Japanese viewpoint on amniotic fluid embolism

TO THE EDITORS: Clark et al[1] described the pathophysiology of amniotic fluid embolism (AFE) and proposed uniform criteria for its diagnosis. The first AFE research center has been established in the United States. We are deeply respectful for their contribution to Amniotic Fluid Embolism Foundation.

The diagnosis of AFE through the exclusion of other fatal diseases without any prevalent serum markers is confusing. AFE is recognized initially by its clinical course only, which includes severe genital bleeding and disseminated intravascular coagulation (DIC) with uterine atony soon after delivery and cardiopulmonary collapse during the peripartum period. Careful pregnancy screening or imaging studies are not useful for diagnosing AFE. In practical settings, patients with AFE with an unknown cause experience postpartum hemorrhage with fibrinolysis-dominant DIC, which includes a sudden and abrupt decrease in fibrinogen, and have cardiopulmonary malfunctions, often leading to arrest without recovery. Obstetricians and researchers must investigate risk factors and clinical settings in connection with large-scale databases to integrate the disease concept through each region. Regarding proposed diagnostic criteria, we consider DIC to be an important part of the pathophysiologic condition of AFE. Atypical cases without DIC need to be excluded. Although some cases may experience symptoms 1 or 2 hours after placental expulsion, we approve the concept that the clinical onset of AFE is abrupt within the early stage of delivery. Our institution plays an important role as a Japanese AFE center.[2] Serum obtained from patients suspected of AFE during pregnancy and delivery and uterine tissue after hysterectomy for hemostasis are delivered to our institution. We present acute inflammation in the myometrium after delivery in accordance with uterine contractile dysfunction as "postpartum acute myometritis."[3] Complement activation, as evidenced by large numbers of C5a receptors in the edematous myometrium, may be the first step in the development of postpartum acute myometritis by inflammatory cell infiltration, including neutrophils and macrophages, and anaphylactoid reactions secondary to mast cell degranulation. We also propose the importance of C1 esterase inhibitors in the onset of AFE and its severity to regulate immunologic reactions that include the complement and kinin-kallikrein systems.[4] When obstetricians diagnose AFE, C1 esterase inhibitors activity is superior as a pathophysiologic indicator to markers that reflect amniotic fluid influx into the maternal circulation.

We preserve the serum, plasma, and even uterine tissues of patients with AFE throughout Japan. We are ready to commence international collaborations on AFE research. The diagnostic criteria proposed herein are significant for worldwide medical care and research. ■

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The authors report no conflict of interest.

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Infant outcomes among women with Zika virus infection during pregnancy: observation on microcephaly

TO THE EDITORS: The report by Adhikari et al[1] is very interesting. The authors reported that "neonatal head circumference percentiles among infants born to women with evidence of possible Zika virus infection during pregnancy were not reduced when compared to infants born to women without infection."[1]

We would like to share ideas and experiences on this observation. Indeed, the Zika virus infection presently spreads worldwide. An interesting finding in South America is the microcephaly infants born to infected mothers. In Thailand, there are already reports of Zika virus–infected pregnant women. Nevertheless, there is no Zika virus–infected infant

born to a mother infected with Zika virus. In other tropical countries in Southeast Asia, the situation is similar.[2]

This observation is consistent with the finding by Adhikari et al.[1] Ronchetti and Bianco[3] noted that there might be some unknown reasons for the high prevalence of abnormal infants born to Zika virus–infected mothers in South America. ■

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REPLY

We appreciate the interest in our recent report on infant outcomes associated with maternal Zika virus infection. We emphasize an important distinction in the epidemiological terms used in characterizing Zika virus spread: epidemic versus endemic. The current Zika epidemic has been primarily confined to the Americas and Pacific Islands, whereas endemic (a constant, low-level) infection has been established in Southeast Asia, including Thailand.[1]

In this context, endemic countries may have occasional clusters of cases but generally not in numbers large enough to be considered an outbreak. Thus, rates of new infections in endemic countries may be relatively low in a predominantly immune population. This differs from our report of Zika infections associated with travel to or from epidemic regions.

We agree, however, that many unanswered questions about the processes that lead to fetal infections in different populations remain. Although both French Polynesian and Brazilian strains of Zika virus have been shown to infect and replicate within placental and fetal tissues, an understanding of the specific factors that make this likely to occur in an individual patient are still elusive.[2,3] We look forward to future research into understanding these factors influencing the burden of disease in different populations. ■

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Limits of current cardiotocography interpretation call for a major rethink

TO THE EDITORS: Clark et al[1] should be commended for a robust retrospective case-control study in a very difficult area with important contributions to the current knowledge base, which should encourage debate and stimulate progress.

But their results were somewhat predictable.[2,3] The study design description in the abstract seems confusing and needs clarification. Is not the condition (1) blind review/interpretation by experts and condition (2) secondary unblinded review of acidemic babies by experts; both using the same published algorithm?[3]

Second, what system of cardiotocography (CTG) interpretation was used by the clinicians in actual practice in the authors' institutes during the study period? Was it the same expert algorithm,[3] especially in 2013? During the blind case-control review, the experts' awareness of the high chance of CTG being abnormal (up to 50%?) could increase detection to 45.8% (even without increasing the false-positive rate).

The paper acknowledges that under actual practice conditions, the detection rate of acidemia would be closer to 30% even with the expert algorithm; thus little improvement. The main pessimistic conclusion about the "limits of CTG"