

coronary tone is much more complicated than just looking at the worse narrowing, or percent stenosis, in an epicardial coronary vessel. Thus, it is almost naive to define such a luminal narrowing as exemplifying the nature of coronary blood flow and coronary artery flow reserve. I believe that we need to deal with the physiology of ischemia (whether it is fractional flow reserve determined using computed tomography or traditional fractional flow reserve determined during coronary angiography or just true angina experienced by a patient) and not the anatomy perceived by “stenosis” during visual inspection of an angiogram.

However, the main focus of my editorial was that atherosclerotic plaque disease is a disorder of the arterial wall, and it escapes detection by coronary angiography (or stress testing or perfusion testing) until it has advanced to be a disorder of the lumen. As I had stated, coronary atherosclerotic disease is a continuum and not a threshold.

Again, I thank Dr Rosenthal for his correspondence.

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## Zika Virus Meningoencephalitis



**To the Editor:** In the March 2017 issue of *Mayo Clinic Proceedings*, Schwartzmann et al<sup>1</sup> reported on a single case of Zika virus meningoencephalitis and concluded that, “In this case, central nervous system involvement and ZIKV propagation to other organs in a disseminated pattern is quite similar to that observed in other fatal Flaviviridae viral infections.” The patient reported by Schwartzmann et al<sup>1</sup> was immunocompromised at the time of Zika virus infection; however, meningoencephalitis accompanying Zika virus infection has also been reported in apparently immunocompetent patients.<sup>2</sup>

An interesting question is whether the immune status has any relationship to the occurrence of meningoencephalitis. In the similar arbovirus infection, dengue infection, meningoencephalitis can also be seen regardless of immune status.<sup>3</sup> In our setting in Southeast Asia, dengue is highly prevalent and Zika virus infection is also endemic. Nevertheless, Zika virus infection is usually asymptomatic and neurological manifestations are extremely rare. Furthermore, despite an extremely high prevalence of dengue in our area (30-224 cases per 100,000<sup>4</sup>), there has never been a report on meningoencephalitis in dengue patients regardless of immune status.

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## In Reply—Zika Virus Meningoencephalitis



**To the Editor:** We read with interest the letter from Joob and Wiwanitkit<sup>1</sup> which reinforced our interpretation that immunosuppression predisposes the central nervous system (CNS) to infection by Zika virus.

It is known that some microbial infections of the CNS—such as those caused by toxoplasma, cryptococcus, and cytomegalovirus—can be related to predisposing underlying diseases. In the Brazilian Amazon region, the tropical climate favors the proliferation of large quantities of insect vectors and their vertebrate reservoirs, thus supporting the natural cycles of many arboviruses that can infect humans. In a study done in the state of Amazonas, cerebrospinal fluid (CSF) samples from 110 patients with meningoencephalitis were tested by reverse transcription-polymerase chain reaction (RT-PCR) for *Orthobunyavirus* and *Flavivirus*.<sup>2</sup> Lymphomonocytosis predominated in all CSF cell counts. Sequencing of RT-PCR products obtained from 3 patients identified Oropouche virus (Peribunyaviridae). Two of the 3 patients infected with Oropouche virus, a 54-year-old man and a 37-year-old woman, had underlying diseases that affected the CNS or the immune system (neurocysticercosis and AIDS,

respectively). In a similar study using RT-PCR<sup>3</sup> followed by nucleotide sequence of amplicons, 2 out of 23 patients from the state of Amazonas had Rocio virus, another Flavivirus, identified in the CSF. They were a 53-year-old man and a 30-year-old woman, both with AIDS. In the above cases, as in the Zika virus reported case,<sup>4</sup> it is very likely that CNS invasion was facilitated by immune deficiency or previous blood-brain barrier damage.

In conclusion, it is important to be aware that in patients who have underlying diseases and additional new CNS manifestations, arbovirus infections should be considered in the differential diagnosis.

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Physicians in the 21st  
 Century: Between  
 Identification With  
 Medicine as a Calling and  
 Self-Diagnosing Burnout,  
 Depression, and Anxiety



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**To the Editor:** The father of medicine, William Osler said: “The practice of

medicine is an art, not a trade; a calling, not a business; a calling in which your heart will be exercised equally with your head. Often the best part of your work will have nothing to do with potions or powders, but with the exercise of an influence of the strong upon the weak, of the righteous upon the wicked, of the wise upon the foolish.”<sup>1</sup>

Jager et al’s<sup>2</sup> article, published in the March 2017 issue of *Mayo Clinic Proceedings*, raised an important association between physician burnout and identification with medicine as a calling. The authors randomly selected and surveyed 2263 physicians from all specialties between 2014 and 2015, using the American Medical Association Physician Masterfile. About one-third of the respondents experienced burnout symptoms. Those who reported burnout symptoms were less likely to be engaged in their profession, find satisfaction, or recognize the importance of their work.<sup>2</sup>

An absent sense of calling in medicine correlates with burnout and other psychopathological illnesses. The relationship between burnout and symptoms of depression has been studied, and their theoretical similarity in the work setting has been supported.<sup>3,4</sup> Previous studies found that burnout, emotional exhaustion, and depersonalization are more common among physicians than among the general US population.<sup>5</sup>

We surveyed medical trainees (students, residents, and fellows) at a medical university between 2013 and 2014 and incorporated screening tools for major depression disorder (MDD) and generalized anxiety disorder (GAD).<sup>6</sup> A total of 462 responded to the survey, and we compared the results to age-matched controls from the National Health and Nutrition Examination Survey database. The prevalence of a positive screen for MDD and GAD was more than 5- and 8-fold higher in medical trainees, respectively.

Even though Jager et al<sup>2</sup> excluded medical residents from their study, we reported both critical psychopathological issues in current and future health care professionals.<sup>6</sup> In addition, both populations work and train under similar medical environments and challenges. As a result, we propose that medical trainees who experience depression and anxiety are likely to experience burnout and are less likely to identify with medicine as a calling. Both physicians and medical trainees may not self-recognize such symptoms and potential illnesses, or may not seek help because of concern for stigma. Interventions are needed at all institutional levels to keep physicians in all specialties, the young vulnerable trainees, and their patients away from the adverse mental health consequences of the medical profession. Lacking the sense of calling can be a critical marker of mental health illnesses.

In this era of fast-moving science and everyday challenges, it is important for every physician and trainee to remember Dr Charlie Mayo’s words: “Medicine is a profession for social service and it developed organization in response to social need. Medicine gives only to those who give, but her reward for those who serve is finer than much fine gold.”<sup>7</sup>

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