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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1. Rosenthal RL. Revisiting the historical origins of clinically meaningful coronary artery obstruction. *Mayo Clin Proc*. 2017;92(8):1312.
2. Rumberger JA. Coronary artery disease: a continuum, not a threshold. *Mayo Clin Proc*. 2017;92(3):323-326.
3. Rosenthal RL. The 50% stenosis. *Am J Cardiol*. 2015;115(8):1162-1165.
4. Gould KL, Lipscomb K. Effect of coronary stenoses on coronary flow and resistance. *Am J Cardiol*. 1974;34(1):48-55.
5. Katz LN, Linder E. Quantitative relations between reactive hyperemia and the myocardial ischemia which it follows. *Am J Physiol*. 1939;126:283-288.
6. Patel MR, Calhoon JH, Dehmer GJ, et al. ACC/AATA/AHA/ASE/ASNC/SCAI/SCCT/STS Appropriate use criteria for coronary revascularization in patients with stable ischemic heart disease: a report of the American College of Cardiology Appropriate Use Criteria Task Force, American Association for Thoracic Surgery, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, and Society of Thoracic Surgeons. *J Am Coll Cardiol*. 2017;69(17):2212-2241.

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Zika Virus Meningoencephalitis

To the Editor: In the March 2017 issue of *Mayo Clinic* Proceedings, Schwartzmann et al[1] 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[1] was immunocompromised at the time of Zika virus infection; however, meningoencephalitis accompanying Zika virus infection has also been reported in apparently immunocompetent patients.[2]

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.[3] 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[4]), there has never been a report on meningoencephalitis in dengue patients regardless of immune status.

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1. Schwartzmann PV, Ramalho LN, Neder L, et al. Zika virus meningoencephalitis in an immunocompromised patient. *Mayo Clin Proc*. 2017;92(3):460-466.
2. Duca LM, Beckham JD, Tyler KL, Pastula DM. Zika virus disease and associated neurologic complications. *Curr Infect Dis Rep*. 2017;19(1):4.
3. Araújo FM, Araújo MS, Nogueira RM, et al. Central nervous system involvement in dengue: a study in fatal cases from a dengue endemic area. *Neurology*. 2012;78(10):736-742.
4. Limkittikul K, Brett J, L'Azou M. Epidemiological trends of dengue disease in Thailand (2000–2011): a systematic literature review. *PLoS Negl Trop Dis*. 2014;8(11):e3241.

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In Reply—Zika Virus Meningoencelphalitis

To the Editor: We read with interest the letter from Joob and Wiwanitkit[1] 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*.[2] 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,