The first trimester concept is outdated

Andrew E. Czeizel
Foundation for the Community Control of Genetic Diseases, Budapest, Hungary

The time factor, i.e., the exact fetal or gestational age when the hazardous environmental factor has an exposure to pregnant women is extremely important at the evaluation of teratogenic risk and the manifestation of congenital abnormalities. In the classic work of Nishimura and Tanimura (1976) we can find an excellent timetable of selected developmental characteristics. Nevertheless, in the human clinical teratology there is an old rule: the most sensitive and vulnerable period of fetal development is equal to the so-called organogenesis and it corresponds to the first trimester of gestation. This old fashion rule needs a change. At present the gestational time is calculated from the first day of the last menstrual period, thus women are not pregnant during the first two weeks of the so-called pregnancy. In addition, the third week is connected with the preimplantation period when zygote is transported from the lateral end of fallopian tube to the uterus, while the implantation occurs in the fourth week of pregnancy. Zygotes and/or blastocysts have omnipotent cells therefore toxic-teratogenic exposure may cause death but not structural developmental defects. It is the well-known "all-or-nothing" rule (i.e., either there are too many cell deaths and no embryos result or the survivors do not have any morphological defect). Mutagens can cause very rarely later manifested fetal defects during this time period, however, this phenomenon is an exception to the rule. (Generoso et al., 1988) Thus, obviously the first month of pregnancy is before the organogenesis therefore it is meaningless to use the first trimester at the evaluation of human teratogens. We evaluate the second and third gestational months as the critical period of most major congenital abnormalities diagnosed after birth (Czeizel et al., 1999). Actually this most sensitive period is between the 5th and 10th gestational weeks, but it is difficult to differentiate weeks, in addition there is some unreliability at the calculation of conception day. However, as a general concept in teratopaedemiological studies, we focus on specific congenital abnormalities since teratogens can induce specific congenital abnormalities without necessarily affecting the overall rate (it is the rule of noxa specificity). The central nervous and skeletal systems have a longer critical period including second and third trimesters, on the other hand some specific congenital abnormalities of male genital organs, such as hypospadias (10-16 weeks) and undescended testis (7-9 months) or urinary tract defects (obstructive defects or kidney dysgenesis) or cardiovascular malformations e.g., patent ductus arteriosus (early postnatal period) have well-defined critical period after the third month of gestation. In conclusion, it is worth calculating the specific critical period of a specific congenital abnormality or if we want to have a preliminary general evaluation of teratogens, the second and third months of gestation can be considered. Thus, the analysis of the so-called first trimester is outdated from scientific aspect.

REFERENCES
Nishimura H, Tanimura T (1976) Clinical Aspects of the Teratogenicity of Drugs. Excerpta Medica, Amsterdam, etc.