# Reply.

Anthony M. Vintzileos MD

John C. Smulian MD, MPH
*Lehigh Valley Health Network*, john.smulian@lvhn.org



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compression (and other nonhypoxic reflex mechanisms) actually causes rapid decelerations?[6] Should all rapid decelerations be defined as variable despite the fact that the decelerations in confirmed cord compression (predominant chemoreceptor mechanism) have descent time often much more than 30 seconds with nadir much later than peak of contractions?[6] Could these be some of the most substantial framing and confirmation fallacies in modern medicine?

The categorization of FHR decelerations is a theoretical/conceptual framework. If it contradicts careful observations and critical analysis, then it would be incompatible with the scientific method/approach and best be corrected for any system of CTG interpretation to be meaningful.[6] ■

Shashikant L. Sholapurkar, MD, DNB, MRCOG
Department of Obstetrics and Gynaecology
Royal United Hospital Bath National Health Service Foundation Trust
Princess Anne Wing
Combe Park
Bath BA1 3LE, United Kingdom
s.sholapurkar@nhs.net

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## REPLY

We would like to thank Dr Sholapurkar for his comments regarding our recent editorial.[1] Dr Sholapurkar makes 4 points.

First, Dr Sholapurkar agrees that studies on longitudinal fetal heart rate (FHR) are desirable, and he believes that such studies should be retrospective in nature but they may be problematic if the study methodology is imprecise and subjective. We agree. In our editorial, we emphasized that such studies can be difficult to perform for a number of reasons including difficulty in choosing the appropriate outcome or outcomes. To that end, we suggested that cord blood gases at birth may be a reasonable gold standard, as outcome, and that the predictor should be the longitudinal FHR changes as depicted in the figure of our editorial. We believe that the longitudinal FHR changes that we described in our editorial, if used correctly, can remove much of the imprecision and subjectivity in the methodology of such future studies. We also would not disregard the benefits of a prospective study that is designed to rigorously capture information on longitudinal FHR tracing interpretation, clinical context, and clinical decision making, which are difficult to assess with an analysis of retrospective data.

The second issue raised by Dr Sholapurkar is that the distinction between absent and minimal (reduced) FHR variability may be difficult and clinically unimportant. We agree and we made this very clear in our editorial. We also agree that a fetal stimulation test may be helpful in decreasing false-positive results, but we doubt the value of fetal scalp blood sampling because this has its own drawbacks and lack of evidence in improving outcome.[2,3]

The third point has to do with the clinical significance of postdeceleration overshoots and that FHR decelerations during the second stage are common and do not warrant intervention. We agree with the inconclusive evidence about postdeceleration overshoots. However, we need to make an important distinction here between the postdeceleration overshoots and what we emphasized in our editorial, which was "the rise of FHR baseline with frequent episodes of tachycardia or continuous tachycardia" in response to decelerations. We agree that decelerations during the second stage of labor may not always warrant intervention, but we should also keep in mind that repetitive prolonged decelerations during the last 30 minutes prior to birth have the highest predictive ability for fetal acidemia.[4]

The fourth point is that most babies born with a pH <7.0 have normal FHR variability and that a less strict definition of gradual and abrupt for early and variable decelerations, respectively, may serve us better. It is true that some of the gradual or abrupt definitions may not encompass all early or variable decelerations, but such definitions correctly identify the majority of decelerations and at the same time provide the framework for creating standard nomenclature and management. ■

Anthony M. Vintzileos, MD
Department of Obstetrics and Gynecology
Winthrop-University Hospital
259 First Street
Mineola, NY 11501
avintzileos@winthrop.org

John C. Smulian, MD, MPH
Department of Obstetrics and Gynecology

Lehigh Valley Health Network
Allentown, PA 18103
University of South Florida-Morsani College of Medicine
12901 Bruce B. Downs Blvd
Tampa, FL 33612

The authors report no conflict of interest.

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# Efficacy of oral valacyclovir in cytomegalovirus-infected fetuses

**TO THE EDITORS:** We read carefully the article of Leruez-Ville et al[1] about the efficacy evaluation of oral valacyclovir for pregnant women carrying a symptomatic cytomegalovirus-infected fetus, who are at high risk for developing both neurosensory and neurological impairments. Symptomatic fetuses, defined by the presence of measurable extracerebral or mild cerebral ultrasound signs, were treated in utero from the prenatal diagnosis, performed at a median age of 25.9 weeks' gestation, to the delivery or the termination of pregnancy. As noted by the authors, high-dosage valacyclovir was effective in improving the outcome of the infected fetuses. At the interim analysis, 8 of 11 women delivered asymptomatic neonates that were still asymptomatic at 12 months old.

Over the last decades, the natural history of the cytomegalovirus (CMV) infection in pregnancy has been slightly changed, being the object of several therapeutic attempts.[2] Vaccination is not available and no prenatal treatment of congenital CMV has yet been validated. The use of CMV-specific hyperimmune globulin to prevent vertical transmission has obtained contrasting results. As suggested, around 10% of infected neonates are symptomatic at birth and their risk of sequelae reaches 58%. On the other hand, the risk of sequelae in asymptomatic newborns is around 13%.[2]

We understood that the difference in viral load of both symptomatic and asymptomatic newborns may be critical, particularly if the predictive value for developing symptoms at birth in an infected fetus is assessed only by interpreting the results of both prenatal imaging and laboratory tests. Increasing the number of data from human studies indicates that human cytomegalovirus infection interferes with the differentiation of trophoblast progenitor cells in the human placenta[3] so that the passive immunization with hyperimmune globulin has been shown to reduce viral replication, to enable the compensatory growth of chorionic villi, to increase the perfused placental surface, and, for some babies, to improve the outcome.[4]

Although this study is not a randomized controlled trial, this is the first one that reports the efficacy of an antiviral drug in cytomegalovirus-infected fetuses. As a consequence, this study should encourage new trials using valacyclovir as a first-line safe and effective treatment in CMV-affected pregnant women and comparing this last one with the new emerging and more potent anticytomegalovirus drugs. However, based on our evaluation of the study by Leruez-Ville et al,[1] it seems that together with prenatal imaging and laboratory tests, the infection natural history in symptomatic and asymptomatic neonates could be better predicted if associated with placenta pathology examination. Once again we thank the authors for bringing these considerations to the forefront. ■

Gianluca Straface, MD
Vincenzo Zanardo
Division of Perinatal Medicine
Policlinico Abano Terme
Abano Terme 35031, Italy
gstraface@casacura.it
glstraface@hotmail.com

Marco De Santis
Catholic University of Sacred Heart
Rome, Italy

The authors report no conflict of interest.

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