Dr Alpesh Gandhi
President FOGSI
DR Anita Singh
Vice President FOGSI
Dr Rakhi Singh
Chairperson of Endocrinology Committee FOGSI
DO,FICOG,FIAOG,DPE, DRM

Senior IVF specialist Abalone IVF center Noida

Editor :Dr Meenu Handa
MS,DNB,FICOG. Senior IVF specialist , Fortis Bloom IVF center Gurugram.

Author- Dr Ashwini Kale

IVF consultant and Chief Embryologist
Ashakiran hospital and Asha IVF centre Pune

Endocrinology Committee of FOGSI

EFFECT OF ENVIRONMENT ON MALE SUB FERTILITY

There is increasing evidence to suggest that **environmental** factors play an important role in the causation of **male infertility**. Our **environment** is contaminated by natural and synthetic chemicals, which could interact with the endocrine system resulting in the reduction of human **fertility**.

Over the last 50 years, there has been a steady decline in the mean sperm count by 50% in the general population. Genetic factors, lifestyle and environmental exposures, all affect semen quality and male fertility. Genetic factors may not alone contribute as the sole cause for this decline, considering the dramatic environmental and lifestyle changes that have occurred over the past few decades. Lifestyle changes such as smoking, alcohol consumption, increased stress and obesity all contribute towards the decline in semen quality. Environmental factors like high temperature, increasing exposure to ionizing radiation and excessive use of cell phones, all have a negative impact on male fertility.

Approximately 15% of couples of reproductive age have fertility problems and about half of these cases are because of male factors .

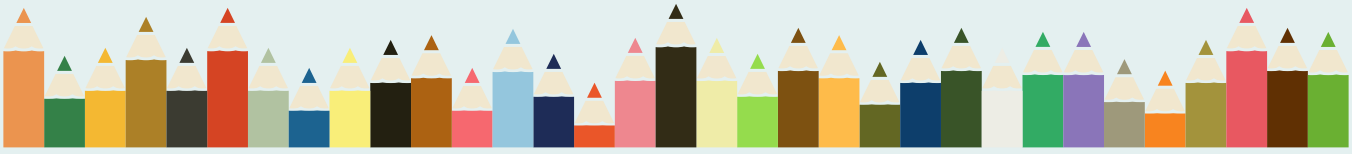
The expansion of the chemical industry in every facet of modern life is one such major environmental change causing increasing damage to men's health. Studies in recent years have proven that endocrine-disrupting chemicals (EDC) may disturb the fertility of men. EDCs are endocrine disrupting chemicals mimicking endogenous hormones, interfering with their biosynthesis, metabolism and normal function. EDCs have potential hazardous effects on male reproductive axis by altering the normal regulatory endocrine system[1].

EDCs are estrogen-like antiandrogenic chemicals in the environment. BisphenolA(BPA), phthalates, polycholorinatedbiphenyls(PCBs) , DDT, dioxin are well known examples of EDCs. The first few EDCs which were reported to act as endocrine disrupters causing spermatogenic failure were Methoxychlor and Vinclozolin.

It has always been difficult to prove a direct effect of fetal EDC exposure and abnormal testicular function in humans. However, many rodent experiments have proved the causal relationship between EDC and disturbed masculinisation. The effect of EDC exposure during early fetal development results in TDS-like features. The entity of testicular dysgenesis syndrome (TDS) comprises of undescended testes, hypospadias and oligozoospermia with increased incidence of testicular germ cell cancer. TDS is thought to originate from exposure of sensitive fetal organs to disturbed androgen action.[2]

Endocrine-disrupting chemicals (EDC) and their mechanism of action

EDCs are exogenous chemical compounds altering the normal metabolism and function of endogenous hormones. EDCs bind to the androgen or estrogen receptor triggering an agonist or antagonist action. This mechanism can lead to increased or decreased gene expression of sex specific genes. EDCs also act on steroidogenic enzymes, inhibit 5-α reductase activity and suppress the production of dihydrotestosterone. All these effects disrupt the regulation of masculinisation of the external genitalia and the prostate. Furthermore, P450 enzymes in the liver that metabolize steroid hormones may also be affected by EDCs.



Masculinisation programming window (MPW)

The timing of the EDC exposure appears to be of clear importance in men, even if a strict MPW cannot be identified as seen by the experiments done in rodents. It is clear that fetal development period between 8-14 weeks in humans is extremely crucial for optimal fetal testicular development. It is also known that the exposure to EDCs prior to puberty can still lead to adult disease and testicular dysfunction.

Anogenital distance (AGD) is often used as a marker for antiandrogen exposure. Many studies have shown AGD association with sperm concentration and count, total motile count and morphology. AGD also provides a reliable lifelong indicator of antiandrogen exposure within the MPW and has been proven to be a sensitive marker for antiandrogen toxicity.[3]

1. **Bisphenol A (BPA) –** It is a ubiquitous particle found in mineral water bottles, medical devices and food packaging materials. It is known to be endocrine disrupter and can cause testicular dysfunction ranging from hypospadias, cryptorchidism to low sperm counts. It is also one of the important causes of occupational infertility. Nonylphenol is a synthetic plastic additive found in detergents, paints and personal care products. As it has estrogenic properties, adult exposure to this chemical for a prolonged time can cause reduce sperm counts.[4]

2. **DDT& Dioxins –** DDT is a pesticide with estrogenic effects. It has detrimental consequence on sperm chromatin condensation and decreases sperm motility. Dioxin also causes decreased spermatogenic activity. Many fertilizers and compounds used in food industries as preservatives like Cabendazium also decrease spermatogenesis and act as EDCs.

3. **Heavy Metals & Phthalates-** According to WHO, exposure to even low levels of Lead and Cadmium (400ugm/L and 10ugm/L respectively) can significantly impair semen quality. Cadmium can damage Sertoli cells causing oligozoospermia and testicular toxicity. Phthalates are widely used in automobile industries, beverage cans and coating of metal tins. It is known to be a common EDC and decreases sperm production.

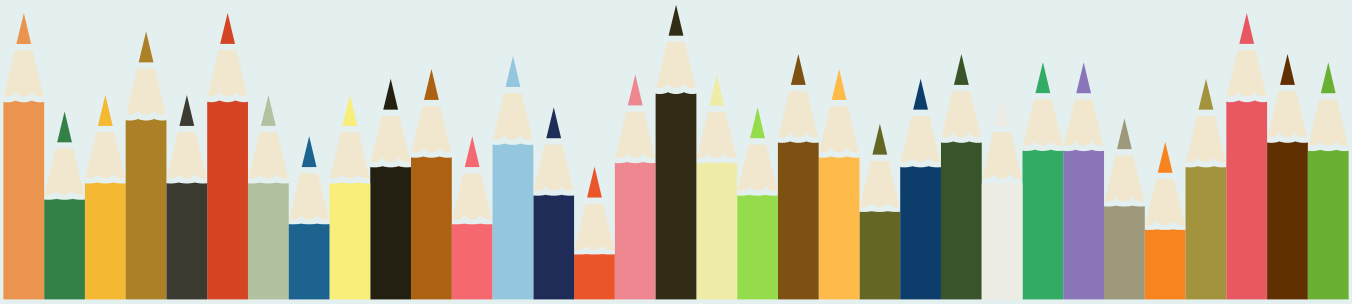
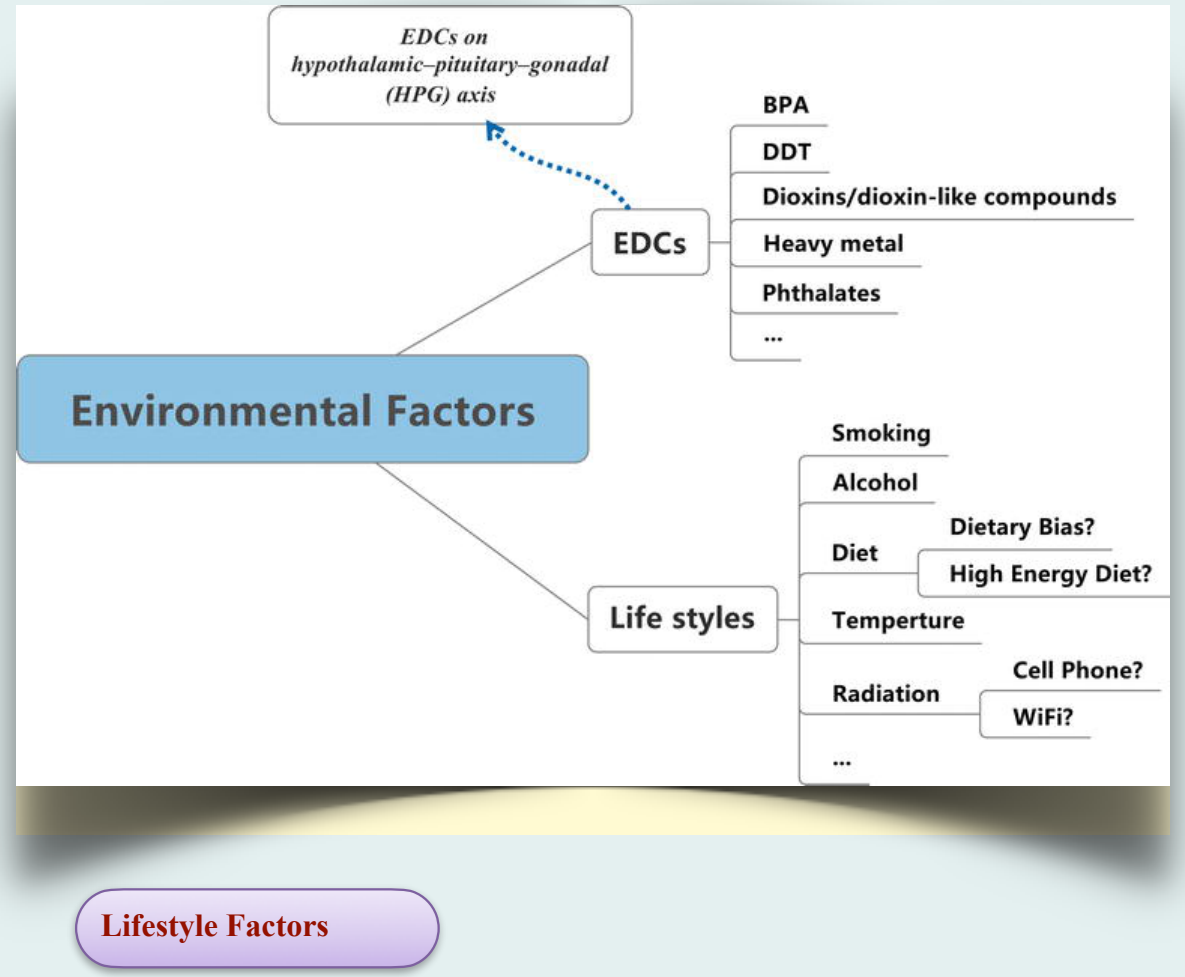


Fig 1- Environmental factors affecting Male fertility:



Lifestyle plays a major role in optimal functioning of the male reproductive system. We have seen a major shift in choices pertaining to our lifestyle over the past 50-100 years. Sedentary lifestyle, lack of physical exercise and increased consumption of alcohol and tobacco has played havoc in our lives.

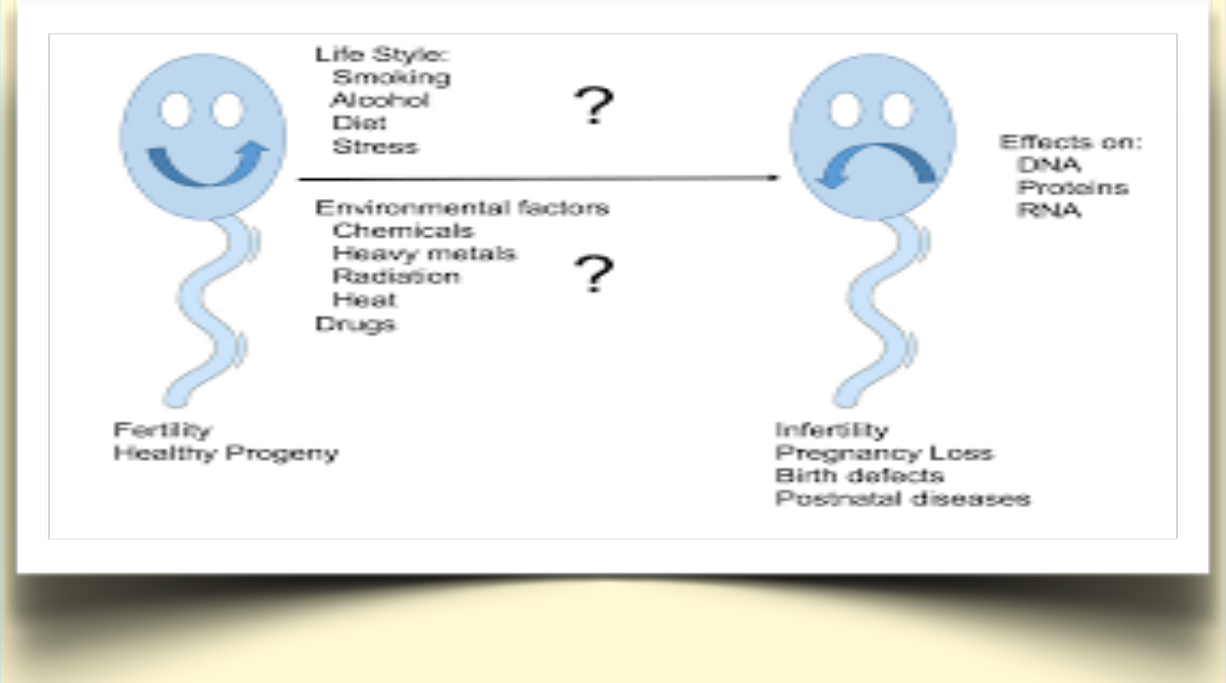
a) **Smoking** – Due to exposure to harmful compounds like alkaloids, nicotine and hydroxycotine, there is increased ROS and oxidative stress in the body. It eventually leads to decreased sperm motility, count, vitality and increased DNA methylation.

b) **Alcohol** – Excessive alcohol consumption leads to decreased testosterone production and can cause decline in libido, erectile dysfunctions, hypogonadism and testicular atrophy.

c) **Obesity** – Men with BMI more than 25 are likely to suffer more from oligozoospermia and increased DNA fragmentation. Excessive visceral adipose tissue enhances the peripheral

conversion of testosterone to estrogen. This subsequently inhibits the Hypothalamic-pituitary-testicular axis and results in hypogonadism. Increased suprapubic fat and inner thigh fat in severely obese men can lead to increased testicular heat stress leading to spermatogenic impairment.

d) **Drugs-** Antibiotics and chemotherapy are known to cause germinal epithelium damage. Many antibiotics (Tetracycline derivatives and sulpha drugs) can inhibit spermatogenesis. Long term steroid use is also known to cause oligozoospermia as they suppress LH secretion and decline in testosterone levels. Hypogonadotropic Hypogonadism is commonly seen in this group.

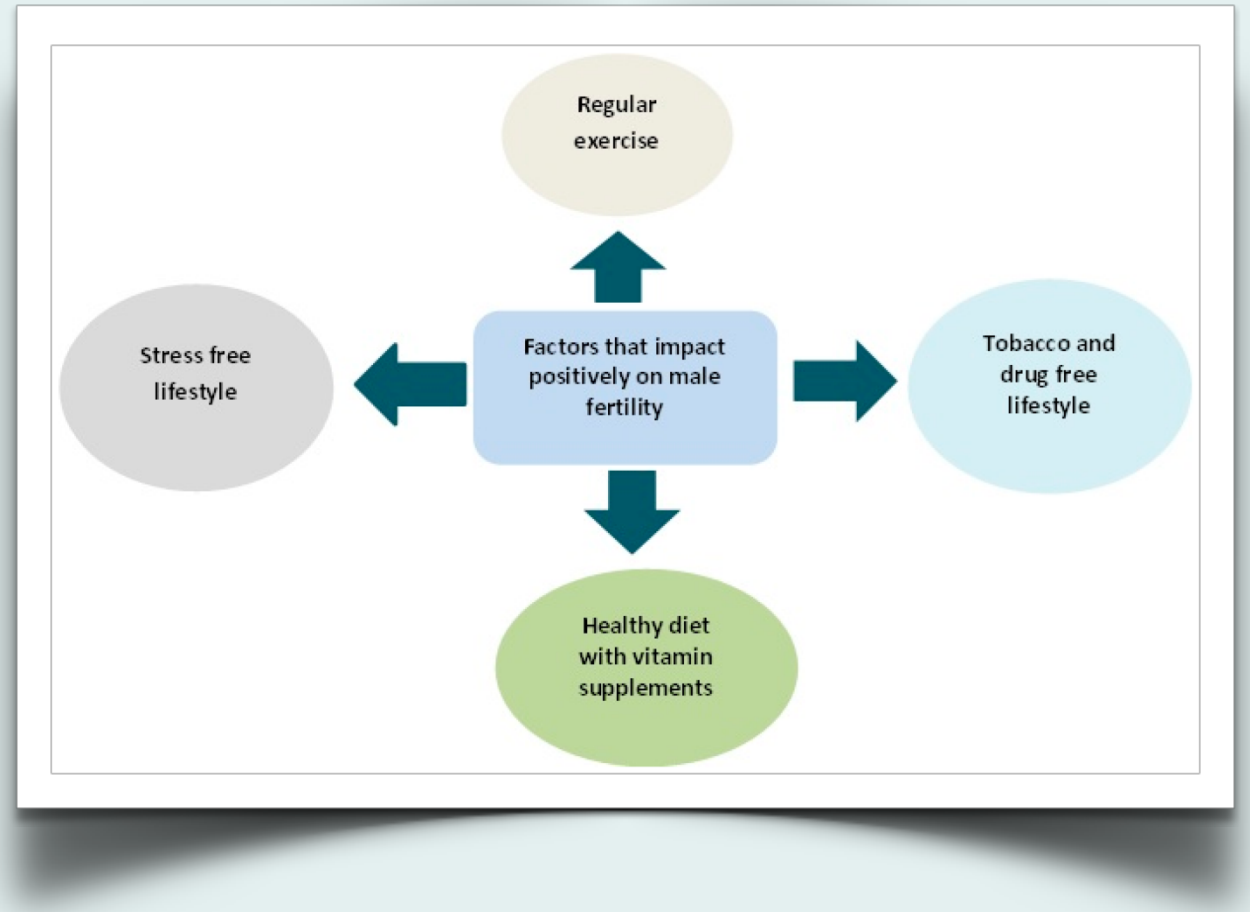


e) **Radiation/ Phones**- Increased semen abnormalities were found in men talking more than 3 hrs/ day on mobiles and in men holding the phones<50cms from the scrotum. Continuous WIFI presence has also shown to increase the sperm DNA fragmentation. The electromagnetic wave-dependent decrease in melatonin predisposes sperm to oxidative stress leading to poor semen quality.

f) **Heat effects** – occupational exposure to heat (welders, ceramic &furnace workers and truck drivers) and sauna/hot baths can elevate scrotal temperatures leading to spermatogenic failure.

g) **Stress-** Mental stress is associated with low levels of antioxidants such as, glutathione (GSH) and higher levels of pro-oxidants which can create oxidative stress and decrease in testosterone levels. These combined effects lead to poor semen quality and erectile dysfunction.

Fig 2 – Positive Lifestyle changes recommended:



CONCLUSION

It is important to recognize the hazardous effects of improper lifestyle on men's health. It is essential to correct inappropriate lifestyle to improve the quality of life. The majority of human studies suggest an association between EDC and disruption of the male reproductive system causing decreased male fertility. It is prudent to check the damage caused by these chemicals on the male reproductive system, notably the TDS.

In a report compiled by IFFS in May 2019, it is suggested that prevention of exposure to EDCs should be a priority for all health professionals with the goal of ensuring global equity and health for all. It has been emphasized to shift the burden of proof of chemical safety from the individual and health care provider to the manufacturers similar to the licensing of medical drugs. It is time to introspect, intervene and improvise for a better tomorrow.

REFERENCES

1. Antti Perheentupa, MD. Male infertility and environmental factors.IFFS Brief Report. Global Reproductive Health(2019)4:e28
2. Skakkebaek NE, Rajpert-De Meyts E, Main KM. Testicular dysgenesis syndrome: an increasingly common developmental disorder with environmental aspects. Hum Repro 2001; 16:972–8.
3. Thankamony A, Pasterski V, Ong KK, et al. Anogenital distance as a marker of androgen exposure in humans. Andrology 2016;4:616–25
4. Di Nisio A, Sabovic I, Valente U.et al. Endocrine disruption of androgenic activity by perfluoroalkyl substances: clinical and experimental evidence. J Clin Endocrinol Metab. 104(4):1259-1271, April 2019


Butterflies may be better indicators of the health of our environment than birds.
Roger Tory Peterson