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Fetal Congenital Heart Disease in Twins with fully identified Zygosity: genetic or epigenetic?That is the question perhaps answered by an international multicenter study of 144 monozygotic twins.

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Twins allow understanding of malformations and provide data of their cause and genetic component. The incidence of cardiac malformations (FHD) is higher in monozygotic (MZ) than in dizygotic and singletons. MZ have a similar environment. This multicenter prenatal study is the first to collect a large number of MZ, 144 sets of MZ with fully identified zygosity. Acardiac and FHD in twin to twin transfusion were excluded. Our purposes were to answer the following questions:1-what was rate of concordance, genetic or not? 2-what were the phenotypes of the FHD? (we used Clark's classification) 3- could we suspect any influence of epigenetic factor, in particular placentation? Prenatal diagnosis of the FHD was performed using Dopplerechocardiography(2D). Extremes for gestational age were 16-35 weeks. Whenever intra-uterine death or termination of pregnancy occurred, fetopathological examination was done. All neonates had 2D. Fetal karyotypes were obtained with microdeletion 22q11 testing. Zygosity was assessed taking account fetal gender, gonosomal complement, placental phenotype and microsatellite analysis. Placental examination was performed. Only 16 sets of MZ presented each a FHD, but there were discordant, however there was one exception,.one MZ presented twins with aortic and mitral atresia. We also found that an extracardiac malformation (ECM) was found in the twin with FHD in 18% of the MZ. The answer to first question is discordance for FHD and the ECM when present. The FHD phenotype showed that type II (flow lesions) and type I (conotruncal malformations) accounted for 75% of the phenotype with a predominance of the abnormal flow, followed by type IV (atrioventricular canal) and only two were type VI (looping anomalies). The placentation showed relevant information, there was an abnormal incidence of velamentous or marginal cords. This result has been already reported in MZ with ECM (Machin, G.A., 1996). Velamentous or marginal cord were found significantly more frequent in MZ with FHD. In conclusion this multicenter study in MZ showed discordance in FHD. This observed discordance probably occurs as a postzygotic event. We have strong indication that one of the epigenetic factors maybe abnormal cord insertion,others are searched such as factors of methylation.