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Invited Review Article

Impact of chronic stress on reproductive functions in animals

D. Banerjee[1*], J. Mukherjee[1], P. K. Das[1], P. R. Ghosh[1] and K. Das[1]

[1]Department of Veterinary Physiology, Faculty of Veterinary and Animal Sciences, West Bengal University of Animal and Fishery Sciences, Kolkata- 700 037, West Bengal, India

Abstract

Chronic stress is a widespread condition with a profound negative impact on animal reproductive functions such as fertility, pregnancy and offspring production. The persistent activation of the hypothalamic-pituitary-gonadal (HPG) axis under chronic stress conditions leads to hormonal imbalances as elevated cortisol levels can suppress the-reproductive hormone secretion. Hormonal imbalances adversely affect key reproductive processes such as ovulation, spermatogenesis, fertilization and embryo development. In livestock, these impairments significantly reduce reproductive efficiency, hence contributing to substantial economic losses in animal production systems. Furthermore, chronic stress induces oxidative stress, resulting in cellular damage to reproductive tissues and modulating immune system function, exacerbating the decline in reproductive health. Stressors which result into significant impact on animal production in daily basis are from poor managemental conditions, amongst which heat stress due to global climate change. All these stressors have compounded to reproductive challenges imposed by chronic stress. Heat stress, driven by higher ambient temperatures, further disrupts reproductive processes by altering hormonal balance, reducing gamete quality, impairing embryo survival and increasing pregnancy complications. The synergistic effect of chronic stress and heat stresses creates an additional burden on reproductive functions, particularly for less heat-intolerant livestock. This review critically explores the multifaceted mechanisms by which chronic stress disrupts reproductive function in animals, emphasizing the roles of hormonal dysregulation, oxidative stress and immune system alterations. Thus, addressing both environmental and physiological factors is of utmost importance to improve the reproductive functions of domestic animals.

Keywords: Animal reproduction, Chronic stress, Global climate change, Hormonal imbalance, Reproductive failure

Highlights

- Chronic stress disrupts the HPG axis, causing hormonal imbalances that impair fertility in animals.
- Elevated glucocorticoids from chronic stress inhibit gonadal hormones, reducing reproductive success.
- Understanding the impact of chronic stress on reproduction aids welfare in conservation and management.

INTRODUCTION

Stress is a natural part of life, functioning as self-protective mechanism to adapt and respond to environmental challenges. This stress response is essential for survival in acute situations, facilitating the body's ability to cope with immediate threats by activating physiological responses such as the hypothalamic-pituitary-adrenal (HPA) axis (Sapolsky, 2000). However, when stress becomes chronic in case of prolonged or repeated exposure to stressors, it can cause detrimental effects on multiple physiological systems, including reproduction. Chronic stress disturbs the finely tuned hormonal balance, leading to reproductive dysfunction and reduced fertility (Dobson and Smith, 2000). Reproductive success is vital not only for the survival of species but also for the economic viability of animal husbandry. In the livestock sector, where reproduction underpins productivity, chronic stress can severely impair reproductive outcomes, affecting both animal health and farm profitability (Marai and Habeeb, 2010).

The effects of chronic stress on reproduction are profound and multifaceted. Its impact on fertility, pregnancy outcomes, and offspring survival is clearly shown by altering reproductive hormone levels, increasing oxidative stress, and modulating immune responses (Agarwal *et al*., 2005). Furthermore, chronic stress affects both male and female reproduction differently, with distinct effects on spermatogenesis, oogenesis, and maternal behavior (Tilbrook *et al*., 2000).

This review provides an in-depth examination of the mechanisms through which chronic stress impairs reproductive function, on the role of the HPA axis, oxidative stress, and immune responses.

Common stressors on animal reproductive functions

Stressors on animal production include poor housing conditions, overcrowding, nutritional deficiencies,

*Corresponding Author, E-mail: dipakndri@gmail.com

extreme environmental temperature, handling, and transport (Moberg and Mench, 2000). These stressors lead to continuous activation of the HPA axis and ultimately disrupt the HPG axis, which, over time, irregulates productive hormone production-and reduces fertility (De Rensis and Scaramuzzi, 2003).

Besides these common stressors, global warming is increasingly becoming a significant cause of chronic stress for both livestock and wild animal populations. Rising environmental temperatures due to climate change exacerbate thermal stress in livestock, disrupting reproductive functions, particularly in heat-sensitive species (Rojas-Downing *et al*., 2017). Similarly, temperature-dependent sex determination in reptiles is being skewed by global warming, leading to imbalanced sex ratios and potentially threatening species survival (Hulin *et al*., 2009). In migratory birds, shifting climate patterns are altering the timing of reproduction, resulting in asynchrony between breeding periods and food availability, which impacts reproductive success (Both *et al*., 2009). Marine species, such as fish, are also affected by ocean warming, which disrupts spawning cycles and threatens the sustainability of fisheries (Pankhurst and Munday, 2011). Wild animals succumbed to chronic stress due to climate change, habitat degradation, and enormous human activities, further disrupting the natural reproductive cycles and affecting population sustainability (Romero, 2004).

Hypothalamic-pituitary-adrenal (HPA) axis and reproduction

The hypothalamic-pituitary-adrenal (HPA) axis is the central stress-response system in mammals, birds, reptiles and fish. Upon exposure to stress, the hypothalamus releases corticotropin-releasing hormone (CRH), which stimulates the anterior pituitary gland to secrete adrenocorticotropic hormone (ACTH). ACTH then triggers the adrenal glands to produce glucocorticoids, such as cortisol in mammals and corticosterone in birds and reptiles (Moberg and Mench, 2000). These glucocorticoids regulate the body's metabolism, immune function and energy use to help the organism cope with stress.

In short-term or acute stress situations, the HPA axis plays a beneficial role by mobilizing resources to respond to the stressor. However, when stress is prolonged, the continuous release of glucocorticoids has a suppressive effect on the reproductive system. Chronic elevation of cortisol levels will interfere with the hypothalamic-pituitary-gonadal (HPG) axis, which regulates the reproductive steroid hormones (Sapolsky, 2000). Disruption of the HPG axis leads to decreased secretion of gonadotropin-releasing hormone (GnRH), which in turn reduces luteinizing hormone (LH) and follicle-stimulating hormone (FSH) production.

This hormonal imbalance negatively affects reproductive processes such as spermatogenesis, oogenesis, and estrous cycle. For example, climate-induced chronic stressors like rising environmental temperatures due to global warming exacerbate, leading to disruptions in reproductive function. High ambient air temperatures have been shown to increase glucocorticoid secretion, further suppressing reproductive hormone production and impairing reproductive success, particularly in heat-sensitive species like livestock and reptiles (Hulin *et al*., 2009; Rojas-Downing *et al*., 2017). The chronic elevation of glucocorticoids can also reduce the sensitivity of gonadal tissues to LH and FSH, further impairing reproductive function. For example, high cortisol levels inhibit ovarian steroidogenesis, reduce estrogen production and lead to impaired follicular development and ovulation (Rivier and Rivest, 1991).

Additionally, in migratory birds, climate change-induced shifts in environmental stressors, such as altered breeding seasons and food scarcity, which can lead to prolonged activation of the HPA axis, further disrupting reproductive cycles (Both *et al*., 2009). These effects of chronic stress related to climate change highlight the importance of understanding the global environmental variation impacting the HPA and HPG axis, consequently on animal reproductive health.

Gonadotropin-inhibitory hormone (GnIH) and reproductive function

Gonadotropin-inhibitory hormone (GnIH) has emerged as a critical regulator in the modulation of reproductive processes under chronic stress conditions. GnIH inhibits the release of gonadotropins by acting on the hypothalamus and pituitary, consequently reducing reproductive capacity (Tsutsui *et al*., 2013). Chronic stress elevates GnIH levels, which has downstream effects on reproductive hormone levels, leading to disruptions in the reproductive axis (Kirby *et al*., 2009).

In mammals, prolonged exposure to stressors has been shown to significantly upregulate GnIH expression, dampening the hypothalamic-pituitary-gonadal (HPG) axis activity and reducing fertility rates (Calisi *et al*., 2008). For example,-exposure to chronic unpredictable stress highlight a marked increase in hypothalamic GnIH expression, which correlates with reduced luteinizing hormone (LH) secretion and altered estrous cyclicity in rodents (Tsutsui *et al*., 2012).

Moreover, the ecological context in which animals are exposed to stress plays a vital role in GnIH regulation. In avian species, environmental stressors

such as habitat loss and climate change trigger GnIH activity, reducing reproductive success and impacting population dynamics. This is particularly evident in migratory birds, where shifting climate patterns disrupt reproductive timing, leading to asynchrony between breeding and resource availability (Both *et al*., 2009).

Reactive oxygen species and reproductive function

Chronic stress is known to exacerbate oxidative stress, a condition marked by an overproduction of reactive oxygen species (ROS) that overwhelms the antioxidant defence systems, leading to cellular damage and impaired reproductive function. Persistent activation of the hypothalamic-pituitary-adrenal (HPA) axis during chronic stress results in elevated glucocorticoid levels, which not only impair mitochondrial function but also reduce the activity of key antioxidant enzymes like superoxide dismutase (SOD) and glutathione peroxidase (GPx), increasing ROS production (Sapolsky, 2000; Picard *et al*., 2014). In reproductive tissues, oxidative stress is linked to disruptions in follicular development, oocyte quality, and sperm function, ultimately reducing fertility (Aitken and Baker, 2006; Agarwal *et al*., 2012). The ovaries are particularly vulnerable to ROS accumulation, causing apoptosis in granulosa cells and impaired ovulation. In males, sperm ROS-mediated lipid peroxidation and DNA damage contribute to reduced motility and fertility (Aitken and Baker, 2006; Agarwal *et al*., 2012). Furthermore, pro-inflammatory cytokines such as TNF-α and IL-6, which are elevated during chronic stress, exacerbate oxidative damage in reproductive tissues (Agarwal *et al*., 2012). To mitigate these effects, antioxidant supplementation of vitamins C and E, along with selenium, has been shown to alleviate ROS-induced reproductive damage (Agarwal *et al*., 2008). Therefore, understanding the relationship between chronic stress, oxidative stress, and reproductive health is essential for developing targeted interventions to maintain fertility in stressed animals.

Chronic stress and immune system interactions

Chronic stress significantly influences the immune system, triggering profound effects on reproductive health through immune-endocrine interactions (Webster Marketon and Glaser, 2008; Dhabhar, 2014). Prolonged activation of the hypothalamic-pituitary-adrenal (HPA) axis during chronic stress elevates glucocorticoid levels, which suppress immune function and promote systemic inflammation by altering cytokine production (Elenkov and Chrousos, 2002). This immunosuppressive effect is particularly harmful in the reproductive system, where immune homeostasis is crucial for maintaining healthy tissue function. For example, chronic stress can lead to elevated levels of pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), which disrupt ovarian and uterine function by promoting oxidative damage and impairing normal folliculogenesis, implantation and early embryo development (Palomba *et al*., 2018). In males, stress-induced immune dysregulation can result in increased infiltration of immune cells like macrophages into the testes, leading to inflammation, impaired spermatogenesis and reduced testosterone production (Zou *et al*., 2019; Khambata *et al*., 2021; Ye *et al*., 2021). Furthermore, the interaction between the immune system and reproductive hormones, such as estrogen and progesterone, plays a key role in modulating the inflammatory response, and chronic stress can disturb this balance, exacerbating reproductive dysfunction (Straub, 2007). Targeted therapies, including anti-inflammatory agents and stress reduction techniques, are thus critical in mitigating the adverse immune-mediated effects of chronic stress on reproduction (Dhabhar, 2009).

Impact of chronic stress on male reproduction

Spermatogenesis and sperm quality: Chronic stress has a profound impact on spermatogenesis and sperm quality, primarily through the dysregulation of the hypothalamic-pituitary-gonadal (HPG) axis and the exacerbation of oxidative stress. Consequence of prolonged stress is increased glucocorticoid levels, which will inhibit gonadotropin-releasing hormone (GnRH) secretion, ultimately leading to a reduction in both the luteinizing hormone (LH) and follicle-stimulating hormone (FSH) levels. This hormonal imbalance disrupts spermatogenesis, contributing to suboptimal sperm parameters such as reduced sperm count, motility, and viability (Sengupta *et al*., 2017) and diminishes testosterone production. Additionally, chronic stress induces reactive oxygen species (ROS) level that causes lipid peroxidation of the sperm membrane, compromising its integrity, reducing motility and the ability to fertilize an oocyte (Kaltsas, 2023).

Furthermore, stress-induced inflammation results due to infiltration of immune cells, such as macrophages, into testicular tissue, leading to chronic testicular inflammation and damage to the blood testis barrier. Sperm DNA fragmentation caused by oxidative stress is strongly associated with impaired fertilization, poor embryo quality, and increased miscarriage rates (Aitken and Baker, 2006). Mitigating these effects involves antioxidant therapy, such as supplementation with vitamin C and E, selenium, and zinc, which have been shown to protect sperm from oxidative damage and improve overall sperm quality (Ahmadi *et al*., 2016;

Hajjar *et al*., 2020). Reducing environmental stressors and implementing stress management strategies are essential for preserving normal spermatogenesis and ensuring optimal male fertility.

Suppression of testosterone production: Chronic stress significantly suppresses testosterone production, primarily through its dysregulation of the hypothalamic-pituitary-gonadal (HPG) axis. Stress-induced activation of the hypothalamic-pituitary-adrenal (HPA) axis elevates glucocorticoid levels, particularly cortisol, which negatively affects the secretion of gonadotropin-releasing hormone (GnRH) from the hypothalamus. Reduced GnRH levels will decrease luteinizing hormone (LH) release from the anterior pituitary, which is required to stimulate Leydig cells in the testes for testosterone secretion (Xiong *et al*., 2022; Mbiydzenyuy and Qulu, 2024). This suppression disrupts spermatogenesis and can lead to reduced libido and impaired sexual function in males (Sengupta *et al*., 2017).

Moreover, chronic stress enhances oxidative stress and inflammation within the testes, which further suppresses testosterone synthesis (Xiong *et al*., 2022). Reactive oxygen species (ROS) damage Leydig cells and reduces their capacity to produce testosterone (Darbandi *et al*., 2018), while pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α), inhibit steroidogenic enzymes essential for testosterone biosynthesis (Hong *et al*., 2004). This stress-induced reduction in testosterone not only compromises reproductive function but also leads to systemic health issues, including reduced muscle mass fatigue and mood disturbances (Zitzmann, 2024).

Mitigation strategies to counter testosterone suppression focus on stress management interventions, including behavioral therapies, physical exercise, and pharmacological approaches like selective glucocorticoid receptor antagonists. Additionally, antioxidant supplementation, such as vitamins C and E, has shown potential in protecting Leydig cells from further oxidative damage and support-the testosterone production (Ryan *et al*., 2010).

Testicular damage and apoptosis: Chronic stress induces significant testicular damage and apoptosis, primarily through the activation of oxidative stress, inflammation, and hormonal dysregulation (Turner and Lysiak, 2008; Ojo *et al*., 2023). Elevated glucocorticoids during chronic stress disrupt the hypothalamic-pituitary-gonadal (HPG) axis, impairing testosterone production and promoting oxidative stress within the testes (Whirledge and Cidlowski, 2013; Darbandi *et al*., 2018; Mbiydzenyuy and Qulu, 2024). Reactive oxygen species (ROS) accumulate in testicular tissue, causes lipid peroxidation, DNA fragmentation, and protein damage, leading to apoptosis of germ cells and structural deterioration of the seminiferous tubules (Agarwal *et al*., 2014; Darbandi *et al*., 2018). Oxidative damage to the Sertoli cells, which are essential for nurturing developing sperm, further exacerbates germ cell apoptosis and impairs spermatogenesis (Yang *et al*., 2021).

Inflammatory cytokines, such as TNF-α and interleukin-6 (IL-6), are also upregulated during chronic stress and play a crucial role in mediating testicular damage (Dutta *et al*., 2021). These cytokines activate pro-apoptotic pathways in Leydig and germ cells by upregulating caspase enzymes, leading to increased cell death. Moreover, the integrity of the blood-testis barrier (BTB), which protects the developing sperm from harmful substances and immune responses, is compromised under stress-induced inflammation and oxidative stress, further facilitating cellular damage and apoptosis (Shen *et al*., 2022). The cumulative result of these processes is reduced sperm count, motility and overall fertility.

Mitigating testicular damage and apoptosis involves targeting oxidative stress and inflammation. Antioxidants such as vitamins C and E, zinc and selenium have been shown to protect testicular tissue by scavenging ROS and reducing apoptosis (Sengupta *et al*., 2004; Besong *et al*., 2023). Additionally, anti-inflammatory agents and lifestyle modifications aimed at reducing chronic stress can preserve testicular function and fertility in stressed animals.

Impact of chronic stress on female reproduction

Ovarian function and oocyte quality: Chronic stress negatively impacts ovarian function and poor oocyte quality, primarily through the dysregulation of the hypothalamic-pituitary-gonadal (HPG) axis and the resultant hormonal imbalances. Prolonged activation of the hypothalamic-pituitary-adrenal (HPA) axis during stress leads to elevated glucocorticoid levels, which can suppress the release of gonadotropin-releasing hormone (GnRH) from the hypothalamus, thereby reduces luteinizing hormone (LH) and follicle-stimulating hormone (FSH) secretions from the pituitary gland (Mbiydzenyuy and Qulu, 2024). This disruption in hormonal signaling adversely affects ovarian follicular development and maturation, leading to impaired ovulation and decreased fertility.

Moreover, chronic stress induces oxidative stress in ovarian tissues, characterized by an increase in reactive oxygen species (ROS) that can damage oocytes and surrounding granulosa cells. Elevated ROS levels can

lead to lipid peroxidation, DNA fragmentation, and mitochondrial dysfunction in oocytes, compromising their quality and developmental potential (Song *et al*., 2024). Oxidative stress can also trigger apoptosis in granulosa cells, further impairing the microenvironment necessary for oocyte maturation and health (Yang *et al*., 2017; Yan *et al*., 2022).

The inflammatory response associated with chronic stress also plays a critical role in ovarian dysfunction. Increased levels of pro-inflammatory cytokines, such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), can disrupt normal ovarian function by promoting follicular atresia and inhibiting normal steroidogenesis (Yamamoto *et al*., 2015; Samir *et al*., 2017). This immune dysregulation affects not only the quantity of follicles but also their quality, leading to suboptimal oocyte health and viability.

Interventions aimed at mitigating the effects of chronic stress on ovarian function include antioxidant therapy, which can counteract oxidative damage and support oocyte quality (Rakha *et al*., 2022). In addition, stress reduction techniques such as behavioral therapies, physical activity, and nutritional support by improving ovarian function and enhance reproductive outcomes in females undergoing chronic stress (Gitsi *et al*., 2024).

Estrous cycle disruptions: Chronic stress is known to cause significant disruptions in the estrous cycle, which can adversely affect female reproductive health and fertility (Casillas *et al*., 2021; Poitras *et al*., 2024). Stress-induced activation of the hypothalamic-pituitary-adrenal (HPA) axis leads to elevated levels of glucocorticoids, can interfere with the normal functioning of the hypothalamic-pituitary-gonadal (HPG) axis. This ultimately alters the secretion of gonadotropin-releasing hormone (GnRH), luteinizing hormone (LH), and follicle-stimulating hormone (FSH), which are essential for the regulation of the ovarian cycle including the follicular and luteal phases.

One of the primary effects of chronic stress is either prolongation or irregularity of the estrous cycle, often resulting in anovulation or missed estrous cycles (Casillas *et al*., 2021). Increased levels of stress hormones can inhibit the pre-ovulatory LH-surge, leading to incomplete follicular phase (Wagenmaker *et al*., 2009). Additionally, the influence of chronic stress on ovarian function can lead to decreased estrogen production, which is crucial for maintaining normal follicular wave dynamics during estrous cycle and prepares the endometrium for potential implantation.

Furthermore, chronic stress is associated with increased oxidative stress and inflammation in reproductive tissues, leading to disruption of the estrous cycle. Elevated reactive oxygen species (ROS) and pro-inflammatory cytokines, such as TNF-α and IL-6, have been shown to impair the quality of oocytes production and the health of the endometrium, further complicating the estrous cycle and reproductive failure.

Pregnancy and gestation: Chronic stress during pregnancy can have profound implications for both maternal health and fetal development, affecting gestational outcomes and long-term offspring health (Coussons-Read, 2013). The activation of the hypothalamic-pituitary-adrenal (HPA) axis in response to stress leads to increased production of glucocorticoids, primarily cortisol, which can cross the placental barrier and influence fetal development (Dahlerup *et al*., 2018). Elevated maternal cortisol levels have been associated with adverse outcomes, including low birth weight, preterm birth, and developmental delays in offspring (Zijlmans *et al*., 2015).

Stress during pregnancy can disrupt the hormonal balance, which is critical for maintaining a healthy gestation (Entringer, 2013). Increased levels of glucocorticoids can interfere with the production of reproductive hormones, such as progesterone and estrogen, which are essential for sustaining pregnancy and supporting placental function (Whirledge and Cidlowski, 2010). Additionally, chronic stress is linked to heighten inflammation, characterized by increased levels of pro-inflammatory cytokines like interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), which can adversely affect placental health and fetal growth (Palomba *et al*., 2018).

The impact of chronic stress on pregnancy does not end with birth; it can have lasting effects on the offspring as well. Prenatal stress exposure has been linked to increased susceptibility to metabolic disorders, behavioral issues, and cognitive impairments in later life (Coussons-Read, 2013; Jagtap *et al*., 2023). The offspring of chronically stressed mothers may exhibit alterations in stress response systems, leading to increased vulnerability to stress-related disorders in adulthood (Majer *et al*., 2023).

Lactation and maternal behavior: Chronic stress during the peripartum period can significantly impact lactation and maternal behavior, ultimately affecting offspring health and development. Elevated stress levels activate the hypothalamic-pituitary-adrenal (HPA) axis, resulting in increased glucocorticoid production, particularly cortisol. These hormonal changes can interfere with prolactin secretion, a key hormone essential for milk synthesis and secretion (Levine and Muneyyirci-Delale, 2018). Prolonged stress may cause

reduced milk yield and altered milk composition, which can negatively affect the growth and development of neonates (Josefson *et al*., 2023; Chen *et al*., 2024).

Chronic stress associated with impaired maternal behavior, is characterized by reduced maternal care and bonding with the offspring (Millie *et al*., 2024). Elevated glucocorticoid levels can diminish the responsiveness of mothers to their young, impairing behaviors such as grooming, nursing, and protective responses. This reduction in maternal care can further impact offspring development, leading to behavioral issues and increased vulnerability to stress later in life.

Additionally, stress can influence the neurobiological mechanisms underlying maternal behavior. Increased stress hormones can alter neurohormonal secretions, such as oxytocin and dopamine, which are critical for promoting maternal bonding and nurturing behaviors (Baskerville and Douglas, 2010). Oxytocin is a lactogenic hormone and has a significant role in maternal bonding. Dysregulation in oxytocin secretion due to chronic stress can hinder the establishment of a strong mother-offspring relationship (Olff *et al*., 2013).

Conclusion

Chronic stress exerts profound and often detrimental effects on reproductive functions across animal species, significantly influencing fertility, reproductive behavior and overall reproductive success. The mechanisms underpinning these effects are multifaceted, involving the dysregulation of the hypothalamic-pituitary-gonadal (HPG) axis, alterations in gonadal steroid hormones and heightened levels of glucocorticoids. These hormonal imbalances impair various stages of reproductive processes, from gametogenesis to different postpartum reproductive phases such as in the expression of abnormal reproductive behaviors, reduced fertility and compromised offspring viability. The impact of chronic stress on animal reproduction requires further research to explore interspecies variations and identify potential resilience mechanisms that some species may employ. An improved understanding on molecular, physiological and behavioral responses to chronic stress will help to advance the development of interventions aimed at mitigating these effects. Such insights will not only benefit reproductive science but also have applications in wildlife conservation and animal husbandry, where managing stress is critical for promoting reproductive health and population sustainability.

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REFERENCES

Agarwal A, Aponte-Mellado A, Premkumar BJ, Shaman A and Gupta S, 2012. The effects of oxidative stress on female reproduction: A review. Reprod Biol Endocrinol, 29: 1-31, doi: 10.1186/1477-7827-10-49

Agarwal A, Gupta S and Sharma R, 2005. Oxidative stress and its implications in female infertility- A clinician's perspective. Reprod Biomed Online, 11(5): 641-650, doi: 10.1016/s1472-6483(10)61174-1

Agarwal A, Gupta S, Sekhon L and Shah R, 2008. Redox considerations in female reproductive function and assisted reproduction: from molecular mechanisms to health implications. Antioxid Redox Signal, 10(8): 1375-1403, doi: 10.1089/ars.2007.1964

Agarwal A, Virk G, Ong C and du Plessis SS, 2014. Effect of oxidative stress on male reproduction. World J Mens Health, 32(1): 1-17, doi: 10.5534/wjmh.2014.32.1.1

Ahmadi S, Bashiri R, Ghadiri-Anari A and Nadjarzadeh A, 2016. Antioxidant supplements and semen parameters: An evidence based review. Int J Reprod Biomed, 14(12): 729-736

Aitken RJ and Baker MA, 2006. Oxidative stress, sperm survival, and fertility control. Mol Cell Endocrinol, 250(1-2): 66-69, doi: 10.1016/j.mce.2005.12.026

Baskerville TA and Douglas AJ, 2010. Dopamine and oxytocin interactions underlying behaviors: potential contributions to behavioral disorders. CNS Neurosci Ther, 16(3): e92-12, doi: 10.1111/j.1755-5949.2010.00154.x

Besong EE, Ashonibare PJ, Obembe OO, Folawiyo MA, Adeyemi DH *et al*., 2023. Zinc protects against lead-induced testicular damage via modulation of steroidogenic and xanthine oxidase/uric acid/caspase 3-mediated apoptotic signaling in male Wistar rats. Aging Male, 26(1): 2224428, doi: 10.1080/13685538.2023.2224428

Both C, van Asch M, Bijlsma RG, van den Burg AB, Visser ME *et al*., 2009. Climate change and unequal phenological changes across four trophic levels: constraints or adaptations? J Anim Ecol, 78(1): 73-83, doi: 10.1111/j.1365-2656.2008.01458.x

Calisi RM, Rizzo NO and Bentley GE, 2008. Seasonal differences in hypothalamic EGR-1 and GnIH expression following capture-handling stress in house sparrows (*Passer domesticus*). Gen Comp Endocrinol, 157(3): 283-287, doi: 10.1016/j.ygcen.2008.05.010

Casillas F, Betancourt M, Juárez-Rojas L, Ducolomb Y, López A *et al*., 2021. Chronic stress detrimentally affects *in vivo* maturation in rat oocytes and oocyte viability at all phases of the estrous cycle. Animals (Basel), 11(9): 2478, doi: 10.3390/ani11092478

Chen L, Thorup VM, Kudahl AB and Østergaard S, 2024. Effects of heat stress on feed intake, milk yield, milk composition, and feed efficiency in dairy cows: A meta-analysis. J Dairy Sci, 107(5): 3207-3218, doi: 10.3168/jds.2023-24059

Coussons-Read ME, 2013. Effects of prenatal stress on pregnancy and human development: mechanisms and pathways. Obstet Med, 6(2): 52-57, doi: 10.1177/1753495X12473751

Dahlerup BR, Egsmose EL, Siersma V, Mortensen EL, Hedegaard M *et al*., 2018. Maternal stress and placental function, a study using questionnaires and biomarkers at birth. PLoS One, 13(11): e0207184, doi: 10.1371/journal.pone.0207184

Darbandi M, Darbandi S, Agarwal A, Sengupta P, Durairajanayagam D *et al*., 2018. Reactive oxygen species and male reproductive hormones. Reprod Biol Endocrinol, 16(1): 87, doi: 10.1186/s12958-018-0406-2

De Rensis F and Scaramuzzi RJ, 2003. Heat stress and seasonal effects on reproduction in the dairy cow- A review. Theriogenology, 60(6): 1139-1151, doi: 10.1016/s0093-691x(03)00126-2

Dhabhar FS, 2009. Enhancing versus suppressive effects of stress on immune function: implications for immunoprotection and immunopathology. Neuro-immunomodulation, 16(5): 300-317, doi: 10.1159/000216188

Dhabhar FS, 2014. Effects of stress on immune function: the good, the bad, and the beautiful. Immunol Res, 58(2-3): 193-210, doi: 10.1007/s12026-014-8517-0

Dobson H and Smith RF, 2000. What is stress, and how does it affect reproduction? Anim Reprod Sci, 2(60-61): 743-752, doi: 10.1016/s0378-4320(00)00080-4

Dutta S, Sengupta P, Slama P and Roychoudhury S, 2021. Oxidative stress, testicular inflammatory pathways, and male reproduction. Int J Mol Sci, 22(18): 10043, doi: 10.3390/ijms221810043

Elenkov IJ and Chrousos GP, 2002. Stress hormones, pro-inflammatory and anti-inflammatory cytokines, and autoimmunity. Ann N Y Acad Sci, 966: 290-303, doi: 10.1111/j.1749-6632.2002.tb04229.x

Entringer S, 2013. Impact of stress and stress physiology during pregnancy on child metabolic function and obesity risk. Curr Opin Clin Nutr Metab Care, 16(3): 320-327, doi: 10.1097/MCO.0b013e32835e8d80

Gitsi E, Livadas S and Argyrakopoulou G, 2024. Nutritional and exercise interventions to improve conception in women suffering from obesity and distinct nosological entities. Front Endocrinol (Lausanne), 28(15): 1426542, doi: 10.3389/fendo.2024.1426542

Hajjar T, Soleymani F and Vatanchian M, 2020. Protective effect of vitamin C and zinc as an antioxidant against chemotherapy-induced male reproductive toxicity. J Med Life, 13(2): 138-143, doi: 10.25122/jml-2019-0107

Hong CY, Park JH, Ahn RS, Im SY, Choi HS *et al*., 2004. Molecular mechanism of suppression of testicular steroidogenesis by pro-inflammatory cytokine tumor necrosis factor alpha. Mol Cell Biol, 24(7): 2593-604, doi: 10.1128/MCB.24.7.2593-2604.2004

Hulin V, Delmas V, Girondot M, Godfrey MH and Guillon JM, 2009. Temperature-dependent sex determination and global change: Are some species at greater risk? Oecologia, 160(3): 493-506

Jagtap A, Jagtap B, Jagtap R, Lamture Y and Gomase K, 2023. Effects of prenatal stress on behavior, cognition, and psychopathology: A comprehensive review. Cureus, 15(10): e47044, doi: 10.7759/cureus.47044

Josefson CC, De Moura Pereira L and Skibiel AL, 2023. Chronic stress decreases lactation performance. Integr Comp Biol, 63(3): 557-568, doi: 10.1093/icb/icad044

Kaltsas A, 2023. Oxidative stress and male infertility: The protective role of antioxidants. Medicina (Kaunas), 59(10): 1769, doi: 10.3390/medicina59101769

Khambata K, Modi DN and Gupta SK, 2021. Immunoregulation in the testis and its implication in fertility and infections. Explor Immunol, 1: 309-324, doi: 10.37349/ei.2021.00021

Kirby ED, Geraghty AC, Ubuka T, Bentley GE and Kaufer D, 2009. Stress increases putative gonadotropin inhibitory hormone and decreases luteinizing hormone in male rats. Proc Natl Acad Sci, 106 (27): 11324-11329, doi: 10.1073/pnas.0901176106

Levine S and Muneyyirci-Delale O, 2018. Stress-induced hyperprolactinemia: pathophysiology and clinical approach. Obstet Gynecol Int, 3: 9253083, doi: 10.1155/2018/9253083

Majer AD, Paitz RT, Tricola GM, Geduldig JE, Litwa HP *et al*., 2023. The response to stressors in adulthood depends on the interaction between prenatal exposure to glucocorticoids and environmental context. Sci Rep, 13(1): 6180, doi: 10.1038/s41598-023-33447-x

Marai IFM and Habeeb AAM, 2010. Buffalo's biological functions as affected by heat stress- A review. Livest Sci, 127(2-3): 89-109, doi: 10.1016/j.livsci.2009.08.001

Mbiydzenyuy N and Qulu LA, 2024. Stress, hypothalamic-pituitary-adrenal axis, hypothalamic-pituitary-gonadal axis, and aggression. Metab Brain Dis, 39(8): 1613-1636, doi: 10.1007/s11011-024-01393-w

Millie Rincón-Cortés, 2024. Stress-induced modulation of maternal behavior and mesolimbic dopamine function, Curr Opin Behav Sci, 60: 101445, doi: 10.1016/j.cobeha.2024.101445

Moberg GP and Mench JA (Eds.), 2000. The Biology of Animal Stress: Basic Principles and Implications for Animal Welfare. CABI Publishing, New York, pp 1-21, doi: 10.1079/9780851993591.0001

Ojo OA, Nwafor-Ezeh PI, Rotimi DE, Iyobhebhe M, Ogunlakin AD *et al*., 2023. Apoptosis, inflammation, and oxidative stress in infertility: A mini review. Toxicol Rep, 10: 448-462, doi: 10.1016/j.toxrep.2023.04.006

Olff M, Frijling JL, Kubzansky LD, Bradley B, Ellenbogen MA *et al*., 2013. The role of oxytocin in social bonding, stress regulation and mental health: An update on the moderating effects of context and interindividual differences. Psychoneuroendocrinology, 38(9): 1883-1894, doi: 10.1016/j.psyneuen.2013.06.019

Palomba S, Daolio J, Romeo S, Battaglia FA, Marci R *et al*., 2018. Lifestyle and fertility: The influence of stress and quality of life on female fertility. Reprod Biol Endocrinol, 16(1): 113, doi: 10.1186/s12958-018-0434-y

Pankhurst NW and Munday PL, 2011. Effect of climate change on fish reproduction and early life history stages. Mar Freshw Res, 62(9): 1015-1026

Picard M, Juster RP and McEwen BS, 2014. Mitochondrial allostatic load puts the 'gluc' back in glucocorticoids. Nat Rev Endocrinol, 10(5): 303-310, doi: 10.1038/nrendo.2014.22

Poitras M, Lebeau M and Plamondon H, 2024. The cycle of stress: A systematic review of the impact of chronic psychological stress models on the rodent estrous cycle. Neurosci Biobehav Rev, 162: 105730, doi: 10.1016/j.neubiorev.2024.105730

Rakha SI, Elmetwally MA, El-Sheikh Ali H, Balboula A, Md. Montaser A *et al*., 2022. Importance of antioxidant supplementation during *in vitro* maturation of mammalian

oocytes. Vet Sci, 9(8): 439, doi: 10.3390/vetsci9080439
Rivier C and Rivest S, 1991. Effect of stress on the activity of the hypothalamic-pituitary-gonadal axis: peripheral and central mechanisms. Biol Reprod, 45(4): 523-532, doi: 10.1095/biolreprod45.4.523
Rojas-Downing MM, Nejadhashemi AP, Harrigan T and Woznicki SA, 2017. Climate change and livestock: impacts, adaptation, and mitigation. Clim Risk Manag, 16: 145-163, doi: 10.1016/j.crm.2017.02.001
Romero LM, 2004. Physiological stress in ecology: lessons from biomedical research. Trends Ecol Evol, 19(5): 249-255, doi: 10.1016/j.tree.2004.03.008
Ryan MJ, Dudash HJ, Docherty M, Geronilla KB, Baker BA *et al*., 2010. Vitamin E and C supplementation reduces oxidative stress, improves antioxidant enzymes and positive muscle work in chronically loaded muscles of aged rats. Exp Gerontol, 45(11): 882-895, doi: 10.1016/j.exger.2010.08.002
Samir M, Glister C, Mattar D, Laird M and Knight PG, 2017. Follicular expression of pro-inflammatory cytokines tumour necrosis factor-α (TNFα), interleukin 6 (IL6) and their receptors in cattle: TNFα, IL6 and macrophages suppress thecal androgen production *in vitro*. Reproduction, 154(1): 35-49, doi: 10.1530/REP-17-0053
Sapolsky RM, 2000. Glucocorticoids and hippocampal atrophy in neuropsychiatric disorders. Arch Gen Psychiatry, 57(10): 925-935, doi: 10.1001/archpsyc.57.10.925
Sapolsky RM, Romero LM and Munck AU, 2000. How do glucocorticoids influence stress responses? Integrating permissive, suppressive, stimulatory, and preparative actions. Endocr Rev, 21: 55-89
Sengupta P, Dutta S and Krajewska-Kulak E, 2017. The disappearing sperms: analysis of reports published between 1980 and 2015. Am J Mens Health, 11(4): 1279-1304, doi: 10.1177/1557988316643383
Sengupta R, Sengupta E, Dhakal BK, Thakur AR and Ahnn J, 2004. Vitamin C and vitamin E protect the rat testes from cadmium-induced reactive oxygen species. Mol Cells, 17(1): 132-139
Shen Y, You Y, Zhu K, Fang C, Yu X *et al*., 2022. Bibliometric and visual analysis of blood-testis barrier research. Front Pharmacol, 13: 969257, doi: 10.3389/fphar.2022.969257
Song J, Xiao L, Zhang Z, Wang Y, Kouis P *et al*., 2024. Effects of reactive oxygen species and mitochondrial dysfunction on reproductive aging. Front Cell Dev Biol, 12: 1347286, doi: 10.3389/fcell.2024.1347286
Straub RH, 2007. The complex role of estrogens in inflammation. Endocr Rev, 28(5): 521-574, doi: 10.1210/er.2007-0001
Tilbrook AJ, Turner AI and Clarke IJ, 2000. Effects of stress on reproduction in non-rodent mammals: The role of glucocorticoids and sex differences. Rev Reprod, 5(2): 105-113, doi: 10.1530/ror.0.0050105
Tsutsui K, Ubuka T, Bentley GE and Kriegsfeld LJ, 2012. Gonadotropin-inhibitory hormone (GnIH): discovery, progress and prospect. Gen Comp Endocrinol, 177(3): 305-314, doi: 10.1016/j.ygcen.2012.02.013
Tsutsui K, Ubuka T, Bentley GE and Kriegsfeld LJ, 2013. Review: regulatory mechanisms of gonadotropin-inhibitory hormone (GnIH) synthesis and release in photoperiodic animals. Front Neurosci, 7: 60, doi: 10.3389/fnins.2013.00060
Turner TT and Lysiak JJ, 2008. Oxidative stress: A common factor in testicular dysfunction. J Androl, 29(5): 488-498, doi: 10.2164/jandrol.108.005132
Wagenmaker ER, Breen KM, Oakley AE, Pierce BN, Tilbrook AJ *et al*., 2009. Cortisol interferes with the estradiol-induced surge of luteinizing hormone in the ewe. Biol Reprod, 80(3): 458-463, doi: 10.1095/biolreprod.108.074252
Webster Marketon JI and Glaser R, 2008. Stress hormones and immune function. Cell Immunol, 252(1-2): 16-26, doi: 10.1016/j.cellimm.2007.09.006
Whirledge S and Cidlowski JA, 2010. Glucocorticoids, stress, and fertility. Minerva Endocrinol, 35(2): 109-125
Whirledge S and Cidlowski JA, 2013. A role for glucocorticoids in stress-impaired reproduction: beyond the hypothalamus and pituitary. Endocrinology, 154(12): 4450-4468, doi: 10.1210/en.2013-1652
Xiong X, Wu Q, Zhang L, Gao S, Li R *et al*., 2022. Chronic stress inhibits testosterone synthesis in Leydig cells through mitochondrial damage via Atp5a1. J Cell Mol Med, 26(2): 354-363, doi: 10.1111/jcmm.17085
Yamamoto Y, Kuwahara A, Taniguchi Y, Yamasaki M, Tanaka Y *et al*., 2015. Tumor necrosis factor alpha inhibits ovulation and induces granulosa cell death in rat ovaries. Reprod Med Biol, 14(3): 107-115, doi: 10.1007/s12522-014-0201-5
Yan F, Zhao Q, Li Y, Zheng Z, Kong X *et al*., 2022. The role of oxidative stress in ovarian aging: A review. J Ovarian Res, 1: 100, doi: 10.1186/s13048-022-01032-x
Yang H, Xie Y, Yang D and Ren D, 2017. Oxidative stress-induced apoptosis in granulosa cells involves JNK, p53 and Puma. Oncotarget, 8(15): 25310-25322, doi: 10.18632/oncotarget.15813
Yang X, Liu P, Zhang X, Zhang J, Cui Y *et al*., 2021. T-2 toxin causes dysfunction of Sertoli cells by inducing oxidative stress. Ecotoxicol Environ Saf, 225: 112702, doi: 10.1016/j.ecoenv.2021.112702
Ye L, Huang W, Liu S, Cai S, Hong L *et al*., 2021. Impacts of immunometabolism on male reproduction. Front Immunol, 12: 658432, doi: 10.3389/fimmu.2021.658432
Zijlmans MA, Riksen-Walraven JM and de Weerth C, 2015. Associations between maternal prenatal cortisol concentrations and child outcomes: A systematic review. Neurosci Biobehav Rev: 1-24, doi: 10.1016/j.neubiorev.2015.02.015
Zitzmann M, 2024.Testosterone deficiency and chronic kidney disease. J Clin Transl Endocrinol, 37: 100365, doi: 10.1016/j.jcte.2024.100365
Zou P, Wang X, Yang W, Liu C, Chen Q *et al*., 2019. Mechanisms of stress-induced spermatogenesis impairment in male rats following unpredictable chronic mild stress (uCMS). Int J Mol Sci, 20(18): 4470, doi: 10.3390/ijms20184470

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