta H$. These ideas were put down in his only publication in 1824 entitled Reflections on the Motive Power of Fire. This became a key work in the history of physics.

Carnot thought of the production of motive force from heat as nature’s response to a disturbance from a normally balanced state, not unlike the production of electricity or the perturbation of a pendulum from its equilibrium. Carnot viewed the steam engine as another way of disturbing a normal state which gives nature an opportunity to restore the disturbance back to its the original state. This heat engine Carnot imagined was the “ideal heat engine,” one which is considered
weightless with no heat loss to friction or conduction. Most of his readers interpreted his description of heat as a weightless “subtle fluid” that Lavoisier had called caloric. Caloric was one of those imponderable substances. (see Editor's Corner, September 2017 Links) When these imponderable substances were combined with material bodies or matter, these bodies were warmed. How much caloric was present was a measure of the matters temperature. The temperature of the air in the chamber of a steam engine depended on how caloric was present in the volume of the chamber. With these assumptions, Carnot was able to explain how disturbing and restoring an equilibrium state could tell us how a steam engine is able to produce motive force. Imagine a cylinder with a movable piston that expands the volume of the cylinder on its upstroke then compresses the volume on its downstroke. In the equilibrium state, there is no movement. Carnot assumed that nature would maintain that equilibrium. Now bring on the heat, extra caloric into the cylinder. This is done by bringing the cylinder into contact with a body made hot by steam. Nature maintains the equilibrium by expansion, moving the chamber up as it was disturbed by the increasing temperature. Now remove the cylinder from its contact with the hot body, no more steam flows in, at this point the piston continues up expanding the volume of the chamber briefly resulting in another unstable situation. The temperature now drops from the increasing temperature. The amount of caloric has been reduced. Nature restores equilibrium by bringing the cylinder into contact with a cold body. Nature allows the caloric to flow to the cold body thus contracting the volume of the cylinder and moving the piston down. The downward movement of the piston continues beyond the equilibrium which perpetuates the cycle similar to the simple harmonic motion or oscillation of a pendulum, spring or in this case a piston under ideal circumstances. From this analysis, Carnot learned that the motive power of the engine depended on two factors: the amount of heat produced and the availability of cold - that is the size of the fall in temperature or the delta $\Delta H$ - “without the latter, the heat is useless.”

This brings us back to the original questions about the relationships among forces, electrical and mechanical as pointed out above. Is heat made use of to produce motive force or is heat used up to produce motive force. Carnot states that “the production of motive power is then due in steam engines not to an actual consumption of caloric but due to its transportation from a warm body to a cold body,” in its reestablishment to equilibrium. He believes heat was conserved. Most importantly to produce a motive force there must be a drop in temperature akin to Norman Shumway’s great quote, “all water flows downhill.” To answer the question about which substances are better at producing a given motive force, if motive power depended on the difference in temperature of the hot body and the cold body, then the substance used to supply the heat was not important. He concluded that all ideal reversible heat engines must have the same efficiency. This was just the beginning of the new science of thermodynamics. For this, Carnot is considered the father of thermodynamics.

Now fast forward to the technological explosion of extracorporeal life support systems where such systems assume the work of the heart and/or the lungs. Consider the production of heat and its effect on clot formation. What about the sources of energy necessary for ventricular assist devices? When the energy is “used up” where does it go other than producing a motive force for circulation? What about the heat? What effect does this heat from motion and friction have on our patients and
on ourselves? Think not just about how hot or if it clots, but think about “sudden” changes in temperature. Of course, is the energy perpetual, renewable or when batteries or back up batteries must be changed? Imponderable questions?

Before we finish here, rethink or reflect on heat, France and Carnot, then think about sewing two vascular structures together successfully to allow blood flow with the least amount of friction, resistance or heat. Let’s not confuse Nicolas Leonard Sadi Carnot (1796 – 1832) – Father of Thermodynamics with Marie François Sadi Carnot (1837 – 1894), the President of France from 1887 until he was assassinated in 1894. Nicolas Carnot was Marie Carnot’s uncle. Anyway, a fatal stab wound to the abdomen of the nephew Carnot in 1894 profoundly influenced a French surgeon, Dr Alexis Carrel (1873 – 1944), to consider the possibility of repairing the severed abdominal vessels. Carrel’s pioneering vascular surgical techniques paved the way to his Nobel Prize in 1912. Further, with the assistance of Charles Lindbergh, Carrel in his effort to keep tissues and organs alive, extracorporeally, invented the “perfusion pump” in the 1930’s which unlocked the door to open heart surgery and organ transplantation.

Need we simply end here with all these “links” related to France, heat, motion, rotaries, propulsion, travel, transplantation, replacement therapies and extracorporeal life support? Or should we go in circles and swing back and forth like a pendulum in a frictionless vacuum like an idealized steam engine in perpetuity. What came first? The chicken or the egg, science or technology, or the theory or the application? Where are we today? Soon it will be Nice.

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