EDITORIAL

Advancements and challenges in Peyronie's disease: a personal journey and current perspectives

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It is truly an honor to be invited to write the introduction to this special issue in the International Journal of Impotence Research on Peyronie's disease (PD). PD has become very much part of my life since the late 1980s, when I first encountered a colleague doing research on tendon repair. He explained to me that calcium channel blockers had been shown to change the behavior of fibroblasts. This was truly a "Eureka moment" and triggered the first clinical study using intralesional verapamil for treatment of PD. Prior to that time, I had likely only seen 2 or 3 men with PD during my residency training and was beginning to see more as a junior faculty member at University of Chicago Medical Center. Since the publication of my first paper on intralesional verapamil in 1994, as a treatment for PD, I have remained fascinated by this enigmatic disease [1]. Over the past 30 years, I have continued to see more and more men with this both physically and psychologically devastating condition and during that time, I have published with many colleagues, residents and fellows almost 100 peer-reviewed articles, 19 book chapters and two books with emphasis on evaluation as well as non-surgical and surgical treatment of PD. Thanks to these efforts, I was recently recognized as "the author with the most articles published on PD" [2] (Fig. 1).

We still do not understand the pathophysiology of PD, nor do we have a reliable nonsurgical treatment for it. Although I expect in time research will guide us to the key to unlock the mystery of this scarring disorder at the current time, surgery remains the gold standard of treatment if the goal is to attempt to get the penis back, as close as possible, to its pre-PD configuration. I think we have learned very important lessons over the last several decades about how men with PD respond differently with respect to their expectations and trepidations towards treatment. The relatively recent introduction of Collagenase Clostridium Histolyticum (CCH) has taught me that many men will be satisfied with any improvement in their erect deformity and will accept the risks of intralesional therapy, whereas others insist on whatever it takes, including the most invasive approaches to be functionally straight and functional [3].

We have seen advancements in the quality of published papers on PD as well, where objective measures of deformity are routinely being reported, as compared to the past, where success was frequently being reported as reduction in plaque volume with either physician or patient reported improvement of deformity without any objective measure. We still have issues with accurately measuring erect curvature, even with a goniometer- I can easily create a 10 degree discrepancy with minor adjustments of the goniometer limbs. Therefore, to me any reported curvature reduction can be reduced by as much as 10 degrees. Placebo-controlled trials are now the norm for nonsurgical treatment. Much of this is likely because Centers of Excellence have been established worldwide, drawing more patients to be able to do such studies. In addition, more men are coming forward with PD due in part to a general reduction in the negative stigma associated with sexual dysfunction and a greater involvement by industry with advertisements suggesting the PD penis is similar to a bent carrot.

There remain many important unanswered questions about PD including- Why is it that it tends to occur primarily in middle-aged men? Why is it that once the disease is stable it rarely recurs? Why is it that there are so many variations in the deformities seen? I think we have learned that calcification, which was previously thought to be associated with more severe and aging scar, is just a different sub-type of PD. Men with calcification likely have osteoblastic genes triggering calcification which can be identified on ultrasound almost immediately after onset of plaque formation [4]. I am not sure we will answer the question soon as to why the scar occurs in the first place, but we have had some insight as to once the scar presents, why doesn't it go away as would happen with normal wound healing. Research done in my lab years ago found that the metalloproteases (MPs) responsible for scar remodeling are blocked by tissue inhibitors of metalloproteinases (TIMPs) [5]. Research to safely shut off these TIMPs would seem a good idea. Sorting out why the scar tissue does not resolve could also help provide relief for other types of wound healing disorders including Dupuytren's contracture and pulmonary fibrosis. Historically, research in PD was limited in part due to lack of interest by industry or government sources.

At this time, it appears that the available non-surgical treatment options may help prevent progression during the acute phase and possibly even result in adequate correction of deformity for some men, especially those with mild-moderate deformity. But for those with severe deformity including curvature, shortening and indentation, I have come to believe that surgery is the gold standard. Surgical treatment of PD, like much of surgery can become routine when performed frequently enough but correction of severe deformity associated with PD, requires specialized training and experience. As I frequently say, a man cares about 2 things in his body, his brain and his penis. When something goes wrong with the penis, it can oftentimes consume him and be devastating psychologically. The PD surgeon must recognize the distress of their patient as well as set appropriate expectations about treatment outcomes. If surgery is chosen, we must be clear about its risks including erectile dysfunction, incomplete correction of deformity, sensory changes and shortening.

In this issue, we have many well-done manuscripts which will hopefully provide useful information, push back the frontiers of Peyronie's disease a bit and possibly trigger in some of you an urge to perform your own research. All these outcomes are worthwhile and explains why I have chosen to be an academic surgeon. I have been blessed by my interest in PD as it has taken

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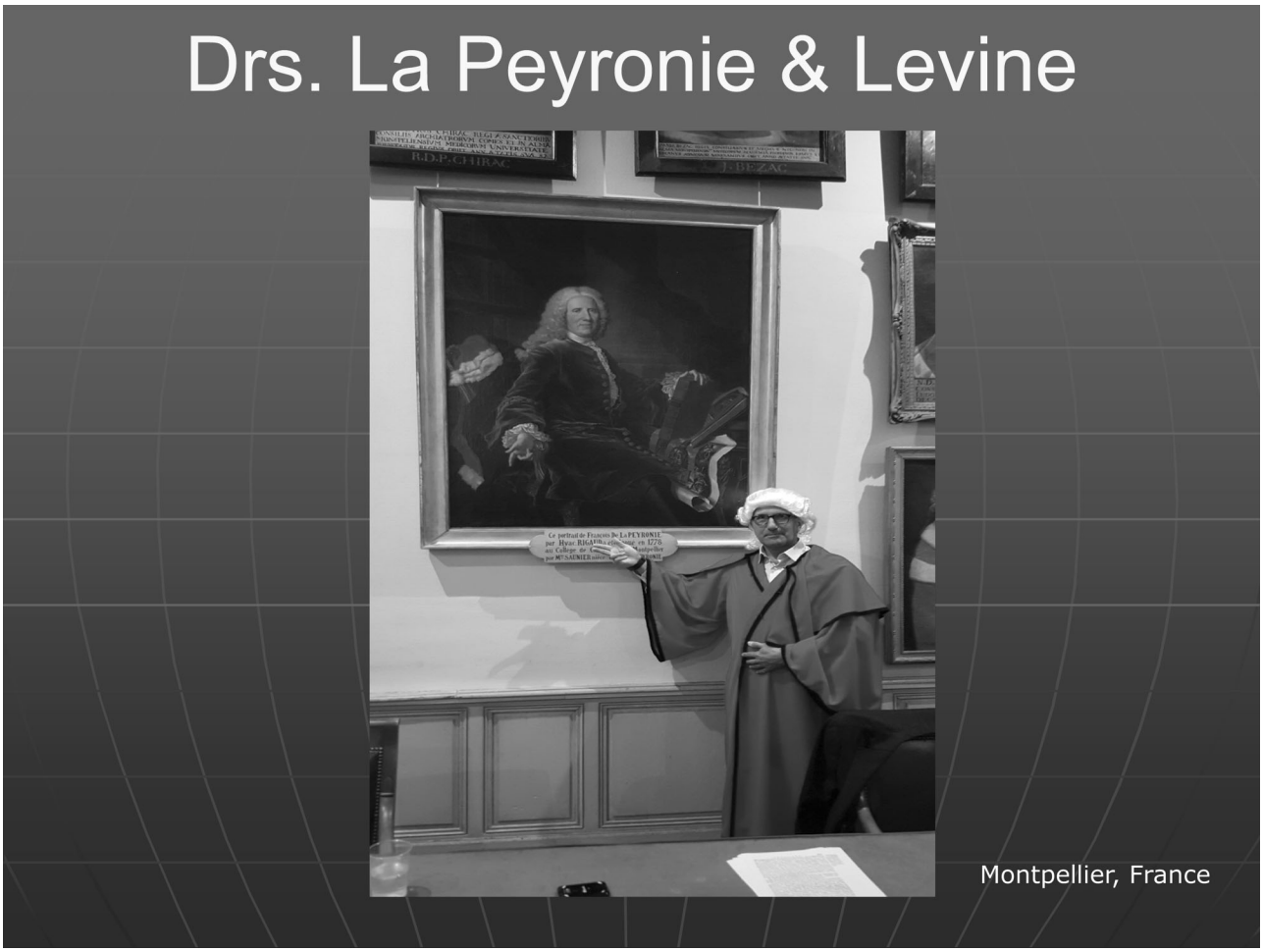

Fig. 1 A photo taken during my trip to Montpellier, France the home of F.G. de la Peyronie, in 2016.

me around the world and introduced me to new friends and colleagues as well as lasting relationships with many of my patients. It has been a good run and I hope to keep going.

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