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Editor: Deborah Sesok-Pizzini, MD, MBA, professor, Department of Clinical Pathology and Laboratory Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia, and chief, Division of Transfusion Medicine, Children's Hospital of Philadelphia.

Etiology and clinical presentation of birth defects: a population-based study

Birth defects are inborn errors of development and include any structural or functional anomaly that impacts physical, intellectual, or social well-being. They are a considerable and growing clinical and public health challenge. Major birth defects are common and costly. Collectively, they are estimated to occur in one in 33 births, which translates into approximately 7.9 million babies affected worldwide. In the United States alone, the cost of care during a single year (2004) was estimated to be $2.6 billion. Birth defects are the leading cause of infant mortality in the United States, estimated at one in every five deaths in the first year of life. The authors conducted a study in which they investigated cases of birth defects in children born between 2005 and 2009 in Utah as an initial step to characterize the etiology, morphology, and pathogenesis of birth defects. They used Utah's statewide population-based public health surveillance system, which monitors birth defects among all pregnancy outcomes in Utah residents, for their clinical case review. They found 5,504 cases among 270,878 births (prevalence, 2.03 percent), excluding mild isolated conditions, such as muscular ventricular septal defects and distal hypospadias. The authors measured the proportion of birth defects with a known etiology or unknown etiology by morphology and pathogenesis. Their results showed that a definite cause was assigned in only 20.2 percent of cases: chromosomal or genetic conditions accounted for 94.4 percent, teratogens for 4.1 percent (mostly poorly controlled pregestational diabetes), and twinning for 1.4 percent (conjoined or acardiac). The remaining 79.8 percent of cases were classified as unknown etiology. The authors noted that these findings underscore the gaps in knowledge regarding causes of birth defects. They concluded that for causes that are known, such as smoking or diabetes, assigning causation of birth defects is still challenging. However, they state the importance of studying the impact of these exposures on fetal development so appropriate interventions can be designed. For unknown causes, better strategies are needed, including greater integration of etiology, morphology, and pathogenesis into epidemiologic studies; closer collaboration between researchers, clinicians, and epidemiologists; and better ways to measure fetal exposures.

Feldkamp ML, Carey JC, Byrne JLB, et al. Etiology and clinical presentation of birth defects: population based study. *BMJ.* 2017;357:j2249. doi:10.1136/bmj.j2249.

Correspondence: Dr. M. L. Feldkamp at marcia.feldkamp@hsc.utah.edu

Outcomes of Blood Group Antigen Matching Influence on Gestational Outcomes study

The approach to red blood cell matching of females of childbearing potential to prevent alloimmunization varies among health care centers. Some centers will use extended matching to prevent RBC alloimmunization to non-D RBC antigens to decrease the future pregnancy risk of hemolytic disease of the fetus and newborn (HDFN). This may include K, C, E, or c matching. The authors conducted a multinational retrospective study of women with offspring affected by severe HDFN requiring neonatal transfusion or intrauterine exchange, or both, to determine if blood bank policies of prospective antigen matching are effective in decreasing the risk of HDFN. They compared mothers treated at centers that provide extended antigen-negative RBCs (Match, five centers) and those that do not (NoMatch, nine centers). The results showed that 293 mothers had at least one affected pregnancy: 179 at Match centers and 114 at NoMatch centers. Eighty-three percent of the alloimmunizations were due to a previous pregnancy, three percent to transfusion, and 14 percent undetermined. Only 50 mothers received transfusions; 13

at Match and four at NoMatch centers had HDFN due to anti-K. Most of the anti-K HDFN (12 of 13) cases at Match centers were due to K+ paternal antigen status. The study concluded that mothers at the Match centers do not appear to be protected from HDFN due to K, C, c, and E antibodies. However, a limitation of the study was the low number of females of childbearing potential who received transfusions and the lack of uniformity between matching policies. The authors concluded that these results showed that the causal stimulus of antibodies that cause HDFN is predominantly from a previous pregnancy. The authors were unable to show a positive effect with extended RBC antigen matching. They also concluded that as more blood centers work to provide RBC antigen typing or genotyping data on RBC units to transfusion services, the feasibility of providing matched units for HDFN prevention, even at small numbers, will improve.

Delaney M, Wikman A, van de Watering L, et al. Blood Group Antigen Matching Influence on Gestational Outcomes (AMIGO) study. *Transfusion.* 2017;57:525–532.

Correspondence: Dr. Meghan Delaney at meghand@bloodworksnw.org