60^{+} years since *Silent Spring:* Where are we now?

An examination of the possible biological impacts of human exposure to endocrine-disrupting chemicals on early life, sexual identity and male fertility decline.

Don Maisch PhD

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Prologue: The WHO enters the fray
February 16, 2024

That which is not spoken of – it is taboo. So that no one steps over the boundary, there are guardians who, via lobbying or mobbing, disarm those who are guilty of the unacceptable. At the same time this means that the free furtherance of knowledge, the prime task of researchers, is hindered.

French philosopher Michael Foucault

Prologue: The WHO enters the fray

Feb 16, 2024

On December 18 2023 The World Health Organisation (WHO) announced the establishment of a panel tasked with developing national guidelines for countries on how to best treat transgender and gender diverse people (gender dysphoria). Referred to as providing "gender-inclusive care", the panel's emphasis is on promoting the access to hormone replacement therapy, such as puberty blockers and gender reassignment surgery. Researching possible external environmental factors which may be having an influence on the incidence of gender dysphoria, appears to be outside the panel's area of responsibility and at this time does not appear to be an area of scientific inquiry with the WHO.

To quote from the WHO press release:

> *This new guideline will provide evidence and implementation guidance on health sector interventions aimed at increasing access and utilization of quality and respectful health services by trans and gender diverse people. The guideline will focus in 5 areas: provision of gender-affirming care, including hormones; health workers' education and training for the provision of gender-inclusive care; provision of health care for trans and gender diverse people who suffered interpersonal violence based on their needs; health policies that support gender-inclusive care, and legal recognition of self-determined gender identity.*[1]

Although these are laudable efforts to help people currently dealing with gender issues nothing is said by the WHO departments responsible for the implementation of the guidelines [2] about a need to address possible contributing factors, such as exposure to endocrine disruptive chemicals (EDCs). Evidence indicates that in-utero EDC exposures have an ability to influence early gender identity and thus pose a potential risk for exposed populations. For example:

In a 2022 global overview of EDCs they were found to be universal in the environment, and low concentrations ($\mu g/L$ to ng/L) could severely impact human health and wildlife due to transgenerational and multigenerational effects.[3]

In a scientific statement by the *Endocrine Society* in 2009 the authors presented evidence that EDCs have effects on male and female reproduction, breast development and various cancers. They report that results from animal models, human clinical observations and epidemiological studies implicate EDCs as a significant concern to public health. The authors made a number of recommendations, including increased basic and clinical research and the involvement of individual and scientific society stakeholders in communicating and implementing changes in public policy and awareness. [4]

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[1] WHO press release: WHO announces the development of a guideline on the health of trans and gender diverse people, 18 december 2023,

[2] WHO departments of Gender, Rights and Equity-Diversity, Equity and Inclusion (GRE-DEI), Global HIV, Hepatitis and Sexually Transmitted Infections Programmes (HHS), and Sexual and Reproductive Health and Research (SRH).

[3] Puri, M., Gandhi, K. & Suresh Kumar, M. A global overview of endocrine disrupting chemicals in the environment: occurrence, effects, and treatment methods. *Int. J. Environ. Sci. Technol.* Vol. 20, pp. 12875–12902 (2023).

[4] Diamanti-Kandarakis E,, Bourguignon J-P., Giudice L., Hauser R., Prins G., SotoA., Gore A., "Endocrine-Disrupting Chemicals: An Endocrine Society Scientific Statement", *Endocrine Review*, Vol 30, no.4, pp.293-342, June 2009. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2726844/

For the WHO to enter the fray in 2023 with its new expert panel while ignoring the possible role of EDCs as a contributing factor in some instances of gender dysphoria, despite available evidence to the contrary, can best be described as disingenuous.

It must be asknowledged, however, that for people who presently are dealing with gender identity issues, the WHO guidelines promise to be an important initiative to help them deal with their present day life situation. Evidence indicates however, the additional importance of research to identify possible environmental factors which could be impacting upon present and future generations. Failure to do so means the proposed WHO guidelines are presently incomplete in failing to address the controversial issue of possible causation.

The danger inherent in the WHO's developing guidelines is that they give an impression that trans and gender diverse identity are exclusively natural human conditions needing only societal intervention. This is unfortunate as it discourages scientific research examining possible environmental contributing factors, such as the increasing levels of EDCs and other artificial chemicals widely used in today's world.

For women planning on having children in the future and families with young children, being aware of, and avoiding unnessary exposures to plastic items containing EDCs, needs wider discussion and awareness than presently is the case.

The attached paper examines these potential environmental influences in detail.

Don Maisch PhD

60+ years since *Silent Spring:* Where are we now?

Endocrine-disrupting chemical exposures in early life, sexual identity and male fertility decline. Is there a connection?

Don Maisch PhD

Overview

It was Rachel Carson's book *Silent Spring,* published in 1962, that launched the modern environmental movement, by drawing attention to evidence on the biological dangers of the widespread use of DDT and other pesticides. Informed by interviews with scientists and physicians with relevant experience, Carson wrote that pesticides should more properly be called "biocides" because of their impact on organisms other than the intended target pests. She warned that the widespread use of pesticides would result in an accumulation of the chemicals in the environment resulting in an increased risk to human and animal health. Since *Silent Spring* was published, concerns for possible health hazards have grown as a myriad of other chemicals, many of which can interfere with the human endocrine system (endocrine disrupters), have been introduced. There has been little research conducted on the unintended long-term impacts of their use on human health.

Early Research

The scientific evidence of endocrine disruption from chemical exposures was extensively examined in a 1992 book chapter: *Chemically-Induced Alterations in Sexual and Functional Development: The Wildlife/Human Connection* by Theo Colborn and Coralie Clement.(1) The chapter was a synthesis of relevant reports from the previous decade that examined concentrations of organochlorine contaminants in human reproductive tissues, adipose (body fat) tissue, breast milk and blood from the general population, excluding industrial exposures. Measurable amounts of these contaminants (2) were found in human tissue worldwide. They persist in the environment and bioaccumulate and biomagnify within food chains to eventually reach measurable concentrations in human tissue (as Carson warned in 1962). The chapter's concluding discussion noted that the concentrations of these chemicals in human tissue are at levels that can have untoward effects on wildlife and humans.(3)

The 1991 Wingspread Consensus Statement

By the early 1990s it was becoming obvious that many endocrine disrupting chemicals were accumulating in the environment which were capable of disrupting the endocrine systems of animals, including marine life, wildlife and humans. As a consequence of this growing awareness, a multidisciplinary group of experts met at Wingspread, Racine, Wisconsin in July 1991 in order to assess what was known about the issue. Participants included experts in the fields of anthropology, ecology, endocrinology, histopathology, immunology, medicine, law, psychiatry, psycho-neuroendocrinology, reproductive physiology, toxicology, wildlife management, tumor biology, and zoology.(4) The statement from the Wingspread meeting confirmed the warnings originally given in Carson's 1962 book *Silent Spring*. To quote in part from the 1991 Wingspread consensus statement:

> *Some of the developmental impairments reported in humans today are seen in adult offspring of parents exposed to synthetic hormone disruptors (agonists and antagonists) released in the environment. The concentrations of a number of synthetic sex hormone agonists and antagonists measured in the US human population today are well within the range and dosages at which effects are seen in wildlife populations. In fact, experimental results are being seen at the low level of current environmental concentrations.*
>
> *Unless the environmental load of synthetic hormone disruptors is abated and controlled, large scale dysfunction at the population level is possible. The scope and potential hazard to wildlife and humans are great because of the probability of repeated and/or constant exposure to numerous synthetic chemicals that are known to be endocrine disruptors.* (5)

Swedish research on chemical exposures in the workplace

During the 1990's the Swedish trade union movement, notably the Swedish Confederation of Professional Employees (TCO), the central organization for professional workers, and the Union of Clerical and Technical Employees in Industry (SIF), the largest trade union within the TCO, led the world in actively tackling and working on solutions for the growing problem of both chemical and electromagnetic field (EMF) pollution in the workplace. In several trade union publications from the 1990s the importance of protecting the health of workers by addressing the issues of chemical and EMF hazards in the workplace was emphasised. The level of cooperation between SIF and the academic sector such as the University of Lund, the Lulea University of Technology and the Karolinska Institute was notable.(6)

An emphasis on chemical pollution and its possible role in affecting health was initiated by a research project led by Gunilla Lindstrom, Professor of Environmental Chemistry at Orebro University which compared stored blood samples from the 1940s to the 1980s. Although traces of polychlorinated biphenyls (PCB's) were present in both groups (PCB was widely in use since 1929 in electrical equipment) the 1940 samples were almost free of synthetic chemicals such as brominated flame retardants (BFRs) which were not in use in the 1940s.(7)

Later research on BFRs by the National Swedish Food Administration and the Karolinska Institute measured the BFRs in breast milk. They found large differences in the samples which couldn't be explained by food intake, age, body weight, alcohol consumption or smoking. A few women had up to ten times the average levels of the overall group. Subsequent follow-up studies found that the BFR levels in breast milk increased annually with the levels doubling every five years. The researchers suggested that exposure to electronic equipment outgassing could be a possible source of exposure.(8)

The SIF publication *NO RISK in the IT environment* (1999) makes the point that employees who were working with the older model CRT computer monitors would have been breathing in a chemical mixture during their working day, five days a week, composed of flame retardants, furanes, formaldehyde, Isocyanates and other chemicals not identified.(9)

The obvious concern in the above Swedish publications was the uncertainty over the possible long-term health effects on people who were being exposed to this mix of new chemical compounds, many of which are endocrine disrupters. There was a special concern for pregnant women and infants who may be ingesting

contaminated milk from birth. The subsequent research examined in this paper only adds to that concern.

Research in Sweden in the early 1990s had found that chemical emissions were an important factor in electromagnetic hypersensitivity (EHS) from electronic equipment. The research indicated that chemical exposures were possibly an initiating factor in EHS.(10)

In 1997, a Swedish study published in *Oncology Reports* found increased concentrations of polybrominated diphenyl ethers (PBDE) in the same study population previously found to have elevated levels of polychlorinated biphenyls and chlordane compounds in adipose tissue (11) from patients with non-Hodgkin's lymphoma. Non-Hodgkin's lymphoma is a common disease among transplant patients who take immune suppression drugs. This was the first study in Sweden to find elevated levels of PBDEs in all subjects previously tested. The researchers considered that the main source of exposure was through the food chain. They saw the environmental situation for PBDEs as similar to that of PCBs a few decades earlier. (12)

In 2004 a joint research paper from the environmental departments of the Swedish Orebro and Stockholm Universities reported on tests for perfluoroalkylated compounds (PFAS) (13) in whole blood plasma from the Swedish population. The study findings of 5 PFAS compounds tested indicated that the Swedish population are exposed to a large number of PFAS chemicals.(14) PFAS chemicals act as endocrine-disrupting chemicals (EDCs) due to their ability to interfere with hormone systems.

In 2008 a Swedish pilot study published in *Electromagnetic Biology and Medicine* found increased concentrations of polybrominated diphenyl ethers (PBDEs) in people who reported suffering from electromagnetic hypersensitivity (EHS).(15) Although this was a small study, it indicated a larger study was warranted on the possible causative role of chemical exposures with EHS.

Also in 2008, a paper was published in *Atmospheric Environment* by researchers from the Lawrence Berkeley National Laboratory (Environmental Energy Technologies Division, Indoor Environment Department) that reviewed the available data and information specific to indoor chemical pollutants emitted by office equipment. The abstract states (in part):

> *There is concern that potentially harmful pollutants may be emitted from office equipment. Although office equipment has been a focal point for governmental efforts to promote energy efficiency through programs such as the US EPA's Energy Star, little is known about the relationship between office equipment use and indoor air quality, and information on pollutant emissions is sparse… We then observe that personal exposures may be significantly larger than those estimated through average pollutant indoor concentrations, due to proximity of users to the sources over extended periods of time. Finally, we observe that the magnitude of emissions, the link from emissions to personal exposure, the toxicological significance of the chemicals emitted, and the costs and impacts of alternate materials should all be considered in order to evaluate potential importance of human exposures and health risks.*(16)

A list of some of the chemicals examined in the paper included volatile organic chemicals (VOCs), ozone, particulate matter and several semi-volatile organic chemicals (SVOCs) such as phthalate esters, brominated flame retardants,

organophosphate flame retardants and polycyclic aromatic hydrocarbons (PAHs).

Later research raises concerns

In 2020, Dunzhu *et al* investigated the use of plastic feeding bottles during formula preparation. The researchers found that the recommended high-temperature process for sterilizing plastic bottles and preparing formula milk caused bottles to shed millions of microplastics and trillions of even smaller nanoplastics. The researchers called for the urgent need to assess whether exposure to microplastics at these levels poses a risk to infant health.(17)

In a 2022 Italian pilot study, breast milk from 34 women was analysed by Raman Microspectroscopy, for microplastic (MP) contamination. Microplastic chemical contamination was found in 26 out of 34 samples with the most abundant composed of polyethylene, polyvinyl chloride and polypropylene - all of which contain endocrine disruptors.(18) It is not clear if the source of the chemical contamination was from the milk itself or from plastic baby bottles?

A 2023 paper, *Brominated flame retardants in breast milk from the United States: "First detection of bromophenols in U.S. breast milk,* found that BFRs have been widely detected in breast milk, posing a potential health risk for breastfeeding infants. The researchers concluded, "The presence of phased-out polybrominated diphenyl ethers (PBDEs), bromophenols, and other current-use flame retardants in breast milk reflects ongoing prenatal exposure and increased risk for adverse impacts on infant development. More than 25 different types of BFRs of various levels were detected in every sample of breast milk tested."(19) BFRs are used in plastic TV and computer casings and other electronics, including internal circuit boards to prevent fire risks but humans can be exposed to them through outgassing BFR emissions as the equipment heats up, especially in new equipment.

A Chemical Brave New World

During the Second World War in the 1940s, research on military uses of plastic products was intensified as part of the war effort. After the war in the 1950s a wide range of plastic consumer products was created, ushering in a new plastic age. In the 1970s with the introduction of personal computers and photocopiers in the office workplace environment, millions of office workers were exposed to a novel mix of chemicals that had not previously existed in the environment and had not been tested for toxicity. Essentially modernity had entered a chemical 'Brave New World'(20) with many possible unintended consequences for children conceived in this environment. In addition, the widespread introduction and use of pesticides and herbicides in agriculture and growth hormones in farm animals exposed humans to new chemicals on which no long term research had been conducted.

By way of example, in Puerto Rico in the early 1980s, approximately 3,000 children were affected by abnormal sexual development. Typical examples were a young girl under the age of one starting to menstruate, a boy with an estrogen level exceeding that of an ovulating adult woman, and a young girl with fully developed breasts and adult sized ovaries. Medical exams found high levels of estrogen in the blood in up to 80 % of the children tested. The suspected source of the estrogen was thought to be from the use of animal growth stimulants containing artificial forms of estrogen used by farmers wanting to have bigger animals to sell and thereby increase their profit margins. When doctors recommended to the parents to remove locally produced poultry, milk, eggs and sometimes beef from the children's diet

the condition improved.(21) In a paper published in Journal of Pediatrics in 1985 the authors concluded that they suspected that the early sexual development was caused by exogenous estrogen contamination in the food ingested by the children and by their mothers. (22)

Although the risk of cancer lies outside the main topic in this paper there are a number of research papers that found a connection between non-Hodgkin lymphoma (NHL) and pesticide exposure. For example, in a 1999 Swedish case control study of 442 cases and over 800 controls, found an increased risk of NHL with exposure to herbicides containing phenoxyacetic acids such as 2, 4D. (23) In a later 2008 case control study of male and female subjects living in Sweden, researchers confirmed an association between NHL and exposure to the agricultural herbicides containing phenoxyacetic acid and Glyphosate (Roundup).(24)

A possible link between reproductive and developmental disorders and pesticide exposures was indicated in a 2004 study of agricultural workers which found an increased risk of specific morphological abnormalities in sperm, including a decreased sperm count and less viable sperm. An increased risk of congenital malformations in the children of the workers, including orofacial clefts, birthmarks, as well as musculoskeletal and nervous system defects was reported. There are also some indications that exposure to pesticides may contribute to stillbirth and female infertility. (25)

Are endocrine disrupting chemicals a factor in gender dysphoria in adolescents?

In a paper published in 2018 in *Adolescent Health, Medicine and Therapeutics* the authors examined the treatment regime for increasing numbers of adolescents, seeking treatment for gender dysphoria (GD) in Western countries. The authors note that while gender dysphoria intensifies during puberty, "virtually nothing is known regarding adolescent-onset GD, its progression and factors that influence the completion of the developmental tasks of adolescence among young people with GD and/or transgender identity. Identity development is a central development goal of adolescence, but we still do not know enough about how gender identity and gender variance evolve." (26).

Considering the high level of uncertainty and a lack of understanding of the fundamental causes of the increasing incidence of gender dysphoria, it should be imperative that the evidence that exposure to chemicals in utero and early life should be investigated and corrective action taken as a matter of urgency.

It was in 1996 that warnings were given in *Our Stolen Future: Are We Threatening Our Fertility, Intelligence and Survival?* The authors examined the health and environmental threats posed by our widespread use of chemicals used in plastic products and warned of the potential of these new chemicals to interfere with hormones in both humans and wildlife. To quote: "Endocrine disrupting chemicals alter the development of the fetus in the womb by interfering with the natural hormonal signals directing fetal growth. Their impacts, sometimes not detectable until years or decades after exposure, include reduced disease resistance, diminished fertility, and compromised intelligence and behavior".(27)

While social and psychological causes are commonly canvassed as possible contributing factors in GD, the possibility of exposure to chemicals is not receiving the attention it deserves. The controversy was examined by Nigel Barber, Ph.D., an evolutionary psychologist writing in *Psychology Today*, November 2019.

Barber examined the evidence that exposure to phthalates**, (**a group of chemicals used to make plastics more durable) and polychlorinated biphenyls (PCBs), which are both endocrine disruptors, are one of the factors predicting gender dysphoria, particularly in the case of male-to-female transgender. Barber notes that there is a reluctance on part of the transgender community to accept that what is seen as a voluntary choice may partly be due to involuntary environmental chemical exposures in early life. Barber acknowledges that there are obvious psychological factors in gender dysphoria, such as childhood trauma and abusive parenting, but they do not invalidate the influence of hormone disruptors. He suggests that there may be a similar connection in brain development and that it is short-sighted to ignore the evidence that chemical environmental threats can influence brain development.(28)

Writing in *Neuroendocrinology* Mark Gordon mentions that the widespread use of endocrine disrupting chemicals (EDCs) in a wide range of consumer products, as well in industrial manufacturing, end up as environmental contaminants. There is increasing evidence that EDCs can interfere with the endocrine system leading to adverse health effects on both human and wildlife, including gender identity ambiguity.(29)

The importance of natural endocrine hormone influences on sexual orientation and childhood behavior is explored in detail in a review by Melissa Hines, writing in *Frontiers in Neuroendocrinology*. Hines explores the importance of natural prenatal hormones such as testosterone, estrogen and progesterone, in influencing the development of gender based interests in childhood and sexual orientation in later life, with the effectiveness of these hormones to influence later sexual orientation occurring early in life, particularly prenatally and neonatally.(30) Although the issue of the possible impact of exposure to artificial endocrine disruptive chemicals in early life was not explored in the review, the importance of endocrine hormones in influencing later sexual orientation brings into question the possible impact of EDCs on early human development.

The possible role of the endocrine disrupting chemical, Bisphenol A (BPA) in transsexuality was examined in a paper published in *Endocrine Abstracts* (conference poster presentation) by Yurekli et al. (2015.) The authors noted that the main mechanism in sexual differentiation appears to involve a direct effect of testosterone on the developing brain in boys and a lack of this effect in girls. This is identified as a crucial factor in the development of male and female gender identity. Exposure to BPA in utero may affect the sexual differentiation of the brain and cause a reversal of differentiation in male to a female transsexual self identity, as BPA acts as an estrogen mimic hormone and may target the estrogen receptors in the developing brain. The authors conclude that transsexuality is most likely a combination of a genetic background and an early effect of the interaction of sex hormones with the developing brain during the foetal period. They hypothesized that exposure to BPA at that critical period may be a cause for transsexualism.(31)

Male sperm counts declining globally

As far as associated health issues are concerned another related issue that deserves attention is the decline of male sperm count globally that may be due to exposure to toxic pollutants. This was a topic of a *BBC Future* program "How pollution is causing a male fertility crisis."(32)

In a 2023 systematic review by Levine H. et al, the research found that between 1973 and 2018 from all continents, a reduction in sperm counts of slightly over 50%. The researchers concluded: "Furthermore the data suggest that this world-wide decline is continuing in the 21st century at an accelerated pace. Research on the causes of this continuing decline and actions to prevent further disruption of male reproductive health are urgently needed." As for the causes of this decline it is largely unknown but the lead author Hagai Levine suggested that damage to the male reproductive system may begin in the womb. "We know that stress of the mother, maternal smoking and especially exposure to manmade chemicals that are in plastic such as phthalates, disrupt the development of the male reproductive system".(33)

On October 12, 2023 *Nature Reviews Urology* published a paper, authored by an international consortium of 26 fertility experts, led by the University of Melbourne's Professor Moira O'Bryan. The paper, titled: "Frequency, morbidity and equity- the case for increased research on male fertility", called for a research effort to understand why, and how the increasing incidence of male infertility can be reversed. Professor O'Bryan said that *"the real issue is that we don't know what the individual causal problems are we won't until we studies. Decreasing semen quality and increasing frequency of testicular cancer and congenital effects in the urogenital system indicate that globally male productive health has declined. Research is needed to understand why, and how this trend can be reversed"*. The consortium said that more rigorous tests of impacts on males of compounds such as endocrine-disrupting chemicals in consumer products, the workplace, and general environment are needed. (34)

Another concern for male fertility is the commonly used herbicide Atrazine, an EDC. It has been banned in Europe since 2004 but is still allowed in Australia. It is used to control weeds in summer crops such as sorghum, maize and sugarcane, and it is also widely used in Western Australia for control of weeds in lupin and canola crops as well on pasture and golf courses. The herbicide has been detected in Australian tap water, especially in Queensland, New South Wales and Tasmania. In a study from the School of Biosciences at the University of Melbourne in 2019 the researchers found significant effects on the reproductive and general health of male rats exposed to both low doses and high doses of the chemical. The authors explained that lower doses over a long exposure time may potentially do more damage than a high dose. This is because the low doses are likely to be similar in concentration to the body's own hormones while the very high dose can be too high to generate a response. The researchers concluded:

> *We have highlighted the importance of investigating chronic exposure to low doses of endocrine disruptors. These doses are used to calculate the current government-approved safe level – and may have different physiological effects than previously seen. There is a lot more we need to know about these chemicals to protect the health of humans and animals.*(35)

According to a study by researchers from the University of California, Berkeley, atrazine has a devastating effect on male frogs, with the exposed frogs missing testosterone and all the things that testosterone controls, including sperm, with their fertility as low as 10% of normal male frogs. Atrazine exposure can also turn affected male frogs into females something not seen in the natural environment. As for the long–term effect of this the researchers commented:

> *These kinds of problems, like sex-reversing animals skewing sex ratios, are much more dangerous than any chemical that would kill off a population of frogs…In exposed*

populations, it looks like there are frogs breeding but, in fact, the population is being very slowly degraded by the introduction of these altered animals.(36)

Subsequent research by the Berkeley researchers found adverse hormonal effects on several species of frogs including tadpoles raised in atrazine contaminated water becoming hermaphrodites, developing both female (ovaries) and male (testes) gonads. This occurred at atrazine levels as low as 0.1 parts billion (ppb) which is 30 times lower than the levels allowed in American drinking water by the EPA. Other frog species were found to have eggs in their testes and low testosterone levels in ponds up to 1,000 miles from where atrazine had been applied to fields.(37)

Sources of endocrine disrupting chemicals (EDCs) in today's world

In an investigative article published in *Penn State Extension* (39) on microplastics (2022) , the author found virtually all domestic and natural water sources worldwide are contaminated with microplastics or nanoplastics which can leach chemicals into the environment, eventually making their way to land and water sources. The research indicates that these plastics can attract and concentrate heavy metals and organic pollutants dissolved in the water. Of concern are polychlorinated biphenyls (PCBs). Even though PCBs have been banned, they are still present and persistent in the natural environment worldwide in both land and aquatic environments. Plastic debris accumulates pollutants up to 100,000-1,000,000 times the levels found in seawater, according to US National Oceanic and Atmospheric Administration (NOAA). What the long-term effects will be on humans is presently unknown. Still, given the massive amount of plastic waste discarded in the oceans (approximately eight million metric tons annually) more research needs to be done on what adverse effects they may have. (39)
Similar to the findings of the previous study, a paper published in *Environment International* in 2019 found that micro and meso-plastics, either originating from plastic manufacturing or dumped in the marine environment, are able to absorb harmful substances such as EDCs with the potential to cause adverse effects to organisms. The authors called for future studies to determine the contribution of plastic–bound EDCs in the human diet because the concentrations of these plastics may change in the future. (40)

An earlier paper published in *Environmental Health Perspectives* in 2011 found that most plastic products, from sippy cups to food wraps, can release chemicals (EDCs) that act like the sex hormone estrogen. The study found that even products that didn't contain the endocrine disrupter chemical BPA, still contained EDCs. The researchers tested 455 plastic items advertised as "BPA free", such as baby bottles, food packaging and flexible bags, and found that 70% of the products tested released chemicals that acted as estrogen. When these plastic products were stress tested such as being placed in a dishwasher, or microwave oven, more than 90% tested positive for EDCs.(41)

In addition to the above list of commonly used products with EDCs, in 2019, ANSES, the French Agency for Food, Environmental and Occupational Health Safety (ANSES) highlighted the health risks to babies associated with the presence of chemicals of concern in single-use disposable diapers. To protect the health of very young children, ANSES submitted a restriction proposal to the European Chemicals Agency to make it possible to regulate the sale of single use disposable diapers on the European market. The chemicals of concern found in single use diapers were polycyclic aromatic hydrocarbons (PAHs), polychlorodibenzo-p-

dioxins (dioxins or PCDDs), polychlorodibenzofurans (furans or PCDFs), polychlorobiphenyls (PCBs) and/or formaldehyde. PAHs, formaldehyde, PCDD/Fs and Dioxin-like PCBs (DL-PCBs).(42)

In a paper published in *Frontiers in Toxicology* in 2023, researchers reported that biologically active microplastics and nanoplastics have a significant impact on ecosystems, wildlife, and human health. These pollutants as have been shown to cause increased oxidative stress, inflammation and altered metabolism leading to cellular damage which ultimately affects tissue and organismal homeostasis in numerous animal species and human cells. Of concern is the ability of these plastic particles to carry contaminants, toxic chemicals, pesticides, and bioactive compounds, such as EDCs which are a risk to both animal and human health. The researchers point out however, that knowledge of full effect of these pollutants on health is limited. The authors concluded:

> *Although this review provides insight into the potential mechanisms of microplastics (MPs) and nanoplastics (NPs) toxicity in humans, more research is needed on the bioaccumulation, distribution, and transcriptomic changes caused by MPs and NPs inappropriate test models. Moreover, human biomonitoring studies are crucial in determining MPs and NPs' presence in biological fluids. This would offer a comprehensive understanding and possibly unravel any associated health issues.*(43)

Concluding Discussion: The Anthropocene Epoch

It was about 4 billion years ago that life arose from a primordial soup of chemicals after amino acids somehow managed to link together to form proteins and then later hormones from which the basic molecules of biological life formed, leading to life as we know it. All hormones in the human body (except sex hormones and those from the adrenal cortex) are proteins or protein derivatives. They are the body's chemical messengers and affect many different processes, including growth and development, metabolism, sexual function, reproduction and mental state – all products of many millions of years of evolution. It is a finely tuned biological system where, in response to specific stimuli, the endocrine glands release hormones into the bloodstream for a specific purpose and maintain a stable internal environment. It stands to reason that anything that interferes with this process by triggering an inappropriate hormone response will most likely disrupt this natural biological process with unknown consequences. A prime example of this disruption would be artificial chemical compounds which can mimic natural hormones and can therefore interfere with the body's endocrine system – the endocrine disrupters.

Today there are about 350,000 artificial chemicals in our environment used in plastics, pesticides, industrial chemicals, cosmetics, antibiotics and a wide range of drugs with very few of these chemicals tested for possible long-term health hazards. This problem was examined in a 2016 paper by Bijlsma and Cohen in which they called for concerted action to better understand the risk to health that lifetime environmental exposures pose for the individual. The authors saw such action as necessary at all levels of society, from individual patients, clinicians, medical educators, regulators, government and non-government organisations corporations to the wider civil society. (44)

The massive amount of plastic products and chemicals in the modern global environment has led some scientists to identify this feature as a hallmark of the Anthropocene Epoch, a geological age (the plastic age) in which human activities have to come to dominate the planet, after the bronze and iron ages. Microplastics

are now ubiquitous in the earth, from the deepest oceans to high mountains and even in the air of the Arctic and freshly fallen snow in Antarctica. Since the early days of plastic production in the 1950s global production has increased 50-fold with the projected increase in production to triple by 2050 compared to 2010. This has caused concerns that this rapidly expanding production of new substances not previously known to the Earth is a cause of concern at the global level because these products exhibit persistence and widespread distribution and accumulation in organisms in the environment with the potential for negative impacts on vital Earth system processes.(45)

This paper does not suggest that gender dysphoria is purely a condition resulting purely from artificial chemical exposures to a fetus in utero and/or in infancy. This conclusion would be incorrect. Transgender people have existed in society since long before the invention of the artificial chemicals mentioned here. There is an extensive history of transgender people in many parts of the world dating from the ancient Roman and Greek civilizations .(46)

Gender dysphoria has previously been considered a relatively rare condition. However, in recent years there has been a significant increase in the number of referrals to both adult and child and adolescent gender clinics, with services being described as "becoming overwhelmed".(47)

This paper seeks to draw attention to evidence that indicates that the recent increase in gender disphoria and the declining male sperm counts globally may in part be due to exposure to endocrine disrupting chemicals within a pervasive chemical environment that interferes with sexual identity and male fertility at a crucial stage in early life development. Any additional long-term effects that may occur from these exposures remain to be uncovered. For the future of humanity, the implications of the current state of knowledge needs urgent attention and corrective action for what constitutes a major public health crisis.

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