The protective effect of periconceptional folate on congenital heart defects (CHDs) presented by Van Beynum et al. (2006) contributes to the governing folate paradigm. The researchers showed a quantitative trait effect between MTHFR 677 > CT heterozygosity and homozgyosity (TT) and a modification by periconceptional folate supplementation. In addition, using the family-based transmission disequilibrium test (TDT), they identified this polymorphism in the mother as a risk factor for CHDs in their progeny, independent of its presence in the foetus. Similar results were found in relation with cleft lip with or without cleft palate. Studies on the relation between MTHFR 677 > T polymorphism and congenital anomalies as a consequence of mildly elevated plasma homocysteine (Hcy) – presume an extensive reduction of migrating cardiac neural crest cells during early development. The connection of a very broad spectrum of chromosomal aberrations, constitutional diseases with MTHFR polymorphisms support the concept of non-optimal maturation of the oocyte as causal pathway into adverse progeny as suggested by Wynn and Wynn (1993), who moved the attention away from teratological disturbances during the early months of pregnancy into the maturation of the oocyte. In fact, deficiency of folate in rhesus monkeys is known to depress the concentration of oestradiol and progestagen and to slow down the replication of granulosa cells, being the principal cells in the ovarian follicle. This deficiency results in a reduction of the growth of the follicle and in delayed ova-lation, as markers for retardation of embryonic growth and malformations. Therefore, they presume that folic acid is the prerequisite for optimum maturation of the oocyte and inherent favourable outcome.

Heterozygous and homozygous carrier ship of these polymorphisms implies increased plasma of total Hcy and, thus lower folate concentration threatening optimal maturation of the oocyte and embryonic development. Non-optimal maturation of the oocyte or over-riness of the egg in animal experiments and observations has been shown to be associated with a wide spectrum of chromosomal and development anom alies. It has also been presumed in a range of conditions in which the maturation of the oocyte is at stake, such as very premature and advanced reproductive age, postpartum restoration of the ovula-tory pattern, seasonally bound transitional stages of it, etc. This is in line with the association between follicular fluid Hcy levels and detrimental effect on embryo quality in couples undergoing assisted reproductive techniques (ART), as well as with the greater risk for miscarriage, particularly when foetal chromosomal anomalies are present.

Low folate concentrations connected with over-riness ovopathy, therefore, may play a role in the causal pathway of unfavourable pregnancy outcomes. This concept not only explains the broad spectrum of chromosomal aberrations, congenital anomalies, and constitutional diseases, but also their pleitropic pattern and male preponderance, and finally, the analogy with the above-mentioned high-risk conception categories.

References

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Selene, the goddess of the moon: does she shine on men only?

First of all I would like to congratulate Nawrot et al., on their convincing and important analysis on yet another selenium (Se)-dependent health issue, i.e. the inverse correlation of blood Se with blood pressure. This report represents the latest addition to an ever-growing list of sex-specific effects mediated by this particular trace element which has been named after Selene, the Greek goddess of the moon. Low Se status causes male infertility in both humans and animals, thereby its honorary title ‘XY nutraceutical’ is well deserved.

Chromoprevention trials by Se supplementa- tion generally report stronger effects for male participants, most pronounced usually for prostate cancer. Therefore, a large, expensive, long range, and men-only follow-up study on the chromopreventive effects of Se has recently been initiated by the NIH (www.cancer.gov/selecl). Moreover, a prospective multicentre study on mortality from sepsis yielded positive effects of