Environmental Pollution and Infertility

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Giorgio Cavallini

17.1 Introduction

A decline in sperm counts has emerged in recent years [1–3]. Consequently, it has been argued that male fertility is declining, and it is further proposed that environmental pollutants may play an active role [4–10]. By contrast, no apparent and clear decrease in population fertility has been noted in epidemiologic studies [11, 12]. Decline in sperm count of healthy men of reproductive age over the years has been higher in some regions (Denmark, Scotland, USA east coast) than in others (USA west coast, south of France, Baltic countries). Genetic and racial factors may also be involved [7–12].

It has been hypothesized that environmental chemicals with estrogenic properties, heavy metals, and solvents constitute detrimental factors for sperm count [13–18], even though the epidemiologic consequences are unclear. Nevertheless, some kind of toxicologic effect on spermatogenesis is hypothesized; clinical and laboratory research indicates that of all the changes in male reproductive health seem to be interrelated and may have a common origin in fetal life or childhood [19–23]. Furthermore, some epidemiologic studies confirm that exposure to endocrine disruptors, solvents, and heavy metals may play a role in male reproductive disorders [24].

Three categories of potential reproductive disruptor pollutants have been found: endocrine disruptors, heavy metals, and organic solvents.

G. Cavallini
Andrological Section, Gynepro-Medical Team,
via Tranquillo Cremona 8, 40137 Bologna, Italy
e-mail: giorgiocavallini@libero.it

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17.2 Endocrine Disruptors

Endocrine disruptors affect the male genital tract during fetal testis and germinal cell development (testicular dysgenesis syndrome), targeting pituitary gonadotropins [25] or the genetic regulation of steroidogenesis [26] at either the genomic [27] or proteomic [28, 29] levels. Gene pathways targeted include cholesterol transport and steroidogenesis, pathways involved in intracellular cholesterol/lipid homeostasis, insulin signaling, transcriptional regulation, oxidative stress [27], α-inhibin (which is essential for physiologic Sertoli cell development), and genes involved with communication between Sertoli cells and gonocytes [27]. Environmental pollutants are thought to induce oxidative stress, peroxidation [30], and germ cell apoptosis in the human fetal testis [31].

There exists a critical period of exposure: diethylstilbestrol (an estrogenic compound) exposure during the perinatal period can influence behavior, accessory glands, and reproductive structures in humans and rodents [32] via hormonal or epigenetic mechanisms [33].

Given that animals represent an accepted experimental model for human male reproduction, it is noteworthy that pollutants are regarded as etiologic factors in the reproductive decline of wildlife [34, 35]. Perinatal exposure is critical for the development of testicular dysgenesis syndrome in animals [36–38]. A severe problem of pollutants is that some of these chemicals have long half-lives and have been detected in environmental samples 10–20 years after they were banned for use [39].

Pesticides, fungicides, heavy metals, defoliants, and other chemical weapons, in addition to oils and cleaning agents [40–44], are regarded as the main environmental pollutants capable of disrupting the human and wildlife endocrine system (endocrine disruptor chemicals or EDCs).

Endocrine disruption is a mechanism of toxicity that hinders the ability of cells, tissues, and organs to communicate hormonally [45], provoking reduced fertility and fecundity [17], spontaneous abortion, skewed sex ratios [46], male and female reproductive tract abnormalities [47–49], precocious puberty [50, 51], polycystic ovary syndrome [52], neurobehavioral disorders, impaired immune function, and a wide variety of cancers [53, 54]. Endocrine disruptors represent a wide range of chemical classes and include agonists of the estrogen receptor, androgen receptor antagonists, and aryl hydrocarbon receptor agonists [55]. Some chemicals have more than one mechanism of action [56]. A list of endocrine disruptors is shown in Table 17.1. Many of these chemicals persist in the environment. Some are lipophilic and, hence, sequestered in adipose tissue and secreted in milk, whereas others may only be present for short periods of time but at critical periods of development.

17.3 Heavy Metals

All heavy metals are toxic and can affect the seminiferous epithelium [57–59]. Cadmium interacts with the zinc-dependent stability of the human sperm chromatin [60]. Salts of arsenic, cadmium, mercury, lead, and antimony are all toxic for

Table 17.1 Environmental pollutants: their sources and health effects [66]

Pollutant	Origin	Health effects	
		During development	During adulthood
[a]Bisfenol A	Component of polycarbonate plastic and epoxy resins	Modified prostate development and puberty onset, hormonal changes, decreased semen quality, obesity	Decreased semen and oocyte quality, recurrent miscarriages
[a]Dioxin/furans	Manufacture or burning of products containing chlorine	Urologic malformations	Menstrual irregularities, epigenetic disorders
[a]Organochlorine pesticides	Largely banned in Western countries, still persist in the food chain (DDT)	Altered sex ratio, altered puberty onset, decreased semen quality	Altered puberty onset, decreased semen quality, endometriosis, fetal loss
[a]Pentachlorophenol	Wood preservative, railroad ties	Reduced fertility	Reduced fertility
[a]Ethylene oxide	Chemical sterilizer for dental practice	?	Decreased semen quality, miscarriage
[a]Glycol ethers	Paints, enamels, wood stains; printing inks, cosmetics	?	Reduced fertility, decreased semen quality, fetal loss, menstrual irregularities
[a]Nonylphenol, octylphenol	Detergents, pesticides, paints, plasticizers	Hormonal changes, altered puberty onset, decreased testicular size, decreased semen quality	?
[a]Perfluorinated compounds	Water-repellent treatments	Hormonal changes, fetal loss, reduced birth weight	?
[a]Phthalates	Cosmetics, toys, lubricants	Malformations of reproductive tract, hormonal changes, decreased semen quality	Earlier menarche, menstrual irregularities, endometriosis, ovulation alterations, decreased semen quality, fetal loss
[a]Polybrominated diphenyl esters	Flame retardants	?	Decreased semen quality
[b]Mercury	Thermometers, dental filling	Decreased semen quality	Decreased semen quality
[b]Cadmium	Batteries, pigments, some metal alloys	Sertoli cell and testicle damage	Toxic to Sertoli cells and spermatogenesis
[b]Lead	Batteries, ammunition, metal products, X-ray shields	Hormonal and pubertal onset alterations	Hormonal alterations, menstrual alterations, reduced fertility, fetal loss, altered puberty, reduced spermatogenesis

(continued)

Table 17.1 (continued)

Pollutant	Origin	Health effects	
		During development	During adulthood
[b]Manganese	Dietary supplements, ceramics, pesticides, fertilizers	Hormonal changes, altered puberty onset	Hormonal changes, menstrual irregularities, fetal loss, altered puberty onset, damage to Sertoli cells and spermatogenesis
Organic solvents: benzene, toluene, 1-bromopropane, 2-bromopropane, perchloroethylene, trichloroethylene, etc	Plastic, resin, rubbers, synthetic fibers, lubricants, dyes, detergents, drugs, pesticides, fingernail polish, cleaning products, detergents, lacquers, fiberglass, food containers	Hormonal changes, pubertal onset alterations, reduced fertility, menstrual irregularities, miscarriage and fetal loss, decreased semen quality	Hormonal changes, reduced fertility, menstrual irregularities, miscarriage and fetal loss, decreased semen quality

[a]Chlorinated hydrocarbons (endocrine disruptors)
[b]Heavy metals

spermatogenesis in humans and animal models [61, 62]. Heavy metals are also present in some welding fluxes [63].

17.4 Solvents

Various organic solvents are also known to cause infertility, including glycol ethers [64], which are used in the printing industry and are also found in some paints (e.g., as used on naval vessels). Perchloroethylene, used in the dry cleaning industry, can also cause subfertility, but its effects on sperm morphology and kinematics are subtle, and their impact on fertility remains unclear [65].

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