JOURNAL OF INTERNATIONAL CRISIS AND RISK COMMUNICATION RESEARCH
ISSN: 2576-0017
2024, VOL 7, NO S5

Endocrine Disruptors and Their Role in Metabolic Disorders: A Systematic Review of Evidence in Internal Medicine Practice

Mohammad Khalid Halabi[1], Dr.Bassam Mohammed Saleh Bandugh[2], khaled ibraheem alqurashe[3], Anas Saifullah A Jan[4], Hamid Musaad Zaid Alsharif[5], Ahmad Musa A Almalki[6], HANI khalid Mahjoub[7], Mohammed Ahmed Melibari[8], Faisal Abdulmonem Al Ruwayshid[9], Abdulrahman Khalid Alzamzami[10], Rahaf Mustafa Idrees Albensari[11], Mutaz Mohammad Alandonisi[12], Ibraheem Saaed Sadan Alzahrani[13], Khalid Mohammed Bin Ahmed Alqarni[14]

1. family medicine, PHC Alshehri 2
2. consultant Family Medicine, Family Medicine Academy at Makkah health cluster
3. Family Medicine, alnoor hospital
4. Registrar-Family Medicine, Al - Taneem PHC
5. Medicine specialist, King Abdulaziz Hosptial jeddah first health cluster
6. Neurology, King Faisal Hospital, Makkah
7. Family Medicine Resident, Executive director of puplic Health and Prison Health
8. Endocrinology & Internal Medicine consultant, Alnoor specialist hospital
9. Family Medicine Resident, BARNCH OF MINISTRY OF HEALTH IN MAKKAH
10. Family Medicine Resident, BARNCH OF MINISTRY OF HEALTH IN MAKKAH
11. FAMILY MEDICINE, ALNOOR SPECIALIST HOSPITAL
12. CENTER General physician, ALESKAN PHC
13. Family medicine senior registrar, Al-Nawariyah PHC
14. Senior Registrar-Family Medicine, Alaziziah PHC

Abstract

Endocrine disruptors (EDs) are exogenous chemicals that interfere with the normal functioning of the endocrine system, leading to disruptions in hormone signaling and metabolic processes. Increasing evidence suggests that EDs play a significant role in the development and progression of metabolic disorders, including obesity, type 2 diabetes, thyroid dysfunction, and cardiovascular disease. These substances, found in common environmental sources such as plastics, pesticides, and personal care products, have the potential to mimic, block, or alter the actions of natural hormones, resulting in adverse health outcomes. This systematic review aims to synthesize current evidence on the mechanisms by which EDs contribute to metabolic disorders and their clinical implications for internal medicine practice. By examining the most recent research, this review highlights the link between ED exposure and metabolic dysfunction, emphasizing the need for internal medicine professionals to incorporate environmental health assessments into routine clinical care. The review also discusses prevention strategies, including patient education on minimizing ED exposure, and the importance of early intervention to address the root causes of metabolic disorders. Ultimately, as the understanding of EDs advances, internal medicine must lead efforts to identify, mitigate, and manage the health consequences of these environmental toxins, with a focus on prevention and long-term health outcomes.

Keywords: Endocrine Disruptors, Metabolic Disorders, Obesity, Type 2 Diabetes, Thyroid Dysfunction, Insulin Resistance, Hormonal Disruption, Environmental Health, Internal Medicine, Prevention Strategies, Patient Education, Environmental Toxins, Bioaccumulation, Cardiovascular Disease, Endocrine System, Hormonal Mimicry, Hormonal Antagonism

Introduction

Endocrine disruptors are natural or synthetic chemicals that can mimic, block, or interfere with the body's endocrine system—the network of glands that produce hormones to regulate essential functions such as growth, metabolism, and reproduction. These disruptors can alter the normal functioning of hormones, leading to various health issues. In wildlife, exposure to endocrine disruptors has been associated with reproductive abnormalities, developmental delays, and changes in behavior. In humans, the effects are similarly concerning, with links to conditions such as obesity, diabetes, thyroid dysfunction, infertility, and certain cancers. Common sources of endocrine disruptors include chemicals found in plastics (e.g., Bisphenol A), pesticides (e.g., DDT), and industrial pollutants. The growing body of evidence regarding the harmful effects of these chemicals underscores the need for increased regulation and greater awareness of their role in public health.[1].

Metabolic disorders, such as obesity, diabetes mellitus, and thyroid dysfunction, have become increasingly prevalent worldwide, posing significant challenges to public health and internal medicine practice [2]. While genetic predisposition and lifestyle factors are well-established contributors to these disorders, environmental influences have garnered growing attention. Among these, endocrine disruptors (EDs) exogenous chemicals that interfere with the endocrine system's normal functioning—are emerging as pivotal players in the etiology of metabolic disorders.

Endocrine disruptors include a diverse range of synthetic and natural substances found in plastics, pesticides, personal care products, and industrial chemicals. They mimic or antagonize natural hormones, disrupt hormonal synthesis, or alter receptor activity, leading to dysregulation in metabolic processes. The ubiquitous exposure to EDs, such as bisphenol A (BPA), phthalates, and polychlorinated biphenyls (PCBs), raises concerns about their long-term implications for human health [3]. The most important EDCs that have been suspected in the development of obesity and obesity-associated metabolic disorders are the plastic additive bisphenol A (BPA) and the phthalate-based plasticizers [2].

This systematic review aims to synthesize evidence on the role of endocrine disruptors in the development and progression of metabolic disorders, focusing on their relevance to internal medicine practice. By analyzing the current literature, this study seeks to elucidate the mechanisms by which EDs impact metabolic health, identify high-risk populations, and highlight strategies for mitigating exposure and associated health risks. Ultimately, this review will provide a foundation for informed clinical decision-making and policy recommendations to address the growing burden of metabolic disorders in an environmentally influenced world.

The Endocrine System

The endocrine system is a complex network of glands and tissues that produce, secrete, and regulate hormones—chemical messengers critical for maintaining homeostasis in the body. These hormones control a wide array of physiological processes, including growth, metabolism, reproduction, and stress response. The precise interplay between hormones and their target organs ensures that various bodily functions operate in harmony. The Endocrine Society has defined EDCs as “exogenous chemicals, or mixture of chemicals, that can interfere with any aspect of hormone action” [4]. he WHO defined endocrine disruptors as: “an exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub)-populations” [5].

Endocrine glands, distributed throughout the body, produce the hormones that act as signaling molecules after release into the circulatory system. The human body is dependent on hormones for a healthy endocrine system, which controls many biological processes like normal growth, fertility,

and reproduction. Hormones act in extremely small amounts, and minor disruptions in those levels may cause significant developmental and biological effects [6].

EDCs Characteristics

Over 1,000 synthesized chemical compounds are considered to be EDCs, such as plastics (bisphenol A), plasticizers (phthalates), industrial solvents/lubricants, and their byproducts (polychlorinated biphenyls, polybrominated biphenyls, dioxins), pesticides (methoxychlor, chlorpyrifos, dichlorodiphenyltrichloroethane), fungicides (vinclozolin), and pharmaceutical agents (diethylstilbestrol) [6].

There are multiple routes of exposure to the above EDCs, including air, water, food, and consumer products. Some of them have low accumulation in the human body (BPA, phthalates), while others are very lipophilic, accumulating easily in the food chain and the adipose tissue (persistent organic pollutants - POPs). EDCs can also be found in various biological fluids, including sera, urine, amniotic fluid, and breast milk [7]. There are some key characteristics that define them and enable us to better understand their mechanism of action and their consequences. Key Characteristics of Endocrine Disruptors are:

1. Hormone Mimicry

- EDs can imitate natural hormones such as estrogen, androgen, or thyroid hormones by binding to their receptors.
- This mimicry can activate or suppress normal hormonal pathways, leading to inappropriate cellular responses.
- Example: Bisphenol A (BPA) acts as an estrogen mimic, potentially influencing reproductive and metabolic health [8].

2. Antagonistic Action

- Some EDs block the action of natural hormones by occupying hormone receptors without activating them.
- This receptor blockade can disrupt normal signaling and physiological processes.
- Example: Certain pesticides block androgen receptors, affecting male reproductive development and metabolism.

3. Alteration of Hormone Synthesis and Metabolism

- EDs can interfere with the production, transport, or breakdown of endogenous hormones, leading to imbalances.
- Example: Phthalates disrupt steroidogenesis, reducing testosterone synthesis [9].

4. Disruption of Hormonal Feedback Mechanisms

- EDs can disturb feedback loops within the endocrine system, causing sustained overproduction or suppression of hormones.
- Example: Persistent organic pollutants (POPs) may interfere with the hypothalamic-pituitary-thyroid (HPT) axis, disrupting metabolic regulation.

5. Bioaccumulation and Persistence

- Many EDs are lipophilic (fat-soluble) and persist in the environment or human tissue, leading to prolonged exposure.
- This bioaccumulation enhances their impact over time, especially in individuals with higher body fat percentages.
- Example: Polychlorinated biphenyls (PCBs) accumulate in adipose tissue, affecting metabolic and immune functions.

6. Low-Dose and Non-Monotonic Effects [10]:

- Unlike traditional toxicants, EDs can exert significant effects even at low doses.
- Non-monotonic dose-response relationships mean that their effects do not always increase linearly with dose, complicating risk assessments.
- Example: Low-dose BPA exposure has been linked to obesity and insulin resistance.

7. Transgenerational Effects

- ED exposure can affect not only the exposed individual but also subsequent generations through epigenetic modifications.
- Example: Diethylstilbestrol (DES) exposure in pregnant women has been linked to reproductive issues in their offspring.

8. Ubiquity in the Environment

- EDs are widespread in everyday products such as plastics, cosmetics, food packaging, and agricultural chemicals, making human exposure almost unavoidable.
- Example: Phthalates are commonly found in personal care products and household items.

Consequences of Endocrine Disruption [11]:

1. **Metabolic Disorders**:
    - Increased risk of obesity, insulin resistance, and type 2 diabetes.
    - Dysregulation of lipid metabolism and energy balance.
2. **Reproductive Health Issues**:
    - Infertility, hormonal imbalances, and developmental abnormalities.
3. **Neurodevelopmental Disorders**:
    - Impact on brain development, cognitive function, and behavior due to thyroid hormone disruption.
4. **Chronic Diseases**:
    - Links to cardiovascular disease, cancer, and immune system dysfunction.

Review of Evidence in Internal Medicine Practice

The evidence on endocrine disruptors (EDs) in internal medicine highlights their profound impact on the development and progression of metabolic disorders. As environmental exposures become increasingly recognized as critical health determinants, internal medicine practitioners must consider the role of EDs in their clinical assessments and patient management strategies [12]. This section reviews the current literature on the interplay between endocrine disruptors and key metabolic disorders, focusing on the implications for internal medicine practice.

1. Obesity and Adipogenesis

- **Evidence**: Numerous studies link EDs, such as bisphenol A (BPA) and phthalates, to increased adipogenesis and disrupt lipid metabolism. These chemicals act on the peroxisome proliferator-activated receptor gamma (PPAR-γ) and estrogen receptors to promote fat cell differentiation and accumulation [13].
- **Clinical Implications**:
    - Patients presenting with obesity and unexplained weight gain may benefit from environmental exposure assessments.
    - Intervention strategies could include counseling minimizing exposure to obesogenic EDs in everyday products.

2. Insulin Resistance and Type 2 Diabetes Mellitus

- **Evidence**: EDs interfere with insulin signaling pathways, contributing to insulin resistance. Persistent organic pollutants (POPs) and organochlorines have been implicated in altered glucose metabolism and pancreatic beta-cell dysfunction.
- **Clinical Implications**:
    - Screening for diabetes in populations with high environmental toxin exposure.
    - Encouraging dietary modifications and reducing ED exposure to mitigate risk factors.

3. Thyroid Dysfunction

- **Evidence**: Chemicals such as polybrominated diphenyl ethers (PBDEs) and perchlorates interfere with thyroid hormone synthesis, metabolism, and transport. These disruptions are linked to hypothyroidism, hyperthyroidism, and altered energy homeostasis.
- **Clinical Implications**:
    - Thyroid function tests should consider possible environmental contributors in unexplained thyroid disorders.
    - Lifestyle advice could focus on reducing exposure to known thyroid disruptors.

4. Polycystic Ovary Syndrome (PCOS)

- **Evidence**: Exposure to phthalates and BPA has been associated with hormonal imbalances characteristic of PCOS, such as hyperandrogenism and insulin resistance.
- **Clinical Implications**:
    - Treatment plans for PCOS could include education on environmental risk factors.
    - Further research may help refine diagnostic criteria and treatment protocols considering ED exposure.

5. Cardiovascular Health

- **Evidence**: EDs contribute to cardiovascular risks by promoting oxidative stress, inflammation, and endothelial dysfunction. Chemicals like BPA have been linked to hypertension and atherosclerosis.
- **Clinical Implications**:
    - Cardiovascular risk assessments may incorporate exposure histories, especially in high-risk populations.
    - Emphasizing lifestyle changes to reduce exposure to EDs may complement pharmacologic interventions.

6. Developmental and Lifespan Impacts

- **Evidence**: Early-life exposure to EDs can result in epigenetic changes affecting metabolic health throughout life. Transgenerational effects have been observed, underscoring the need for preventive measures in vulnerable populations.
- **Clinical Implications**:
    - Pediatric and prenatal care guidelines might include advice on avoiding exposure to EDs during critical developmental windows.
    - Lifelong monitoring of individuals with significant early-life exposures.

Interventions and Mitigation Strategies

Internal medicine practitioners can adopt various strategies to address ED-related health impacts:

- **Patient Education**: Informing patients about EDs and providing practical tips for minimizing exposure (e.g., avoiding plastic containers, choosing organic produce).

- **Advocacy**: Supporting public health initiatives to regulate and reduce EDs in the environment.
- **Research and Training**: Encouraging interdisciplinary research and integrating environmental health topics into medical education [15].

Future Directions in Internal Medicine

As the understanding of endocrine disruptors (EDs) advances, incorporating environmental health assessments into routine clinical practice could become a vital aspect of patient care. Given the growing body of evidence linking EDs to metabolic disorders and other chronic health conditions, internal medicine has a critical role to play in leading efforts to identify, mitigate, and manage the health consequences of these environmental toxins [16]. By integrating environmental health considerations into clinical evaluations, internal medicine practitioners can help identify at-risk populations early, provide targeted prevention strategies, and recommend lifestyle interventions to minimize exposure to EDs. This proactive approach not only helps address the root causes of metabolic disorders but also promotes long-term health outcomes for patients.

Emphasizing prevention and early intervention will be key in reducing the impact of EDs. Educating patients about lifestyle modifications—such as reducing exposure to plastics, pesticides, and other common sources of EDs—can empower individuals to take control of their health. Additionally, internal medicine can advocate for policy changes that regulate the use and disposal of EDs, as well as push for greater awareness and research into their long-term effects on human health. Ultimately, the evolving understanding of EDs presents an opportunity for internal medicine to be at the forefront of a paradigm shift in healthcare—one that addresses environmental factors as integral contributors to disease prevention and management.

Conclusion

Endocrine disruptors (EDs) have emerged as critical environmental factors influencing metabolic disorders, including obesity, type 2 diabetes, thyroid dysfunction, and cardiovascular disease. Their ability to mimic, block, or alter hormone actions disrupts the delicate balance of the endocrine system, leading to long-term health consequences. As internal medicine practice increasingly acknowledges the environmental determinants of disease, understanding the mechanisms by which EDs contribute to metabolic disorders is essential for clinical practice.

The evidence reviewed highlights the complex and often insidious role of EDs in disrupting normal metabolic processes. From promoting adipogenesis and insulin resistance to interfering with thyroid function and reproductive health, EDs pose a significant challenge to the prevention and management of metabolic diseases. The persistence of these chemicals in the environment and their potential for bioaccumulation further exacerbates their impact, especially in vulnerable populations.

Internal medicine practitioners play a pivotal role in recognizing the clinical signs of ED exposure and integrating environmental health considerations into patient management. By incorporating assessments of endocrine disruptor exposure into routine evaluations, clinicians can better address the root causes of metabolic disorders and provide more targeted interventions. Additionally, patient education on minimizing ED exposure and advocating for public health policies to regulate these harmful substances are crucial components of a comprehensive approach to mitigating their health risks.

Ultimately, continued research is needed to deepen our understanding of the long-term effects of EDs, their mechanisms of action, and the most effective strategies for reducing exposure. As the body of evidence grows, internal medicine can take the lead in integrating environmental health

into clinical care, ensuring that metabolic disorders are addressed holistically, with consideration for both genetic and environmental factors.

References

1. World Obesity Federation. World Obesity Atlas 2023. Available online: **https://data.worldobesity.org/publications/?cat=19** (accessed on 14 November 2023).
2. Dalamaga, M., Kounatidis, D., Tsilingiris, D., Vallianou, N. G., Karampela, I., Psallida, S., & Papavassiliou, A. G. (2024). The Role of Endocrine Disruptors Bisphenols and Phthalates in Obesity: Current Evidence, Perspectives and Controversies. *International Journal of Molecular Sciences*, *25*(1), 675. https://doi.org/10.3390/ijms25010675
3. Haverinen E, Fernandez MF, Mustieles V, Tolonen H. Metabolic Syndrome and Endocrine Disrupting Chemicals: An Overview of Exposure and Health Effects. Int J Environ Res Public Health. 2021 Dec 10;18(24):13047. doi: 10.3390/ijerph182413047. PMID: 34948652; PMCID: PMC8701112.
4. Zoeller R.T., Brown T.R., Doan L.L., Gore A.C., Skakkebaek N.E., Soto A.M., Woodruff T.J., Vom Saal F.S. Endocrine-disrupting chemicals and public health protection: A statement of principles from The Endocrine Society. Endocrinology. 2012;153:4097–4110. doi: 10.1210/en.2012-1422.
5. Endocrine Society: Common EDCs and Where They Are Found. Available: https://www.endocrine.org/topics/edc/what-edcs-are/common-edcs [accessed 16 November 2024].
6. Bergman A., Heindel J.J., Jobling S., Kidd K.A., Zoeller R.T. State of the Science of Endocrine Disrupting Chemicals 2012: Summary for Decision-Makers. United Nations Environment Programme and the World Health Organization: 2013. [(accessed on 1 December 2021)]. Available online: https://apps.who.int/iris/bitstream/handle/10665/78102/WHO_HSE_PHE_IHE_2013.1_eng.pdf?sequence=1&isAllowed=y
7. Koch CA, Diamanti-Kandarakis E. Introduction to endocrine disrupting chemicals–is it time to act? *Rev Endocr Metabol Disord.* (2015) 16:269–70. doi: 10.1007/s11154-016-9338-3
8. Vandenberg LN, Colborn T, Hayes TB, Heindel JJ, Jacobs DR, Jr., Lee DH, et al. Hormones and endocrine-disrupting chemicals: low-dose effects and nonmonotonic dose responses. *Endocr Rev.* (2012) 33:378–455. doi: 10.1210/er.2011-1050
9. Pataky MW, Young WF, Nair KS. Hormonal and Metabolic Changes of Aging and the Influence of Lifestyle Modifications. Mayo Clin Proc. 2021 Mar;96(3):788-814. doi: 10.1016/j.mayocp.2020.07.033. PMID: 33673927; PMCID: PMC8020896.
10. Vandenberg LN, Colborn T, Hayes TB, Heindel JJ, Jacobs DR Jr, Lee DH, Shioda T, Soto AM, vom Saal FS, Welshons WV, Zoeller RT, Myers JP. Hormones and endocrine-disrupting chemicals: low-dose effects and nonmonotonic dose responses. Endocr Rev. 2012 Jun;33(3):378-455. doi: 10.1210/er.2011-1050. Epub 2012 Mar 14. PMID: 22419778; PMCID: PMC3365860.
11. Gibert Y, Sargis RM, Nadal A. Editorial: Endocrine Disrupters and Metabolism. Front Endocrinol (Lausanne). 2019 Dec 10;10:859. doi: 10.3389/fendo.2019.00859. PMID: 31920972; PMCID: PMC6914735.

12. Küblbeck J, Vuorio T, Niskanen J, Fortino V, Braeuning A, Abass K, Rautio A, Hakkola J, Honkakoski P, Levonen AL. The EDCMET Project: Metabolic Effects of Endocrine Disruptors. Int J Mol Sci. 2020 Apr 24;21(8):3021. doi: 10.3390/ijms21083021. PMID: 32344727; PMCID: PMC7215524.
13. González-Casanova JE, Pertuz-Cruz SL, Caicedo-Ortega NH, Rojas-Gomez DM. Adipogenesis Regulation and Endocrine Disruptors: Emerging Insights in Obesity. Biomed Res Int. 2020 Feb 18;2020:7453786. doi: 10.1155/2020/7453786. PMID: 32149131; PMCID: PMC7049431.
14. Dalamaga M, Kounatidis D, Tsilingiris D, Vallianou NG, Karampela I, Psallida S, Papavassiliou AG. The Role of Endocrine Disruptors Bisphenols and Phthalates in Obesity: Current Evidence, Perspectives and Controversies. Int J Mol Sci. 2024 Jan 4;25(1):675. doi: 10.3390/ijms25010675. PMID: 38203845; PMCID: PMC10779569.
15. García García, M., Picó, Y., & Morales-Suárez-Varela, M. (2024). Effects of Bisphenol A on the Risk of Developing Obesity. *Nutrients*, *16*(21), 3740. https://doi.org/10.3390/nu16213740.
16. Knight DRT, Confiado SM, Bruno KA, Fairweather D, Seymour-Sonnier AM, Jain A, Gehin JM, Whelan ER, Culberson JH, Munipalli B, Dawson NL, Rozen TD, Wick JJ, Kotha A. Establishing an Ehlers-Danlos Syndrome Clinic: Lessons Learned. SN Compr Clin Med. 2022;4(1):138. doi: 10.1007/s42399-022-01218-w. Epub 2022 Jul 5. PMID: 35811641; PMCID: PMC9255530.