Apophenia and the Crafting of a *Circulation: Heart Failure* Issue

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Apophenia: the spontaneous perception of connections and meaningfulness in unrelated phenomena

It is our nature as human beings to look for connections—and often to discern them where none actually exist, something known as illusory correlation. This is wired into our brains, for a number of reasons. The ability to discern a true pattern quickly can be a time saver—and one would expect evolutionarily that it may have been a life saver as well. Apophenia exists in many species. Skinner[1] demonstrated the existence of illusory correlation or superstition in pigeons. In a series of experiments, pigeons apparently associated a food reward with unusual behavior (for a pigeon), such as bowing, scraping, dancing, or neck turns. The bird would then begin repeating that motion, and every subsequent food reward would further reinforce the behavior. Apophenia is a tool humans use to exert control over a chaotic world. Research has shown that doing relaxation exercises can lower the chances of succumbing to such illusory pattern perception.[2]

Apophenia is an important force to acknowledge in scientific research and publishing. Many of the papers we receive report associations between two phenomena, such as a biomarker and heart failure events. It is in our nature as humans to infer causality in these associations, and as journal editors, we often require authors to propose a potentially causal mechanism when describing such associations. It is important to recognize that while this is natural and important as it imparts scientific rigor to the work we publish, we are likely often fooling ourselves in believing these connections are real. The field of heart failure is riddled with excellent, mechanistic hypotheses that haven't really borne out. The potential for positive inotropes to improve outcomes in heart failure is one example, with an appealing and logical rationale, accompanied by multiple negative randomized trials often occurring in the context of prior repeatedly negative outcomes in the active therapy arm with similar drugs. The promise of angiotensin system blockade in heart failure with preserved ejection fraction is another example, where the allure of blocking a system known to be active in hypertrophied ventricles and hypertensive patients persists, despite randomized trials showing no difference in outcomes. As I often say on rounds in the hospital, we are excellent at coming up with a unifying diagnosis and story to link clinical events together, but a good physician knows that those connections may be illusory—we can never stop looking for the zebras.

As a journal editor, it is similarly appealing to identify themes and build journal issues around topics of interest. While desirable, this is challenging, as good science comes in rapidly at *Circulation: Heart Failure*, and often without obvious thematic connections. We take seriously our charge to respond rapidly to submissions, to make decisions promptly, and to shorten the time from submission to publication. While it is often our wish to hold a paper for some time in order to allow a thematic

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link with other papers to emerge in an issue, this is not consistent with our mission of making science available rapidly. So while the editors at *Circulation: Heart Failure* are interested in publishing thematic issues, what we call Spotlight features, most of our volumes will be filled with wide-ranging but excellent science on the cutting edge of heart failure.

Nevertheless, 2018 is a special year. It is the 50th anniversary year of the first human-to-human heart transplants, performed November 17, 1967, by Dr Christiaan Barnard in Cape Town, South Africa, and on January 6, 1968, by Dr Norman Shumway at Stanford. Considered a radical innovation at the time, the next 50 years were filled with remarkable and sometimes unbelievable advances in the care of patients with heart failure. Transplant is now a routine therapy for advanced heart failure. Beginning in the 1950s, work was underway to design implantable pumps that would allow patients with heart failure to survive despite complete cardiac failure, and in 2018, patients are implanted daily and discharged home on left ventricular assist devices that provide significant improvements in survival and quality of life. It has been a remarkable 5 decades in our field.

Turning an apophenic eye to this issue of *Circulation: Heart Failure*, we honor this legacy with a number of articles highlighting the challenges and progress we have made in our Spotlight on application of advanced therapies in heart failure. Several articles explore the current practice and experience with mechanical circulatory support therapies, including the article by Brinkley et al[3] demonstrating similar outcomes at implanting centers both with and without transplant programs and the article by Agrawal et al[4] exploring the reasons behind 30-day readmissions after mechanical circulatory support implantation. We have 2 articles that examine the experience of advanced therapies in patients with hypertrophic and restrictive cardiomyopathies, patients who clearly respond less well to mechanical circulatory support implantation. Wever-Pinzon et al[5] examine outcomes in patients listed for heart transplant with hypertrophic cardiopmyopathy as an underlying cause of heart failure, while Topkara et al[6] examine mechanical circulatory support use and transplant outcomes in a population with underlying restrictive and hypertrophic diagnoses. These articles are timely in light of upcoming changes in heart allocation that acknowledge the difficulties faced by this population. Finally, several articles address more global, societal issues affecting transplant practice, including the article by Topkara et al[7] highlighting the impact of socioeconomic disparities in outcomes after heart transplantation and the On My Mind by Rajab[8] proposing that we seriously examine reducing barriers to use of deceased cardiac donors as donors for heart transplant in addition to other organs. I can think of no more fitting tribute to the explorers, innovators, and pioneers of the last 50 years than to put together this collection of remarkable scientific work that while acknowledging the remarkable life-saving advances made also illustrates some of the thorny issues we face daily when caring for these patients.

Of course, there is much more in this issue besides the Spotlight feature. This includes fascinating basic science by Dr Koch and colleagues[9] examining mechanisms by which caloric restriction may improve function of the failing heart and by Dr Kass and colleagues[10] revealing important cellular signaling and localization pathways that may differentiate the effects of phosphodiesterase 5 soluble guanlyate cyclase inhibition and sGC stimulation on G protein signaling in failing myocytes. There is an important study by Thacker et al[11] demonstrating a shocking rate of cognitive decline in patients with heart failure and a brief communication by Catino and colleagues[11] highlighting vascular effects of sunitinib in oncology patients receiving this drug.[12] Dr Catino is our highlighted Emerging Investigator this month. Watch for our upcoming Twitter journal club with Dr Catino, and if you missed them, check out the prior Twitter journal clubs with prior Emerging Investigators Dr Rebecca Cogswell (https://storify.com/CircHF/emerging-investigator-rebecca-cogswell) and Dr Bettina Heidecker (https://twitter.com/i/moments/940981613541851136). Our Twitter journal club is an energizing forum of scientific engagement, dialogue, and exploration, led by Dr John Ryan, that has engaged all participants and which we continue to highlight and grow.

Any theme in this issue beyond great science with potential to impact care of patients with advanced heart disease may in fact be illusory. But the new team of editors at *Circulation: Heart Failure* will do our prescribed relaxation exercises to reduce any tendency to apophenia and forge on to find the most reliable links and patterns in the great content we work to bring you every month.

DISCLOSURES

None.

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FOOTNOTES

Circ Heart Fail is available at http://circheartfailure.ahajournals.org.

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