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Commentary

Impact of pesticides on gonads and human health: An updated commentary

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Abstract

The consequence of pesticides on human health is a significant area of research. Different types of pesticides can cause various side effects on our body systems, including our organs and glands. One notable effect is on the gonads, which are the glands responsible for producing male and female sex hormones. The effects can be severe, leading to infertility in men and women, as well as other health issues. Thus, it is essential to focus on developing plant-based pesticides, known as botanical pesticides, which are derived from the various parts of plants (such as roots, stems, leaves, flowers, seeds, and fruits) and can be used in either dry powder or liquid form. Additionally, there is a need for innovation in creating new artificial pesticides, or synthetic pesticides, in laboratories. This includes modifying existing pesticides to make them biodegradable over time, that is they have minimal or no adverse effects on human health.

Keywords: Pesticides, Endocrine system, Gonads, Human health

Introduction

This article provides an overview of the effects of pesticides on reproductive organs and overall human health. It highlights recent findings and offers an updated perspective on how exposure to these chemicals can influence gonadal function and cause various health issues. To ensure that every individual globally has access to food, the "Green Revolution" was initiated, starting in numerous nations post-World War II and at the end of the 19th century into the early 20th century, and continuing thereafter. This agrarian transformation included biotechnology, genetic modification, and pest management. In pest management, different chemicals, including pesticides, were produced to mitigate damage caused by pests, thereby allowing for the production and storage of crops for the necessary duration. Literature surveys indicate that these pesticides directly or indirectly enter the human body since humans are at the highest level in all food chains [1–11]. Various categories of these pesticides have distinct impacts on the body's systems: digestive, respiratory, circulatory, excretory, reproductive, endocrine, and nervous system. Additionally, our focus here is solely on reproductive systems, specifically gonads.

Commentary Discussion

The production and secretion of male (♂) and female (♀) sex hormones are intricately regulated by gonadotropic hormones released by the master gland, as shown in **Figure 1**. When these vital processes are disrupted by pesticides, serious health issues can arise, including the abnormal functioning of organs. Extensive literature reviews underscore the alarming link between various pesticides (considering their types, levels of exposure, and detrimental impacts) and gonadal health, which directly influences human well-being [12–23]. It is crucial to address these concerns to protect our health interests.

Castiello and Freire [8] found that (i) exposure to organophosphate pesticides is connected to delayed sexual maturation in both boys and girls, (ii) childhood exposure to pyrethroids is related to

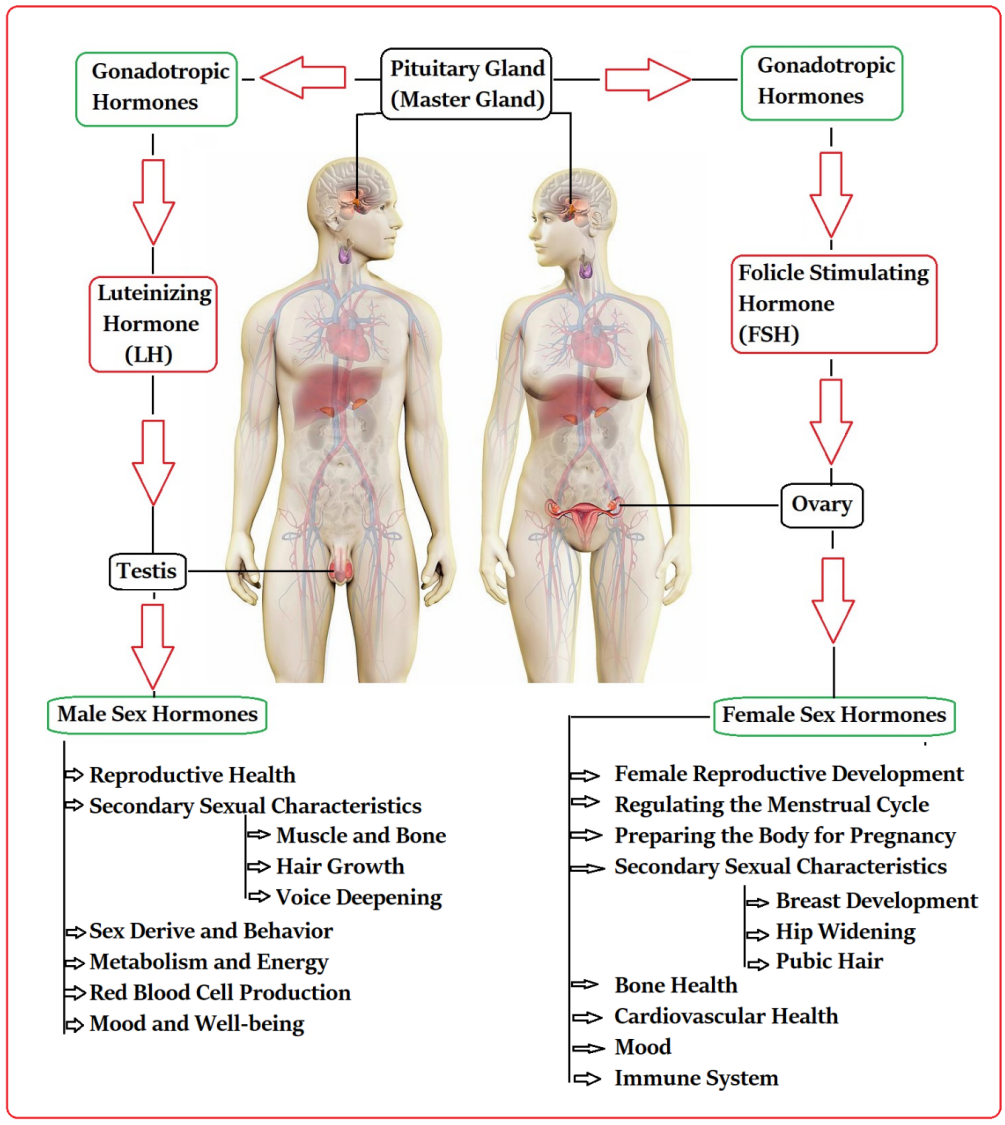

Figure 1. Mechanism of release of sex hormones from the gonads.

delayed puberty in girls and earlier puberty in boys, and (iii) prenatal/childhood exposure to various pesticides has been associated with earlier puberty onset in girls and delayed puberty in boys.

Bretveld *et al.* [15] authored a review titled, "Pesticide exposure: the hormonal function of the female reproductive system disrupted?" This review outlined various ways pesticides can interfere with the hormonal function of the female reproductive system, specifically the ovarian cycle. They determined that contact with pesticides could be linked to disruptions in the menstrual cycle, decreased fertility, extended time to conceive, miscarriage, stillbirths, and developmental abnormalities. Farr *et al.* [16] employed Cox proportional hazards modeling to investigate the relationship between pesticide use and age at menopause in 8,038 women residing and working on farms in Iowa and North Carolina. The research indicated that the median time to menopause rose by about 3 months for women exposed to pesticides (hazard ratio = 0.87, 95% confidence interval: 0.78, 0.97) and by roughly 5 months for those who used hormonally active pesticides (hazard ratio = 0.77, 95% confidence interval: 0.65, 0.92).

Roychoudhury *et al.* [17] also discussed pesticide contamination in their review. They documented the impacts of pesticides on (i) altered levels of luteinizing hormone (LH), follicle-stimulating hormone (FSH), and testosterone caused by imidacloprid, (ii) anti-androgenic effects and hormonal imbalances in the body displayed by hypogonadism from dichlorodiphenyltrichloroethane (DDT) exposure, and (iii) reduced testosterone concentrations from acute exposure to carbamates, thio- and dithiocarbamates, pyrethroids, chlorophenoxy acids, chloromethylphosphonic acids, and organophosphates. Research featured by Glover *et al.* in the Journal of Endocrinological Investigation [18] indicated that exposure to the insecticide chlorpyrifos and various organophosphates (OPs) are positively linked to the onset of erectile dysfunction (ED). ED, referred to as impotence, is the challenge of achieving or maintaining

an erection. ED leads to drawbacks such as a diminished sex life, depression, reduced self-worth, and troubled relationships, along with possible health concerns like an increased risk of heart disease, stroke, and various circulatory problems. It can lead to discomfort for both the person and their partner. Kaur *et al*. [19] revealed the possible mechanisms of pesticide effects on erectile function, a contributing factor in male infertility. They discovered that acetamiprid has the most harmful impact, leading to erectile dysfunction by affecting various inhibitory pathways. Acetamiprid is a neonicotinoid pesticide that manages a variety of sucking and chewing insects, including aphids, whiteflies, and leafhoppers, by affecting the insect's central nervous system. In 2023, Hamed *et al*. [20] in their meta-analysis used a total of 766 male subjects, out of which 349 were exposed to OP pesticides and rest 417 were unexposed controls. The findings of this research indicate that exposure to OP pesticide leads to decreased sperm count, concentration, total and progressive motility, and normal sperm morphology, potentially through a mechanism independent of testosterone. These results reinforce the current evidence in the literature regarding the adverse effects of OP pesticide exposure on semen quality. Cremonese *et al*. [21] documented the effects of agricultural pesticides on reproductive hormones, semen quality, and genital measurements in young men in the southern region of Brazil. Rural men exposed to agricultural pesticides exhibited worse sperm morphology, increased sperm count, and reduced LH levels compared to urban individuals. They determined that prolonged occupational exposure to contemporary pesticides could influence reproductive results in young males.

La Merrill *et al*. [7] authored a research paper titled, "Prenatal Exposure to the Pesticide DDT and Hypertension Diagnosed in Women before Age 50: A Longitudinal Birth Cohort Study" and found that (i) adult women may experience heightened hypertension due to exposure to p,p′-DDT in early life, and (ii) the link between DDT exposure and hypertension may originate early in developmental stages. Tyagi *et al*. [5] determined in their study that the concentration of organochlorine pesticides (OCPs) in the environment may significantly influence the development of diabetes. Mohammadkhani *et al*. stated that exposure to OCPs is linked to a higher risk of Cardiovascular disease (CVD) and mortality from CVD, mediated by atherogenic and inflammatory molecular mechanisms affecting fatty acid and glucose metabolism [6]. Three pesticides namely malathion, diazinon, and glyphosate were classified category 2A carcinogens to humans [9–11].

Every class of plants of India (algae [24], bryophytes [25], pteridophytes [26], gymnosperms [27], and angiosperms [28]) possesses particular medicinal or toxicological properties, or sometimes both [29]. Plants act as natural pesticides by producing secondary metabolites (alkaloids, terpenes, limonoids, etc.) that may repel, harm, or affect the development of pests [30]. Certain plants that possess pesticidal characteristics (botanical pesticides) are familiar to us. Examples include neem (azadirachtin) [31], *Chrysanthemum cinerariifolium* (pyrethrum) [32], Leguminosae family plants (rotenone) [33], strychnine tree (strychnine) [34], clove, coriander, and mint plants (repellent activity) [35], among others. Azadirachtin serves as an effective insect growth regulator and antifeedant, deterring pests while interfering with their growth and reproduction without causing instant death. Neem oil, a widely used neem pesticide, is derived from fruits and seeds, containing these active ingredients, necessitating emulsifiers to blend with water for application [31]. Pyrethrins originate from the desiccated flower blooms of the *Chrysanthemum* plant. Pyrethrins consist of a blend of six insecticidal substances, which include cinerin, jasmolin, and different types of pyrethrins. Pyrethrins function as a quick-acting contact insecticide, affecting the nervous system of insects and leading to swift paralysis, or "knockdown". The derived compounds are utilized to produce a range of insecticidal items, including sprays and lotions, aimed at managing pests such as flies, mosquitoes, and fleas [32]. Rotenone is utilized globally due to its wide-ranging insecticidal, acaricidal, and various pesticidal characteristics. All plants recognized for producing rotenone belong to the natural order Leguminos. Rotenone is utilized globally due to its wide-ranging insecticidal, acaricidal, and additional pesticidal characteristics [33]. All plants recognized for producing rotenone belong to the natural order Leguminos. Rotenone is extremely poisonous to various insects but completely safe for humans and all warm-blooded vertebrates. Although not every insect is vulnerable to its harmful effects, it has been demonstrated, in the form of sprays and various formulations, to be fifteen times more toxic than a nicotine spray when applied as a contact poison on aphids, and thirty times more toxic than lead arsenate, when evaluated as an internal poison against specific caterpillars. The seeds of the strychnine tree (Strychnos nux-vomica) hold the extremely poisonous alkaloid strychnine, which has been commonly utilized as a potent yet hazardous pesticide. It is mainly utilized to eliminate small vertebrates, including rodents and birds [34]. Botanical pesticides are typically less harmful to non-target species, humans, and the ecosystem. They decompose into non-toxic materials, minimizing environmental harm. They provide a sustainable and renewable option to artificial pesticides. The intricate and varied chemical makeup can hinder pests from developing resistance more effectively. Thus, the main aim of botanists should be to search for other wild plants that have pesticidal properties.

Conclusion

There are already all classes of plants with natural pesticidal properties; therefore, their use should be increased and encouraged globally among farmers. Because exposure to some pesticides (synthetic) resulted in: (i) early/delayed puberty in boys, (ii) decreased semen quality (including low sperm count, reduced sperm mobility, failure to inseminate the ovum), (iii) erectile dysfunction in male, (iv) early puberty (fertility) and early menopause (infertility) in girls, (v) loss of gestation in females (natural implantation of embryo in uterus), (vi) other health issues including (vii) aggressiveness, (viii) anxiety, (ix) hypertension, (x) diabetes, (xi) cardiovascular disease and (xii) cancer. Therefore, we commented that attention should be given to time dependent biodegradable synthetic pesticides (chemicals) with no/minimal side effects and more attention is given to natural (botanical) pesticides.

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