



IMPACT OF ADULTHOOD LIFESTYLE ON MALE INFERTILITY: A CRITICAL REVIEW OF THE CURRENT LITERATURE

PURUSHOTTAM PRAMANIK

Post graduate, Department of Physiology Hooghly, Mohsin College,

ABSTRACT

Human infertility has been increasing worldwide but the exact causes are not yet known. Male infertility, which currently accounts for approximately half of all cases, has been increasing faster than female. While certain cases of male infertility are due to anatomical abnormalities, an estimated 40-49% of cases are due to deficient sperm production of unidentifiable origin. There is growing body of scientific evidence supporting the idea that sperm counts have declined considerably over the last 50 years. Over the last few decades, there have been progressive changes in aspects of our diet, lifestyle as well as environment. Report in recent years has shown that the incident of male infertility has increased as a result of various factors such as environmental pollution, stress and lifestyle. Among lifestyle, factors such as tobacco smoking, smokeless tobacco chewing, alcohol intake, high temperature, some modern electronic gadget and obesity have shown to adversely affect reproduction. These factors may impair male fertility by interfering with spermatogenesis, spermiogenesis, motility, sperm DNA and chromatin integrity, hormonal regulation or by reducing the fertilizing capacity of spermatozoa. Most of the lifestyle factors decrease semen quality by inducing oxidative stress from imbalance between rate of formation of reactive oxygen species and their scavenging capacity by antioxidant system. In conclusion it is strongly encouraged to research into antioxidants for greater understanding of the effects of ROS on sperm parameters and it will be beneficial way of finding solutions to human male infertility.

Key words: Sperm parameters, heat, tobacco, alcohol, cell phone, obesity

INTRODUCTION

Human fertility is remarkably low in comparison to most of the animals. An estimated 6% of adult males are thought to be infertile (Steven,2000). Infertility is defined as the inability to achieve a pregnancy after one year of unprotected intercourse. Conception is normally achieved within 12 months in 80-85% of couples using no contraceptive measures, thus an estimated 15% of couples attempting their first pregnancy will have difficulty in conceiving. While certain cases of male infertility are due to anatomical abnormalities such as varicoceles, ductal obstructions or ejaculatory disorders, an estimated 40-49% of cases are due to deficient sperm production of unidentifiable origin (Griffin and

Wilson, 1994). There is growing body of scientific evidence supporting the idea that sperm counts have declined considerably over the last 50 years. Carlsen et al.(1993 and 1992) reported that sperm density declined from 113 million/ml in 1940 to 66 million /ml in 1990 and seminal volume decreased from an average of 3.4ml to 2.75 ml. Other recent reports also found the decline of semen quality among donors over the last 20 years(Carlsen et.al., 1995; Van Waeleghem , 1996).

There are sufficient evidences of increasing trends in a number of human health problems like cancers, reproductive and developmental defects, cardiovascular problem

etc. Factors like Environmental, lifestyle, dietary or occupational may play an important role behind these trends. Over the last few decades, there have been progressive changes in aspects of our diet, lifestyle as well as environment. Report in recent years has shown that the incident of male infertility has increased as a result of various factors such as environmental pollution, stress and lifestyle (Mishra et al., 2012). Among lifestyle, factors such as tobacco smoking, smokeless tobacco chewing, alcohol intake etc have a profound negative impact on general health. The association of lifestyle factors on deterioration of reproductive health receiving attention i.e., tobacco smoking and chewing, alcohol, high temperature and some modern electronic gadget have shown to affect reproduction adversely. These factors may impair male fertility by interfering with spermatogenesis, spermiogenesis, motility, sperm DNA and chromatin integrity, hormonal regulation or by reducing the fertilizing capacity of spermatozoa. Therefore, in this chapter, the impact of lifestyle factors on male fertility will be considered.

HEAT

Temperature influences the development of germ cells as well reproductive cycle of living beings. Nature has kept the scrotum outside the body cavity so that the temperature of the testes remains lower than that of the body temperature. Testicular descent into the scrotum normally occurs by birth in boys and failure of testicular descent, especially when this extends into puberty and adulthood, results in absence of spermatogenesis. The testes into the scrotum in order that their temperature can be kept 3-4°C below core body temperature as maintenance at normal body temperature are incompatible with spermatogenesis (Setchell, 1998). It is probably also important that the testes are descended into the bottom of the scrotum rather than being placed at top where their proximity to the body surface is likely to impair cooling of the testes. As well as testis position, two other key elements in ensuring cooling of the testis are the presence of a vascular-rich corrugated scrotal surface via which heat loss can occur and the presence of an arterio-venous plexus (the pampiniform plexus) in the spermatic cord and which has the function as a heat exchanger to cool incoming blood to the testis by

heat exchange with the cooler venous blood that is exiting the testis (Maddocks et al.1993; Piner et al. 2002). Normal functioning of the plexus is important for maintaining testicular coolness and it is potentially susceptible by disorders such as varicocele in which the veins in the plexus are varicosed (Turner, 2001). Therefore any things that impede scrotal heat loss will affect testicular temperature, then the greater will be the detrimental effect on the spermatogenesis (Setchell, 1998).

Moderate or physiological elevation in scrotal skin temperature is associated with a substantially reduced sperm concentration, which results in a poor semen quality (Hjollund et al. 2000). Wang et al. (1997) reported elevation of testicular temperature by 1°C above the base line depresses spermatogenesis by 14% and there by decreases sperm output. They also mentioned that exposure to high temperature results in modification of sperm morphology. The mean value sperm with abnormal morphology rises from 30-60% within 6-8 months of exposure to high temperature (Dada et al. 2003 and 2001).

The most obvious things that can affect scrotal heat loss are a febrile illness such as influenza, exposure to an exogenous heat source, such as occupationally (bakers, welders, foundry workers) or via taking a hot bath (Mieusset and Bujan, 1995). A 30 min soak of laboratory animal in a moderately hot bath (40-42°C) impairs spermatogenesis (1), and it can induce germ cell apoptosis and DNA damage (Paul et al. 2008a and 2008b).

Lifestyle and occupational factor now a days cause men to spend a long time in a sedentary position. When seated, air does not circulate too easily around the scrotum and therefore there is less efficient cooling, an effect likely to be exacerbated if wearing tight underpants or trousers. In studies of men in whom scrotal temperature was measured continuously in relation to position and activity, scrotal temperature increased progressively with duration of sedentation and this was associated with lower sperm counts (Hjollund 2002a and 2002b). Studies in lorry and taxi drivers, who spend a long time seated, have also produced evidence for detrimental effects on semen quality (Bujan et al. 2000). Other studies have investigated the impact of wearing tight versus loose underwear and

reached similar conclusions (Mieusset and Bujan, 1995). The most recent scenario investigated has been the impact on scrotal temperature of using laptop computer (Sheynkin, 2005).

Paul et al. (2009) suggested that heat exposure causes hypoxia and oxidative stress responses in germ cells, which is manifested as increased expression of hypoxia inducible factors that push the germ cells towards apoptosis.

ALCOHOL

Humans have consumed alcoholic beverage since pre-historic times for a variety of reasons. Alcoholic beverages are found to affect different system of the human body including reproductive system. It has been observed that chronic alcohol was common among infertile men (Tsujiura et al. 2004). The testes have been shown to be highly susceptible to ethanol as it cross the blood testes barrier (Maneesh et al. 2005). Chronic ethanol consumption causes sexual defunct (VanThiel, 1979). Early histological studies indicate that testis may be even more sensitive to ethanol than the liver (Arlitt and Wells, 1997). Chronic alcoholics are often associated with impotence, loss of libido, premature or delayed ejaculation and sterility (Bayden and Pamerter, 1983). Alcohol intakes have been shown to increase number of teratozoospermia (Villalta et al. 1997). Impaired sperm motility was noted in chronic ethanol users (Kucheria et al. 1985; Gomathi et al. 1993) as well as alcohol treated rats (Pramanik and Ghosh, 2011). A numbers of clinical and experimental studies have shown impaired spermatogenesis under chronic ethanol consumption (Haider, 1985). Low sperm count was reported in cauda of epididymis of alcohol treated rat (Pramanik and Ghosh, 2011; Anderson, 1983).

Male reproductive system consists of three parts: hypothalamus, anterior pituitary and testes and is finely controlled through a classic negative feedback mechanism (Maneesh et al. 2006). Hypothalamus produces LHRH which is released in hypothalamo-hypophyseal portal system and circulates to anterior pituitary. It stimulate release of LH and FSH from anterior pituitary. LH and FSH circulate to testes via general circulation. LH stimulates testosterone production from Leydig cell of testes. FSH promotes spermatogenesis and sperm maturation. Testosterone circulates back to

the hypothalamic-pituitary unit and regulates the further production and secretion of LHRH and LH by negative feedback. When the system is functioning normally low testosterone level results in a rise of LH and FSH. Chronic alcohol consumption negatively impacts all level of hypothalamic-pituitary gonadal axis (Emanuele and Emanuele, 2001). Ethanol treatment decreases testosterone level in serum, testis as well as epididymis (Adams et al. 1991). Alcohol impairs testosterone production (Maneesh et al. 2006). Alcohol administration has been shown to reduce in the testes the activity of enzymes crucial to the synthesis of testosterone (Chiao and VanThiel, 1983). Alcohol Increased oxidative stress is a well accepted mechanism Alcohol-induced low testosterone level is associated with low level of LH. Thus alcohol is toxic not only to the testis but also to the hypothalamus or the pituitary (or both). Alcohol administration is associated with a reduction in the production and secretion of LHRH by the hypothalamus (Ching, 1988).

Increased oxidative stress is a well accepted mechanism of alcohol-induced injury of various tissues including testis (Emanuele et al. 2001). Low testosterone is due to increased oxidative stress which can damage testosterone secreting Leydig cell (Maneesh et al. 2006). Oxidative stress has been established as one of the cause of male infertility (Makker, 2009). Oxidative stress is a cellular condition associated with an imbalance between the production of reactive oxygen species (ROS) and their scavenging capacity by antioxidants. When the production of ROS exceeds the available antioxidant defense, significant oxidative damage occurs to many cellular organelles due to damage of lipid, proteins, carbohydrates and DNA. These processes can ultimately lead to cell death. Sperm is susceptible to oxidative damage as it content high poly unsaturated fatty acid in its plasma membrane (Sanocke and Kurpisz, 2004). Though antioxidant defense system is active in the semen its activity is limited as the amount of cytoplasm of the sperm is low (Lewis, 1997). Activity of antioxidant enzyme, super oxide dismutase (SOD) was significantly low in testes and epididymis in alcohol treated rats (Pramanik and Ghosh 2011). Alcohol treatment also decreases level of vitamin-C in testes and epididymis (Pramanik and Ghosh, 2011).

Testicular alcohol dehydrogenase normally functions to convert retinol to retinal, a compound essential for normal spermatogenesis. When the alcohol dehydrogenase in the testes is pre-empted to metabolize alcohol, retinal synthesis is blocked and spermatogenesis is impaired (Van Thiel, 1974).

CELL PHONE USE

Cell phone has become an indispensable device in our daily life and such a phone with 2000 MHz infrequency bands emits radiofrequency electromagnetic waves (EMW). However, health risk associated with their usage are often overlooked. Recently adverse effects of radio frequency EMW on brain, heart, endocrine system and DNA of humans and animals are widely reported. The recent evidences from several studies supports a growing claim that cell phone usage may have a detrimental effect on sperm parameters leading to increase the risk of male infertility. The reports available show an effect of cell phone on sperm motility in humans (Fejes et al. 2005; Davoudi et al. 2002). Animal studies indicate that EMW may have a wide range of damaging effects on the testicular functions and male germ line (Dasdag et al. 1999; Itken et al. 2005). The use of cell phones by men is associated with a decrease in semen quality. The decrease in sperm count, motility, viability and normal morphology is related to the duration of exposure to cell phones (Agarwal et al. 2008). Cell phone use is associated with low testicular weight and destruction of Leydig cells (Kesari et al. 2010)

EMW can possibly affect reproductive function via three mechanism: i) an EMW-specific effect; ii) a thermal molecular effect; or iii) a combination of these (Blackwell, 1979). Wang et al. (2003) suggested that Leydig cells are most susceptible cells to EMW, and injury to Leydig cell may affect spermatogenesis. Increase in tissue or body temperature on exposure to EMW may also cause reversible disruption of spermatogenesis (Saunders et al 1991; Kandeel et al. 1988; Jung and Schill, 2000). EMW-dependent decrease in melatonin, an antioxidant, can predispose sperm to oxidative stress (Burch et al. 1998). Agarwal et al. (2009) suggested that cell phone use increases ROS production and decreases total antioxidant capacity leads to

increase in oxidative stress. A decrease in motility and viability of sperm is linked to concentration of superoxide anions.

Recent observation suggests that the adverse effects of cell phone usage on male reproductive parameters have been due to over production of ROS by an induced field of EMW (Kesari et al. 2010; Agarwal et al. 2011). This can trigger cell differentiation by its action on PKC which may have adverse effect on spermatogenesis. Further research is needed to identify the mechanism of action of EMW emitted from cell phones on the male reproductive system.

SMOKING

A number of studies have shown higher incidence of abnormal morphology of sperm (Gour et al. 2007; Lewin et al 1991), decrease sperm motility, decrease sperm density and damaged DNA (Kunzle et al. 2003; Stillman et al. 1986; Vine et al. 1986) in men who smoked. Exposure of spermatozoa to seminal plasma from smokers resulted in a significant reduction in sperm viability and possibly their fertilizing ability (Zovos et al. 1998a; Zovos et al. 1998b). Cigarette smoking reduced testosterone production (Luqman et al. 2008). It is also reported that nicotine inhibits LH secretion in males (Funabashi et al. 2005). Thus nicotine-induced suppression of hypothalamo-pituitary-testicular axis is one of the causes of smoking-induced adverse effects on male fertility. Cigarette smokers were also shown to have higher level of circulating estradiol which potentially impact spermatogenesis (Steven 2000). Smoking also causes erectile dysfunction (Kumar, 2010).

Saleh et al. (2002) reported that cigarette smoking significantly increased level of seminal ROS which caused oxidative stress. ROS in the seminal plasma arises from imbalance between antioxidant capacity of spermatozoa and the amount of ROS production (Saleh et al. 2002; Rajpukar et al. 2000). In smokers there is increase risk of sperm aneuploidy, alteration of sperm plasma membrane and sperm DNA fragmentation have been documented (Mandiola et al. 2009).

SMOKELESS TOBACCO USE

The use of tobacco without burning is known as smokeless tobacco (SLT) use. Chewing tobacco and snuff are the two types of SLT. Chewing

tobacco is sold in loose leaf, plug or twist form and the user's places in small amount between the cheek and lower gum for sucking or chewing. Snuff a moist or dry tobacco that of finely ground or shredded is pinched or dipped and placed between cheek and lower gum. SLT use has increased rapidly throughout the world in recent years especially among adolescent boys and young men. Because of vigorous efforts toward increasing awareness of the adverse effects of the tobacco, smoking has declined paradoxically and the use of SLT has greatly increased (Christen et al. 1989). Smokeless tobacco is now considered as safe alternative of smoking (Christen et al. 1989). Like cigarette the main ingredient of SLT is tobacco and tobacco contains along with other harmful materials like nicotine.

Decrease of semen quality including sperm motility, sperm viability and sperm morphological abnormality has been reported in tobacco chewers (Said et al. 2005). Chronic treatment of rat with extract of 'khaini' as well as 'gutkha' (types of chewing tobacco use in India) adversely affect male reproductive indices including decrease epididymal sperm count, decrease sperm motility and increase sperm abnormality (Pramanik and Mondal 2011). SLT-induced sperm abnormality associated with defective tails (Zovos et al. 1998b). Chronic treatment of albino rats with SLT extract significantly decreased testicular weight (Pramanik and Mondal, 2011).

Like smoked tobacco the main ingredient of SLT is nicotine. SLT consistently produces levels of nicotine higher than those seen with smoking (Gupta 2004). Because of prolonged absorption, overall nicotine exposure was twice as large after single exposure to SLT compared with cigarette smoking (Benowitz et al. 1988). Ultra structural change was noted in testis following nicotine treatment (Aydos et al. 2001). Nicotine acts as sperm toxic agent on maturing or matured spermatozoa (Pacifci et al. 1995). Chronic nicotine treatment is associated with decrease fertility indices of male rats (Oyeyipo et al. 2011). Like cigarette SLT is responsible for oxidative stress (Stegmayr et al. 1993). Thus SLT-induced

decrease of semen quality may be due to either direct effect of nicotine of nicotine-induced oxidative stress.

OBESITY

Obesity is lifestyle dependent factor and is often associated with people who are generally less active, which could roughly mean period of prolonged sitting. Several studies have shown up to a threefold higher incidence of obesity in infertile men than in those with normal semen quality (Magnusdottir et al. 2005; Hammoud et al. 2008). Obesity is associated with negative impact on male fertility. BMI of more than 25 is associated with an average 25% reduction in sperm count and sperm motility (Hammoud et al. 2008; Nielsen et al. 2007).

Abnormal spermatogenesis in men is often hormone related. Obesity in men is associated with reduced blood testosterone level, this reduction being proportional to the degree of obesity (Techernof et al. 1995; Gould et al. 2007). In addition there may be an increase in circulating estradiol (Raman and Schlegel 2002; Shafik and Olfat 1981). Suppression of estradiol levels in obese men using aromatase inhibitor normalizes the testosterone: estradiol ratio and improve semen quality (Raman and Schlegel 2002). Shafik and Olfat (1981) suggested that number of Sertoli cell is low in obese persons than nonobese subject. Reduced Sertoli cell number permanently produced lower sperm count.

Another explanation for reduced spermatogenesis in obese men could be deposition of fat around the scrotal blood vessels, leading to impaired blood cooling and elevated testicular temperature (Sharpe 2010).

DNA fragmentation is the process in which chromatin DNA is cleaved during apoptosis, or when a cell dies. Literature survey suggests that there is direct correlation between BMI and DNA fragmentation (Hammoud et al. 2008). However, although there is sufficient evidence to support lower sperm count and DNA fragmentation due to obesity, there is yet to understand why sperm morphology appears to be affected.

Table-1: Effect of principal life style related factors on male sperm parameters

Mechanism/factor	Life style	Effect on sperm parameters	Reference
Heat	Hot bath	Low sperm count	Hjollund et al. 2000;
	Tight dresses	Abnormal sperm	Dada et al. 2001
	Working with sitting		
	Use of laptop Automobile driving		
Alcohol	Beverage	Low sperm count	Pramanik and Ghosh, 2011;
		Abnormal sperm Decrease sperm motility Low testosterone	
			Adams et al. 1991
Tobacco	Smoking	Low sperm count Abnormal sperm Decrease sperm motility Decrease sperm viability	Gour et al. 2007;Kunzle et al. 2003;Luqman et al. 2008
	Smokeless tobacco	Low sperm count Abnormal sperm Decrease sperm motility	Said et al. 2005; Pramanik and Mondal 2010.
Obesity	Less physical work high caloric diet	Low sperm count Abnormal sperm Decrease sperm motility Low testosterone	Hammoudt et al., 2008; Gould et al., 2007.
Electromagnetic wave	Cell phone	Low sperm count Abnormal sperm Decrease sperm motility Decrease sperm viability Destruction of Leydig cell Testicular apoptosis	Agarwal et al., 2008; kesari et al., 2010; Agarwal et al., 2011.

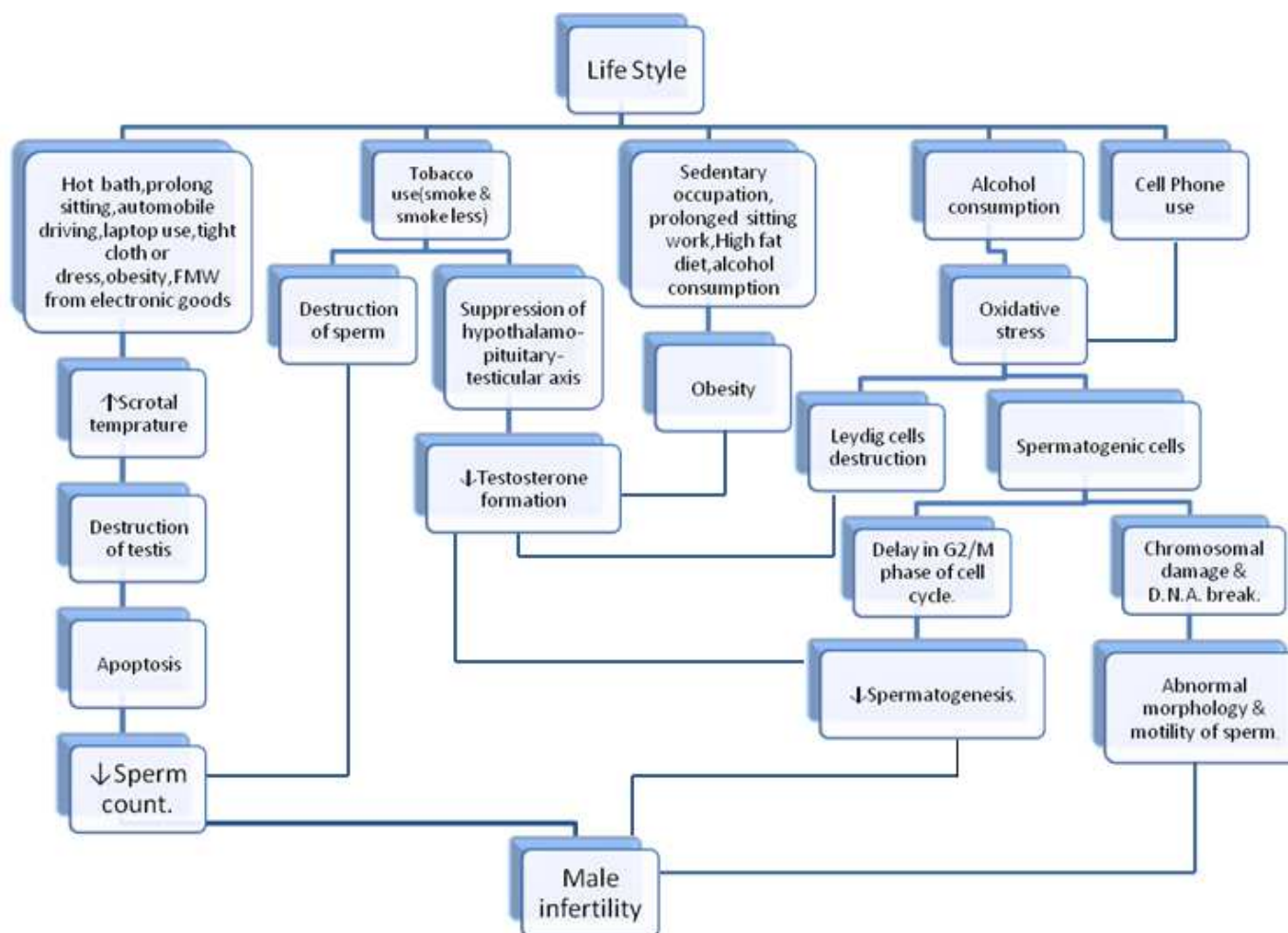


Figure 1: A summaries of the effects of adulthood life style on male reproductive pattern

CONCLUSION

1. Most of the lifestyle factors including smoking, tobacco chewing, alcohol intake as well as cell phone use decrease semen quality by inducing oxidative stress. Vitamin-C, vitamin-E and Selenium provide strong antioxidant properties to fight free radical damage and maintain the integrity of sperm cells. Thus antioxidant rich food should be incorporated in daily food list.

2. Healthy weight should be maintained and exercise must be done regularly. Having an increase amount of body fat may interfere with production of androgens and can contribute to the production of abnormal sperm.

3. Heavy drinking can also interfere with sperm quality and cause more abnormal sperm production. Thus alcohol intake should be controlled.

4. Hot tubs and hot baths must be avoided because spending longer than 30 minutes in over 100 °F can affect the number of normal sperm present as well as an increased scrotal temperature can interfere with sperm production and contributes to sperm abnormality.

5. Riding a bike for longer than 30 minutes, wearing tight shorts, working in a hot environment and sitting with laptop on lap can all cause an increased number of abnormal sperm.

ACKNOWLEDGEMENT

I am thankful to Mr Sunirmal Bhattacharya and Mr. Indra Narayan Ganguli of Hooghly Mohsin College and my son Parthiba Pramanik for their assistance in preparation of manuscript. I also thank to my wife, Mrs. Basudha Pramanik for her continuous inspiration.

REFERENCES

1. Adams ML, Little PJ, Bell B and Cicero TJ. Alcohol affects rat testicular interstitial fluid volume and testicular secretion of testosterone and beta endorphin. *J Pharmacol Exp Ther.* 1991; 258: 1008-1014.
2. Agarwal A, Fnu D, Sharma RK, Ranga G and Li J. Effect of cell phones usage on semen analysis in men attending infertility clinic: an observational study. *Fertil Steril.* 2008; 89: 124-128.
3. Agarwal A, Nisarg D, Makker K, Varghese A, Mouradi R, Sabanegh E and Sharma R. Effects of radio frequency electromagnetic waves from cellular phones on human ejaculated semen: an in vitro pilot study. *Fertility and sterility.* 2009; 92: 1318-1325.
4. Agarwal A, Sing A and Kesari K. Cell phone and male infertility: a review of recent innovations in technology and consequences. *Int Braz J Urol.* 2011; 37: 432-454.
5. Anderson RA Jr, Willis BR, Oswald C and Zeneveld LJD. Ethanol-induced male infertility; impairment of spermatozoa. *J Pharmacol exp Ther.* 1983; 225; 479-486.
6. Arlitt A and Wells A. The effect of alcohol on reproductive tissues. *J Expt med.* 1997; 26; 769-782.
7. Aydos k, Guven MC, Can B and Ergun A. Nicotine toxicity to the ultrastructure of testis in rat. *B J U Int.* 2001; 88: 622-626.
8. Bayden TW and Pamenter RW. Effects of ethanol on male hypothalamic-pituitary-gonadal axis. *Endo Rev.* 1983; 4; 389-395.
9. Benowitz NL, Porchet H, Shiener L and Jacob P. Nicotine absorption and cardiovascular effects with smokeless tobacco use; comparison with cigarette with nicotine gum. *Clin Pharmacol Ther.* 1988; 44: 23-28.
10. Blackwell RP. Standards for microwave radiation. *Nature.* 1979; 282: 360.
11. Bujan L, Daudin M, Charlet JP, Thonneau P and Mieusset R. Increase in scrotal temperature in car drivers. *Hum Reprod.* 2000; 15: 1355-1357.
12. Burch JB, Reif JS, Yost MG, Keefe TJ and Pitral CA. Nocturnal excretion of urinary melatonin metabolite among electric utility workers. *Scand J Work Environ Health.* 1998; 24: 183-189.
13. Carlsen E, Giwerman AJ, Keiding N and Skakkeback NE. Evidence for decreasing quality of semen during past 50 years. *B.M.J.* 1992; 305: 609-613.
14. Carlsen E, Giwerman AJ, Keiding N and Skakkeback NE. Decline in semen quality from 1930 to 1991. *Ugeskr Laeger.* 1993; 155: 2230-2235.
15. Carlsen E, Giwerman AJ, Keiding N and Skakkeback NE. Declining semen quality and increasing incident of testicular cancer: is there a common cause? *Environ health Perspect.* 1995; 103: 137-139.
16. Chiao YB and VanThiel DH. Biochemical mechanism that contribute to alcohol-induced hypogonadism in the male. *Alcoholism Clin Exp Res.* 1983; 7(2): 131-134.
17. Ching M, Valenca M and Negro-Vilar A. Acute ethanol treatment lowers hypophyseal portal plasma LHRH and systemic LH levels in orchidectomized rats. *Brain Res.* 1988; 443: 325-328.
18. Christen AG, McDonald JL, JrOlson BL and Christen JA. Smokeless tobacco addiction: a heart to the oral and systemic of the child and adolescent. *Pediatrician.* 1989; 16: 170-177.
19. Dada R, Gupta NP and Kucheria K. Deterioration of sperm morphology in men exposed to high temperature. *J Anatomical Soc India.* 2001; 50: 107.
20. Dada R, Gupta NP and Kucheria K. Spermatogenic arrest in men with testicular hyperthermia. *Teratog Carcinog mutagen.* 2003; 23: 235.
21. Dasdag M, Ketani MA, Akbag Z, Ersay AR, Sari I and Demirtas OC. Whole body microwave exposure emitted by cellular phones and testicular function of rats. *Urol Res.* 1999; 27: 219-223.
22. Davoudi M, Brossner c and Kuber W. The influence of electromagnetic waves on sperm motility. *Urol Urogynaecol.* 2002; 19: 18-22.
23. Emanuele MA and Emanuele N. Alcohol and male reproductive system. *Alcohol Res Health.* 2001; 25: 282-287.

24. Emanuele N, Lapigli N, Ateiner J, Colantoni A, VanThiel DH and Emanuele MA. Peripubertal paternal ethanol exposure. *Endocrinology*. 2001; 14; 213-219.
25. Fejes I, Zavaczki Z, Szollosi j, Koloszar S, Daru J and Kovacs L. Is there a relationship between cell phone use and semen quality? *Arch Androl*. 2005; 51: 385-393.
26. Funabashi T, Sona A, Mitsushima d and Kimura F. Nicotine Inhibit Pulsatile LH secretion in human males but not in human females and tolerance to this nicotine effect loss within one week of quitting smoking. *J Clin Endocrinol Metab*. 2005; 90; 3908-3913.
27. Gomathi C, Balsubramanian K, Vijayabanu N, Srikanth V and Govindarajulu P. Effects of chronic alcoholism on semen studies on lipid profiles. *Int J Androl*. 1993; 16: 175-181.
28. Gould DC, Kirby RS and Amoroso P. Hypoandrogen –metabolic syndrome: a potentially common and under diagnosed condition in men. *Int J Clin Pract*. 2007; 61: 341-344.
29. Gour DS, Talekar M and Pathak VP. Effect of cigarette smoking on semen quality of infertile men. *Singapur Med J*. 2007; 48: 119-123.
30. Griffin E and Wilson D. Disorders of the testes in: Isselbacher K, Braunwald E, Wilson J, Martin B, eds *Harrison's Principles of Internal Medicine*. 13th ed. New York, Mcgraw Hill; 2006-2017; 1994.
31. Gupta R. Smokeless tobacco and cardiovascular risk. *Arch Intern med*. 2004; 164: 1845-1849.
32. Haider SG, Haffmann N and Passia D. Morphological and enzyme histochemical observation on alcohol-induced disturbances in testis of two patients. *Andrologica*. 1985; 17; 532-540.
33. Hammoud AO, Gibson M, Petersen CM, Hamilton BD and Carrell DT. Obesity and male reproductive potential. *J Androl*. 2006; 27: 619-626.
34. Hammoud AO, Gibson M, Petersen CM, Meikle AW and Carrell DT. Impact of male obesity on infertility: a critical review. *Fertil Steril*. 2008; 90: 897-904.
35. Hjollund N H, Bonde J P, Jensen TK and Olsen J. Diurnal scrotal skin temperature and semen quality. *Int J Androl*. 2000; 23: 309.
36. Hjollund NH, Storgaard L, Ernst E, Bonde JP and Olsen J. The relation between daily activities and scrotal temperature. *Reprod toxicol*. 2002a; 16: 209-214.
37. Hjollund NH, Storgaard L, Ernst E, Bonde JP and Olsen J. Impact of diurnal scrotal temperature on semen quality. *Reprod Toxicol*. 2002b; 16: 215-221.
38. Itken RJ, Bennetts LE, Sawyer D, Wiklendt AM and King BV. Impact of radio frequency electromagnetic radiation on DNA integrity in the male germ line. *Int J Androl*. 2005; 28; 171-179.
39. Jung A and Schill WB. Male infertility. Current lifestyle could be responsible for infertility. *MMW Fortschr Med*. 2000; 142: 31-33 (German).
40. Kandeel FR, Swerdloff RS. Role of temperature in regulation of spermatogenesis and the use of heating as a method for contraception. *Fertil Steril*. 1988; 49: 1-23.
41. Kesari KK, Kumar S and Behari J. Mobile phone usage and male infertility in wistar rats. *Indian J Exp Biol*. 2010; 47: 987-992.
42. Kucheria K, Saxena R and Mohan D. semen analysis in alcohol dependence syndrome. *Andrologica*. 1985; 17: 558-563.
43. Kumar R. The association between smoking and male fertility and sexual health. *Indian J Cancer*. 2010; 47: 107-108.
44. Kunzle R, Mueller MD, Hanggi W, Birkhauser MH, Drescher h and Bersinger NA. semen quality of male smokers and nonsmokers in infertile couples. *Fertil Steril*. 2003; 79: 287-291.
45. Lewin A, Gonen O, Orvieto R and Schenker JG. Effect of smoking on concentration, motility and zona-free hamster test on human sperm. *Arch Androl*. 1991; 275: 51-54.
46. Lewis SE, Sterling ES, Young IS and Thompson W. Comparison of of individual antioxidants of sperm and seminal plasma in fertile and infertile men. *Fertil Steril*. 1997; 67: 142-147.

47. Luqman AO, Emmanuel OE, OLuseguss RJ, Olaide KG, Ayokunle O, Abidun GJ and Sikiru A. effect of cigarette smoking on urinary testosterone excretion in men. *Biokemistri*. 2008; 20: 129-32.
48. Maddocks S, Hargreave T B, Reddie K, Fraser H M, Kerr j B and Sharpe R M. Intra testicular hormone level and the route of secretion of hormones from the testis of the rat, guineapig, monkey and human. *Int J Androl*. 1993; 16: 272-278.
49. Magnusdottir EV, Thorsteinsson T, Thossteindottir S, Heimisdottir M and Olafsdottir K. Persistent Organochlorines , Sedentary occupation, obesity and human male sub fertility. *Hum Reprod*. 2005; 20: 208-215.
50. Makker k, Agarwal A and Sharma R. Oxidative stress and male infertility. *Indian J Med Res*. 2009; 129: 357-367.
51. Mandiola J, Torres-Cantero AM and Agarwal A. Life style factors and male infertility: an evidence based review. *Arch Med Sci*. 2009; 5: S3-S12.
52. Maneesh M, Joylakshmi H, Dutta S, Chakraborty a and Basudevan DM. Role of oxidative stress in ethanol-induced germ cell apoptosis as experimental study in rats. *Indian j Clin Biochem*. 2005; 20: 62-67.
53. Maneesh M, Dutta S, Chakraborty A and Basudevan DM. Alcohol abuse duration dependent decrease in plasma testosterone and antioxidants. *Indian J Physiol Pharmacol*. 2006; 50: 291-296.
54. Mieusset R and Bujan L. Testicular heating and its possible contribution to male infertility: a review. *Int j Androl*. 1995; 17: 186-191.
55. Mishra RK, Verma HP, Singh N and Singh SK. Male infertility; Lifestyle and oriental remedies. *J Scientific res*. 2012; 56: 93-101.
56. Nielsen TL, Hagen C, Wraae K, Brixen K, Petersen PH, Haug E, Larsen R and Andersen M. Visceral and subcutaneous adipose tissue assessed by magnetic resonance imaging in relation to circulating androgens, sex hormone binding globulin and LH in young men. *J Clin Endocrinol Metab*. 2007; 92: 2696-2705.
57. Oyeyipo IP, Raji Y, Emikpe BO and Bolarinwa AF. Effects of nicotine on sperm characteristic and fertility profile in adult male rats; a possible role of cessation. 2011; 12(3): 201-207.
58. Pacifici R, Altieri I, Gandini L, Lenzi A, Passa AR and Pichini S. Environmental tobacco smoke: nicotine and conitine concentration in semen. *Environ Res*. 1995; 68(1): 69-72.
59. Paul C, Murray AA, Spears N and Saunders PTK. Do heat stress and deficits in DNA repair pathway have a negative impact on male fertility? *Mol Hum Reprod*. 2008a; 14: 1-08.
60. Paul C, Murray AA, Spears N and Saunders PTK. A single, mild transient scrotal heat stress causes DNA damage, sub fertility and impairs formation of blastocysts in mice. *Reproduction*. 2008b 136: 73-84.
61. Paul C, Teng S and Saunders PTK. A single, mild transient scrotal heat stress causes hypoxia and oxidative stress in mouse testes, which induces germ cell death. *Biol Reprod*. 2009; 80: 913-919.
62. Piner J, Sutherland M, Millar M, Turner K J, Newall D and Sharpe R M. Changes in vascular dynamics of the adult rat testis leading to transient accumulation of a novel 5-hydroxytryptamine agonist. *Reprod Toxicol*. 2002; 16: 141-450.
63. Pramanik P and Mondal P. Effect of crude extracts of smokeless tobacco on gonads of male albino rats. *Indian J Physiol Allied Sci*. 2010; 64(40): 155-164.
64. Pramanik P and Ghosh M. Effect of alcoholic beverage mahua on male reproductive indices of adult albino rats. *Indian j Biol Sci*. 2011; 17; 39-48.
65. Rajpukar A, Dhaduwalla CB, Jiang Y and Li H. Chronic cigarette smoking induces an oxidant-antioxidant imbalance in the testis. *J Environ Pathol Toxicol Oncol*. 2000; 19: 369-373.
66. Raman JD and Schlegel PN. Aromatase inhibitors for male infertility. *J Urol*. 2002; 167: 624-629.
67. Said TM, Ranga G and Agarwal A. Relationship between semen quality and tobacco chewing in men undergoing

- infertility evaluation. *Fertil Steril.* 2005; 84: 649-653.
68. Saleh RA, Agarwal A, Sharma RK and Nebon DR. Effect of cigarette smoking on levels of seminal oxidative stress in infertile men: a prospective study. *Fertil Steril.* 2002; 78: 491-499.
69. Sanocke D and Kurpysz M. Reactive oxygen species and sperm cells. *Reprod Biol Endocrinol.* 2004; 2: 12.
70. Saunders R, Sienkiewicz Z and Kowalczyk C. Biological effect of electromagnetic field and radiation. *J Radiol Prot.* 1991; 11: 27-42.
71. Setchell B P. Heat and the testis. *J Reprod Fertil.* 1998; 114: 179-184.
72. Shafik A and Olfat S. Scrotal lipomatosis. *Br J Urol.* 1981; 53: 50-54.
73. Sharpe RM. Environmental/lifestyle effects on spermatogenesis. *Phil Trans R Soc B.* 2010; 365: 1697-1712.
74. Sheynkin Y, Jung M, Yoo P, Schulsinger D and komaroff E. Increase in scrotal temperature in laptop computer users. *Hum Reprod.* 2005; 20: 452-455.
75. Stegmayr B, Johansson I, Moser U and Asplund K. Use of smokeless tobacco and cigarette- effects on plasma level of antioxidant vitamins. *Int J Vit Nutr Res.* 1993; 63: 195-200.
76. Steven S. Male infertility: Nutrition and environmental consideration. *Altern Med Rev.* 2000; 1: 28-38.
77. Stillman RJ, Rosenberg MJ an. Vogt HF, Heller WD and Borelli S. Sperm quality of healthy smokers, ex-smokers and nonsmokers d Sachs BP. Smoking and reproduction. *Fertility.* 46; 545-566; 1986.
78. Techernof A, Despres JP, Belanger A, Dupont A, Prud'homme D, Moorjani S, Lupien PJ and Labrie F. Reduced testosterone and adrenal c19 steroid levels in obese men. *Metabolism.* 1995; 44: 513-519.
79. Tsujimura A, Matsumiya K, Takahashi T, yamanka M, Koga M, Miura H, Nishimura K, Takeyama M, Fujioka H, Okamoto Y, Iwamoto T and Okuyama A. Effects of life style factors on infertility in men. *Arch Androl.* 2004; 50: 15.
80. Turner T T. The study of varicocele through the use of animal model. *Hum Reprod Update.* 2001; 7: 78-84.
81. Van Thiel DH, Gavalier JS and Lester R. Ethanol inhibition of vitamin-a metabolism in the testes: possible mechanism for sterility in alcoholics. *Science.* 1974; 186: 941-942.
82. VanThiel DH and Lester r. The effects of chronic ethanol abuse on sexual functions. *Clin Endo Metab.* 1979; 8: 499-510.
83. Van Waeleghem k, De Clerq N and Vermeulen L. Deterioration of sperm quality in young healthy Belgian men. *Hum Reprod.* 1996; 11: 325-329.
84. Villalta J, Balleza JL, Nicole JM, Marfinzer-de-osaba MJ, Antunez E and Pimental C. Testicular function in asymptomatic chronic alcoholics: relation to ethanol intake. *Alcohol Clin Res.* 1997; 21: 128-133.
85. Vine MF, Tse CK, Hu P and Truong KY. Cigarette smoking and semen quality. *Fertil Steril.* 1986; 65: 835-842.
86. Wang C, McDonald V, Leung A, Suiperlano L. Bermaan N, Hull L and Swerdloff RS. Effect of increase scrotal temperature on sperm production in normal men. *Fertil Steril.* 1997; 68:334.
87. Wang SM, Wang DW, Peng RY, Gao YB, Yang Y and HU WH. Effect of electromagnetic pulse irradiation on structure and function of Leydig cells in mice. *Zhonghua Nan Ke Xue.* 2003; 9: 327-330 (Chinese).
88. Zovos PM, Correa JR, Antypas S, Zarmakoupis –zovos PN and, Zarmakoupis CN. Effect of seminal plasma from cigarette smokers on sperm viability and longevity. *Fertil Steril.* 1998a; 69: 425-429.
89. Zovos PM, Correa JR, Karagounis CS, Ahparaki A, Phoroglou C, Hicks CL and , Zarmakoupis –zovos PN. An electron microscope study of the axonemal ultra structure in human spermatozoa from male smokers and nonsmokers. *Fertil Steril.* 1998b; 69: 430-434.