Endocrine disrupters and male reproduction

Trine B. Haugen

Faculty of Health Sciences, Oslo University College, Oslo, Norway
E-mail: trine.b.haugen@hf.hio.no  Telephone: +47 22 45 25 42  Telefax: +47 22 45 23 55

Testicular dysgenesis syndrome is thought to have increased in most Western countries over the past decades (1,2). The syndrome comprises testicular cancer, hypospadias (incomplete closure of the urethral fold), cryptorchidism (undescended testis) and poor semen quality. All of these conditions are considered to originate in utero. In 1993, Sharpe and Skakkebæk launched the so-called oestrogen hypothesis, suggesting that increased exposure to endogenous or exogenous oestrogens in utero could be a cause of declining sperm count and disorders of the male reproductive tract (3). Increased exposure to oestrogens early in foetal life may have adverse effect on both Sertoli and Leydig cells, and thus also on germ cells. Since 1993, the oestrogen hypothesis has been expanded to include also environmental antiandrogens with potential adverse effects on male reproductive health (2). By blocking androgen action, exposure to an antiandrogen may cause changes similar to those associated with oestrogen exposure, and in addition, several environmental estrogen receptor agonists are also androgen receptor antagonists.

In most Western countries the incidence of testicular cancer has increased during the last fifty years, and there are large ethnic and regional differences. Finland has the lowest incidence among the Nordic countries and similar to the Baltic area, whereas Norway and Denmark have the highest incidence of testicular cancer in the world (4).

Geographic differences in semen quality are found in several studies. An east-west gradient in semen quality has been observed in the Nordic-Baltic area, and the total sperm count seems to be inversely correlated to the testicular cancer incidence (5). Geographic differences in semen quality have also been reported for fertile men in USA. In this study there was found a reduced sperm concentration and sperm motility in agricultural areas compared to urban areas (6).

Also geographic difference in prevalence of congenital cryptorchidism as well as hypospadias has been reported. The prevalence of cryptorchidism at 3 months of age, was 1.9% in Denmark and 1.0% in Finland (7), whereas the prevalence of hypospadias was 1.0 and 0.3% at birth in Denmark and Finland, respectively (8).

Although studies with animal models have revealed effects of endocrine disrupting chemicals (EDCs) on reproductive function, there are few studies showing effects in human. However, a recent study showed that several
phthalate metabolites measured in maternal urine samples during pregnancy were negatively correlated to anogenital index (anogenital distance/weight) (9). Furthermore, boys with lower AGIs were more likely to experience incomplete testicular descent, indicating that exposure to phthalates may be associated with cryptorchidism. Such effect may be exerted by affecting Leydig cell function and suppressing testosterone and insulin-like factor 3 production (2).

It should be emphasized that there is no evidence for a decrease in male fertility, and that the decrease in fertility rates is mainly due to socioeconomic factors. Furthermore, no evidence for a uniform temporal increase in hypospadias, cryptorchidism, or a decline in sperm quality has been found. Although studies have shown effect of EDCs on male reproductive health, the hypothesis that EDCs represent a threat to male reproduction still remains controversial. Other factors, including diet and lifestyle, should also be considered as risk factors.

References