EDITORIAL

Congenital Anomalies: Current Knowledge and Future Prospects

Issues about congenital anomalies are of great importance in public health. Even excluding early fetal loss, it has been estimated that as many as 3.5% of all live births had some level of major abnormality, which are referred to as birth defects. Incidences can vary dramatically according to geographic region, cultural background, ethnic group, and the efficiency of detection and reporting systems. If minor abnormalities are included, the incidence would be close to 5%. Worldwide, birth defects are one of the causes of infant mortality and add extensively to the public healthcare burden.

The cause of birth defects is not necessarily genetic, and various etiologic mechanisms may be applied: chromosomal anomalies, polygenic disorders, single-gene disorders, environmental/teratogenic factors, multifactorial scenarios, and other, unknown, causes. Generally speaking, at least 1% of human births have one or more clinically significant chromosomal abnormalities. Before birth, the effect of natural selection removes the vast majority of genetically abnormal embryos. At conception, aneuploidy may affect any chromosome, but only trisomies of sex chromosomes or of autosomes for chromosomes 13, 18, or 21, or monosomy of the X chromosome is compatible for carriers to survive to the end of pregnancy.

In terms of incidence, clear chromosome-specific variations exist, in which larger autosomes (chromosomes 1–12) are under-represented; as chromosome 16 stands out as most frequent, followed by chromosomes 22, 21 and 15. Sex chromosome trisomies are not normally seen in spontaneous abortions. At conception, aneuploidy may affect any chromosome, but only trisomies of sex chromosomes or of autosomes for chromosomes 13, 18, or 21, or monosomy of the X chromosome is compatible for carriers to survive to the end of pregnancy.

In comparison to X chromosome trisomy, which has a survival rate of 94%, cases with 47, XXY have 100% survival. Trisomies of chromosomes 13, 18 and 21 are among the few surviving to birth with uncertain chances. At birth, trisomy 21, leading to Down’s syndrome, has an incidence of 1.3 per 1000, trisomy 18 and trisomy 13 (Patau syndrome) have incidences of 0.05 per 1000 (Edward syndrome) and 0.1 per 1000, respectively.

Structural anomalies of chromosomes, including chromosome breakage and abnormal reunion, also occur frequently in humans. Either they occur following reciprocal translocations (the exchange of segments between non-homologous chromosomes), or two or more breaks within a chromosome, causing a shift in the position or reversal of sequence (inversions) at the freed segment of chromatin. This is particularly the case with Robertsonian translocation, involving chromosomes 13–15 and 21–22, so-called “acrocentrics”, in which the centromere is close to the end of the chromosome with a net outcome of reduction in chromosome number by one without a phenotypic effect. Reciprocal translocations occur in 1 in 500 people and Robertsonian translocations in approximately 1 per 1000, mostly affecting chromosomes 13 and 14, or 14 and 21. Chromosomal inversions are relatively rare without an exact reported incidence, as many cases are not detected.

As to well-characterized risk factors for chromosomal abnormalities, the most critical one is older maternal age. Among recognizable pregnancies, trisomy is at greatest risk for older mothers, with age-specific rates of 0.07%, 0.11% and 1% for mothers in their 20s, 30s, and 40s or above, respectively. Nonetheless, there are exceptions for trisomy X, which normally happen at a younger age for mothers. When estimates of maternal trisomy were calculated, the outcome suggested that in women aged 40 or more, the majority of oocytes may be aneuploid. The other well-known risk factor of bearing a chromosomally abnormal child is that one of the couples carries a gonadal or germinal mosaic for a trisomic cell line, which happens during mitosis in premeiotic divisions of the germ cells and may affect one or several germ cells. In this kind of trisomic syndrome (translocation, gonadal, or germinal mosaicism), cases occur independently of maternal age.

Taiwan’s government started setting up programs to protect and promote maternal health from 1945. Birth registry reporting by medical practitioners was officially launched by the Department of Health of Taiwan in 1995, and later transferred to the Bureau of Health Promotion, Department of Health, Taiwan in 2001. Its regulations require reporting of births with a gestational age of ≥ 20 weeks, including live births and miscarriages. However, further studies into the
incidence rates of congenital anomalies and their risk factors are still warranted in Taiwan.  

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