

**POISONING THE FUTURE:
THE CASE OF ENDOCRINE DISRUPTORS**

RUEL A. AVILLA



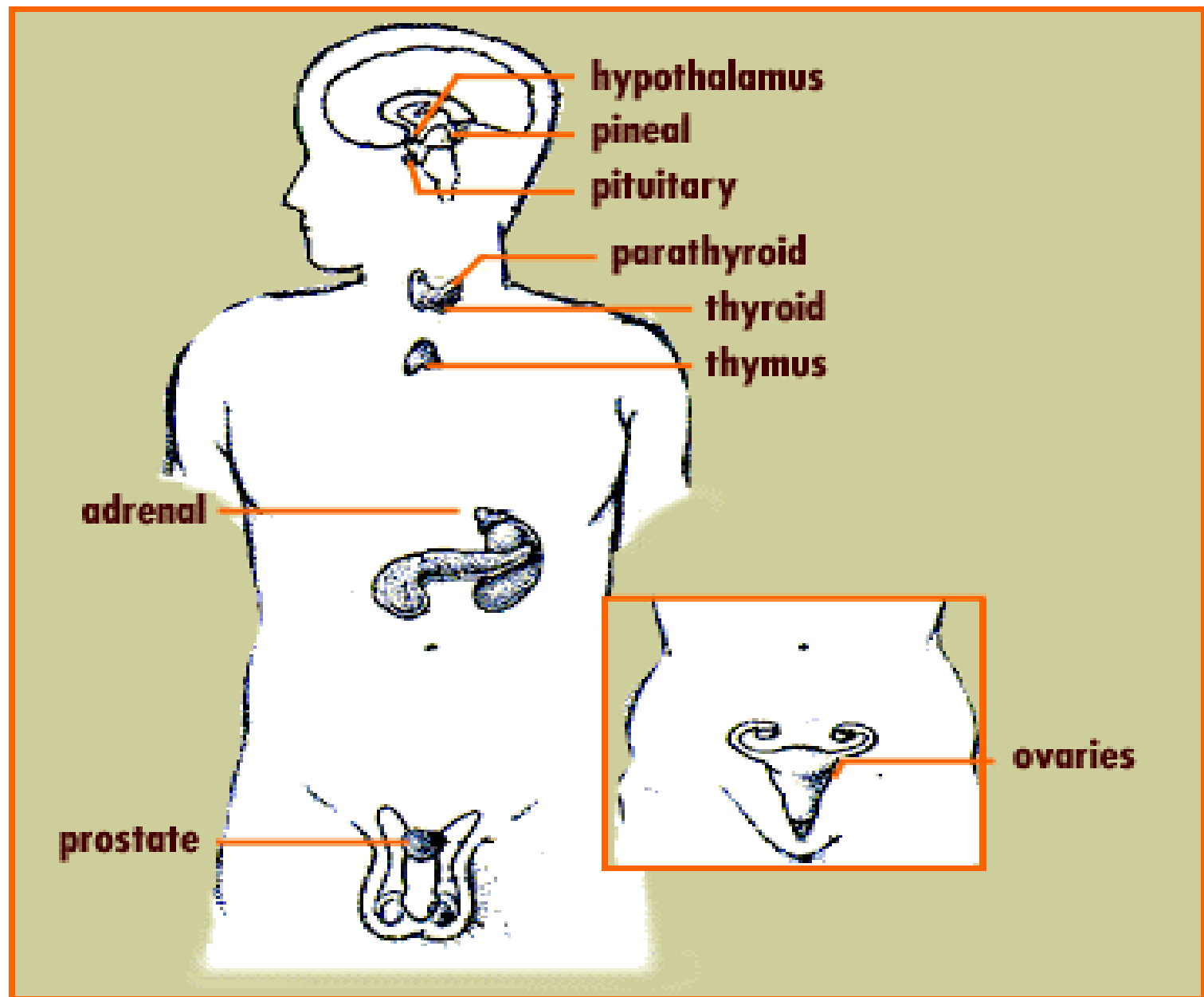


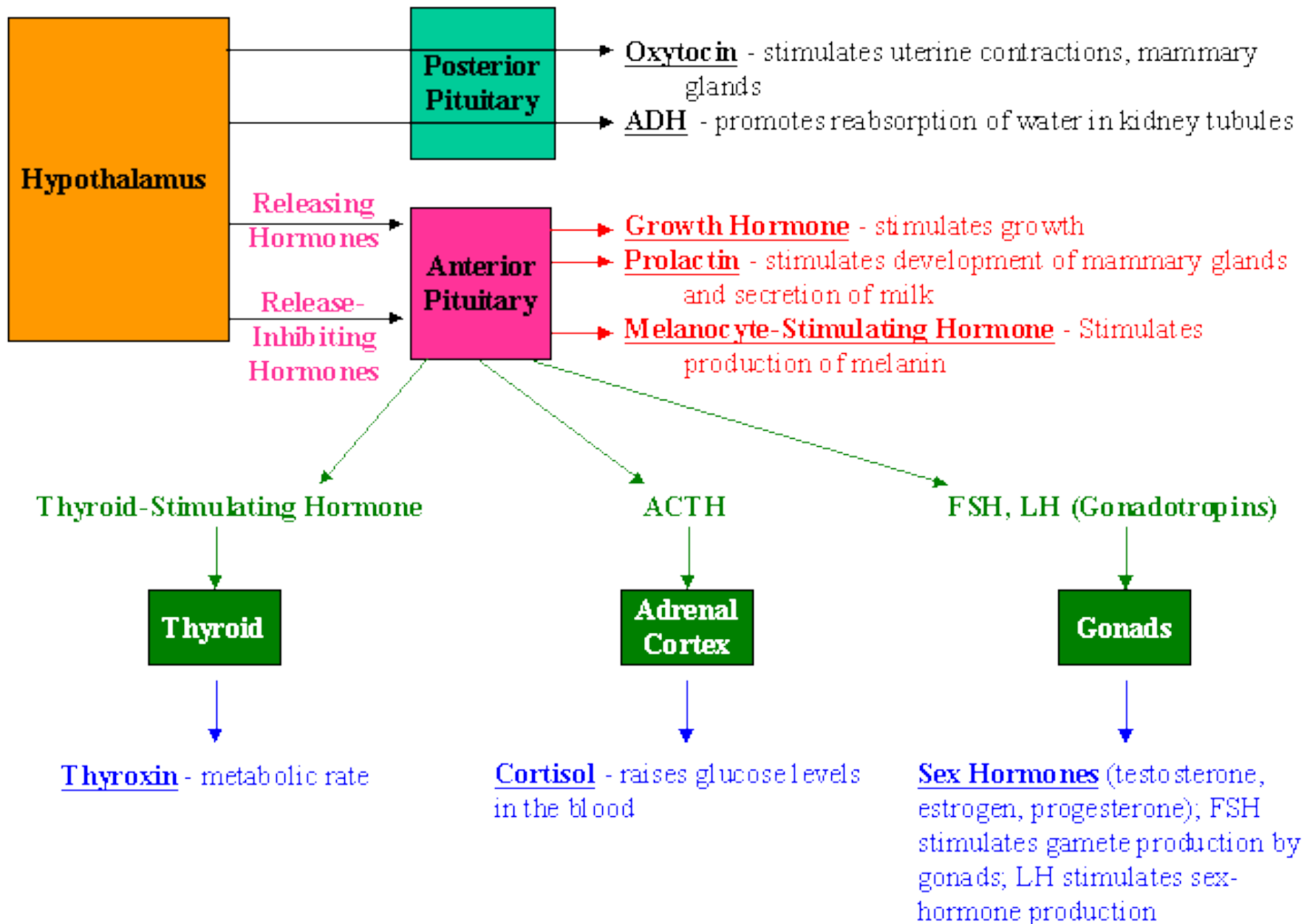
The body has three marvelous communication systems

- The nervous system
- The immune system
- The endocrine system, a network of glands which release hormones

The endocrine system is a network of glands that release many different hormones, that regulates many of the body's functions

- Hormones control growth, sexual and mental development, metabolism, and many other functions

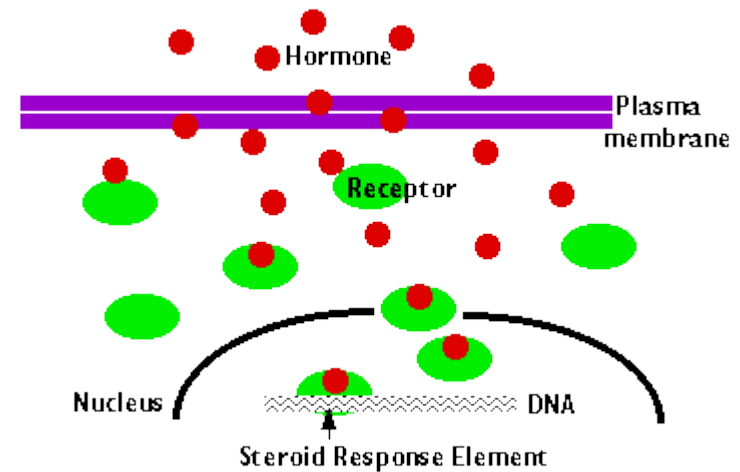
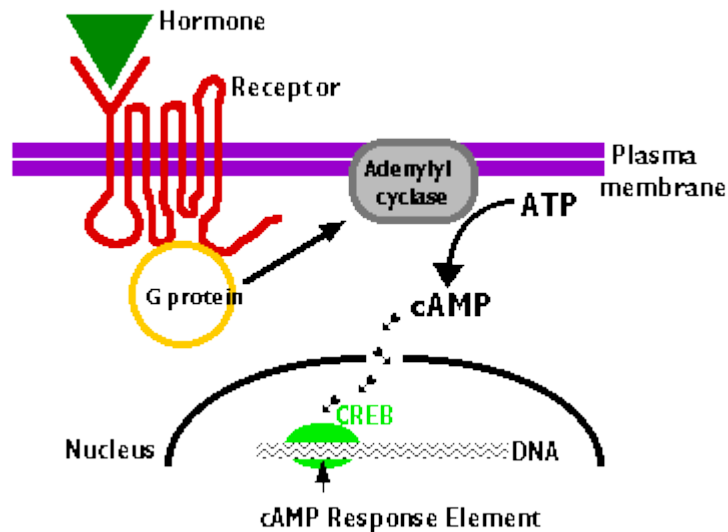




Kinds of Hormones

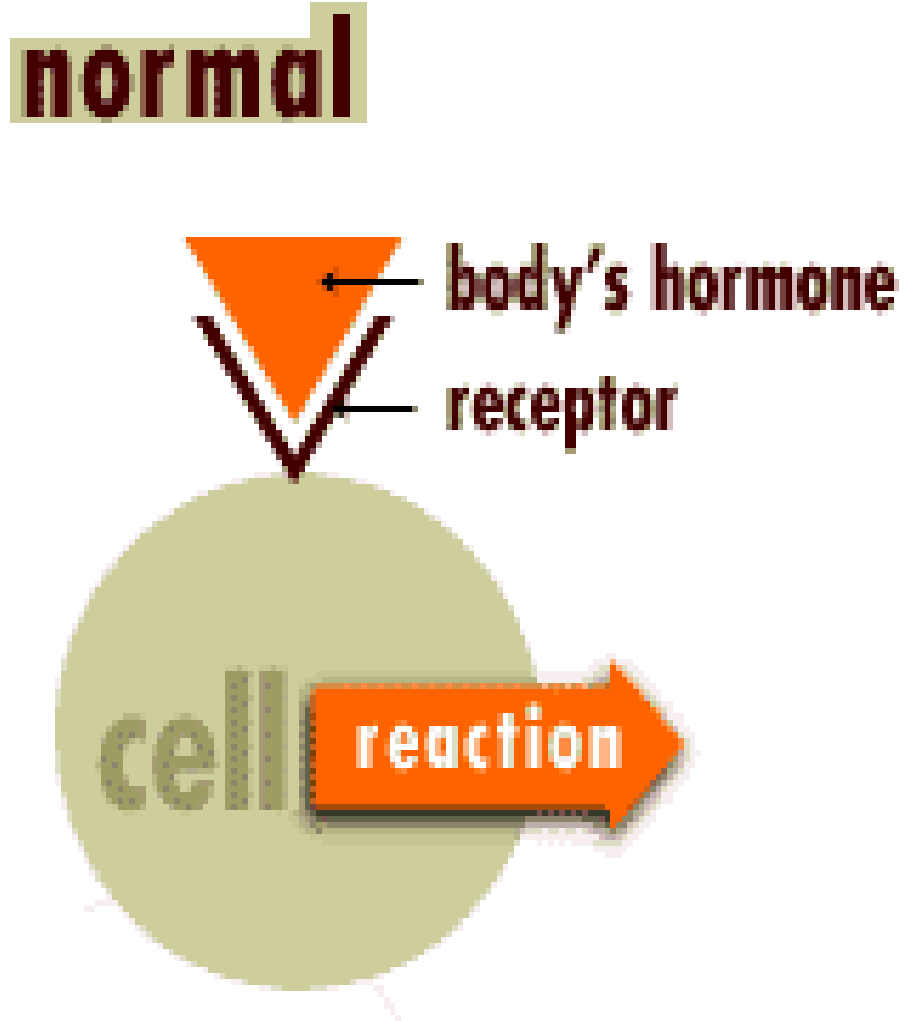
Protein, peptides

Steroids



Normally, hormones

- travel through the blood until they reach their particular receptor cell
- where they fit, like a key in a lock, to turn on or off functions

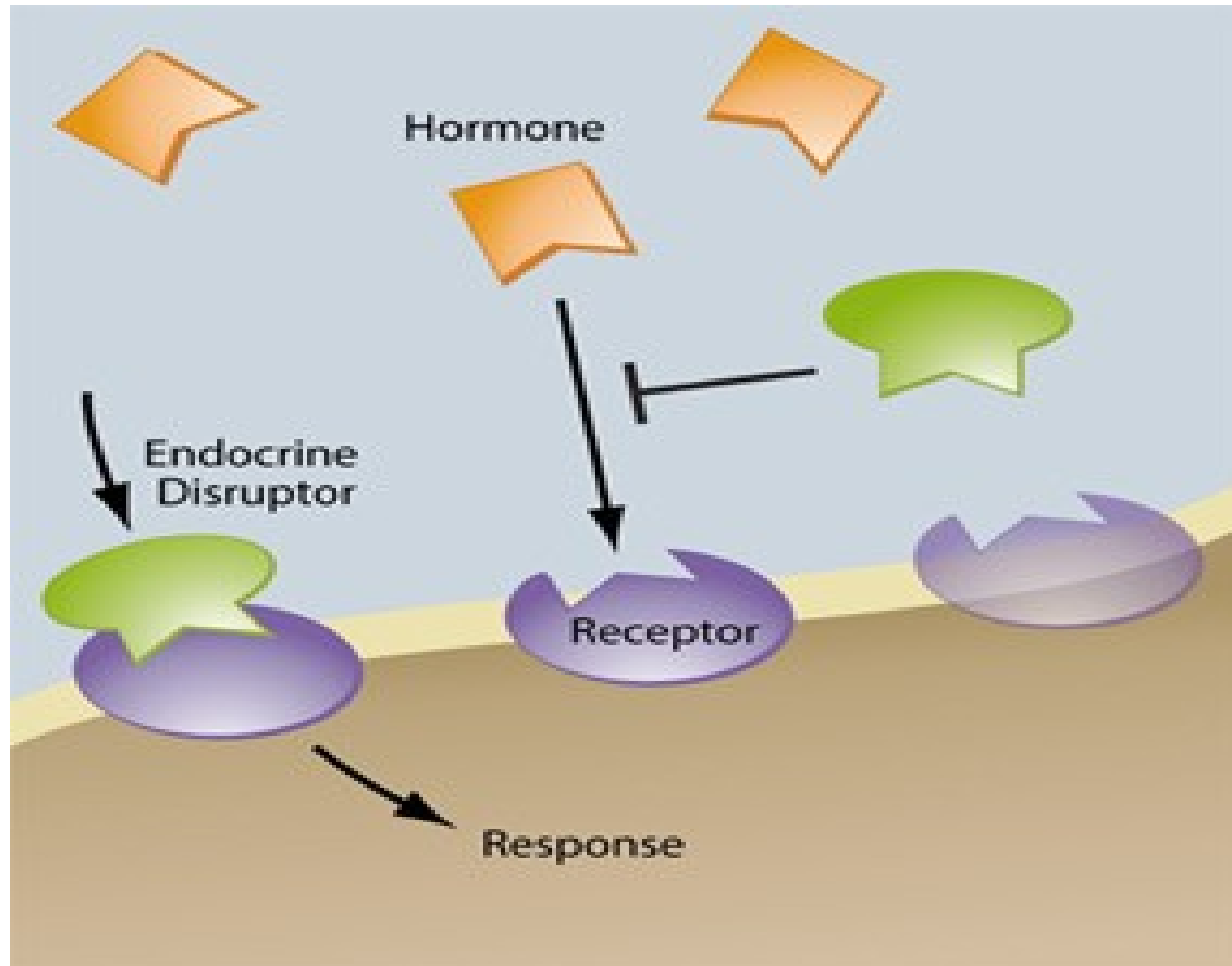


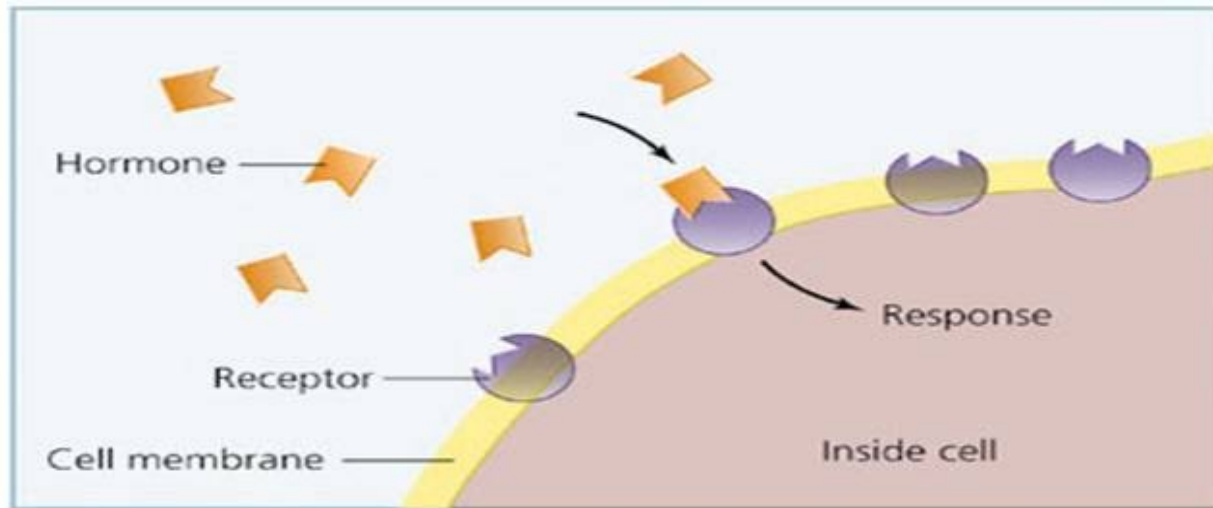
Endocrine Disruptors

- Mimic or Block natural hormone action
- Can be synthetic (most) or naturally occurring (phytoestrogens)
- May or may not have structural similarity with endogenous hormone
- Alter gene expression *not* structure (not mutagens)
- Are lipophilic

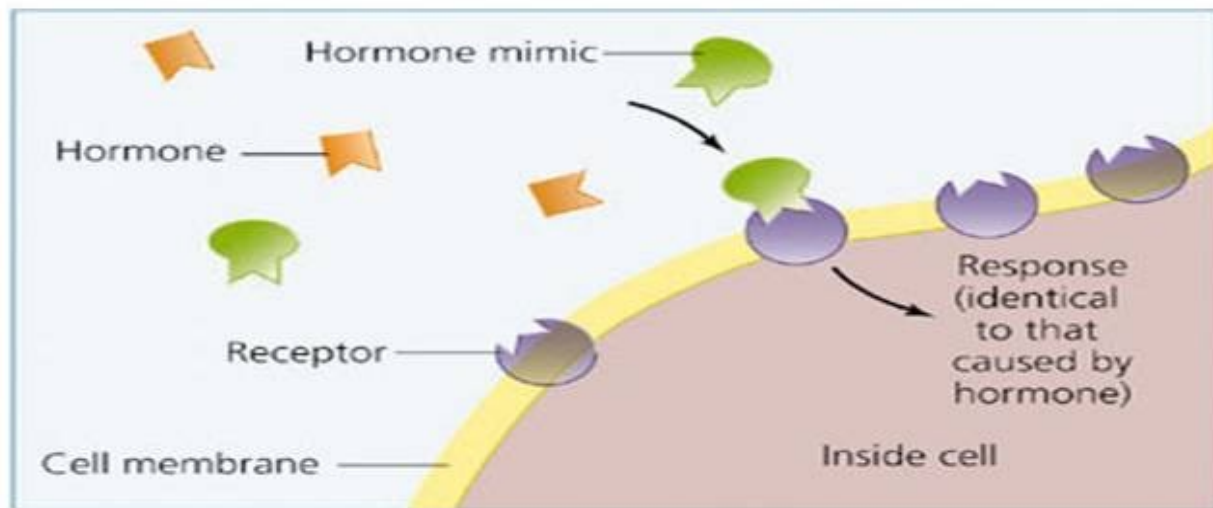
Modes of Actions of EDC's

- Mimics - bind and activate receptors just as the natural hormone
- Antagonists - bind but do not activate receptors
- Inhibitors of synthesis of natural hormone
- Inhibitors of degradation/removal of natural hormone
- Interfere with transport from





(a) Normal hormone binding



(b) Hormone mimicry

Sources of EDC's

plastics: Chemicals used in PVC and in the production of other plastics including certain phthalate plasticizers.

organohalogen chemicals: Particularly those containing chlorine (organochlorines), including PCBs, dioxins

pesticides: a variety of different pesticides used in agriculture.

industrial chemicals: various industrial chemicals, including alkylphenols which are derived from chemicals used in detergents and other products.

Food Antioxidant

Compound	Hormone system affected	Mechanism
<u>Butylated hydroxyanisole (BHA)</u>	Estrogen	Inhibits binding to the estrogen receptor.

Persistent organohalogens

Compound(s)	Hormone system affected	Mechanism if known
Benzenhexachloride (BHC)	Thyroid	
1,2-dibromoethane	Reproductive	
Chloroform	Reproductive	
Dioxins and furans (in order of antiestrogenic potency : 2,3,7,8-tetrachlorodibenzo-p-dioxin > 2,3,7,8-tetrachlorodibenzofuran > 2,3,4,7,8-pentachlorodibenzo-furan > 1,2,3,7,9-pentachlorodibenzofuran > 1,3,6,8-tetrachlorodibenzofuran)	Estrogen	work as anti-estrogen through binding with Ah receptor, which then inhibits estrogen receptor binding to estrogen response elements, thereby inhibiting estrogen action

PCBs (in order of antiestrogenic potency: 3,3'-pentachlorobiphenyl > 3,3,4,4,5,5'-hexachlorobiphenyl 3,3',4,4'-tetrachlorobiphenyl > 2,3,3',4,4',5'-hexa, 2,3,3',4,4'-and 2,3,4,4',5'-pentachlorobiphenyl > Aroclors 1221, 1232. 1248, 1254, and 1260 were inactive as antiestrogens at the highest concentrations used in this study (10⁻⁶ Ni)	Estrogen/androgen/Thyroid Adverse outcomes in reproductive systems.	Inhibits estrogen binding to the receptor; works as anti-estrogen. anti-androgenic via Ah receptor interaction
PCB, hydroxylated	Thyroid	Binds to thyroid hormone binding protein, but not to the thyroid hormone receptor.

Pesticides

<u>DDT</u>	Estrogen	DDT and related compounds act in a number of ways to disrupt endocrine function by binding with the estrogen receptor, including estrogen mimicry and antagonism, altering the pattern of synthesis or metabolism of hormones, and (4) modifying hormone receptor levels
<u>DDT Metabolite, p,p'-DDE</u>	Androgen	Inhibits androgen binding to the androgen receptor, androgen-induced transcriptional activity, and androgen action in developing, pubertal and adult male rats.

Phthalates

Compound	Hormones affected	Mechanism
<u>Butyl benzyl phthalate (BBP)</u>	Estrogen	Inhibits binding to the estrogen receptor
<u>Di-n-butyl phthalate (DBP)</u>	Estrogen Androgen	Inhibits binding to the estrogen receptor. anti-androgenic
<u>Di-ethylhexyl phthalate (DEHP)</u>	Estrogen Androgen	Inhibits binding to the estrogen receptor. anti-androgenic

Metals

Compound	Hormones affected	Mechanism
<u>Arsenic</u>	Glucocorticoid	Selective inhibition of DNA transcription normally stimulated by the glucocorticoid-GR complex.
<u>Cadmium</u>	Estrogenic	Activates estrogen receptor through an interaction with the hormone-binding domain of the receptor.

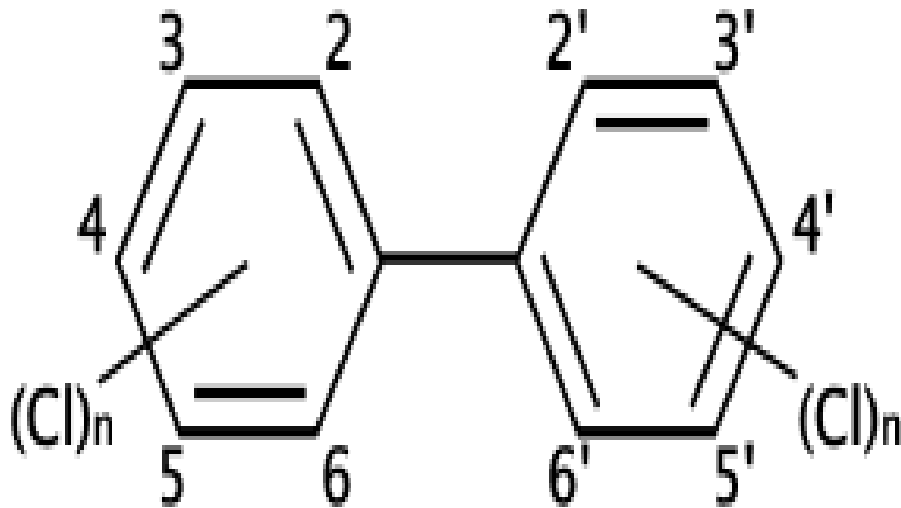
Other Compounds

Compound	Hormones affected	Mechanism
<u>Benzophenone</u>	Estrogen	Binds weakly to estrogen receptors, roles of its metabolite remain to be clarified.
<u>Bisphenol A</u>	Estrogen	Estrogenic; binds to estrogen receptor
Bisphenol F	Estrogen	Estrogenic; binds to estrogen receptor
<u>Benzo(a)pyrene</u>	Androgen	anti-androgenic

Many studies link EDCs to:

- Reproductive disorders
- Immune system dysfunction
- Certain cancers, especially of reproductive organs
- Birth defects of the penis and falling sperm counts
- Neurological effects
- Attention deficit disorder and poor memory
- Low IQ

Evidences of EDC's

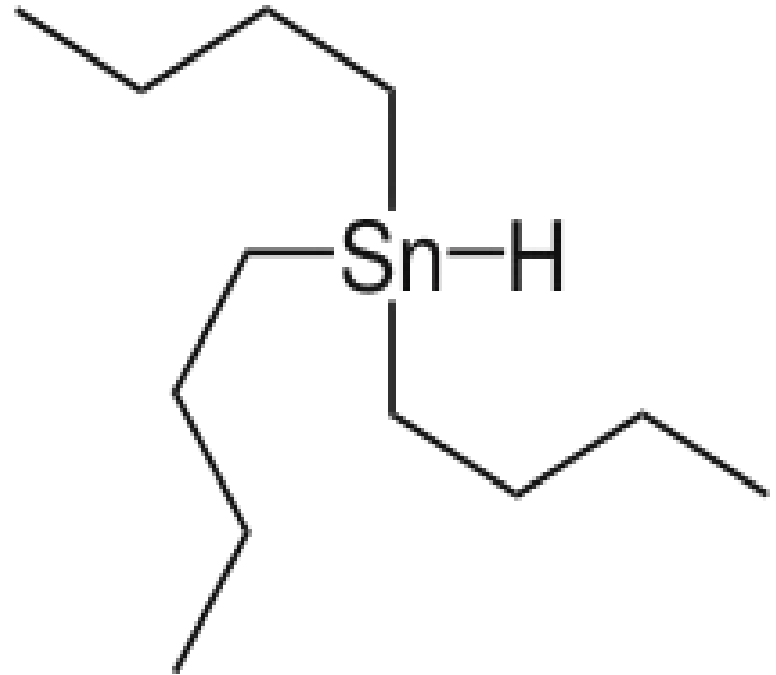


A particular signal blocked during early pregnancy can affect both children and adults

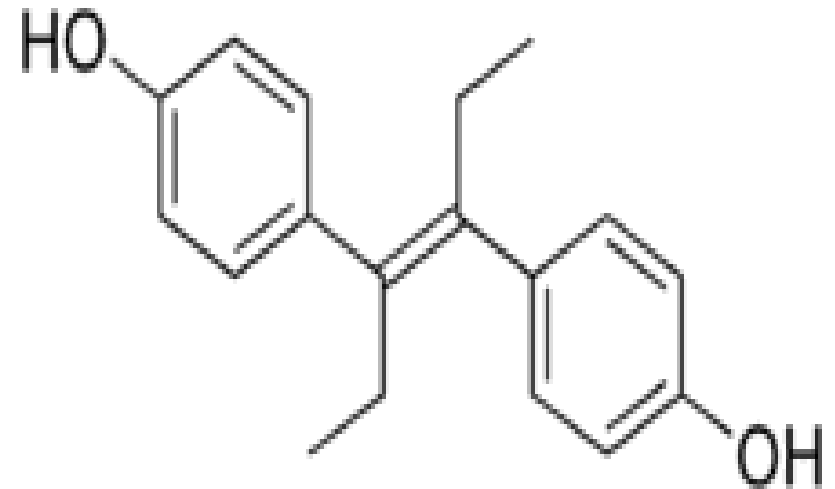
For example, children of mothers who ate low doses of PCBs in fish from Lake Michigan show effects 11 years later

Tributyltin (TBT)

- Used as an anti-foulant for boats, and now banned for all small boats. Still legal on large boats and used on clothing to inhibit fungal growth. Most female snails in British Columbia harbours have *imposex*, including penises,



- Drugs such as birth control pills, DES, and cimetidine, especially in sewage water



*DES,
diethylstilbestrol,
given to mothers
to prevent
morning
sickness, caused
genital cancers in*

"Really?"

Yes...

desPLEX

to prevent ABORTION, MISCARRIAGE and PREMATURE LABOR

recommended for use in ALL pregnancies...

96 per cent live delivery with desPLEX in one series of 1,000 patients...

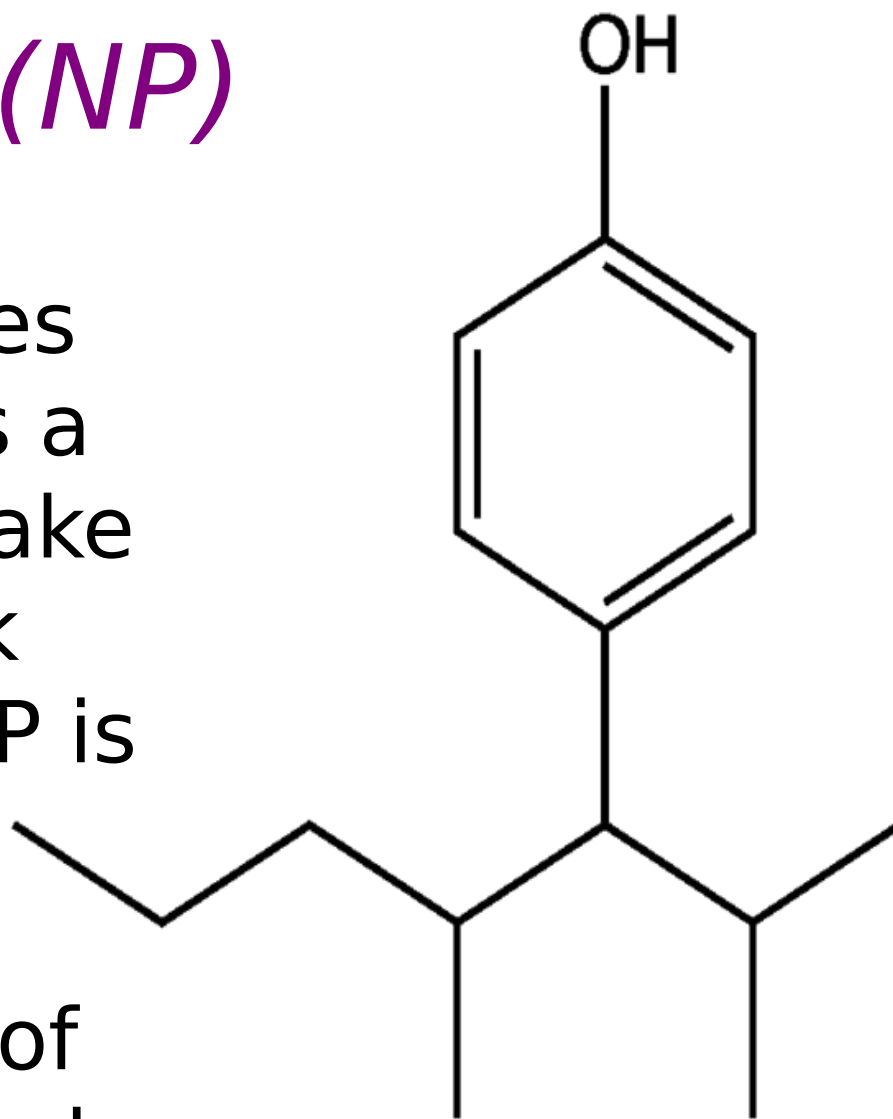
— bigger and stronger babies, too.

No gastric or other side effects with desPLEX

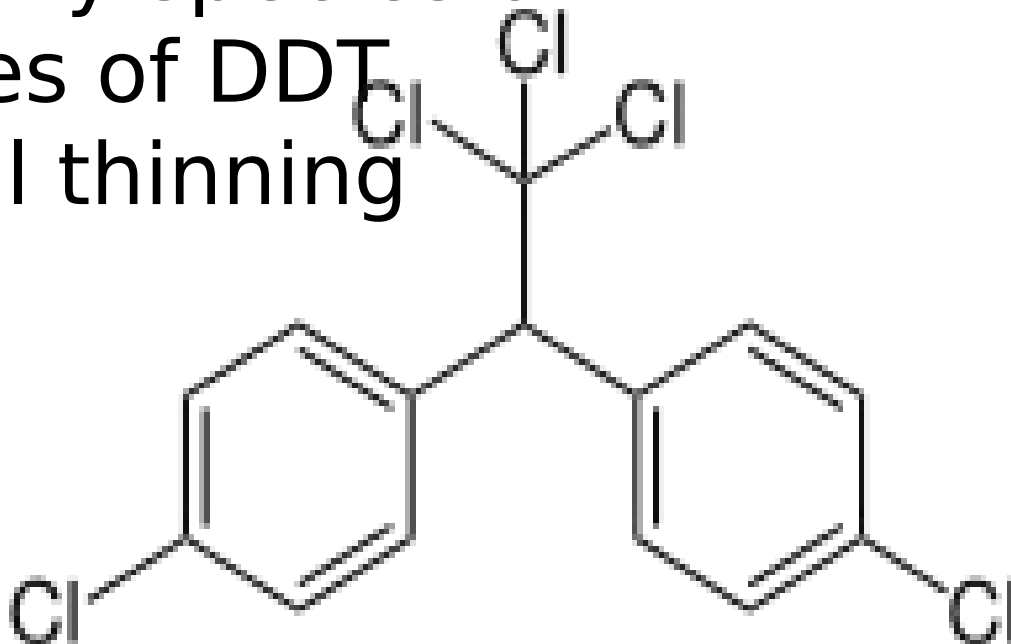
— in either high or low dosage 1-4-4

Nonylphenol (NP)

Added to pesticides and detergents as a “surfactant” to make the chemical work better in water, NP is one of the agents suspected of changing the sex of fish in rivers around the world.



DDT is toxic to a wide range of animals in addition to insects, including marine animals such as crayfish, sea shrimp and many species of fish. Metabolites of DDT cause egg shell thinning



In other words,
Endocrine Disrupting Chemicals
are everywhere

People are organizing, and
governments are paying
attention, to change this.
Right now EDCs are in our food,
in the water, in the air, in a
mother's milk,
and in the womb.

Are There Solutions?

- Phase out the worst substances immediately:
 - Persistent, bioaccumulative toxic chemicals
 - Known endocrine-disrupting chemicals and others as identified.
- Zero Discharge
 - Design Factories and plants so that they do not release their waste into the environment – in or outside the plant gates!

- If there is reason to doubt the safety of a discharge, don't do it! In the absence of scientific certainty, err on the side of precaution.

Personal Precautions

- Avoid heating food in plastic containers, or storing fatty foods in plastics containers or plastic wrap
- Avoid fatty foods
- Do not give young children soft plastic teethers or toys
- Avoid using pesticides in your home or yard
- Buy organic food when possible
- Educate yourself about endocrine disruptors
- Share this information to your family and friends