This month's feature highlights three articles, one of which focuses on COVID-19, that appear in the current issue of Mayo Clinic Proceedings. These articles are also featured on the Mayo Clinic Proceedings' YouTube Channel (https://youtu.be/GD7YUqXt2Vo).

THE POWER AND PRECISION OF PREDICTIVE GENOMIC TESTING

The interplay of "nature and nurture" is uniquely relevant to disease susceptibility as the latter is governed by genetic and environmental/behavioral determinants. Environmental and behavioral factors that reduce such risk are widely agreed upon - clean air and water, sanitation, cardiorespiratory fitness, a Mediterranean-based diet, stress reduction, and avoidance of smoking, among others. Of rapidly growing interest are the genetic factors that lurk unseen in otherwise healthy individuals and which may be harbingers or determinants of subsequent disease. The development of next generation sequencing and related technologies has significantly advanced the exploration of such genetic determinants, broadening genetic testing from its relatively constricted focus of probing for a single or a limited number of genes in individuals with a relevant personal/family history to a more expansive and encompassing one termed predictive genetic screening. Such screening examines panels of genes and their respective variants. In the present issue of Mayo Clinic Proceedings, Anderson et al report on their retrospective analysis of findings derived from predictive genomic testing undertaken in the clinical setting. The study population involved essentially healthy individuals followed in the Mayo Clinic Executive Health Program who chose to undergo such testing. In the pretest phase these participants met with a genomic nurse and genetic counselor, and a three-generation pedigree and family risk evaluation was undertaken in each participant. Thereafter, participants selected one of the three available predictive genomic testing platforms, and in the event that a personal or family history raised particular concerns, participants were counseled by genetic counselors on the platform that may be the most appropriate. Variants were categorized into one of three groups: 1) clinically actionable genes based on the compilation of 59 genes by the American College of Medical Genetics and Genomics Working Group and which are mainly incriminated in cancer syndromes and cardiovascular disease; 2) risk alleles; and 3) carrier status. The findings of Anderson et al demonstrate that almost 12% of participants had at least one clinically actionable result, with genetic variants largely involving pseudocholinesterase deficiency; familial hypercholesterolemia; cardiomyopathy; myopathy; and hereditary syndromes involving breast and colorectal cancers, breast and ovarian cancers, and colorectal cancers. Approximately 50% of participants with clinically actionable results involving hereditary cancer genes warranted genetic assessment according to the guidelines of the National Comprehensive Cancer Network; some 50% of participants with clinically actionable results were without a relevant personal or family history for the gene that was detected. Well over 50% of participants were carriers of a recessive condition, and more than 40% of
participants exhibited a variant for a multifactorial disorder. This analysis by Anderson et al is important and timely from several perspectives including the following: First, it is one of very few studies, if not the only study, which undertook such an analysis in a clinical “real-world” setting, and not within the context of a research protocol. Second, it uncovers the relatively high prevalence of such genetic variants with clinically actionable findings in otherwise healthy individuals. Third, it underscores the discerning power of this technology as pathogenic variants are detected in a substantial number of individuals without any personal or family history for hereditary diseases. Fourth, it provides a paradigm and process for predictive genetic screening in large medical centers. Fifth, over the 5-year time frame in which the analyses were conducted, it shows how newer platforms and updates can be effectively incorporated, a particularly relevant consideration since innovation and refinement in these technologies will indubitably occur in the coming years. And sixth, it holds out the hope—a broadly held one in the provision of health care and medical practice—that by detecting pathogenetic footprints which presage the development of disease, remedying or mitigating the disease and its consequences may be more likely achieved.


Fecal Microbiota Transplantation in the Time of COVID-19

A major cause of health care–associated infections, Clostridioides difficile infection (CDI) afflicts approximately 500,000 individuals each year in the United States, is recurrent in more than 80,000 patients, and imposes almost $5 billion in health care costs; each year CDI causes some 30,000 deaths. For patients with recurrent CDI, experts recommend fecal microbiota transplantation (FMT) as a preventive strategy because of the remarkable efficacy with which FMT decreases recurrence of CDI (Cho JM, Pardi DS, Khanna S. Update on treatment of Clostridioides difficile infection. Mayo Clin Proc. 2020;95(4):758-769). However, as is true for so many aspects of health care, the practice of FMT has been challenged and constrained by the current COVID-19 pandemic for reasons that include, among others, the following: 1) FMT is generally considered an elective procedure, and at certain stages of the pandemic especially during surge situations, elective procedures were placed on hold; 2) SARS-CoV-2 can be transmitted via the fecal-oral route, but the likelihood and duration of such transmission of SARS-CoV-2 in asymptomatic individuals are currently unknown; potential stool donors thus need to be effectively screened so as to avoid the transmission of SARS-CoV-2 during FMT; 3) a validated test to determine the presence of transmissible SARS-CoV-2 in stool is currently unavailable; and 4) supplies of donor stool obtained and banked before December 2019 (that is, well before the start of the pandemic in the United States) have steadily decreased in medical centers and in critical non-profit stool donor banks, such as OpenBiome, the latter currently unable to supply donor stool for FMT. In the present issue of Mayo Clinic Proceedings, Khanna et al report on their experience with FMT during the pandemic. The donor aspect of this experience involved 2 institutions, Mayo Clinic and University of Minnesota, both of which have had established donor programs. Every 2 weeks donors were screened for symptoms and a history of exposure to cases of COVID-19, by a nasopharyngeal PCR test for SARS-CoV-2, and, in the case of the program at Mayo Clinic, by appropriate serologies to delineate past exposure. Two donors in the donor program at Mayo Clinic during the pandemic tested negative for SARS-CoV-2 and donated stool samples used for FMT. Two donors of the six
donors during the pandemic at the University of Minnesota tested positive for COVID-19; because of adequate donor material collected and manufactured before December 2019 at this center, donor supplies obtained during the pandemic have not been used to-date for FMT. FMT was performed in 57 patients from May 26, 2020, through September 30, 2020, at Mayo Clinic. Three of the 19 patients who developed symptoms of recurrent CDI (rCDI) after FMT tested positive for rCDI, and, after FMT, there were no documented cases of COVID-19 within the period of follow-up, the latter being at least four weeks after FMT. This study by Khanna et al is significant for numerous reasons: It calls attention to yet another aspect of health care adversely impacted by the pandemic; it shows how experiences at two medical centers inform responses to challenges imposed by the pandemic in caring for patients with rCDI; it demonstrates how an FMT program for rCDI can be currently maintained in these challenging times, with such a program not only conferring its expected efficacy but also avoiding the transmission of COVID-19; it offers recommendations derived from this experience; and it highlights the need for further understanding of the likelihood, temporal profile, and pathobiologic significance of the excretion of SARS-CoV-2 in the stool in infected patients as well as the need for a test that reproducibly and accurately assesses such viral presence in stool.


PHYSICIANS WHO ARE OR WILL BE MOTHERS MUST RECEIVE MORE SUPPORT

Physician mothers face two sets of challenges: The first set arises because of the challenges and inequities traditionally encountered by women in pursuing careers in medicine; the second set originates from motherhood itself, its ramifications, and all that it entails. The challenges are complex, multi-layered, and, in some instances, catalytic. For example, because of the duration and demands in medical training (medical school, residency, fellowship, subspecialty fellowship), women may delay pregnancy, and such a delay itself may lead to additional issues such as an increased risk of pregnancy complications, infertility, and the possible need for adoption if parenthood is desired. As another example, reentry after maternity leave into medical training or practice is accompanied by added responsibilities of childcare and parenting; while this issue is certainly not unique to physician mothers, the medical training or practice they are reentering is usually exacting. There are very few, if any, comprehensive reviews of the available literature on this topic, a deficiency now rectified by the discerning article of Chesak et al in the current issue of Mayo Clinic Proceedings. Starting from almost 1200 articles from their search strategy, the authors gleaned 71 that met eligibility criteria and these included a mix of qualitative studies, quantitative studies, and studies using multiple methods. From these studies the authors extracted and compiled salient challenges that were identified and potential solutions that were offered. Challenges delineated in these studies were grouped into those with shared themes, the latter then categorized by Chesak et al according to three levels of influence of these themes. The individual level involved, for example, issues pertaining to work-life balance; career progression; pregnancy complications, infertility, timing of pregnancy, and adoption; and mood disturbances and burnout. Themes at the organizational and health care system level included lack of mentors and networks; impediments to breastfeeding; family leave policies; relatively inflexible schedules with demanding hours; and inadequate support for family planning and child-rearing. Finally, challenges were identified at a societal level and these involved issues pertaining to gender discrimination, maternal bias, and childcare. Chesak et al
also addressed strategies and solutions that may mitigate these challenges, emphasizing the importance of mentoring, the support of childbearing and childcare, improving family leave policy, promoting professional fulfillment and work-life balance, and dispelling the maternal bias that exists in medicine. While the issues delineated and discussed by Chesak et al are broadly applicable to women irrespective of their profession, career, or occupation, the special importance of the article by Chesak et al is its persuasive clarion call to the medical community that physicians who are, or wish to be, mothers must receive much more support and resources.


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