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OVERVIEW OF ENDOCRINE DISRUPTION – AN AOTEAROA NEW ZEALAND PERSPECTIVE

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EXECUTIVE SUMMARY

The presence of endocrine disrupting chemicals (EDCs) in the environment can disrupt the endocrine system of exposed biota and humans. The resulting endocrine disruption can be harmful because natural hormones modulate multiple processes involved in the reproduction and development of organisms. There are examples of endocrine disruption in both laboratory and field studies. Globally, there is compelling evidence of endocrine disruption in fish living downstream from municipal sewage treatment plant effluent outfalls. In the United States of America, major sexual development abnormalities were observed in alligators exposed to pesticides with androgenic activities. In Aotearoa New Zealand, there is a dearth of information on the presence of EDCs and potential endocrine disruption in exposed biota. Aotearoa New Zealand studies have measured EDCs and endocrine activities in effluent, groundwater and sediment, but up to now, there is no evidence of endocrine disruption in exposed biota. Although the main source of EDCs is sewage effluent, the agriculture sector is also a potential source, especially in areas of intensive dairy activities.

To date, many of the methods used to evaluate the endocrine disruptive potential of chemicals are based on modes of action. The information generated does not always predict whether these biological activities will result in an adverse effect or harm to exposed individuals or populations. This explains why, up until now, there are no regulations specific to EDCs as regulation processes often require that a chemical must induce an adverse effect in whole animals for it to be regulated.

This report summarises the issue of endocrine disruption by providing information on how EDCs exert their effects and examples of adverse outcome pathways leading to impacts. Recommendations to address knowledge gaps and future research and regulatory needs include:

1. Apply the precautionary principle until it can be conclusively determined whether endocrine disruption is occurring in Aotearoa New Zealand.
2. Better characterisation of EDCs at hotspots around main sources such as dairy areas and sewage effluents.
3. The need for a multi-disciplinary approach that includes the research sector, environmental managers and regulators.
4. Engagement with mana whenua and the wider community is needed to develop sustainable solutions to manage EDCs and the risk of endocrine disruption.

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ACRONYMS AND DEFINITIONS

Acronym	Definition
Agonist	Describes a chemical that can bind to a receptor protein and mimic the effects of the natural hormone.
Antagonist	Describes a chemical that can bind to a receptor protein but blocks the cellular response, e.g., the drug tamoxifen blocks estrogenic responses and is used to treat oestrogen-dependent breast cancer.
AOP	Adverse outcome pathway, a framework to represent biological events leading to an adverse effect in whole organisms.
AR	Androgen receptor.
E2	17β-estradiol, an important female sex hormone (but also present and active in males).
EBM	Effect-based methods, where high-throughput cellular or low complexity whole organism assays are used to measure the toxic effect associated with chemical pollutants in an environmental sample.
EDC	Endocrine disrupting chemical: compounds that can interact with the functions of hormones and disrupt the endocrine system of exposed biota and humans.
Epigenetic	Modulation of gene activity without changes to the DNA sequence.
ER	Oestrogen receptor: the effects of oestrogen hormones are modulated by their interaction with the ER, which trigger a range of physiological responses. There are two oestrogen receptor subtypes, alpha (ERα) and beta (ERβ), and membrane ER such as the G protein-coupled ER (GPR30).
Estrogenicity	Biological or physiological response to an oestrogen (or oestrogen mimic) promoting a female-specific effect.
FXR	Farnesoid X receptor, involved in lipid metabolism.
Glucocorticogenicity	Biological or physiological response to glucocorticoids (or mimics), steroid hormones that have systemic effects
GR	Glucocorticoid receptor.
Homeostasis	The process by which organisms maintain a constant internal environment necessary for good biological function, such as a constant pH or temperature.
Imposex	An irreversible condition in which a female animal develops male genital organs (or vice versa).
Ligand	Ligands are molecules that bind to larger molecules (often protein receptors) and initiate or regulate their function. A hormone is a ligand that binds specifically to its receptor.
PPARα and γ	Peroxisome proliferator-activated receptors α and γ, involved in metabolism and cellular differentiation.
PR	Progesterone receptor, involved in reproduction and development.
RAR	Retinoic acid receptor.
RXR	Retinoid X receptor, involved in development, cell differentiation and metabolism.
TR	Thyroid receptor, involved in metabolism and organ development. There are multiple subtypes of the TRs, such as TRβ.
VDR	Vitamin D receptor, involved in metabolism and immune response.

WHO	World Health Organisation.

1. INTRODUCTION - WHAT IS ENDOCRINE DISRUPTION?

The concept of endocrine disruption stems from the presence of endocrine disrupting chemicals (EDCs) in the environment. One of the best definitions of EDCs remains “exogenous agents that interfere with the production, release, transport, metabolism, binding, action, or elimination of the natural hormones in the body (of a human and/or wildlife species) responsible for the maintenance of homeostasis and the regulation of developmental processes” (Kavlock 1999).

Biologically active EDCs can interfere with endocrine systems leading to adverse health effects, such as interference with sexual development, reproduction, metabolism, immune response and behaviour, in both exposed humans and wildlife. This issue has gained increasing interest, particularly since the publication of the book 'Our stolen future' in the 1990s (Colborn et al. 1996).

There have been several excellent reviews on the state of the science on endocrine disruption in the environment (Matthiessen & Gibbs 1998; Tyler & Routledge 1998; WHO/IPCS 2002; Matthiessen 2003; Cheek 2006; Hotchkiss et al. 2008; Kloas et al. 2009; Marty et al. 2010; Bergman et al. 2013; Kabir et al. 2015; Giulivo et al. 2016). The most authoritative and comprehensive assessment remains the 2002 report published by the World Health Organization (WHO) and the International Program on Chemical Safety (IPCS) (WHO/IPCS 2002). While a more recent report has been produced by the WHO and the United Nations Environmental Programme (UNEP) (Bergman et al. 2013), the latter has been criticised for being less systematic (Lamb et al. 2014). The objective of this report is to highlight key aspects of the endocrine disruption issue, including the sources and occurrence of EDCs in the environment and the risk they pose to exposed biota. Recommendations are provided to the PCE to assist their understanding of whether EDCs are an issue in Aotearoa New Zealand.

2. EVIDENCE OF ENDOCRINE DISRUPTION IN THE ENVIRONMENT

This section provides a brief overview of endocrine disruption, including how EDCs exert their effects and examples of EDCs and their sources. Case studies are provided to describe typical adverse effects of endocrine disruption.

2.1. The endocrine system

Briefly, the endocrine system plays important roles in regulating a range of body functions. Some of the physiological processes modulated by hormones include metabolism, growth and development, immune function, development of sexual characteristics and reproduction. Hormones are the chemical signals released by endocrine glands[1], circulating in the blood throughout the body to target organs. The actions of hormones are activated by their binding to specific receptor proteins in the cells of target tissue. The binding of the hormone-receptor complex to DNA has a direct effect on the level of transcription of messenger RNA, which leads to the production of specific proteins (Figure 1). EDCs are molecules that can interfere with the normal actions of hormones, and the following section describes some of the well-established mechanisms.

2.2. Mechanisms of action of EDCs

EDCs encompass many chemical classes that interact with various processes of the endocrine system, i.e. molecules that interact with the production of hormones or their effects. Research to date has focused mainly on the impacts of EDCs on natural steroid hormone processes.

Our understanding of how EDCs might interact with the endocrine system is based on the assumption that molecules with structural similarities to steroid hormones might bind to hormone receptors—for example, how molecules similar to the main female sex steroid hormone 17β-estradiol (E2) might interfere with the oestrogen receptor (ER) (Muller et al. 1995). Binding to receptors can trigger the sequence of physiological processes, potentially leading to endocrine disruption (Ye et al. 2018). These intimate relationships between oestrogen mimics and ERs are now well understood, and the molecular attributes required for binding to ERs to initiate subsequent receptor-mediated effects have been well described (Brzozowski et al. 1997; Ye et al. 2018).

[1] Ductless glands that secrete hormones into the extracellular spaces, from which they diffuse into the circulatory system.

The effects of E2 and other hormones are modulated by a sequence of events that lead to the estrogenic response: E2 binds to a specific recognition site on the ER, which triggers the formation of an E2-ER complex that migrates to the nucleus where it interacts with the oestrogen response element (ERE) on the nuclear DNA. This leads to the switching on or off of oestrogen-specific genes, which in turn stimulates (or inhibits) the production of specific proteins. These changes ultimately result in the physiological and biochemical effects associated with oestrogens, such as the maturation of reproductive tissues. Figure 1 describes the basic ER-mediated mechanism of E2 mimicry.

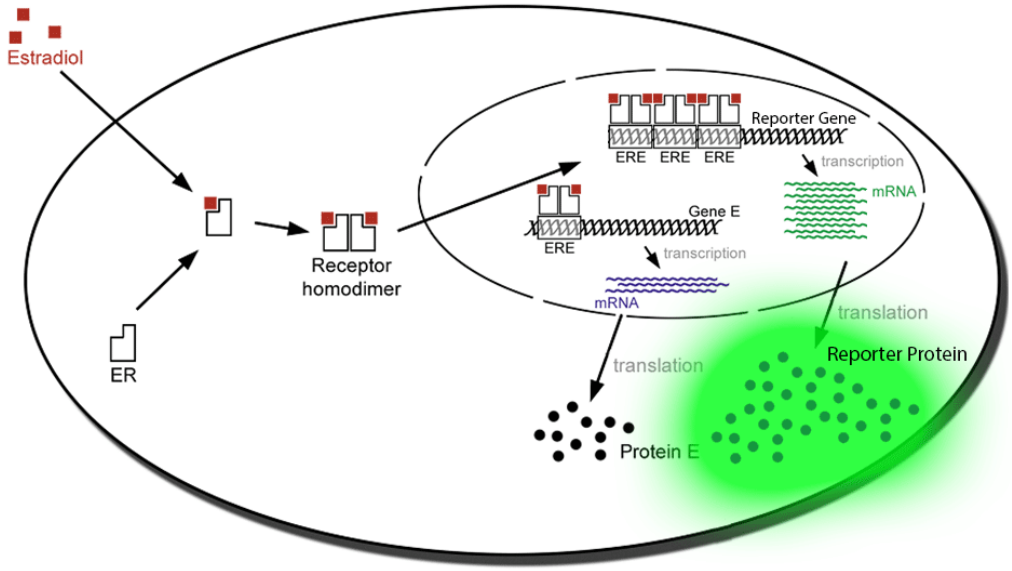

Figure 1. Simplified representation of steroid hormone 17β-estradiol (E2) mechanism leading to the production of specific protein synthesis. The E2 enters the target cells and binds to the oestrogen receptor (ER). The E2-ER complex enters the nucleus and binds to specific oestrogen response elements (ERE) on the DNA. This initiates gene transcription and subsequently the translation of the resulting messenger RNA into new proteins, e.g. vitellogenin, a precursor to egg yolk in egg-laying animals. This principle is used to develop reporter gene assays used to assess the estrogenicity of chemicals.

Hormones can also affect biological systems via non-genomic pathways (Hwang & Choi 2019), through interaction with membrane-bound oestrogen receptors such as the G protein-coupled oestrogen receptor (GPR30). The interaction with the receptor binding site is as described in this section, but the cellular response does not include interaction with DNA. Instead, the membrane-bound ER induces a rapid cellular cascade that can directly affect cellular function (Kelly & Levin 2001; Zhang & Trudeau 2006).

To bind to the ER, a molecule needs specific structural characteristics as illustrated in Figure 2. As such, only a few molecules fit these criteria perfectly, including of course the specific receptor's natural ligand (e.g. E2 for the ER).

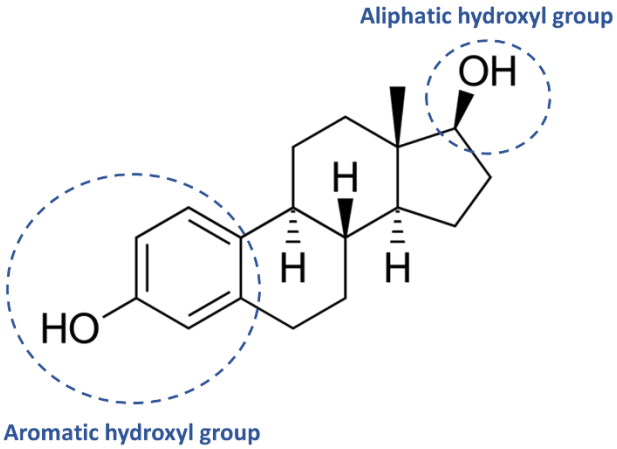

Figure 2. Chemical structure of 17β-estradiol (E2), highlighting the aromatic and aliphatic hydroxyl groups known to be keys to its binding to the oestrogen receptor (ER).

EDCs have varying degrees of affinity to interact and activate ERs; the degree of activation is proportional to the degree of molecular fit. The interactions of EDCs with receptor molecules can lead either to an agonistic or antagonistic effect, i.e. promote or block the response. It is not always easy to predict whether a molecule can be an EDC, but the use of *in vitro* methodologies is a good approach to screen chemicals for their binding affinity for a range of receptors (Huang et al. 2011). For instance, the insecticide DDT[2] does not have any hydroxyl groups, but its two aromatic chlorines are electron withdrawing (i.e. akin to oxygen in hydroxyl groups) and so can still interact with ERs (Figure 3), resulting in agonistic activity. Its relative estrogenicity is low, one million times less than that of E2 (Thomson et al. 2003), because of its poor interaction with the receptor binding site. Other studies have confirmed that the pesticide *o,p*'-DDT binds to the ER but not to the androgen receptor, further illustrating that molecules can have affinities to select receptors based on their chemical structures (Tremblay et al. 2005).

[2] Dichlorodiphenyltrichloroethane, an insecticide used in agriculture that has been banned for use since the 1970s.

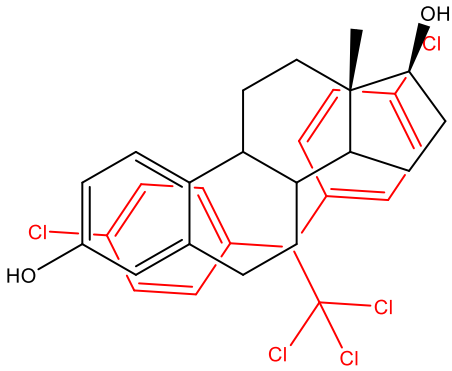

Figure 3. 17β-estradiol (E2) (black) and DDT (red) aligned to show their molecular analogies vis-à-vis binding to the oestrogen receptor (ER). This mechanism of action can explain some of the effects of DDT contaminants on male development in exposed alligators in Lake Apopka, Florida (further explanations in the next section).

As our understanding of mechanisms of estrogenicity and other processes develops, it is likely that more compounds will be considered EDCs. EDCs can interfere with hormone activities in one or more of the following 10 mechanisms of action (Vandenberg 2021):

1. interact with or activate hormone receptors (e.g. receptor agonists)
2. antagonise hormone receptors (e.g. receptor antagonists)
3. alter the expression of hormone receptors
4. alter signal transduction in hormone-responsive cells
5. induce epigenetic modifications in hormone-producing or hormone-responsive cells
6. alter the synthesis of one or more hormones
7. alter the transport of hormones across cell membranes
8. alter the distribution of hormones to the tissues of the body or the circulating concentrations of hormones in blood
9. alter the metabolism of one or more hormones or hormone clearance from the body
10. alter the fate of hormone-producing or hormone-responsive cells.

2.3. Methods to screen and characterise EDCs

Over several decades of research on EDCs, many chemicals have been identified that interfere with the endocrine system (some examples are given in Section 2.3). While most reports and research publications on endocrine disruption have focused on estrogenic EDCs, it is important to notice that EDCs can also interfere with the other endocrine receptors in animals, including other sex hormone receptors such as the androgen receptor (AR), other steroid receptors such as the progesterone (PR)

and glucocorticoid receptors (GR), but also any other hormone receptors such as the thyroid (TR), retinoid (RAR and RXR) and more. For instance, EDCs with glucocorticoid activity have been reported in wastewater where compounds like cortisol, cortisone, prednisone and triamcinolone acetonide were causing the effects (Schriks et al. 2010). Interference with the glucocorticoid receptor can interfere with proper metabolism and the immune response. The progesterone receptor (PR) assay identified active pharmaceutical ingredients and excreted hormones as predominant drivers of PR-mediated activity (Hashmi et al. 2020). Interference with the progesterone receptor (PR) can affect reproduction and gestation, a form of endocrine disruption.

With an estimated 350,000 chemicals and mixtures registered for commercial production and use and their countless transformation products, many of which remain uncharacterised, and it is impossible to analyse all EDCs in a sample with conventional chemical analysis. In addition, some potent EDCs (such as synthetic oestrogens and progestogens) can produce biological effects in exposed organisms at very low concentrations in the parts per quadrillion (pg/L) range. These ultra-trace concentrations can be challenging to measure when using advanced liquid or gas chromatography mass spectrometers (LC/GC-MS), especially when dealing with complex matrices like sewage effluent.

To overcome these limitations, new methodologies such as effect-based methods (EBM) have become essential tools to measure EDCs (Escher & Neale 2021). Effect-based methods detect EDCs not by their chemical structure but by their ability to interfere with endocrine processes, such as by binding to hormone receptors (e.g. receptor binding assays), interfering with hormone production or steroidogenesis, inducing a genomic response (e.g. reporter gene assays, Figure 1). This means that EBM can detect ‘unknown’ EDCs and even provide a measure of the overall mixture effect from bioactive chemicals present in a sample.

There are two main types of bioassays employed in EBM: cell-based and whole-animal bioassays (Robitaille et al. 2022). Cell-based bioassays monitor the response of animal cells to determine if exposure to a particular sample can interfere with the normal hormone-mediated response, often in genetically modified cell lines that amplify that response (Escher & Neale 2021). Cell-based assays are very sensitive to EDCs and capable of detecting potent hormonally active compounds in the pg/L range with proper sample preparation. While not all assays are equal, many of these assays have been shown to be highly reproducible (Leusch et al. 2010) and to correlate well with whole-animal responses (Sonneveld et al. 2011). With water samples, the response in the assay can be compared with established effect-based trigger values to determine if the level of activity measured is likely to pose a risk to exposed humans or ecosystems. Cell-based bioassays are therefore excellent screening tools to test for EDCs in environmental samples.

Cell-based assays also have limitations: they generally do not integrate toxicokinetic elements (such as absorption, distribution, metabolism and excretion) that can affect how whole organisms respond to toxic chemicals like EDCs; they also cannot identify the chemicals that cause the biological response, so are often used in parallel with analytical chemistry to identify the chemicals responsible for the activity.

Whole-animal assays using embryonic and/or transgenic life forms of fish or frogs have also been developed to detect EDCs by their effect on whole organisms (Robitaille et al. 2022). One advantage of these assays is that they incorporate the whole organism (as opposed to a single cell), thereby incorporating a more complete endocrine system with its complex web of interactions and feedback loops. Some of these assays, such as the Xenopus Eleutheroembryonic Thyroid Assay (XETA) (OECD 2019), can also be used in high-throughput format[3], allowing for the testing of many samples in a short amount of time. Overall, however, these techniques are more expensive and less ethically palatable; thus, they are better suited to chemical risk assessment and second tier testing after identifying a positive sample during screening with a cell-based assay. These techniques are not available in Aotearoa New Zealand.

EBMs have been increasingly applied to test environmental samples for endocrine activity (Escher & Neale 2021; Robitaille et al. 2022). Some of these methods have been used in Aotearoa New Zealand to characterise the endocrine disruption potential of sewage and dairy shed effluents and pollutants accumulating in sediment (Leusch et al. 2006b; Sarmah et al. 2006; Gadd et al. 2010; Boehler et al. 2017; Tremblay et al. 2018). The results of these studies are summarised in Section 4.1.1.

With the rapid improvement in in silico technology, it is now possible to model nuclear receptors (such as the ER) and determine how molecules fit into the receptor. This computational technology is increasingly used to provide insights into absorption, distribution, metabolism and elimination/excretion properties of a chemical, all important parameters for the ultimate success or failure of a possible pharmaceutical drug (Leelananda & Lindert 2016). A correlation between in silico-derived parameters (e.g. DockScore) and estrogenicity has been suggested (Eldridge et al. 1997). Along with other methods such as Quantitative Structure Activity Relationship (QSAR), which uses statistical models to predict the biological activity of compounds and can identify potential interactions with receptors, these approaches can be used to predict endocrine disruptive potential as part of future risk minimisation strategies (Sellami et al. 2022).

[3] Platform that allows the concurrent processing of multiple chemicals or extracts through a bioassay.

2.4. Examples of EDCs

There are multiple sources of steroid hormone mimics ranging from pesticides (e.g. vinclozolin, DDT and pyrethroids), industrial effluent contaminants (e.g. lignans from the paper pulp industry, the plasticiser bisphenol A) and pharmaceuticals via sewage effluent (e.g. contraceptive pill ingredients such as 17α-ethinylestradiol and levonorgestrel). A selection of oestrogen mimics is shown in Figure 4 to illustrate their structural analogies to E2 and the wide range of sources of environmental contamination.

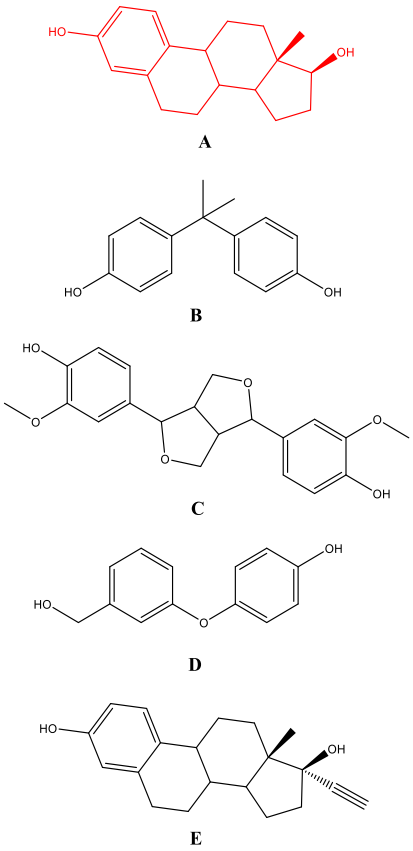

Figure 4. 17β-estradiol (A) and a selection of oestrogen mimics showing their molecular analogies: the chemical additive used in the production of polycarbonate plastics, bisphenol A (B); the lignan pinoresinol (C), which is found in effluent from paper manufacturers; 3-(4-hydroxy-3-phenoxy benzyl alcohol (D), an environmental metabolite of pyrethroid insecticides; one of the contraceptive pill's active ingredients, 17α-ethinylestradiol (E).

Many active pharmaceutical ingredients have been designed to interact with a wide range of nuclear receptors (Table 2). Interference with nuclear receptors is only one mechanism of endocrine disruption, and pharmaceutical ingredients can also affect endocrine function via other mechanisms. For example, somatostatins affect thyroid activity by inhibiting thyroid secreting hormone secretion, and antigonadotropins decrease sex hormones by inhibiting the hypothalamic-pituitary-gonadal axis (the key regulator of sex development and reproduction processes that are initiated through the hypothalamus).

Table 1. Some examples of active pharmaceutical ingredients that are engineered to modulate nuclear receptors to treat human conditions.

Target nuclear receptor*	Active pharmaceutical ingredient	Therapeutic effect
PPARα	Fibrates (e.g. fenofibrate, gemfibrozil, clofibrate)	Cholesterol regulation
PPARγ and RXR	Thiazolidinediones (e.g. pioglitazone, rosiglitazone)	Treatment of diabetes
GR	Synthetic glucocorticoids (e.g. prednisone, betamethasone, dexamethasone, mometasone furoate, triamcinolone acetonide)	Treatment of chronic inflammatory diseases
GR	Mifepristone	Treatment of hyperglycaemia
PR	Mifepristone	Medical abortion, emergency contraception
PR	Progestins (e.g. levonorgestrel, megestrol acetate, norethisterone, norgestrel, drospirenone,	Hormonal birth control, hormone therapy
ER	Oestrogen hormones (e.g. estradiol, estrone)	Hormone replacement therapy
ER	Synthetic oestrogens (e.g. ethinylestradiol, diethylstylbestrol)	Hormonal birth control
ER	Tamoxifen	Treatment of breast cancer
AR	Synthetic antiandrogens (e.g. flutamide, bicalutamide, spironolactone, cyproterone acetate, medroxyprogesterone acetate)	Treatment of prostate cancer, treatment of acne, chemical reduction of sex drive, hormone therapy
AR	Testosterone	Growth promotion, treatment of delayed puberty
AR	Anabolic steroids (e.g. testosterone, nandrolone, stanozol, methyltestosterone)	Body building
TR	Amiodarone	Used to treat heart arrhythmia, affects thyroid receptor as a side effect

Note: many active pharmaceutical ingredients that target nuclear receptors are also used in veterinary medicine and agriculture to treat animal disease or as growth promoters (e.g. the AR agonist trenbolone acetate and the ER antagonist zeranol are used as livestock growth promoters in some countries).
* As defined in the acronym table.

Perhaps the most comprehensive initiative to assess the endocrine potential of chemicals was the Tox21 programme, a collaboration between the US Environmental Protection Agency (USEPA), the National Toxicology Program, and the National Institutes of Health (Huang et al. 2011). The objective of Tox21 is to use a broad spectrum of *in vitro* assays to use high-throughput screening methods to screen many environmental chemicals for their potential to disturb biological pathways that may result in toxicity. As a Tox21 proof-of-concept study, a library consisting of approximately 3,000 environmentally relevant chemicals, such as pesticides,

pharmaceuticals and industrial chemicals, was screened against a panel of 10 human nuclear receptors, including the AR, ERα, GR, and thyroid hormone receptor β (TRβ) (Huang et al. 2011). The study demonstrated that a considerable number of environmentally relevant chemicals can interfere with a wide range of nuclear receptors (Figure 5).

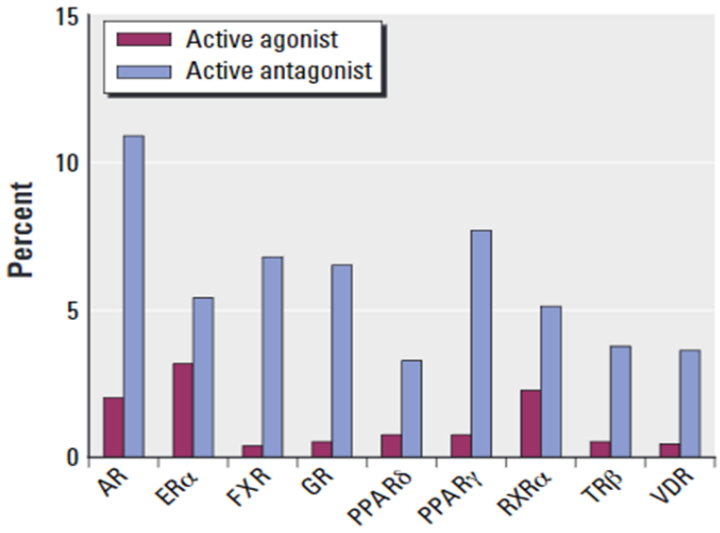

Figure 5. Proportion of tested chemicals that were classified as active agonists or antagonists of 9 different human nuclear receptors. Figure from Huang et al. (2011).

Another study identified 7,135 endocrine active chemicals out of 323,056 (Sipes et al. 2013). Pesticides, pharmaceuticals, consumer use chemicals, and phthalate plasticisers and alternatives were the most active classes of EDCs. This confirms that environmental pollutants can interact with a wide range of endocrine receptors, beyond just effects on the ER. Scientific and medical experts, including representatives from the WHO and the Endocrine Society, have concluded that EDCs pose a risk to the health of humans and wildlife (Vandenberg 2021).

2.5. Effects of EDCs in wildlife

The major WHO/UNEP report listed approximately 800 oestrogen mimics and discussed their impacts on human health and the environment (Bergman et al. 2013). It is now accepted that oestrogen mimics perturb the growth and development of animals and have implications for both human and ecosystem health. The effects range from subtle changes in physiology and sexual behaviour to permanently altered sexual differentiation. A wide range of species and phyla have been affected, including invertebrates, reptiles, amphibians, fish and mammals. Several examples are summarised in Table 2. These studies provide clear evidence that disruption of the endocrine system in a variety of organisms can severely affect the reproductive

capacity of individual organisms and ultimately reduce the survival of affected populations. For some studies, it has been conclusively demonstrated that the adverse effect is mediated via chemical disruption of the endocrine system (labelled as ‘Causation’ in Table 2). In others, the adverse effects are clearly associated with exposure to EDCs, but the exact mechanism has not been conclusively identified (labelled as ‘Association’ in Table 2). This is particularly common in species where we only have a partial understanding of their endocrinology and reproductive biology.

Table 2. Selection of adverse effects reported in wildlife due to endocrine disruption. None of these effects have been observed in Aotearoa New Zealand.

Animal clade	Adverse effect	Strength of the evidence *	Reference
Invertebrates	Imposex in marine gastropods exposed to tributyltin from antifouling paint	Causation	See case study 2 below
Invertebrates	Reproductive abnormalities such as feminisation of male fish associated with discharge of treated wastewater	Causation	(Gagné & Blaise 1998; Gross et al. 2001)
Fish	Reproductive abnormalities associated with discharge of treated wastewater	Causation	See case study 1 below
Fish	Reproductive abnormalities associated with discharge of pulp mill effluent	Causation	(Munkittrick et al. 1998; Parks et al. 2001)
Fish	Complete inhibition of reproduction and ultimate collapse of a fish population exposed to the birth control 17α-ethynylestradiol	Causation	(Kidd et al. 2007)
Reptiles	Developmental abnormalities (shrunken penises) and population decline in alligators exposed to pesticide spill (dicofol, DDE, DDT)	Association	(Guillette et al. 1994; Guillette et al. 2000)
Reptiles	Developmental abnormalities in turtles exposed to PCBs and dioxins	Association	(Bishop et al. 1998; de Solla et al. 1998; de Solla et al. 2001)
Amphibians	Deformities (e.g. extra limb, musculature malformations, eye and central nervous system abnormalities) and sexual abnormalities in frogs exposed to pesticides (incl. atrazine)	Association	(Hayes et al. 1997; Ankley et al. 1998; Hayes et al. 2003; McDaniel et al. 2008)
Birds	Eggshell thinning, skewed sex ratio, altered gonadal development and population decline in birds exposed to DDT/DDE	Causation	(Struger & Weseloh 1985; Fry et al. 1987; Johnstone et al. 1996)
Birds	Reproductive and embryonic abnormalities in fish-eating birds (pesticides)	Association	(Fry et al. 1987; Fry 1995)
Birds	Altered hormone levels and sexual behaviour (nesting, guarding, rearing) in birds exposed to persistent organic pollutants (pesticides, PCBs)	Association	(Fox et al. 1978; McArthur et al. 1983)
Mammals	Compromised endocrine system and reproductive dysfunction in seals exposed to persistent organic pollutants	Association	(Reijnders 1980; Roos et al. 1998; Troisi et al. 2020)
Mammals	Abnormal hormonal levels and pseudo-hermaphroditism in polar bears exposed to high concentrations of PCB	Association	(Wiig et al. 1998; Skaare et al. 2002)
Mammals	Impaired reproduction in sheep exposed to phytoestrogens through clover grazing	Causation	(Bennetts et al. 1946; Adams 1990; Pool et al. 2022)
Mammals	Decline in wild populations of mink and otter exposed to persistent organic pollutants (pesticides, PCBs)	Association	(Roos et al. 2001; Elliott et al. 2018)

* The strength of the evidence is described as either ‘association’ (i.e. the observed effects are associated with elevated EDC concentrations, but there is limited evidence that the adverse effects are mediated through endocrine-dependent mechanisms) and ‘causation’ (i.e. the effect has been demonstrated because of endocrine disruption caused by exposure to EDCs).

Many studies provide clear evidence that disruption of the endocrine system in a variety of organisms can severely affect the reproductive capacity of individual organisms and ultimately reduce survival of exposed populations. One example of drastic effects following exposure to EDCs was reported in alligators from Lake Apopka, Florida following a major pesticide spill in the early 1980s. In the 5 years following the pesticide spill, juvenile recruitment plummeted on Lake Apopka due to decreased clutch viability and increased juvenile mortality (Guillette et al. 2000). The alligators had smaller penises and lower blood testosterone concentrations than those from nearby more pristine Lake Woodruff (Guillette et al. 1994). The sexual development defects of Lake Apopka alligators were attributed to exposure to environmental contaminants, particularly the pesticide DDT. It has been suggested that the antiandrogen characteristics of the DDT metabolite *p,p'*-DDE (and perhaps other environmental pollutants) disrupted male growth and development in alligators (and perhaps other species) via androgen receptor antagonism (Guillette et al. 1994). These findings contributed to a broader understanding of the roles of environmental pollutants and hormone mimicry in environmental impact and the now significant interest in the risks associated with EDCs.

There have been multiple field studies demonstrating endocrine disruption effects in fish that are attributed to the presence of oestrogen mimics in treated wastewater. For example, a study in the United Kingdom showed that male fish caged near sewage outfalls expressed the egg yolk precursor protein vitellogenin, which under normal conditions is specific to females (summarised in Case Study 1 in the box below). Vitellogenin is now recognised as a biomarker of exposure to environmental oestrogen mimic (agonist) in both laboratory and field studies (Sumpter & Jobling 1995; Jones et al. 2000).

Marine pollution by organotin compounds, such as tributyltin (TBT) and triphenyltin (TPT), used in antifouling paints for ships, boats and fishing nets is a good example of endocrine disruption in invertebrates (Horiguchi et al. 1994). The use of organotin-based paints has been banned by the Marine Environmental Protection Committee of the International Maritime Organization since the 1990s. While the ban of TBT antifouling paint products has largely been effective, the levels of TBT remain high, particularly in ports. Unfortunately, some suppliers continue to produce and sell these products in several countries (Beyer et al. 2022). TBT have been shown to induce imposex (the development of male sex organs in females) in neogastropods (see details in Case Study 2). Aotearoa New Zealand is not immune to sediment TBT contamination, as evidenced by elevated sediment levels of TBT at Port Nelson triggered the remediation of the port's seabed to meet the Australia and Aotearoa New Zealand interim sediment quality guidelines (Charry et al. 2020).

Case Study 1: Endocrine disruption in fish exposed to wastewater discharges.

Sexual disruption in fish exposed to municipal wastewater is a well-known example of endocrine disruption in wildlife. It was reported that wild fish in rivers downstream of wastewater discharges exhibited sexual abnormalities, including feminised reproductive organs and expression of vitellogenin in males (Tyler & Routledge 1998). Surveys reported that this disruption was widespread throughout UK rivers, and highest downstream of wastewater discharges (Figure CS1, left) (Jobling et al. 1998; van Aerle et al. 2001). Effects included high levels of vitellogenin in males, high incidences of intersexuality (Figure CS1, right) and altered endocrine status (Christiansen et al. 2002; Jobling & Tyler 2003).

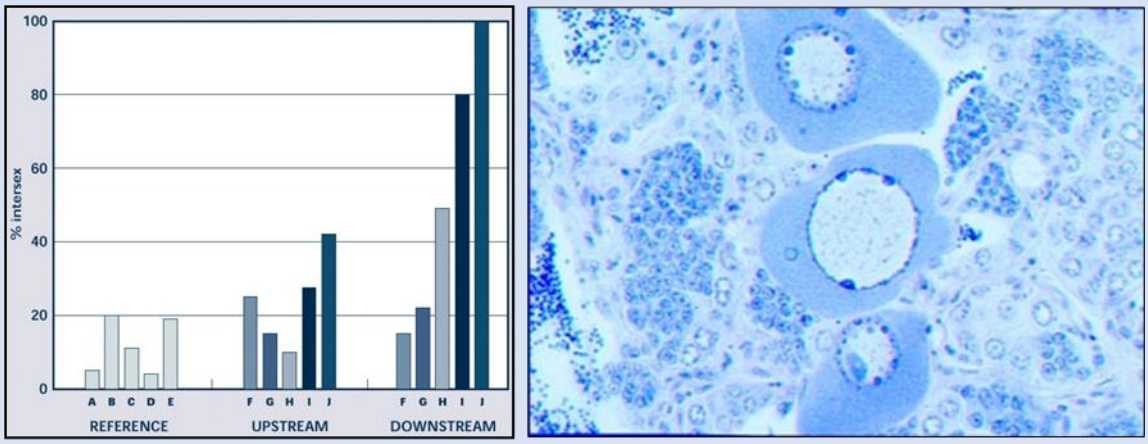

Figure CS1: Left: Incidence of intersexuality in roach captured at reference sites (A-E) and upstream and downstream of wastewater treatment plant discharges (F-J) in UK rivers. Right: Section through fish testes showing the presence of mature oocytes within testicular tissue. Source: Jobling et al. (1998).

These findings were confirmed globally (Folmar et al. 1996; Viganò et al. 2001; Barnhoorn et al. 2004) and in other taxa such as molluscs and crustaceans downstream of wastewater discharges, which likewise exhibited signs of estrogenic effects (Gagné et al. 2001; Gross et al. 2001). It appeared that the situation in the UK was particularly widespread because local environmental regulations required comparatively modest treatment of wastewater before discharge into receiving rivers, and thus wastewater effluent contained higher concentrations of EDCs than in other parts of the world.

By combining chemical and effect-directed analysis, it was demonstrated that wastewater effluent exhibited substantial estrogenic endocrine activity (Purdom et al. 1994), and natural and synthetic oestrogens (estradiol, estrone and 17α-ethinylestradiol) and degradation products of non-ionic surfactants and detergents (e.g. alkyphenol polyethoxylates) were ultimately identified as the drivers of most of the estrogenic activity in UK wastewater and rivers (Desbrow et al. 1998). We now know that pollutants are incompletely removed by wastewater treatment (Melvin & Leusch 2016) and trace amounts of EDCs remain in treated wastewater. This has been demonstrated globally, including in Aotearoa New Zealand (Leusch et al. 2006a).

As the endocrine system is highly sensitive, even trace amounts of EDCs can affect the endocrine system of exposed biota, as this case study demonstrates. An experimental lake was continually dosed with trace concentrations (average exposure concentration of 5-6 ng/L) of the synthetic 17α-ethinylestradiol, the oestrogen in the birth control pill, resulting in a dramatic decrease in reproduction and the eventual collapse of a fish population within 3 years (Kidd et al. 2007), demonstrating that interference with individual reproduction affects the whole population. This is environmentally relevant as 17α-ethinylestradiol has been found in the aquatic environment at concentrations of < 5 ng/L.

Case Study 2: Imposex in marine gastropods exposed to tributyltin from antifouling paint.

In the 1980s, there were worrying signs of population decline in marine gastropods worldwide, and an increasing proportion of marine gastropods were found to exhibit imposex, an irreversible condition in which a female mollusc develops male genital organs such as a penis and vas deferens (Figure CS2, left) (Bryan et al. 1986). This trend was also reported in Aotearoa New Zealand waters (Smith & McVeagh 1991). The consequence of imposex in gastropods includes distortion of sex ratio, reduction in recruitment of juveniles and ultimately reduced population numbers.

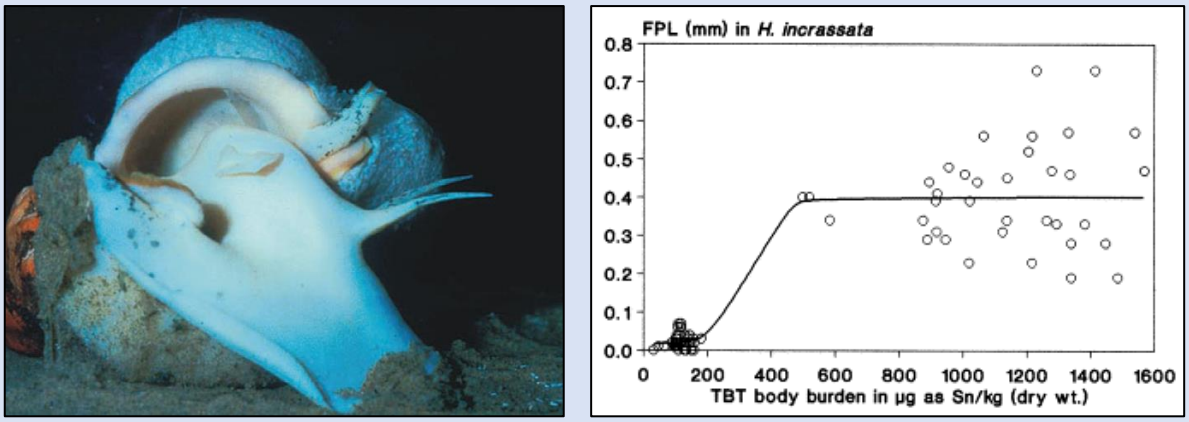

Figure CS2: Left: Female whelk with imposex (small fold on main body, in the middle of the picture). Source: WHO/IPCS (2002). Right: relationship between female penis length (FPL) and tributyltin (TBT) body burden in thin-lipped dogwhelk. Source: Oehlmann et al. (1998).

Exposure to tributyltin (TBT), a compound widely used in antifouling paint applied to the hulls of ships, was identified as the cause of this reproductive abnormality (Matthiessen & Gibbs 1998). TBT was detected in marine sediments worldwide (Fent 1996), even in remote Antarctic marine sediments (Negri et al. 2004).

Laboratory and field experiments demonstrated that the frequency of imposex and the degree of penis development was correlated to the degree of tributyltin exposure (Figure CS1, right) (Bryan et al. 1986; Oehlmann et al. 1998). TBT exposure can also affect reproduction in a wider range of marine molluscs, including oysters, mussels and clams (deFur et al. 1999). It is now know that TBT induces imposex in molluscs via abnormal modulation of the retinoid X receptor (RXR) signalling pathway (Giulianelli et al. 2020).

A global ban on TBT in antifouling paint imposed in 2008 led to a decrease in TBT levels in the marine environment (Jasinska et al. 2015); subsequently, there has been a reduction in imposex and an observed population recovery in many areas previously impacted by TBT, including Aotearoa New Zealand (Holder et al. 2018).

Unfortunately, TBT is still used in antifouling paints in countries in Latin America, Africa and Asia where environmental standards are not as strict, and TBT-induced imposex remains an issue for mollusc populations in those regions (Castro et al. 2018; van Gessellen et al. 2018). Dredging and dumping of TBT-contaminated sediments in harbours can also adversely affect exposed mollusc populations (de Oliveira et al. 2020). In addition, with global shipping, when vessels maintained and repainted in countries using antifouling paints subsequently visit or reside in another country, they can continue to release TBT in those harbours (Kim et al. 2011). Aotearoa New Zealand is not immune to TBT contamination with port sediment concentrations comparable to levels reported internationally (Charry et al. 2020).

3. ENDOCRINE DISRUPTION IN A REGULATORY CONTEXT

The deleterious effects of environmental EDCs on the reproductive success of wildlife populations have been well-documented. This is not an isolated problem and many wildlife populations are potentially at risk (Colborn et al. 1994). Studies have covered a wide range of species, including invertebrates, reptiles, amphibians, birds and mammals. Many of these effects have been associated with (and in some cases conclusively attributed to) the presence of pharmaceuticals, pesticides and other persistent organic pollutants. Unfortunately, there are still no national regulations of EDCs anywhere in the world to remedy this problem. It was estimated that EDC exposure in the USA contributes to disease and dysfunction costing more than 2% of the GDP annually. Some scientists predict that inadequate regulation of EDCs could have serious adverse consequences for future generations (Attina et al. 2016).

Approaches to limit exposure of humans to EDCs have also been slow and insufficient and focused on a limited number of chemicals used in commerce, despite an ever-expanding list of chemicals requiring evaluation for identifying EDCs (Kassotis et al. 2020). To address the risk of EDCs, Australia considered using the European hazard-based criteria as an indicator, triggering further evaluation in risk assessment of a chemical for ongoing use in products (Kassotis et al. 2020). The European environmental policy is based on the precautionary principle that mandates that exposures should be limited when indications of potentially dangerous effects on the environment, human, animal or planetary health exist, even in the absence of scientific certainty (Kassotis et al. 2020).

The Organisation for Economic Co-operation and Development (OECD) has produced a guidance document on standardised test guidelines for evaluating the endocrine disruptive potential of single chemicals based on recommendations from experts (OECD 2018). Many of these methods are based on modes of action and not on particular adverse outcomes or harms. Regulation processes in the United States of America state that a chemical must induce an adverse effect for it to be regulated, and ‘adverse effects’ are defined as occurring in whole animals. Many of the data to evaluate and characterise endocrine mechanisms are from the OECD test guidelines and do not determine if a chemical induces adverse effects in a whole organism or population; thus, the regulatory agencies in the USA, European Union and elsewhere have not yet developed regulations specific to EDCs (Vandenberg 2021). A proposed pathway for the regulation of potential EDCs in invertebrates with greater confidence was based on the Adverse Outcome Pathway (AOP) concept and focused on identifying Molecular Initiating Events (MIEs) within AOPs (Ankley et al. 2010; Crane et al. 2022). The AOP concept is a robust way to organise information on potential harmful EDCs and support regulatory decision-making; however, it requires significant resource investment for development and implementation (Crane et al. 2022). Although the new Toxic Substances Control Act provides authority for the US Environmental Protection Agency to regulate chemicals, request additional safety

testing and gather additional data as needed, endocrine disruption testing is not mentioned (Kassotis et al. 2020).

There are discussions about whether agencies should move forward regulating ‘environmental mixtures’ using effect-based trigger value limits such as the estradiol equivalent concentrations as opposed to single chemical regulation. To date, there has been limited uptake of EBM in regulatory applications, though one prominent example is the use of EBM to monitor recycled water in California (State Water Resources Control Board 2019), which have set health-based monitoring trigger levels of 3.5 ng/L estradiol equivalent (EEQ) for estrogenic activity in a reported gene assay. In addition, there are bottom-up initiatives on EDC detection of wastewater effluents as its own chemical entity are now becoming more prevalent in some regions, e.g. Quebec and Ontario (Canada), California (USA) and Centre-Val de Loire region (France) (Langlois et al. 2022).

4. THE AOTEAROA NEW ZEALAND PERSPECTIVE

A review of international and national literature on emerging organic contaminants (EOCs) was conducted for the Hawke's Bay Regional Council in 2011 and was updated in 2016 for Auckland Council (AC), Environment Canterbury Regional Council (ECan) and Greater Wellington Regional Council (GWRC) (Tremblay et al. 2011; Stewart et al. 2016). These reviews stressed that EOCs with endocrine activities present a risk to the receiving ecosystems. With the improvement of analytical methodologies, a wider range of contaminants of industrial and agricultural origin and from household activities can now be detected including pharmaceutically active compounds and personal care products that can have endocrine disrupting activities. This section provides a brief overview of the current state of knowledge of endocrine disruption in Aotearoa New Zealand.

4.1. What research has been conducted in Aotearoa New Zealand

There has been very limited research on endocrine disruption in Aotearoa New Zealand. While there have been no significant research programmes, a few isolated projects have focused on endocrine disruption, including some student initiatives. As summarised in section 2.2, bioassays have been used to characterise the endocrine disrupting potential of individual chemicals and complex effluent mixtures like sewage effluents. Biochemical and molecular (qPCR) biomarkers, such as vitellogenin, have been developed and used (e.g. in a diquat study in Christchurch (Ataria et al. 2004; Tremblay 2004)). The following section covers the current state of knowledge in Aotearoa New Zealand.

4.1.1. Current state of knowledge on the presence and fate of EDCs in the Aotearoa New Zealand environment

The first study conducted in Aotearoa New Zealand looked at the presence of selected oestrogens and total estrogenicity using an ER competitive binding assay in dairy farm, piggery and municipal effluents in the Waikato region (Sarmah et al. 2006). The results showed the presence of significant amounts of oestrogens in treated animal wastes applied to land or released into streams. Further investigations confirmed the presence of steroid oestrogens and estrogenic activity in dairy shed effluents and in dairy catchments (Gadd et al. 2010; Tremblay et al. 2018). The long-term Predicted No Effect Concentration (PNEC) for E2 is 2 ng/L. While estrogenic activity was generally below < 1 ng/L, one (of 10) stream had activity of 1.4 ng/L, a concentration that could potentially be harmful to aquatic biota (Caldwell et al. 2012). Although this concentration is below the PNEC, the result was from a one-off sampling event, and it is possible that concentrations may exceed the PNEC value, e.g. during periods of low flow over the summer period.

Sewage effluent is a major source of contaminants, and a few studies have investigated the efficacy of sewage treatment plants to remove endocrine activity. A study in Canterbury using estrogenic and androgenic bioassays demonstrated that secondary treatment was the most effective step to remove both estrogenic and androgenic activities from sewage effluent (Leusch et al. 2006b).

A range of estrogenic steroid hormones, including the estrogenic plasticizer bisphenol-A and the preservative paraben, were detected in some samples from a 2018 Aotearoa New Zealand survey of EOCs in groundwater (Close et al. 2021).

Biosolids are a product of the wastewater treatment process and represent another potential source of EDCs (Langdon et al. 2011). A series of commonly found contaminants in Aotearoa New Zealand biosolids were tested and showed a range of endocrine activities, including estrogenicity, androgenicity and anti-androgenicity (Cavanagh et al. 2018). Although biosolids are mostly landfilled, the leachates could represent a source of EDCs.

A study reported estrogenic, androgenic and anti-progestagenic activities in sediment extracts from the Ahuriri (Napier) and New River (Invercargill) Estuaries as measured by bioassays (Boehler et al. 2017). As sediment is a main sink where chemicals introduced into the environment accumulate, it indicates that EDCs are present in the Aotearoa New Zealand environment.

4.1.2. Evidence of impacts

There is indication of endocrine disruption impacts in the literature relating to Aotearoa New Zealand and further research is required to fully confirm the issue in this country. Some of the initial endocrine disruption research has focused on the impacts of pulp and paper effluents. In vitro and in vivo data using mosquitofish and goldfish models showed evidence of androgenic effects (Ellis et al. 2003). However, detectable biological effects were not found in studies of rainbow trout exposed to treated pulp and paper mill effluent or eels caged downstream from a pulp mill effluent outfall (van den Heuvel et al. 2002; van den Heuvel et al. 2006). A study using the invasive brown bullhead catfish in the Waikato River showed some endocrine disruption effects based on circulating sex steroid concentrations, but these effects did not have an impact on populations (West et al. 2006). This group also used the native common bully (*Gobiomorphus cotidianus*) as a bioindicator to assess the impacts of cumulative stressors along the Waikato River (West et al. 2022). Despite the gradual deterioration in water quality in the river, no concomitant cumulative impacts were observed in the common bully. Responses were largely local in nature, responding to point-source discharges. Population responses at the geothermal and the pulp and paper effluent discharge sites warrant further study to investigate possible effects on fish recruitment and identify cause-and-effect relationships.

A study investigated the induction of the vitellogenin gene in the common bully collected across a pollution gradient in Southland's Mataura River (Tremblay et al. 2021). The vitellogenin gene was not induced in fish sampled downstream from a treated municipal sewage outfall. There are multiple reports from other countries strongly suggesting that endocrine disruption is widespread in the environment, but to date, we do not have enough information to confirm whether or not there is endocrine disruption in the Aotearoa New Zealand environment.

4.1.3. Are EDCs monitored?

Municipal wastewater treatment plant (WWTP) effluent is recognised as a source of EDCs entering the environment, but there are no regulations requiring their monitoring. However, some territorial authorities, including Wellington, Auckland and a few others, have commissioned surveys on a range of EOCs (of which some are EDCs) particularly to address conditions of a resource consent. The purpose of these studies has been to either obtain new data on contaminants in support of reapplications to extend resource consents to continue effluent discharge or follow up analysis of EOCs that were included as part of the ongoing monitoring requirements agreed through the reconsenting process. Typically, a series of 80 individual chemicals representing 10 different classes of emerging contaminants is analysed including some with endocrine activities. The main classes of EOCs include some chemicals with endocrine disruption activity:

- industrial alkylphenols (7 compounds)
- parabens (5 compounds)
- pharmaceuticals (10 compounds)
- phthalate esters and plasticisers (13 compounds)
- steroid hormones (16 compounds).

Typical concentrations of these EDCs in a range of Aotearoa New Zealand treated sewage effluent samples is summarised in Appendix 1. A recent study using a combination of passive sampling technology, analytical chemistry and bioassay followed the fate and distribution of estrogenic compounds in the Waikato (Iuele et al. 2022). These authors measured some level of activity in receiving waters but did not investigate whether there were impacts on biota. Some unpublished data from the MBIE project on EOCs measured endocrine disruption activities in both sediment and water samples from Southland and Auckland.

5. FUTURE CONSIDERATIONS

5.1. Addressing the main knowledge gaps

There is a substantial amount of information worldwide describing the impacts of EDCs on ecosystems but very limited research relating specifically to our New Zealand fauna. While there is a dearth of analytical information, only a few studies have reported the presence of endocrine activities in the New Zealand environment. As similar chemicals are used worldwide, it is likely that evidence from other comparable OECD countries can be extrapolated to New Zealand ecosystems in terms of overall effects. We suggest a tiered approach to address some of the key knowledge gaps required to determine whether endocrine disruption is an issue in New Zealand:

5.1.1. Tier 1.

We need to survey the country for the presence of EDCs with an emphasis on suspected hotspots like sewage effluent outfalls and catchments of high intensity dairy farming (Tremblay et al. 2018). An EBM approach is the preferred option, as it allows the measurement of the total endocrine disruption activity in a sample. In doing so, it is important to consider a wider spectrum of hormone receptors to cover endocrine activities other than estrogenicity (Windsor et al. 2018). This survey could be coordinated by the HEPA alongside their recommendation for better mapping of chemical contaminants.

5.1.2. Tier 2.

If sites of high biological endocrine activities are identified in Tier 1, the next step will be to use analytical chemistry to identify the chemicals responsible for these activities and their concentrations, using a process called effect-directed analysis. Once the EDCs are confirmed, it would provide insights into the potential sources so that they can be better managed to reduce the risk.

5.1.3. Tier 3.

The aim of this step would be to determine whether the EDCs identified pose a threat to the health of the receiving environment. One option would be to use the OECD guidance document that would confirm the endocrine disruption potential of the EDCs. There would also be a more basic research component to investigate the effects of the EDCs on species living in the receiving environment and on ecosystem health as a whole, especially at hotspot sites identified in Tiers 1 and 2.

5.2. Potential interactions with other stressors

In the environment, receiving ecosystems are under pressure from multiple stressors. One key question from an environmental management point of view is how do EDCs interact with the stressors deriving from climate change and chemicals with other mechanisms of toxicity. Multiple stressors can lead to unpredictable mixture interactions, including agonistic, antagonistic, additive and even synergistic effects. The concept behind these pharmacological or toxic interactions between agents implies that the effect of the combination somehow deviates from what is expected based on the effects of the single agents (Kortenkamp & Altenburger 1998). An example of a local study demonstrating the effects of multiple stressors focused on the nitrification inhibitor dicyandiamide (DCD) using a mesocosm approach. The authors showed that on its own, DCD may be considered a minor stressor, but when used in combination with other stressors like nutrient enrichment, it can have adverse effects on benthic algal communities (Salis et al. 2019).

5.3. How do EDCs rank against other stressors?

There is evidence from global studies that EDCs can negatively affect the endocrine system of wildlife, with adverse effects on individuals and populations reported across a wide range of species, including invertebrates, reptiles, amphibians, birds and mammals (Table 2). Many of these effects have been associated with the presence of (and in some cases conclusively demonstrated as a consequence of exposure to) pharmaceuticals, pesticides and other persistent organic pollutants. Several studies have tested chemicals for their possible adverse effects on individual organisms. The information generated has provided useful insights into acute toxicity, mechanisms of effects and persistence. However, it is difficult to extrapolate this single-organism data to impacts at the ecosystem level without good knowledge of populations and their natural fluctuations (Johnson & Sumpter 2016).

Another important criterion to consider is the relative risk from EDCs compared to other stressors such as Perfluoroalkyl and Polyfluoroalkyl Substances (PFAS); pesticides such as neonicotinoids; glyphosate; vertebrate pesticides such as brodifacoum; trace metals such as cadmium; microplastics; and also nutrients such as nitrates, which can contribute to harmful algal blooms. It is important that the limited resources to manage and protect the environment from anthropogenic stressors be focused on those posing the highest risks. At this stage, there is insufficient information to rationally prioritise these risks.

6. RECOMMENDATIONS

Although we have presented evidence in this report that EDCs cause adverse effects in wildlife, as shown in international studies, and that some EDCs have been detected in water and sediment in Aotearoa New Zealand, the cause-and-effect relationship between exposure to estrogenic chemicals and the consequent ecosystem health impact cannot yet be confirmed (or rejected). The priority remains to confirm whether the evidence established internationally is occurring here in Aotearoa New Zealand. Below are our recommendations to assess and manage the risk of endocrine disruption in Aotearoa New Zealand:

6.1. Apply the precautionary principle in the chemical registration process

There is still a high level of uncertainty about whether endocrine disruption is occurring in Aotearoa New Zealand, although the evidence from comparable OECD countries indicates it is very likely. In the absence of robust evidence, there should be on-going scrutiny over the potential endocrine disrupting activities of chemicals registered and used in Aotearoa New Zealand. A more stringent assessment of the potential for chemicals to affect the endocrine system (of humans and other living organisms) should be included as part of the national chemical registration process.

6.2. Better characterisation of hotspots

We recommend a tiered approach to determine the level of EDCs and potential endocrine disruption in exposed ecosystems. The focus should be on intensive dairy areas along with municipal sewage and sediment, particularly urban estuaries, that have been identified as potential sources of EDCs. The Australasian Heads of EPA (HEPA) call for a better characterisation of environmental chemical contaminants and the implementation of other initiatives like the NZ EPA chemical mapping project, as the generated information would provide useful data at hotspots where endocrine disruption could occur and guide further investigations into the health of exposed populations.

6.3. The need for a multi-disciplinary approach across sectors

The endocrine disruption issue can be defined as a ‘wicked problem’ requiring a multi-disciplinary approach to manage the risk. The recently formed Intersectorial Centre of Endocrine Disrupting Chemicals (ICEDA) is a good example of a multi-disciplinary team of researchers from environmental and human health, water treatment, analytical chemistry, epidemiology and environmental policies who are working

together to study EDCs (Langlois et al. 2022). A strategy to manage contaminants of emerging concern in Aotearoa New Zealand using a similar approach has been proposed. The strategy was developed as part of the MBIE 'Managing the risk of emerging contaminants' research project (Appendix 2).

6.4. Engagement with mana whenua and the wider community is needed

Another often overlooked aspect of EDCs (and other environmental stressors) is the need to engage with the wider community to raise awareness around the unintended consequences of using chemicals to ensure their benefit while minimising any unintended impacts. A good example is the framework used in the 'Up-the-pipe Solutions' project (Tremblay et al. 2013). Daily individual behavioural patterns play a major role in the chemicals people use, with some of them potentially accumulating in the environment. This is particularly relevant with EDCs, which are often chemicals directly resulting from community activities (e.g. natural hormones, pharmaceuticals including active ingredients in birth control pills, surfactants and additives in consumer products). The public may be more supportive of efforts to control the release of EDCs at the source if they understand the impact of their choices on urban and agricultural waste streams.

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9. APPENDICES

Appendix 1. Concentration of EOCs including EDCs in Aotearoa New Zealand sewage effluent samples.

The concentration of EOCs in the dissolved phase of effluent samples from thirteen wastewater treatment plants representing a broad range of treatment technologies, catchment population, balance of domestic to industrial inputs, and geographic distribution throughout Aotearoa New Zealand.

Concentration in ng/L (ppt)			
Musk fragrance	**Min**	**Max**	**Mean**
Galaxolide	24.4	902	243
Alkylphosphate flame retardant			
TnBP	26.9	499	128
TCPP	70.5	1024	321
TDCP	1.92	630	222
TBEP	N.D.*	3441	783
TPP	6.10	3277	301
Insect repellent			
DEET	15.2	1836	220
Antimicrobial			
Triclosan	4.43	158	38.3
Paraben preservatives			
Ethyl-Paraben	N.D.	39	4.11
Plasticiser			
Bisphenol-A	N.D.	66.9	17.0

* N.D. Not detected.

Appendix 2. Aotearoa New Zealand strategy to manage emergent contaminants.

THE AOTEAROA-NEW ZEALAND STRATEGY FOR EMERGING CONTAMINANTS

PATUA TE TANIWHA KEI TAMARIKI TONU

Assail the Leviathan whilst it is young

OUR VISION

A healthy Aotearoa-NZ safeguarded against emerging contaminants

Whakahaumarutia to tātou taiao i te aranga ake o ngā tāwahawaha kikino

Our Challenge

In Aotearoa-NZ, the main challenge we face with emerging contaminants is our poor understanding of them, and their potential to threaten the health and well-being of our people and unique environment.

The effects of emerging contaminants on people, ecosystems and livelihoods are being documented elsewhere in the world. However, in Aotearoa-NZ research and information about emerging contaminants is limited and un-coordinated. There are currently few studies examining their role and transport in our ecosystems, or food chains and the risk they pose to our economic and cultural wellbeing. We need to move quickly and purposefully to understand current effects and how to manage these and any future risks.

The Aotearoa-NZ Strategy for Emerging Contaminants is a collective initiative that will enable the dissemination of information to advance the understanding of the effects of emerging contaminants in Aotearoa-NZ. The Emerging Contaminants Advisory Panel is comprised of expert colleagues who are currently identifying the key environmental issues related to emerging contaminants.

Tiakina te Mana o Te Taiao – He Oranga Mutunga Kore

Protect the inherent authority of our environment as wellbeing for the future

We embrace a holistic environment approach that advocates respect for Aotearoa-NZ's land, freshwater, atmosphere, coastal and marine areas, including its wildlife and people.

The national strategy on emerging contaminants is important to all and aimed at collectively recognising the national signif cance of our environment and how new threats to its well-being are already in Aotearoa-NZ.

This strategy acknowledges that emerging contaminants may not only negatively affect our environment, but also a range of community and tāngata whenua values and aspirations. It is important that these values and aspirations are supported, and that the ability of our environment to provide for them continues over time.

OUR MISSION

Protecting Aotearoa-NZ's prosperity, heritage and health through leadership, transparency and collaboration on the threats of emerging contaminants

Nā te hautūtanga, kōrero mahuki me te mahi ngātahi ka tiakina te oranga, te taurikura me te koiora o Aotearoa whānui mai i ngā tāwahawaha kikino

OUR GOALS

Goal One

To engage with Māori and stakeholders to improve knowledge and understanding about the increasing role and negative impact of emerging contaminants in an effective and timely manner, in order to protect Aotearoa-NZ's natural environment which underpins our cultural heritage, health and prosperity.

- Ensure Māori in partnership with government are regularly informed about the activities of the Emerging Contaminants group, new research outcomes and supporting information.
- Ensure that Māori and all end-users are provided with relevant contemporary information and advice based on quality science-evidenced data.

Outcomes:

- In partnership with Māori, end users and government are engaged with, and using critical communications pathways to deliver relevant and useful advice.
- International knowledge and research is identified, collated, and communicated to Aotearoa-NZ decision-makers.
- Regular updates are provided to the community on emerging contaminants found in Aotearoa-NZ's environment, and their known effects.

Goal Two

In partnership with Māori identify research and development possibilities for improving our knowledge of the toxicity of ECs to Aotearoa-NZ's people and environment.

Ensure that Aotearoa-NZ has the people, the abilities, the resources and the tools to deliver quality science that advances the knowledge and improves the management of the risks of emerging contaminants to Aotearoa-NZ.

Outcomes:

- Emerging contaminants identification and management is prioritised for Māori and government as well as industry and other productive centres through multi-criteria decision support tools and effects-based prioritisation framework.
- A communication portal / information sharing platform is established for interested partners and agencies, with improved access across multiple information platforms (e.g. science articles, grey literature and information items).
- A specific research programme of work is established to enable the prioritising emerging contaminants research for use in resource management decisions and in aiding policy development.
- Emerging contaminants characterisation remains relevant, current and accurate via the development of a relevant and 'fit for purpose' emerging contaminants framework, which includes annual reviews and updates.

Goal Three

In partnership with Māori provide direction, leadership and support to enable Aotearoa-NZ to undertsand the effects of ECs on Aotearoa-NZ's people and environment.

- Provide in partnership with Māori, leadership that ensures strategic connectivity and clear communication to industry, government, and other stakeholders about issues on the topic of emerging contaminants.
- Provide direction and support through relevant best quality national and international data.

Outcomes:

- Māori are proactively involved in mitigating the negative impact of emerging contaminants on the environment through their mātauranga Māori (inherent knowledge), tikanga (customary processes) and wawata (economic, environmental, cultural and social aspirations).
- Leadership is underpinned by quality international data and targeted national emerging contaminants research.
- Launch of the Strategy and it's socialisation.
- Strategic linkages and transparent communication result in a greater awareness of the risks of emerging contaminants to Aoteoroa-NZ.
- Policy and management sectors develop appropriate and timely responses to manage emerging contaminants in Aotearoa-NZ.

Emerging Contaminants – A definition*

Emerging contaminants (ECs) are micro-organisms and chemicals that have historically not been considered contaminants, but have the potential to enter the environment and cause known or suspected negative impacts on the environment and/or people.

Emerging contaminants are not commonly monitored, but may be present in the environment on a global scale due to activities in our towns and cities, and our agricultural and industrial practices. In some cases, the release of the emerging chemical or micro-organism into the environment has occurred for a long time, but may not have been recognised until new detection methods were developed. In other cases, synthesis of new chemicals or changes in use and disposal of existing chemicals can create new sources of emerging contaminants.

* This definition is derived from the U.S. Geological Survey web site https://toxics.usgs.gov/investigations/cec/index.ph

Disclaimer

All members of the advisory panel participate in this project as individuals with the advice, opinions, or viewpoints given in their personal capacity only, and should not be considered either as endorsed by, nor in any way representative of the views, policies, or strategies of their employers, or any organisation, government agency, business, trust, iwi, hapū or group to which they are affiliated.

* Strategy was developed by the Emerging Contaminant Advisory Panel. MBIE contract: CAWX1708

https://www.cawthron.org.nz/wp-content/uploads/2021/07/Aotearoa-NZ-Strategy-for-Emerging-Organic-Contaminants.pdf