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GENERATIONS

Building the MS Workforce of the Future

"Growing Together"
by Nadia Alkhun

INSIDE

A Publication of the Foundation of the Consortium of Multiple Sclerosis Centers (FCMSC)

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GENERATIONS

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Welcome to the FCMSC and the Workforce of the Future Program

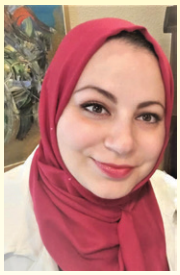
The Foundation of the Consortium of Multiple Sclerosis Centers (FCMSC) was founded in 1999 to stimulate the growth, development, and provision of patient care services, education, and research in the field of multiple sclerosis (MS) and to enhance the quality of life of those affected by MS. Together with the Consortium of MS Centers (CMSC), the Foundation is at the forefront of maintaining and increasing a cadre of trained, dedicated specialists and researchers. Currently, it appears that 1 million people in North America and 2.5 million worldwide have MS, and the patient population is expected to increase annually, which will in turn require greater numbers of professionals to manage their care.

The Workforce of the Future program has supported neurology/neuroimmunology residents, medical students, rehabilitation therapists, and nursing professionals by funding and facilitating fellowships in MS-related research and clinical care, expanding opportunities for CMSC Pilot Research Grants in comprehensive care, and supporting the work of the largest patient-driven MS registry, NARCOMS, which has yielded data about MS itself, contributing factors, and lifestyle implications.

One of the key activities of the FCMSC over the past 5 years has been an MS Mentorship Forum. This mini-conference occurs on the day prior to the CMSC Annual Meeting's opening lecture, and convenes renowned faculty members (experienced experts noted in the subspecialty), peer mentors (neurologists or subspecialists who have completed specialty fellowships or 5-7 years of practice in areas of expertise important to MS care), and neurology residents nominated by their program heads as participants in this career development program. This publication is a natural continuation and expansion of that seminar, offering both career advice and MS research and clinical information and news.

(Continued on page 22)

Cover painting: "Growing Together"



About the artist: Nadia Alkhun is a self-taught contemporary impressionist artist who adores the freedom of imagination and the linkage of art to the state of self. Her artwork reflects her feelings about the human mind's mysteries in health and disease. While most of her art has taken the form of abstraction, one can find representational art in many of her art pieces. In addition to other publications, her painting dedicated to multiple sclerosis patients, "The Unseen But Felt," was featured on the cover of *Neurology*. Recently, Nadia joined the Peck School of Art at the University of Wisconsin in Milwaukee. Contact the artist: nadiaalkhun@gmail.com.

Dear Reader,

I am thrilled to welcome you to *Generations*, a publication designed to inform, engage, and precipitate brainstorming. You are the future and hope, standing on the shoulders of giants and ready to bring joy to people living with multiple sclerosis (MS). You are on your way to discovering the next molecule that will help reorganize the misguided immune cells that prompt MS. You may be the one finding the secrets to placing myelin back where it belongs and observing axons regenerating and reconnecting. You will hold your patients' hands throughout their journey and watch them beat MS. You will provide state-of-the-art clinical care, working in teams that value the concept of multidisciplinary, comprehensive care. You will find yourself eager to learn and grow the bounty of your knowledge in a field where new developments are endless.

Generations is an exciting publication that I hope you will enjoy! In this issue, you will travel through various topics that we feel will interest you as you begin your career. Topics include exploring multiple career pathways and career-life balance, a profile of a "graduate" of the Foundation of the Consortium of Multiple Sclerosis Centers (FCMSC) mentorship program, recent advances in MS therapeutics, and relevant artwork on the cover to enjoy and reflect upon. The editorial team invites you to submit contributions and reflections to publish on the CMSC, FCMSC, and MS Professionals in Training (MS-PiT) websites, and I encourage you to explore the programs offered by the CMSC and FCMSC, and to get involved. Finally, I would like to thank all of the contributors to *Generations*, the CMSC, the FCMSC, and the production team for their hard work and dedication to this publication.

Sincerely,

Ahmed Z. Obeidat, MD, PhD
Editor

Meet the Editor:

Ahmed Z. Obeidat, MD, PhD, received his medical degree with honors from the Jordan University of Science and Technology in 2008. He then joined the graduate program in neuroscience and physiology at Wright State University (WSU), where he received a PhD in 2013 under the mentorship of Professor Timothy Cope. During his time at WSU, he won the graduate student excellence award, served as a president's ambassador, and was selected to join the Phi Kappa Phi honor society. He then entered the University of Cincinnati, where he finished neurology residency training in 2017. During residency, Dr. Obeidat received several junior investigator and travel awards, including the American Academy of Neurology's (AAN) resident annual meeting scholarship. He completed a fellowship in neuroimmunology & multiple sclerosis at the University of Cincinnati, during which he received a 2018 AAN fellow scholarship. He was also awarded a clinical care fellowship by the National Multiple Sclerosis Society (NMSS).

Dr. Obeidat is the current chair of the Multiple Sclerosis Professionals in Training (MS-PiT) special interest group established by the Consortium of Multiple Sclerosis Centers (CMSC). He also serves as a member of the board of governors of the CMSC and is an advisory board member for the Americas Committee for Treatment and Research in MS (ACTRIMS). Dr. Obeidat is currently an Assistant Professor in Neurology, Neuroimmunology, and Multiple Sclerosis at the Medical College of Wisconsin and the founding director of the neuroimmunology and MS fellowship program there.

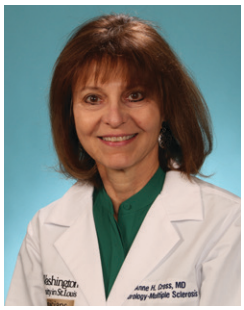
Dr. Obeidat's research aims to advance our understanding of MS clinical phenotypes, disease mimickers, and disease pathogenesis. He also hopes to improve current assessment tools and to integrate technology into MS clinical care. He is also very interested in the intersections among the arts, humanities, and neurology.

MS Career Pathways

During your training, it's important to also be looking toward your future and thinking about your career trajectory and goals. Today, there are many different ways to pursue a career in multiple sclerosis (MS). In this article, we introduce you to career pathways in research, academia, private practice, government, and the pharmaceutical industry.

A CAREER AS A RESEARCHER

RESEARCHER



Anne H. Cross, MD
Professor of Neurology
Washington University School of Medicine
St. Louis, MO

Anne H. Cross, MD, received her medical degree from the University of Alabama School of Medicine (now UAB School of Medicine) in 1980. She did her medical internship at Mercy Hospital and Medical Center in San Diego, CA, and her residency in neurology at George Washington University in Washington, DC. She then did three fellowships from 1984 to 1990 at the National Institutes of Health (NIH), St. Jude Children's Research Hospital in Memphis, TN, and Albert Einstein College of Medicine in The Bronx, NY. The last fellowship was funded by the National Multiple Sclerosis Society (NMSS). Since 1991, she has been at the Washington University School of Medicine in St. Louis, MO, where she has risen to the level of Professor of Neurology and conducts research, focusing almost fully on multiple sclerosis (MS) and related diseases. She has regularly been selected as one of the "Best Doctors in Medicine" and was awarded the John Jay Dystel Prize in 2019 from the NMSS and the American Academy of Neurology. Among many other elected positions and appointments, she is currently Secretary for the Consortium of Multiple Sclerosis (CMSC) Board of Governors.

Q: How did you arrive at your current position?

A: Since I was in high school, I always knew I wanted to go into a scientific research career. I had a family member who had an illness and that drove me into medicine, where I saw how much we didn't know about so many diseases. In medical school, I became very interested in neurology. During my neurology residency, I became interested in MS because at that time there were no disease-modifying therapies (DMTs) for MS, and yet I kept diagnosing a lot of people with MS, including women with the disease who were the same age as me at the time. Yet, there was nothing we could do for them beyond offering corticosteroids. I wanted to make an impact.

Q: What percentage of your work is dedicated to MS?

A: About 98% is MS research. I also do a little teaching and mentoring, and sometimes perform consultations in general neurology.

Q: What are the pros and cons of working as a researcher in an academic setting?

A: The pros are that you get to discover things and you're on the front line of learning how to use new scientific tools. It can be very exciting to work in an

atmosphere where you make discoveries that are potentially important to clinical care; it's like putting the pieces of a big puzzle together. My patients also seem to like that I do research; in fact, many of the patients I see come to me because they know I do research.

The cons are that I have to secure funding to do my research and pay my staff. I am at a soft funding institution, which means I have to generate my own salary and pay for my technicians, supplies and equipment, and equipment maintenance. That can be daunting, especially at first, and I've had many sleepless nights trying to figure out how to support my research. I spend about 50%-60% of my time thinking about, writing, revising, and applying for grants, and then managing the money and writing progress reports and papers.

Q: If you had to do it over, what would you do differently in terms of your career path?

A: I would do most of it in the same way, but worry less about the future. I wish I had known 20 years ago that it would all work out, with hard work and luck. I lost a lot of sleep worrying about funding the research.

Q: How easy is it to achieve work-life balance in your career setting?

A: It's not easy. Academia and research are very demanding, and you're under a lot of pressure to write grants, bring in funding, and produce papers. When I started out, I had two young children, and I would get up in the middle of night to work on grants so I wouldn't take time away from my kids. My husband was also very busy, so I don't know how we did it.

Q: What do you do to achieve work-life balance?

A: I pretty much work all the time, but I like to read for pleasure and take long walks. I consider my work my hobby and avocation, not just my job.

Q: What advice do you have to offer readers about deciding on a career path?

A: Figure out your passion, and what processes and diseases really grab your interest. If you go into academia, seek out the best person in the field to learn from and ask that person to be your mentor. That won't necessarily be the most famous person in the field, but someone who will help you get started and teach you. To find that person, talk to others about who mentored them.

COViMS

COVID-19 Infections in MS & Related Diseases

National Multiple Sclerosis Society

CMSC The Consortium of Multiple Sclerosis Centers

MS Multiple Sclerosis Society of Canada

To obtain additional information about this joint effort or to report a case of COVID-19, please visit:

www.COViMS.org

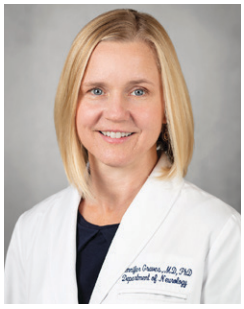
www.covims.org

COVID-19 Infections in MS & Related Diseases (COViMS) is a joint effort of the Consortium of MS Centers (CMSC), the National MS Society (NMSS), and the Multiple Sclerosis Society of Canada (MSSC) to capture information on outcomes of people with MS and other CNS demyelinating diseases (neuromyelitis optica and MOG antibody disease) who have developed COVID-19. Together, the CMSC, NMSS, & MSSC along with several independent experts launched this very important effort on Thursday, April 3, 2020.

COViMS is counting on robust participation and collaboration to provide information to better understand the impact of COVID-19 on patients with MS and other CNS demyelinating diseases.

A CAREER IN ACADEMIA

ACADEMIA



Jennifer Graves, MD, PhD, MAS
Associate Professor of Neurosciences
Director, UCSD Neuro-Immunology Research Program
Director, Rady Children's Pediatric MS Center
University of California, San Diego
La Jolla, CA

Jennifer Graves, MD, PhD, MAS, received her MD/PhD from the University of Texas Southwestern in Dallas, TX. She did her internship at Virginia Mason in Seattle, WA, and her residency in neurology and a fellowship in neuroimmunology at the University of Pennsylvania Perelman School of Medicine in Philadelphia. She also holds a master's degree in epidemiology and biostatistics from the University of California San Francisco (UCSF). She began her career at UCSF, rising to Assistant Professor in the Departments of Neurology and Ophthalmology. Today, she is an Associate Professor in the Department of Neurosciences at the University of California San Diego (UCSD) School of Medicine, Director of the UCSD Neuro-Immunology Research Program, and Director of the Rady Children's Hospital Pediatric MS Center. Her current research focuses on genetic, environmental, and sex-related risk factors driving clinical outcomes in multiple sclerosis (MS) and neuromyelitis optica syndrome disorder (NMOSD). She also studies how age affects patients' experiences of MS.

Q: How did you arrive at your current position?

A: In college, I thought I would go into astrophysics, but then I took a humanities class and read an essay by a woman with MS. It struck me that this disease affects people in their youth and has a profound effect on quality of life. I hadn't made the leap yet that I would go into medicine, but I did think I might have a research career—and this essay planted the first seed that I might want to study MS.

Then, when I was 20, I did a summer research experience in a cell biology lab at the National Institutes of Health (NIH) and I got a lot of exposure to their Medical Science Training Program. I was attracted to the program because it would show me what the important questions are to ask through the eyes of a physician and teach me how to answer those questions through the eyes of a PhD. I decided to do the combined MD/PhD and to specialize in neurology. I did my fellowship in neuro-ophthalmology at the University of Pennsylvania as learning this part of MS clinical care is one of the most challenging and the visual system offers the most precise understandings of the relationship of structural damage to everyday function for MS patients. I did a second clinical research fellowship in MS at UCSF and stayed on there to finish up the work I had started. Today, I'm 8 years out of my fellowships and continuing my career as an Associate Professor at UCSD.

Q: Can you explain the different ways residents and fellows can go into academia?

A: Yes, there are two ways: You can become a clinical educator focusing on teaching and clinical care; you might participate in research, but not as a principal investigator. Or you can go on a basic science or clinical research track, which is what I did.

Q: What are some of the pros and cons of going into research in an academic setting?

A: There are a lot of intellectual rewards to working in academia as a researcher. It is exciting to be fighting a disease on all fronts—research and clinical. Academic research, while often occupying nights

and weekends, does offer more flexibility during the week for parents who may need to get to a lunchtime daycare performance and then make up that time with grant-writing on the "third shift" (after the kids go to bed). But there is less predictability with a research track than a clinical track. You spend a lot of time trying to get funding when you're on a research track, and the university exerts a lot of pressure on investigators. So if you can't handle some of the uncertainty of knowing if you have funding or not, you might do better on a clinical educator path, where you have a salary and your responsibilities are clearly defined.

A challenge for women is that there are still gender differences in the amount of support and the salaries women receive in academia compared to men, but thanks to multiple efforts from different organizations this is slowly improving and is not a reason for women not to go for a career in research! Just make sure you find great mentorship along the way (this is true for MS specialists of all genders).

Q: How much of your job is research and how much is clinical?

A: If you want it to add up to 100%, I'd say about 60% research and 40% clinical. But I actually work a lot, something like 130%! And 100% of my focus is on neuroimmunology and neuro-ophthalmology in patients with MS, NMOSD, and related diseases.

Q: If you had to do it over, what would you do differently in terms of your career path?

A: I wouldn't do things differently, but I'd have more confidence and agonize less over my choices. I would tell my younger self to keep going and not listen to naysayers who said I wouldn't be able to have this career and also have a family—because today I'm married with two kids and doing the exact job I set out to do. It is stressful, but it's recognized that parents in medicine and research are juggling work and home responsibilities. It's still challenging in some environments to be able to leave the lab or office to go pick your kids up from daycare, but at least it's a topic that's discussed now and not something you feel you have to hide.

Q: How easy is it to achieve work-life balance in your career setting?

A: Balance may not be the best word. Juggling might be better. Sometimes you have grant deadlines or very sick patients and you have to give priority to them and utilize babysitters, partners, daycare, grandparents, whomever, to pick up the slack with your kids. And you have to work at not feeling guilty about that. You have to focus on what is important today. On the flip side, sometimes your family just really needs you and you need to set boundaries at work to meet those needs. Life is short and you need to make time for the special people in your life.

Q: What advice do you have to offer readers about deciding on a career path?

A: If they decide to go into academic research, they should educate themselves on what the university expects of them. For instance, if you're starting a research career, you want to know the duration of guaranteed salary they offer, and how they will help support you in setting up a lab, with operating and administrative costs, and the salaries for your staff. You want to become familiar with the requirements for promotion in advance (from assistant to associate professorship and associate to full professorship). I found it helpful to go to the new faculty orientations offered by UCSF and UCSD, and suggest that others do the same. You need to know what is expected of you so you don't get left behind; periodically talk with your chair or division chief to understand exactly what you need to do to be sure you're on track for promotion. Typically, three areas need to be addressed for you to get promoted: (1) you need to do clinical work; (2) you need to do research and get published; and (3) you need to perform service to the university, which consists of things you're not paid to do like helping to promote the university and serving on committees. And of course find good mentors—you need them every step of the way!

A CAREER IN PRIVATE PRACTICE

PRIVATE PRACTICE

Edward J. Fox, MD, PhD
Director
MS Clinic of Central Texas
Central Texas Neurology Consultants
Round Rock, TX

Edward J. Fox, MD, PhD, has been in private practice since he opened a solo practice outside of Austin in Round Rock, TX, in 1992 after completing his neurology residency. He's since grown the practice into Central Texas Neurology Consultants and has partnered with several providers. He personally focuses on multiple sclerosis (MS) and related diseases, and is an investigator in clinical research trials studying MS disease-modifying therapies (DMTs), as well as methods of managing the disease as it worsens. He has received numerous awards, including the Super Doctor award from Texas Monthly *magazine, and is on the Board of Governors for the Consortium of Multiple Sclerosis Centers (CMSC).*

Dr. Fox received his PhD in immunology and a doctorate from Baylor College of Medicine's Medical Scientist Training Program in Houston, where he also did his internship and residency.

Q: How did you arrive at your current position?

A: I went right from residency to opening my own private practice. This was almost 30 years ago, and Round Rock was a small town. Today, it is much larger and is best known as the world headquarters for Dell Computers. I joined the local hospital staff and decided to open a private practice as a solo practitioner. Over time, four other physicians joined the group, so I could focus exclusively on MS and run clinical trials, which I've been doing for the past 20 years. I receive grants from pharmaceutical companies to perform research, which is not uncommon for MS specialists. A lot of research sites are not university based, but rather run out of private practices.

Q: What are the pros and cons of working in a private practice setting?

A: The pluses of working in a private practice are that you get to develop the schedule you want to keep. I also got to hire personnel so I could create my own MS clinic. Of course, at the time I started out in 1992, there were no MS disease-modifying therapies (DMTs) available, so I was able to grow with the subspecialty. Today, a person would have to do an MS fellowship; he or she couldn't learn on the job as I did because there are close to 20 DMTs with different mechanisms of action available and the diagnosis and management of people with MS is much more complex.

It's also difficult to start your own solo practice today, and I wouldn't recommend doing that. But you could go into an established neurology group or hospital system practice as an MS specialist. Having an MS specialist on staff is attractive to groups today because these providers produce a lot of revenue, ordering routine magnetic resonance imaging (MRI) scans and labs, providing infusible DMTs via the establishment of an infusion suite, and referring to physical therapy and other departments.

The cons of private practice are that you are not guaranteed a salary long-term, so you need to find a practice where there is a need for your services. And if you want to do clinical research, you have to understand that it can take years to develop a good

research team. I have found that I couldn't stay in business if I only saw patients for routine medical care; I need to do clinical research, too, to be financially successful.

If you are going to be the MS specialist in a group or hospital practice, you need to have had very good training in a fellowship program because other providers will be looking to you to be the expert. You also need to be part of a national network like the CMSC and the American Academy of Neurology, going to their annual and regional meetings and meeting others in your field. You have to become known in the community by volunteering to give talks at the local National MS Society chapter and other support groups. You also need to be a good business manager as well as a clinician and a researcher, if that's what you want to do.

Q: How easy is it to achieve work-life balance in your career setting?

A: This is one of the great benefits of private practice: Achieving work-life balance can be easy, especially if you work in a suburban or rural area. I set my own hours and I'm not on call as I would be in academic settings. I don't have a long commute (4 minutes each way) and I can go home at a moment's notice if I need to. And there are fewer emergencies to deal with if you are not on call for a busy hospital.

More than 50% of residents going into neurology today are women, and I think that's because early in their careers they can find positions allowing for part-time hours with more freedom for maternity leave and child care. They can also take on shift work at a hospital to manage their schedule so they have family time.

"First, MS is a very satisfying subspecialty that offers providers an opportunity to really impact their patients' lives. Second, I would advise people to start looking for opportunities early."

Q: What advice do you have to offer readers about deciding on a career path?

A: First, MS is a very satisfying subspecialty that offers providers an opportunity to really impact their patients' lives. Second, I would advise people to start looking for opportunities early. You have a limited amount of time in training, so look for a specialty and career track that really piques your interest and investigate it. Interact with established people who are doing what you might like to do, go online to hear about different practice settings, and attend local and national meetings and talk to people about what they do. It's never too early and it's never too late to think about your career track.

Comments, Suggestions?

Generations' editors are eager to hear what you think of the publication. Please complete our short survey.

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Submit comments to the publisher, Joseph D'Onofrio, at jdonofrio@delmedgroup.com.

A CAREER AT A GOVERNMENT AGENCY

GOVERNMENT AGENCY

Shila Azodi, MD
Medical Officer
US Food and Drug Administration
White Oak, MD

Shila Azodi, MD, received her medical degree from Texas Tech University Health Sciences Center in Lubbock, TX. She did her internship and residency at Dell Medical School at the University of Texas in Austin. In 2015, she moved to the National Institutes of Health (NIH) in Bethesda, MD, as a Clinical Research Fellow, and then in 2018 to the Food and Drug Administration (FDA) in White Oak, MD, as a Medical Officer in the Division of Nonprescription Drugs. In June of 2019, in addition to her FDA duties, she began to see neurology patients as an Attending Physician at the Veterans Administration (VA) hospital in Washington, DC.

Q: How did you arrive at your current position?

A: During my medical school interviews, I always listed Dr. Frances Kelsey, a medical officer at the FDA who had blocked the approval of thalidomide, as one of my role models. I didn't know at the time how she had gotten that position, or if it was even an option for me, but I admired Dr. Kelsey's dedication to public health and safety. As a neurology resident, I worked with Consortium of Multiple Sclerosis Centers (CMSC) member Dr. Edward Fox and his clinical research team at the Central Texas Neurology Consultants clinic. While there, I got to see how complex clinical information was being integrated into care for patients with MS and how to provide a holistic approach to care. Dr. Fox nominated me to attend the Foundation of the CMSC Mentorship Program. Learning about advances in MS care as well as all of the challenges that remain from MS leaders like Patricia Coyle, Stephen Krieger, Daniel Pelletier, and Fred Lublin sealed the deal for my dedication to treating patients with MS and pursuing advancement of our understanding of MS. From there, with the help of Dr. Fox, I applied for MS fellowship programs and decided to go to the NIH.

As my fellowship was ending, I started looking at different career options that would combine clinical care and intellectual challenges. The FDA position opened and I thought I might like it, especially if I could combine it with MS clinical care. Luckily, Dr. Mitchell Wallin and Dr. Heidi Maloni were willing to have me work half a day a week in the Washington DC VA MS Center of Excellence!

Q: What are your responsibilities as a Medical Officer?

A: As a Medical Officer, my general mission is to ensure that drugs are safe and effective with truthful and informative product labeling. Specifically, in the nonprescription division, as part of a multidisciplinary team I review investigational new drugs (INDs), new drug applications (NDAs), and post-marketing safety data. Nonprescription products are selected and self-administered without a healthcare intermediary, so I collaborate closely with social scientists in our division to ensure labeling is consumer friendly.

Q: What are the pros and cons of working for a government agency?

A: The big advantage of this job is that it is very impactful. Additionally, the work schedule enables

work-life balance: I work a total of 40 hours a week including professional development time, which I use to work at the Washington DC VA MS Center of Excellence seeing patients. At the clinic, my focus is 100% on neuroimmunology, including patients with MS, neuromyelitis optica spectrum disorder (NMOSD), and other related conditions. I love that I have the flexibility to maintain my clinical skills by working at the VA.

A potential con is that I must make sure I don't have any conflicts of interest. For instance, I can't do a clinical research project with a pharmaceutical company while working for the FDA.

Q: Why did you decide on MS as a subspecialty?

A: As soon I took my first course in neuroscience in medical school, I was thirsty for more knowledge about the brain and diseases that can affect it. I saw that MS can affect women and men at an active and formative time of their lives when they are making big life decisions, including raising families and pursuing careers. I wanted to empower and inform patients to take care of their MS and health so they can lead their ideal lives.

Q: How do you feel supported by the Consortium of Multiple Sclerosis Centers (CMSC) and its Foundation (FCMSC)?

A: Attending the FCMSC Mentorship Program on careers in 2014 was really helpful to me in deciding on a career path. And I've been utilizing the CMSC and FCMSC resources more and more during the pandemic, and have relied on them to get COVID-19 and MS updates. I recently contacted CMSC MS Professionals in Training (MS-PiT) leader Dr. Ahmed Obeidat to learn more about MS curriculum development and he provided excellent resources available from CMSC. I am looking forward to the next annual meeting!

Q: How easy is it to achieve work-life balance in your career setting?

A: Along the spectrum of possible work-life balance as a physician, I think my current setup offers an excellent balance. I have the chance to pre-plan my week—I have work, social activities, chores, exercise, etc., all on the calendar, along with some white space to allow flexibility. When I start my week, I don't waste time worrying about forgetting a deadline or not getting time for family or fun. During the pandemic, outdoor recreation has been really key—my husband and I have been rock climbing and hiking. I really miss seeing my sister and sister-in-law who live in Texas, but we have made weekly Great British Baking Show watch parties, board-game FaceTimes, and Zoom baking a new way to stay connected.

"It is impossible for all aspects of medicine to be represented in a neurology residency program, so I highly encourage you to be creative in planning electives—if you want more exposure to a subspecialty, regulatory science, clinical research, policy, teaching, global medicine, etc., design the elective and go for it!"

Q: What advice do you have to offer readers about deciding on a career path?

A: Medical school and residency may make it seem like there is a very direct path to take to your career. But it is impossible for all aspects of medicine to be represented in a neurology residency program, so I highly encourage you to be creative in planning electives—if you want more exposure to a subspecialty, regulatory science, clinical research, policy, teaching, global medicine, etc., design the elective and go for it! Additionally, not all mentorships will come in the form of a formal mentorship program; with few exceptions, most people working in healthcare will take the time to answer your questions and be a resource.

A CAREER IN THE PHARMACEUTICAL INDUSTRY

PHARMACEUTICAL INDUSTRY

James M. Stankiewicz, MD
Executive Medical Director
Novartis
Boston, MA

James Stankiewicz, MD, graduated from Loyola University Stritch School of Medicine in 2002 and interned in internal medicine at Mount Auburn Hospital in Cambridge, MA. He then did his residency in neurology at Tufts University School of Medicine, and a clinical fellowship in multiple sclerosis (MS)/neuroimaging at Brigham MS Center in Boston, MA. He pursued a clinical career at the Brigham MS Center for a decade while on faculty at Harvard Medical School. In July 2020, he started a new role as Executive Medical Director at Novartis.

Q: How did you arrive at your current position?

A. I had been working in academia and at an MS center for a while and I am a restless person, so I was looking for something new and different. It was tough to leave my patients, but I thought that having the larger platform afforded by Novartis could help me impact the lives of millions of people with MS around the world versus the 1,000 or so patients I followed at the Partners MS Center for nearly a decade and a half.

Q: What are your responsibilities as an Executive Medical Director?

A. I look at my job as one that is dedicated to public health—one in which I generate medical evidence through research studies to help my medical colleagues understand MS medications better in order to use them most efficiently. Specifically, I design and execute clinical trials, educate MS clinicians about Novartis disease-modifying therapies, offer input to the global team about development and additional studies we need to do, give feedback on internally proposed trials, and review external grant proposals and help prioritize funding.

Q: What are the pros and cons of working in industry?

A. A pro is that every day is different—there is no standard workday. I am engaging my mind in different ways than I used to. I need to think about new problems every day, and take deep dives into subjects that I haven't looked at in any depth before. I like that I can now have a larger impact on the MS field than I had as a practicing clinician. I also have the ability to control my schedule better than I did as a clinician. Novartis has a policy that you can work where and when you want to, so you can arrange your hours to take a break in the afternoon, for instance, if you want to run an errand or go for a walk.

A potential downside is that I find that I am attending a lot of meetings. This, however, may be an artifact of the COVID pandemic.

Q: If you had to do it over, what would you do differently in terms of your career path? Were your career choices intentional?

A. I actually haven't done any real planning or strategizing. Instead, I've gone with the flow and that's worked out for me. I'm glad I waited to go into industry, though. I had been told that it was better to join a pharmaceutical company sooner rather than

later in your career, but then I would have been in a junior-level position. By waiting until I was established, I joined Novartis at a senior level and I have the benefit of having been on the other side, working with patients directly and in academia, which offers a broad perspective of the MS field and the needs of patients and providers.

"Remember that if you decide to go down one career path, you can always switch paths in the middle of your career, and even switch back after that."

Q: How easy is it to achieve work-life balance in your career setting?

A. It's not difficult since I work on a corporate schedule. I expect to continue to work from home throughout the pandemic and perhaps beyond.

Q: What advice do you have to offer readers about deciding on a career path?

A. The biggest thing is to listen and explore the opportunities that might be out there. Since we all emerge from an academic background, it's commonly believed that academic medicine is the only career path for many doctors. But there are many other job opportunities out there—in the pharmaceutical world, at the Food and Drug Administration, or in non-governmental organizations—that may suit you well. And you should remember that if you decide to go down one career path, you can always switch paths in the middle of your career, and even switch back after that. Be sure to negotiate any offers you get, though, to ensure they meet your requirements. I had been offered a number of jobs in the pharma industry in the past and declined because they didn't meet my requirements. In retrospect, I see that if I had accepted them, I would have sold myself short.

FOUNDATION
of the Consortium of
Multiple Sclerosis Centers

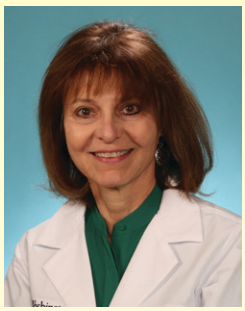
Be sure to routinely monitor the FCMSC website for important initiatives for MS healthcare professionals in training!

Website: https://cmscfoundation.org/

FCMSC Mentor Directory

The following MS specialists have graciously agreed to respond to questions from readers of *Generations*.

Shila Azodi, MD
Topic: Government career
Contact: shilaazodi@gmail.com



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Ahmed Obeidat, MD, PhD
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Laura Piccio, MD, PhD
Topic: Research career
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James M. Stankiewicz, MD
Topics: Pharmaceutical industry, MS center careers
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FCMSC Mentorship Program "Graduate"

Focus on Laura Piccio, MD, PhD

Brain and Mind Centre
The University of Sydney
New South Wales, Australia
and Department of Neurology
Washington University School
of Medicine
St. Louis, MO, USA

Laura Piccio, MD, PhD, first attended a Consortium of Multiple Sclerosis Centers (CMSC) Annual Meeting in 2008, when at the suggestion of her mentor Anne Cross, MD, she applied for and won a Whitaker Research Prize. "I have gone back to the meeting several times since then to network and try to find mentors," she says. "I like the meetings because they blend both clinical and research topics, and they attract top people in the field of multiple sclerosis (MS) that I can meet in person."

Dr. Piccio, who is originally from Italy and did her residency in neurology and her PhD in neurological science at the University of Milan, always knew that she wanted to pursue a research career. "During my residency, I was allowed to spend 1 year abroad, so I went to Washington University School of Medicine in St. Louis to do a research fellowship in immunology," she recalls. There, she pursued Dr. Cross at the suggestion of others at the school, given her interests. "Dr. Cross originally was too busy to talk with me and I followed up a few times, but we didn't connect until just as I was getting ready to return to Italy. I ended up doing a 3-year postdoctoral fellowship with her starting in 2005 that was supported by the National Multiple Sclerosis Society. After that, the University offered me a position as a research instructor in neurology." She was promoted to Assistant Professor in 2010 and then Associate Professor in Neurology in 2016. "I started my own research group, which is still ongoing, although I moved with my husband and son to Sydney, Australia, 2 years ago to work at the University of Sydney." Dr. Piccio currently has joint appointments at both institutions. The position at Washington University is dependent upon her ability to obtain grant funding, while her position in Sydney is salaried. She has several ongoing projects at both institutions, although due to COVID-19 she has not been able to return to St. Louis since March 2020.

Dr. Piccio highly recommends that fellows and early-career physicians/researchers create their own network of contacts and mentors, who can help them in setting career goals for both the short and long term, with an eye to how they see their careers progressing in the future.

Her Research Focus in MS

Dr. Piccio reports that "My research interest is to investigate immune-inflammatory and neurodegenerative mechanisms leading to MS and other neurological diseases," she says, adding, "My research has a strong translational approach, with the goal of applying findings from basic research to the clinic." Currently, she is studying the role played by innate immune cells (macrophages, dendritic cells, and microglia) in MS with a particular interest in the innate immune receptor TREM2. A second area of interest is the effects of intermittent fasting on MS and the complex interplay between the immune system and metabolism.

CMSC Career Support

The CMSC has been critical to Dr. Piccio's career advancement in the MS field. For one thing, she met Michael Racke, MD, Immediate Past-President of the CMSC, by attending the Annual Meeting, who invited her to other events, recommended her to be an Editor-in-Chief of the *Journal of Neuroimmunology*, and still counsels her to this day.

On an everyday basis, "Anne Cross has also been essential to my career," she says. "She was very supportive and gave me guidance and feedback when I was a trainee/fellow and first came onto the faculty. We met regularly and she gave me career advice and encouraged me to apply for grants. Later we started to work together as colleagues on projects. And it was so much easier for me to start my research career because Dr. Cross was supporting me as a member of her research team."

Dr. Piccio highly recommends that fellows and early-career physicians/researchers create their own network of contacts and mentors, who can help them in setting career goals for both the short and long term, with an eye to how they see their careers progressing in the future. "Do you want to pursue an academic career, where you do research in a university setting, or do you want to be a clinician researcher? Many people in the MS field do both clinical care and research, and teach. Clinician researchers are very important because you get a full picture of both the clinical problem and the basic research approach. I am certainly glad that I had that type of preparation myself," she says.

Dr. Piccio has now herself mentored several medical students, visiting researchers, and postdoctoral fellows. "I find it very rewarding to mentor others," she says. "These young investigators have a lot of energy and enthusiasm, which can be contagious. I've learned a lot from my mentees, too. You become very close because you spend a lot of time working together in the lab. And I wouldn't be able to manage a joint appointment today if I didn't have fantastic associates to continue our work in St. Louis when I can't be there."

CMSC Annual Meeting Moved to Fall 2021

We are happy to report that the 2021 Annual Meeting of the Consortium of Multiple Sclerosis Centers (CMSC) has moved location and dates to Orlando, FL! Mark your calendars for Monday, October 25-Thursday, October 28, 2021 to attend our hybrid meeting at the beautiful Rosen Shingle Creek. More information about how you can attend both virtually and live will be announced soon, with details about registration, hotel reservations, and much more.

Please visit our website MSCARE.ORG/2021 for all the updates.

See you in Orlando!

MS Disease-Modifying Therapies (DMTs)

BY AHMED Z. OBEIDAT, MD, PHD

The treatment landscape for multiple sclerosis (MS) is ever-expanding. Our understanding of MS pathogenesis has led to innovations and the development of several disease-modifying therapies (DMTs) with various mechanisms of action (MOAs). In turn, our knowledge of the MOAs of various DMTs has provided insights into MS pathogenesis. This is exciting, as more treatments are being developed, allowing for increased understanding of the immunopathogenesis of MS and continuing to equip patients with the hope to achieve better control of their lifelong disease.[1]

Nearly 20 DMTs are currently approved by the Food and Drug Administration (FDA).[2] Many DMTs share similar MOAs and can be grouped into classes based on that MOA.[1,3] One may also classify DMTs based on their route of administration into injectables, oral medications, or infusions.[2] (see Table, page 18) Alternatively, some may classify DMTs based on their effects on the immune system into categories such as immune modulators, immune suppressants, or agents that result in immune depletion followed by immune reconstitution.

Nearly 20 DMTs are currently approved by the Food and Drug Administration (FDA). Many DMTs share similar MOAs and can be grouped into classes based on that MOA.

Most DMTs require a prolonged treatment duration—for years or even decades to maintain treatment efficacy.[1,3] A few treatments may allow for transient immune depletion followed by partial reconstitution, which provides an alternative way of thinking about the disease process and the ability to maintain remission in subsequent, treatment-free years.[1 3]

In addition to DMTs, autologous hematopoietic stem cell transplant (AHSCT) is currently being tested in randomized, multicenter, clinical trials against the best available non-AHSCT therapies.[4] AHSCT is based on conditioning treatment followed by immune reconstitution.

Classification Based on Route of Administration

Injectable DMTs include interferon beta-1a (Avonex®, Rebif®, Plegridy®), interferon beta-1b (Betaseron®, Extavia®), glatiramer acetate (Copaxone®, glatiramer acetate, and Glatopa®), and more recently, ofatumumab (Kesimpta®). Most can be injected into the subcutaneous tissue, except for Avonex® and Plegridy®, which are administered intramuscularly. Injection was the first route of administration, approved in the early 1990s, for DMTs for MS treatment.

Oral DMTs. In 2010, the FDA approved the first oral medication, fingolimod (Gilenya®). This was a sea change that provided patients with a pill to take, which was revolutionary at the time. Soon after, two other oral medications followed, including teriflunomide (Aubagio®) and dimethyl fumarate (Tecfidera®). Most recently, siponimod (Mayzent®), cladribine (Mavenclad®), ozanimod (Zeposia®), diroximel fumarate (Vumerity®), and monomethyl fumarate (Bafiertam®) have gained FDA approval and were added to the oral DMT profile.

Infusible DMTs. The FDA approved mitoxantrone (Novantrone®) for worsening MS and some progressive MS forms in 2000; this was followed thereafter by natalizumab (Tysabri®), alemtuzumab (Lemtrada®), and ocrelizumab (Ocrevus®) for relapsing forms of MS (RMS).

DMTs by Route of Administration		
Injectable	**Oral**	**Infusible**
Avonex®	Aubagio®	Lemtrada®
Betaseron®	Bafiertam®	Novantrone®
Copaxone®	Gilenya®	Ocrevus®
Extavia®	Mavenclad®	Tysabri®
Glatiramer Acetate	Mayzent®	
Glatopa®	Tecfidera®	
Kesimpta®	Vumerity®	
Plegridy®	Zeposia®	
Rebif®		

Classification Based on MOA

Receptor binding and transcriptional pathway changes. DMTs in this category include the polypeptides interferon beta-1a and interferon beta-1b (average molecular weight [MW]: 40036 Da).[5] Interferons bind to interferon receptors on human cells and act by modulating the immune response through various pathways. Their binding to the human INF receptor can positively impact the JAK/STAT pathway's transcription. This can reduce the proliferation of proinflammatory T cells, but induces regulatory T-cell activity. Furthermore, these drugs may have a favorable effect on specific subsets of B cells, including transitional B cells.[1-3,5] Interferons can also inhibit proinflammatory cytokine production and immune cell migration through the blood-brain barrier (BBB) and destructive effects of matrix metalloproteinases.[1-3,5,6]

Binding to major histocompatibility complex (MHC) molecules. Glatiramer acetate is a synthetic polypeptide (average MW: 7000 Da). The molecule binds to MHC complexes and competes with other antigens presented to T cells. Glatiramer may also directly inhibit some antigen-presenting cells and activate helper T cells type-2, orchestrating a more favorable immune response.[1-3,5]

DNA-acting agents. Mitoxantrone, an organic compound (average MW: 444.4809 Da), directly interferes with DNA repair. It binds to DNA and causes breakage in the nucleic acid. It inhibits immune cell migration and the secretion of proinflammatory cytokines. Another example in this group is cladribine, which was recently approved by the FDA.[1,5] Cladribine is a synthetic purine nucleoside (average MW: 285.687 Da) that exerts its therapeutic effect in MS by DNA strand breakage and inhibition of DNA synthesis and repair in selective cells, resulting in ATP depletion and cell apoptosis. Affected cells mostly include the B and T lymphocytes, and to a lesser extent, other cells such as neutrophils. The selective effect is because cladribine accumulates in cells where its degradation by the adenosine deaminase enzyme is not as effective. Those cells have a higher ratio of phosphorylating to dephosphorylating enzymes, resulting in higher levels of activated cladribine and subsequent DNA damage and cell death.[1-3,5]

Sphingosine 1-phosphate (S1P) modulators. S1P receptors are ubiquitous and have several subtypes. Those of interest for MS include the $S1P_1$ and the $S1P_5$. Fingolimod (average MW: 307.4708 Da) is the prototype and was first approved in 2010. It binds with high affinity to $S1P_{1,3,4,5}$. A second example is siponimod (average MW: 516.605 Da), which binds with high affinity to $S1P_1$ and $S1P_5$. A third example is ozanimod (average MW: 404.47 Da), which binds with high affinity to $S1P_1$ and $S1P_5$. All three are currently FDA-approved to treat RMS. S1P modulators are thought to exert therapeutic effects as sequestering agents by preventing the egress of lymphocytes from lymph nodes, thus reducing the circulation of activated lymphocytes and preventing their migration to the central nervous system (CNS).[1,5,7] Furthermore, growing evidence suggests that S1P modulators may exert direct effects within the CNS through their effects on neurons and glial cells. Further studies are needed to confirm an effect of this class of medications within the CNS. Several other molecules from this class are currently in the pipe-

line. For example, ponesimod (average MW: 460.97 Da), which has a high affinity to $S1P_1$, is currently in phase III randomized clinical trials.[8]

Enzyme inhibitors. Teriflunomide (average MW: 270.2073 Da) is the active metabolite of leflunomide. It is an inhibitor of the mitochondrial enzyme dihydroorotate dehydrogenase, which in turn inhibits pyrimidine synthesis, subsequently leading to inhibition of proinflammatory cytokines and T-cell activation.[1,5] Bruton's tyrosine kinase inhibitors (BTK inhibitors) are a novel class of medications currently being investigated in clinical trials.[9] Second-generation BTK inhibitors mainly target activated B cells. Some covalent BTK inhibitors include evobrutinib (average MW: 429.524 Da) and SAR442168 (average MW: 455.51 Da).[5,9,10] An example of a reversible BTK inhibitor is fenbrutinib (average MW: 664.811 Da).[11] All three molecules are now being investigated in randomized clinical trials.

Nuclear factor (erythroid-derived 2)-like 2 (Nrf2) pathway activators. This group of medications includes several fumarates. First in class for MS is dimethyl fumarate (DMF, average MW: 144.1253 Da). Once ingested, DMF is degraded to monomethyl fumarate (MMF). Diroximel fumarate (average MW: 255.226 Da) was approved by the FDA in 2019, and is also metabolized to MMF. In 2020, MMF (average MW: 130.099 Da) was approved by the FDA for the treatment of MS. For all three products, the MOA in MS is thought to be through the activation of the nuclear factor (erythroid-derived 2)-like 2 (Nrf2) pathway.[1,5,12] However, growing evidence suggests that fumarates may also exert a therapeutic effect by causing a shift toward anti-inflammatory lymphocyte subsets (such as helper T2 and regulatory T cells) and reducing proinflammatory subsets (such as helper T1 and T17 and cytotoxic T cells).[12]

The future holds great opportunities for the upcoming generation of MS professionals to advance immunotherapeutics in MS and discover the molecules that will help the CNS repair some of the damage caused by the autoreactive immune system.

Monoclonal antibodies.

CD20-expressing cell-depleting agents

The first medication of this group used to treat MS, off label, was rituximab (Rituxan®) (average MW:143859.7 Da). Ocrelizumab (average MW: 145000.0 Da) was the first drug in this class to be approved by the FDA for the treatment of RMS as well as for primary-progressive MS. Most recently, ofatumumab (average MW: 146100.0 Da) was FDA-approved to treat RMS. Ublituximab (average MW: 144500 Da) is currently in phase III clinical trials. This class of medications exerts a therapeutic effect by depleting circulating B lymphocytes, which are implicated in MS immunopathogenesis.[1,5,13]

CD52-expressing cell-depleting agent

Alemtuzumab (average MW: 145453.8 Da) is FDA-approved to treat RMS. Alemtuzumab exerts its therapeutic effect by depleting immune cells expressing the CD52 antigen through antibody-dependent cytotoxicity.[1,5] The medication is typically given in two treatment cycles over 2 years with the goal of sustained benefit over time. In addition to B and T lymphocytes, alemtuzumab affects other cells, including monocytes and eosinophils.[1,14]

Leukocyte adhesion molecule inhibitors

Natalizumab (MW: 149000 Da) is a monoclonal antibody against the alpha-4 subunit of VLA4 integrin. It works by preventing VLA4 binding to VCAM-1,

which reduces lymphocyte migration into the CNS, thus exerting a therapeutic effect in RMS.[1,5]

AHSCT

AHSCT has been investigated in several relatively small studies.[15] A large multicenter clinical trial is underway titled "Best Available Therapy Versus Autologous Hematopoietic Stem Cell Transplant for Multiple Sclerosis (BEAT-MS)."[16] The concept of immune depletion followed by immune reconstitution applies for AHSCT. Multiple conditioning regimens have been used by various investigators and are classified based on their intensity (high, medium, and low). The feasibility and safety of AHSCT have improved over the past decade. At this point, it is still experimental until its use in clinical practice is approved, which will be based on efficacy and safety findings from large clinical trials.[4,15]

Neurodegeneration and CNS Repair

As discussed above, several treatments have the potential of suppressing visible inflammation in MS. Current treatment goals include the concept of no evidence of disease activity (NEDA). NEDA-3 includes no evidence of clinical relapses, no new magnetic resonance imaging (MRI) activity, and no evidence of disease progression. NEDA-4 adds no brain atrophy, and NEDA-5 adds no neurodegeneration or injury biomarkers.[17] These are ambitious goals of treatment in MS, and while NEDA-3 can be achieved in some patients, the success in achieving NEDA-4 or NEDA-5 remains in early stages.[17]

MS is a complex, heterogeneous disease with multiple pathogenic mechanisms. Most of the available treatments may not cross the inflamed BBB, based on MW or charge, and other chemical characteristics. There is a significant unmet need for centrally acting treatments for MS. Several candidate molecules have been investigated, including biotin, clemastine, statins, anti-lingo, low dose naltrexone, and hormones (estrogens, testosterone, and thyroid).[18] Other interventions being investigated include aerobic exercise, dietary modifications, and stem cell injection.[18,19] None of the efforts has proven successful for CNS repair in MS to date. One possibility is that a single approach may not be sufficient, and one needs to employ combination therapies to target complex neuropathogenic mechanisms of the disease.

The future holds great opportunities for the upcoming generation of MS professionals to advance immunotherapeutics in MS and discover the molecules that will help the CNS repair some of the damage caused by the autoreactive immune system.

Beyond DMTs: Clinical Care for People Living with MS

MS often visits with no warning and is mostly accompanied by uncertainty. People with MS may not exhibit visible physical symptoms, thanks to brain reserve and neural plasticity. However, they could be suffering and in need of comprehensive medical care. Fatigue, depression, pain, spasticity, bladder, bowel, and cognitive challenges are just some of what can be considered invisible symptoms related to MS. As a future care partner to your patients, it is essential to openly discuss all aspects of their lives with MS. Having an open dialogue and being a great listener are vital for your success in caring for people with MS. Remember that you are part of a team, and that team starts at their home and their circle of support. Try to be one member of this circle and connect them to other people like you who can provide additional help. Remember to discuss mental health, overall well-being, and treatment of comorbidities, and encourage a healthy lifestyle. Discuss diet, exercise, water intake, sleep, coping strategies, stress management, and smoking cessation if applicable. No matter how advanced MS is, there is always something you can do to help, even if it simply means yielding a listening ear. To succeed, show support, provide access, encourage questions, keep hope alive, and never give up.

MS care has advanced over the past two decades. A sea change in the therapeutic landscape, coupled with access to multidisciplinary care, has considerably improved the lives of people with MS. The mission continues with education, research, and excellent clinical care.

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Continued from page 2

The CMSC itself has also established an MS Professionals-in-Training Special Interest Group (MS-PiT SIG) that seeks to develop an international network of multidisciplinary professionals-in-training to encourage interest in the treatment and research of MS, and to increase the number of healthcare professionals providing care to people living with this chronic disease.

Check out these websites for more information about MS and the Workforce of the Future:

FOUNDATION of the Consortium of Multiple Sclerosis Centers

Consortium of MS Centers (CMSC): https://www.mscare.org
Foundation of the CMSC: https://cmscfoundation.org/

To view a video of the FCMSC 2020 Virtual Mentorship Forum, visit: https://cmscfoundation.org/ms-workforce-of-the-future-mini-forum-program/

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