

In Memory of Professor Marsh NM: The Researcher who Understood and Lived Celiac Disease

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Professor Michael Newton Marsh passed away on the 13th of July, 2021 and the present memoriam is dedicated in his honor. He has been a robust pillar in the exploration of celiac disease (CD) for the past 50 years and has contributed greatly to the diagnostic criteria and understanding of the gradual process of intestinal destruction in the disease. The first mentions of CD were represented by Aretaeus the Cappadocian (1856), Samuel Gee (1888), Wilhelm Karel Dicke (1950), followed by Margot Shiner (1956) and William Holmes Crosby Jr (1957), whom I consider the first founders of the disease. In fact, Margot Shiner with her rather cumbersome biopsy tube and William Crosby and Kugler H.W. with their improved suction capsule, established the basis for Prof. Marsh NM career in small intestinal morphology in CD. Based on the dialogue with him in 2016 [1], he acknowledged his first medical mentors: Prof. Sir Christopher Booth, Prof. Jerry Trier and many other that influenced his clinical and scientific career. It seems to me that Prof. Marsh NM represent the transitional generation between the above-mentioned fathers of CD and his generation that expanded on the pathophysiological and morphological events that end up with the mucosal damage. His world-wide scientific international achievements formed the basis for his Invitation to inaugurate the first issue of the international Journal of CD, in 2013 [2]. He inspired the intestinal morphologists and immunopathologist all over the world and his scientific legacy will stand for years to come.

Those two publications [1,2] open a narrow window to his long-term career, scientific achievements, personal opinions, critics to his opponents and even to his "non-CD" academical activities.

Along the years, Prof. Marsh's main scientific contributions were:

1. Establishment of the four phases of intestinal injury in CD, namely: normal, infiltrated, infiltrated-hyperplastic and flat mucosa (0, I, II and III Marsh score, respectively).
2. Exploration of the pathophysiology of refractory CD

3. Expanding on the mucosal responses triggered by environmental factors like food components and parasites, host-host immune histocompatibility and tropical-malabsorption syndrome.
4. Elucidated on the cross talks between susceptible genes and consumption of immunocompetent wheat proteins, thus, activating the mucosal T lymphocytes. Only then, in a stepwise cascade, mucosal damage is taken place.
5. Designed a three-dimensional mucosal scheme, based on the adoption of electron microscopy images. In this regard, I had the pleasure to spend time with him when the late Prof. Theodore Iancu invited him, as a visiting Professor, to stay in our pediatric department, Carmel Medical Center, in the early ninetieth. Both published on the enteric electron microscopy aspects of CD [3].
6. Unraveling the coordinated interrelationship between the superficial epithelium, the basal membrane and the crypts in the lamina propria.
7. Exploring the association between CD and obesity
8. Studying iron absorption at the epithelial level

Here is the proper place to highlight his scientific contributions that are not directly related to CD. Although he achieved his world-wide reputation in exploring CD, it turns out that he studied and published in other areas, including humanity domains. Involved in human rights, ethics and medical morals, he published around 20 publications on those topics [1].

And now for some anecdotal self-expressions and from his personal life. Prof. Marsh always knew how to compliment and flatter the previous generation, his senior teachers, hence left a wide opening for future generations to discover the mysteries of CD. Various CD Puzzles occupied him throughout his life. He congratulated the dedicated CD patients' organization and associations for their fruitful and important role in helping the CD population to cope with the disease and with their gluten restricted diet [2].

Prof. Marsh drew the diagram of CD morphological progression (Figure 6, Gastroenterology 1992) [4] in his

home kitchen table, just before submitting, as testified by himself during the dialogue in 2016 [1]. He improved it while staying in Carmel Medical Center, Haifa, Israel. In this regard, I remember him expressing to me his desire to learn Hebrew. “But I was always fascinated by Hebrew—perhaps the characters as well as the language”, “hiring a private tutor to teach me Hebrew” [1].

He had difficulties to accept non-celiac gluten sensitivity as a separate entity and thought that it represents an “attenuated form of innate response, but which does not get sufficient pumped up to cause gluten sensitivity”. Or “what currently I think is a gobble-de-gook amalgam of words (Non-Coeliac Gluten Sensitivity). If you know what that mean, you're a genius!” [1]. Prof. Marsh criticized the authors that develop the notions of “IEL become killer cells”, “massive cell lysis” or “NKG2D killing is the sine qua non of mucosal flattening”. He cynically suggested that “If the perpetrators of those views do not believe this, they should go and read the relevant literature—and maybe educate themselves” [1]. His humor and the way he took life more easily pre-retirement is expressed by his quotes: “there have been some odd tales floating around (“off his head”: “getting a bit soft”: “got ordained”).

He had hard time accepting Dr. Oberhuber's modification of Marsh score [5]. “We must begin to realize that Oberhuber modification to Marsh III stage are fairly useless... they serve no useful practical value—histologically and diagnostically” [2]. Another controversial topic that urged Prof. Marsh to respond, argue and defend his morphometric score was the cut-off level of the IEL invading the epithelium in CD mucosa [6,7,8,9]. “My own view is that Siriweera's paper hardly contributes to this important debate, and certainly does not help in clarifying any of the issues arising” or “My perception is that not many people know about, have understood and even overcome the underlying technical problems involved” [6].

Finally, according to the memoriam and obituaries published [10,11,12], it is possible to understand Prof. Marsh's greatness and his extensive contribution to the understanding celiac disease evolvement and its target organ injury. His uniqueness and his 50 years of historical role in CD mucosal pathology characterization, interpretation and scoring, will pave the way to current and future

healthcare professionals as well as the scientific generation. Many people, all over the world were diagnosed with CD over the years thanks to his dedicated scientific work and the diagnostic score of CD mucosal damage. As a prominent CD guru, Prof. Marsh legacy will last for many years. Thank you for all you have done and all that you have taught us, Prof. Marsh NM.

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