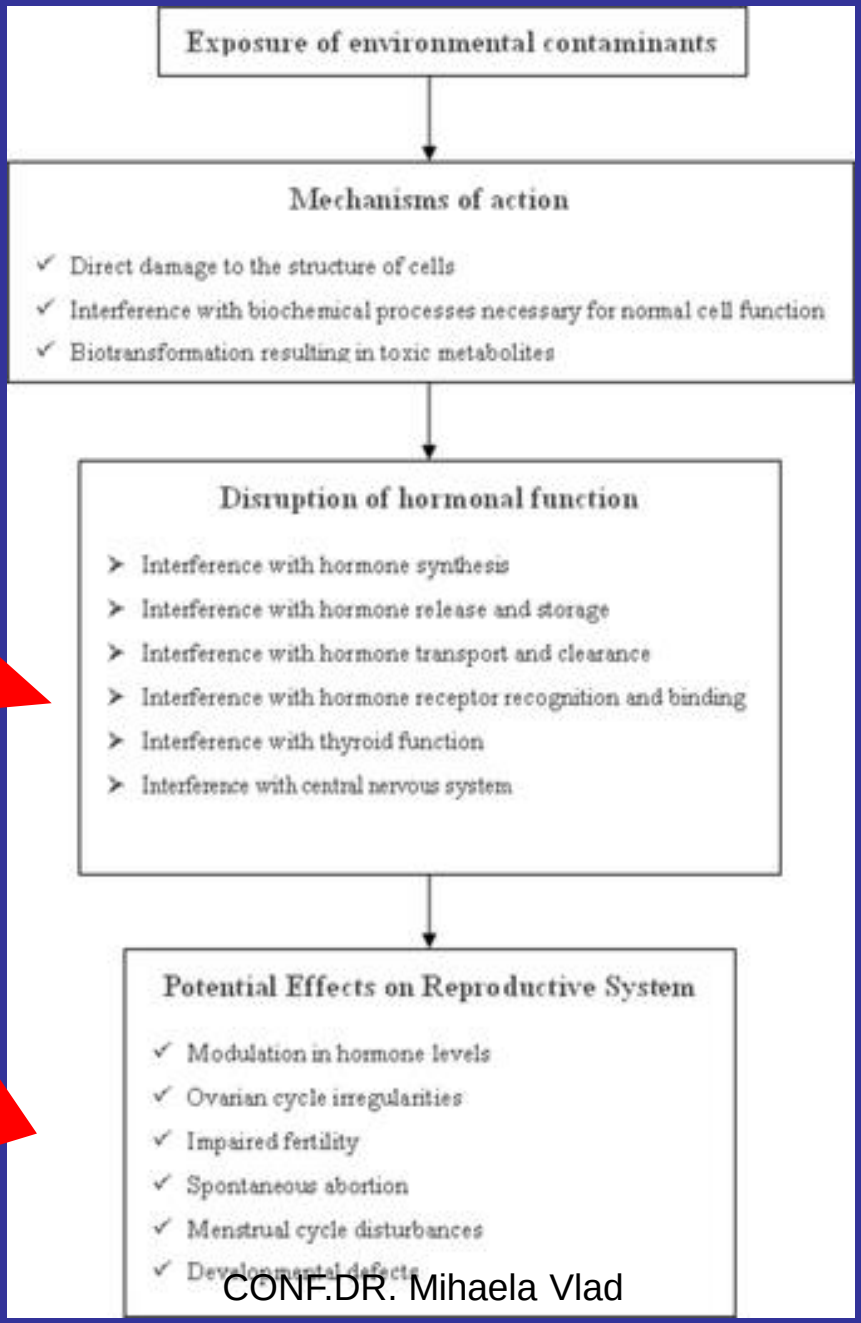
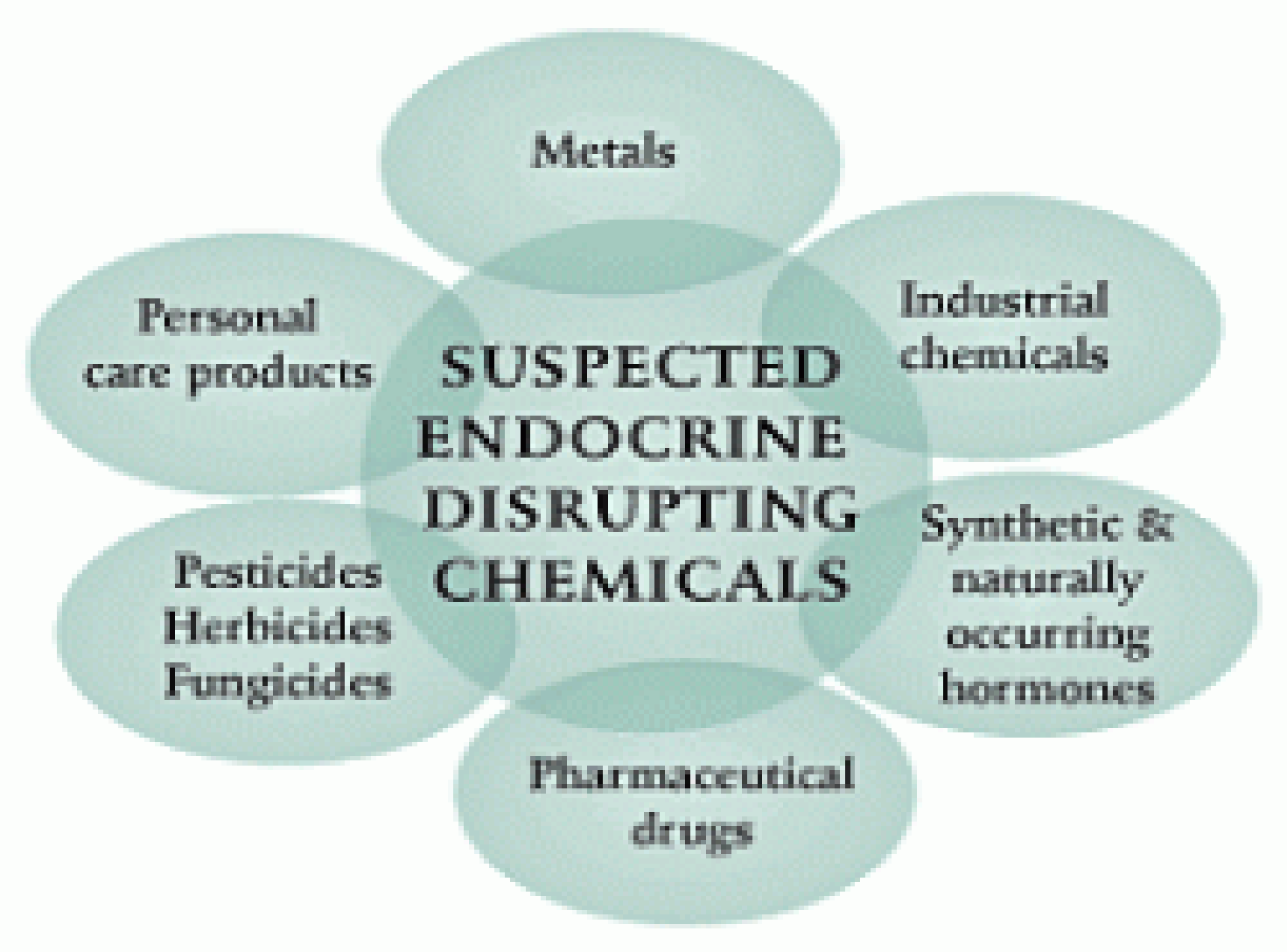
DISRUPTORI (PERTURBATORI) ENDOCRINI

DEFINITIA DISRUPTORILOR ENDOCRINI (EDCs)

- Substante exogene care altereaza functionarea sistemului endocrin si care induc efecte adverse asupra starii de sanatate a organismului sau asupra descendentilor. (WHO)

- Susbtante exogene care interfera cu sinteza, secretia, transportul, metablolismul, legarea de proteinele de transport sau degradarea unor hormoni responsabili de hopeostazia organismului, de reproducere si de dezvoltarea organismului.


Exposure of environmental contaminants
Mechanisms of action
✓ Direct damage to the structure of cells
✓ Interference with biochemical processes necessary for normal cell function
✓ Biotransformation resulting in toxic metabolites
Disruption of hormonal function
➢ Interference with hormone synthesis
➢ Interference with hormone release and storage
➢ Interference with hormone transport and clearance
➢ Interference with hormone receptor recognition and binding
➢ Interference with thyroid function
➢ Interference with central nervous system
Potential Effects on Reproductive System
✓ Modulation in hormone levels
✓ Ovarian cycle irregularities
✓ Impaired fertility
✓ Spontaneous abortion
✓ Menstrual cycle disturbances


Metals
Personal care products
Industrial chemicals
SUSPECTED ENDOCRINE DISRUPTING CHEMICALS
Pesticides Herbicides Fungicides
Synthetic & naturally occurring hormones
Pharmaceutical drugs

Phytoestrogens	Daidzein, genistein, formononetin, biochanin-A, prunetin, pratensein, glycitein, equol, desmetilangolestin, enterolactone, enterodiol, matairesinol, zearalenone
Organohalogens	Dioxins, furans, polychlorinated biphemyls, hexachlorobenzene, pentachlorophenol
Pesticides	Dichlorodiphenyltrichloroethane (DDT), methoxychlor, endosulfan, 2,4-dichlorophenoxyacetic acid, alachlor, aldicarb, amitrol, atrazine, benomyl, dibromo chloropropane, carbaryl, chlordane, ethyl parathion, heptachlor, kepone, ketoconazole, lindane, methomyl, permethrin, malathion, trifluralin, vinclozolin
Phthalates	Diethylhexyl phthalate, butyl benzyl phthalate, di-n butyl phthalate, di-hexyl phthalate, di-propyl phthalate, dichloro hexyl phthalate, diethyl phthalate
Heavy metals	Arsenic, cadmium, uranium, lead, mercury
Drugs	Oral contraceptives, diethylstilbestrol, cimetidine
Industrial products	Bisphenol A, polybrominated biphemyls

Özen S. et al, 2011

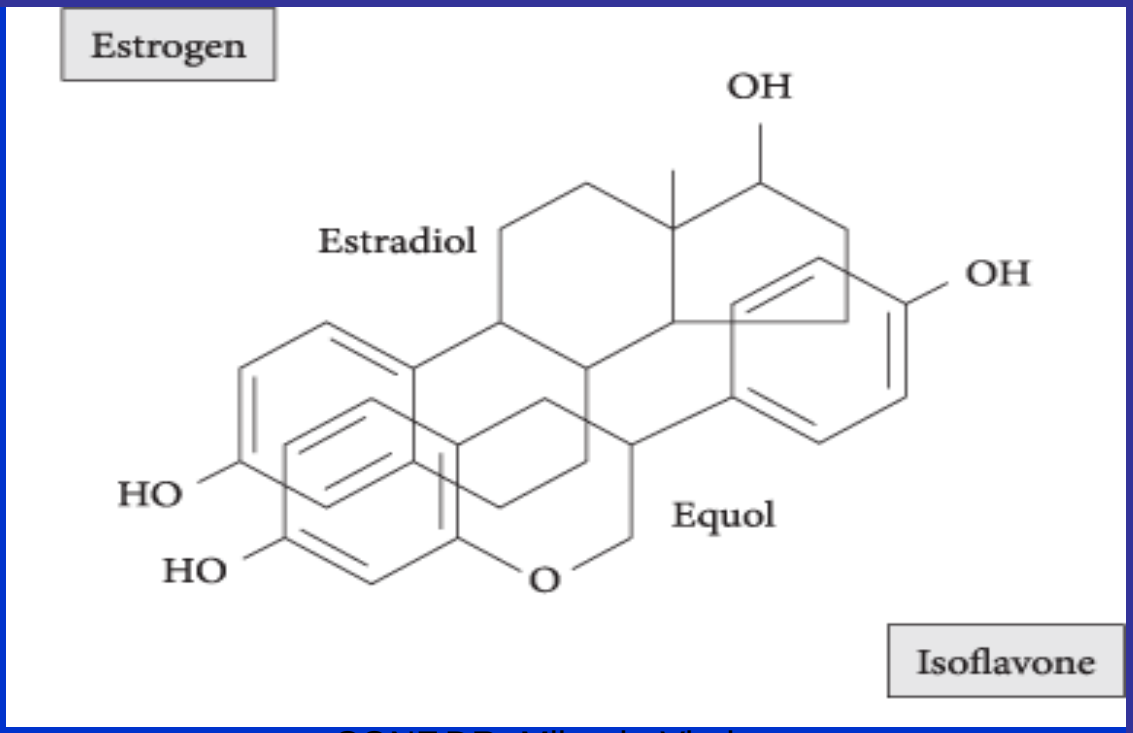
Mecanismul de actiune

Mechanism of action	
Estrogenic	Dichlorodiphenyltrichloroethane (DDT) and its metabolites Methoxychlor Methoprene Phytoestrogens (in high concentrations) Polychlorinated biphenyls (PCBs) Bisphenol A Endosulfan Dioxins
Antiestrogenic	Phytoestrogens (in low concentrations)
Androgenic	Testosterone Trenbolone acetate
Antiandrogenic	Phthalates Dichlorodiphenyltrichloroethane (DDT) Vinclozolin

Ozen et al, 2011

FiTOESTROGENI

Plant compounds similar to mamalian estrogens and their active metabolites.



Phytoestrogens

Coumestans	Isoflavones	Lignans	Prenylflavenoids
Coumestrol	Genistein Diadzein, Glycetein Formononetin	Secoisolariciresinol Matairesinol	Prenylnaringenin
Clover Alfalfa	Beans & Pulses especially Soya	Linseed Small amounts in most cereals	Hops Beers





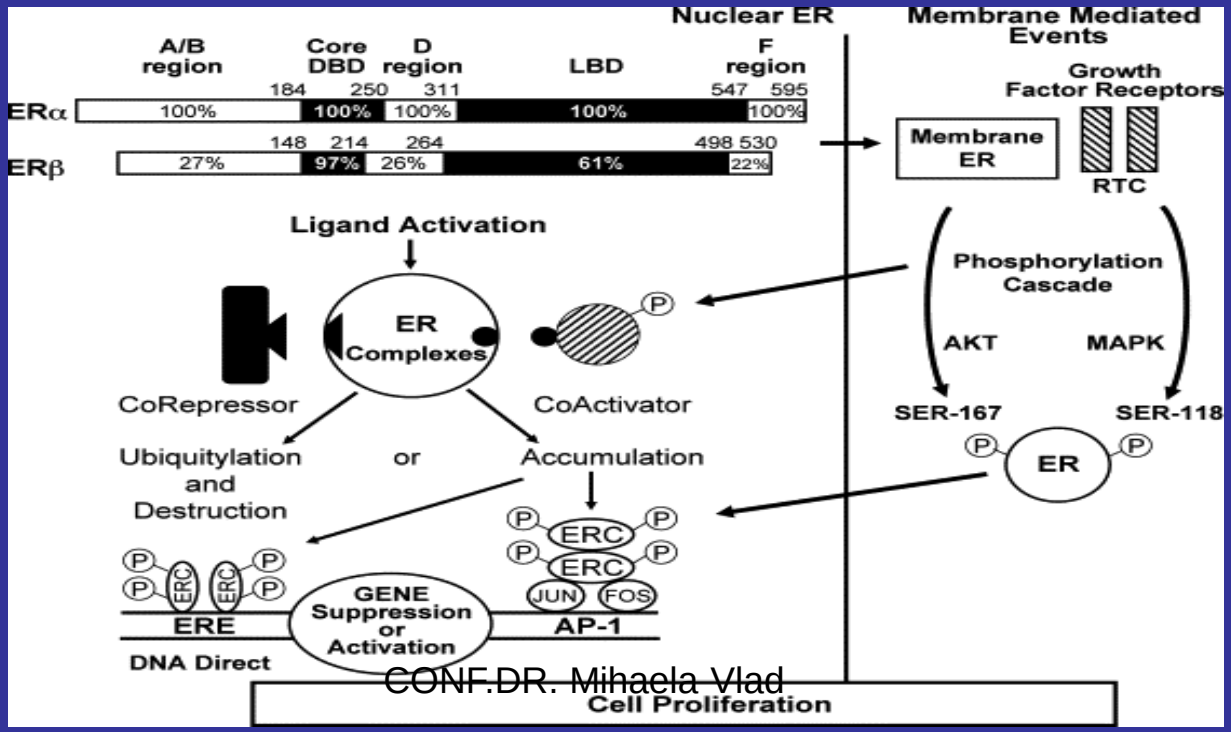




FITOESTROGENI: SOIA

FITOESTROGENI: mecanism de actiune

- *ERα*: endometrium, ovarian stromal cells, hypothalamus, epithelium of the efferent ducts.
- *ERβ*: kidney, brain, bone, heart, lungs, intestinal mucosa, prostate endothelial cells.



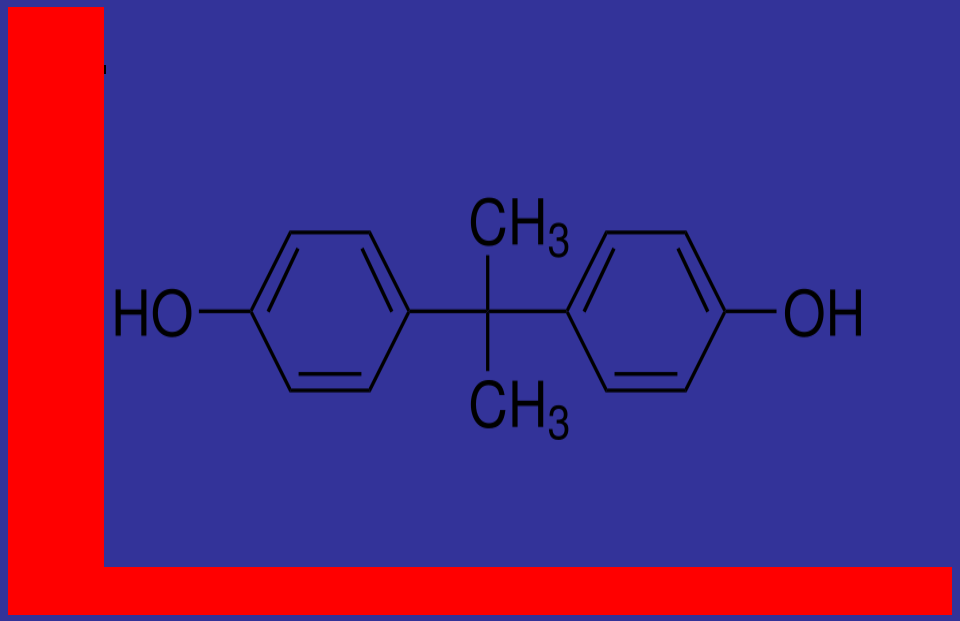
FITOESTROGENI: efecte

- Epigenetic process
- Steroid synthesis
- Steroid transport

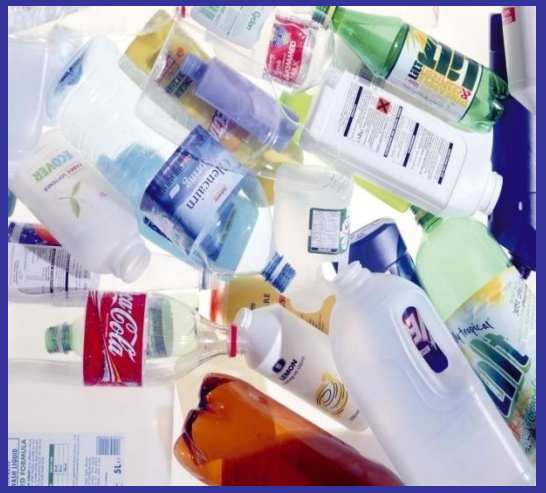
- breast cancer risk
- precocious and delayed puberty
- undermasculinisation of male genital tract (hypospadias, cryptorchidism)
- uterine fibroids development

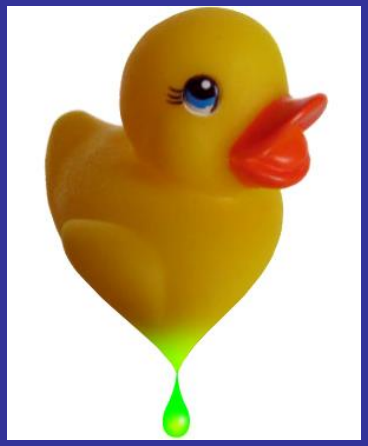
BISFENOL A (BPA)

- 1891
- 1950: polymerized to make polycarbonate plastic



BISFENOL A (BPA)

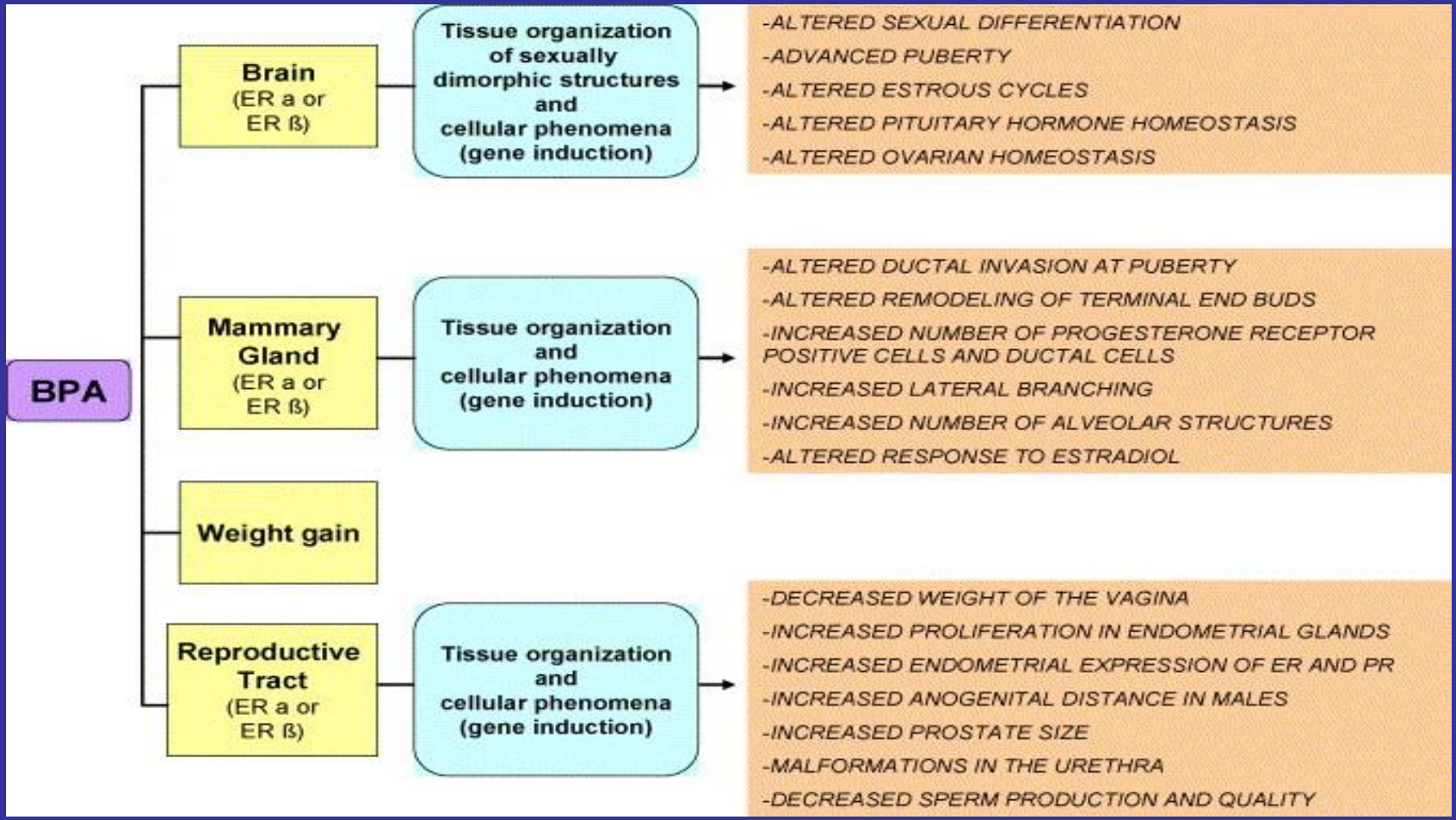




BPA: mecanism de actiune

- IN VITRO: agonist for both α and β ESR
- IN VIVO: agonist for both α and β ESR and GPR 30 and antagonist ESR β

BPA: effects



Maffini et al, 2006


BABY BOTTLE
BPA
POTENTIAL HEALTH EFFECTS:
BEHAVIORAL CHANGES, PREDISPOSITION TO PROSTATE AND BREAST CANCER, EARLY PUBERTY


BPA
Free

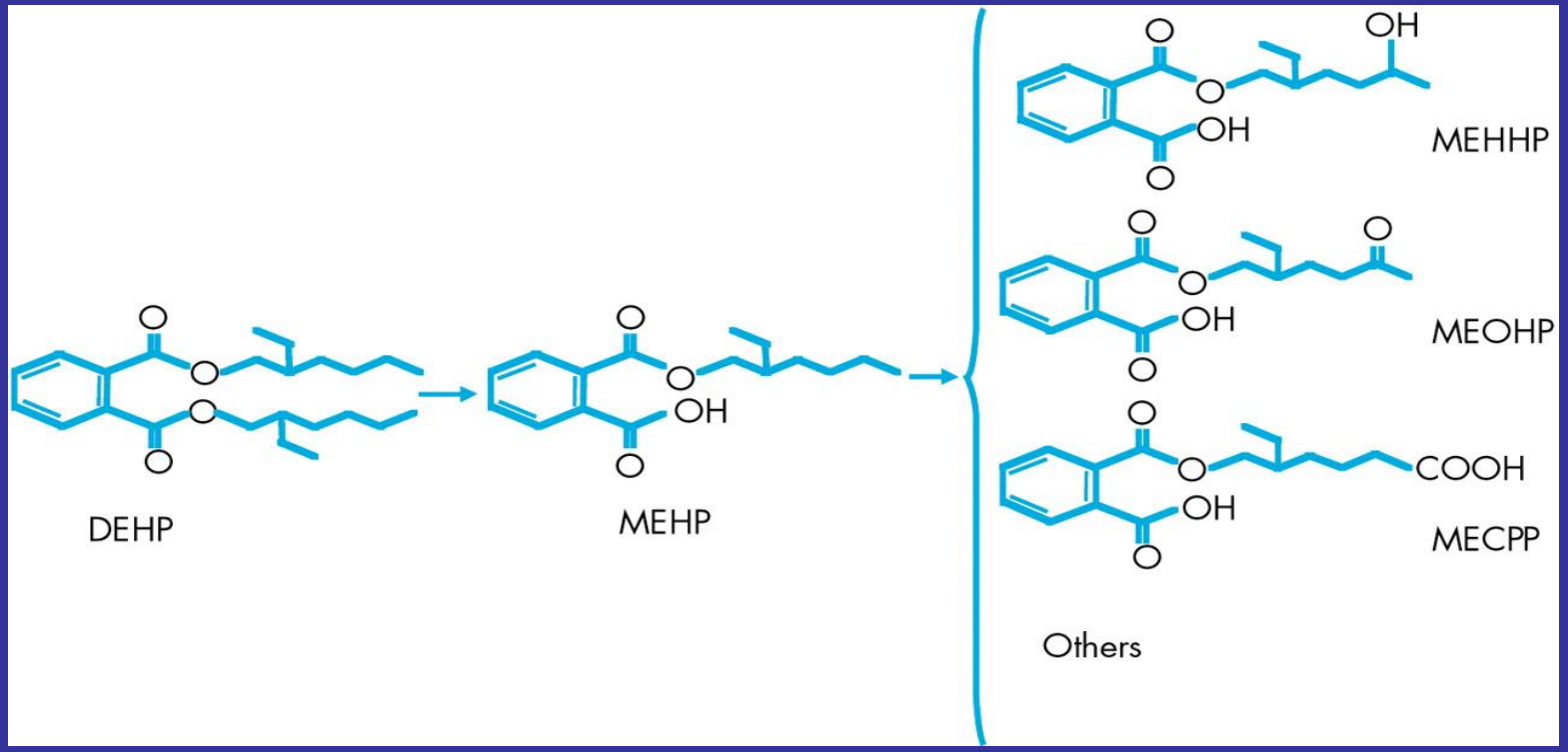

BPA
FREE
This product does not contain any BPA


bpa free


BPA FREE

FTALATI (PHTHALATES)

- Substante chimice utilizate pentru cresterea flexibilatii produselor din plastic.



PHTHALATES

- ↓ estrogen secretion
- ↓ aromatase activity
- reproductive teratogenes

progesterone production

PHTHALATES

Phthalate diester	Potential sources of exposure*	Potential health effects†
Diethyl phthalate	Personal care products (e.g. fragrances), coatings (e.g. pharmaceuticals), dyes, insecticides	Reduced growth rate, food consumption and increased organ weights
Di-n-butyl phthalate	Cellulose acetate plastics, personal care products (e.g. nail polish, cosmetics), lacquers, varnishes, coatings (e.g. pharmaceuticals)	Hepatic and renal effects, developmental and reproductive effects, reduced fetal weight, cryptorchidism, hypospadias, reduced anogenital distance in males.
Butylbenzyl phthalate	Vinyl flooring, adhesives and sealants, car-care products, toys, food packaging, synthetic leather, industrial solvents, personal care products	Testicular toxicity, cryptorchidism, reduced anogenital distance, teratogenic, modulates steroid hormone levels
Di(2-ethylhexyl) phthalate	PVC plastics used in household products (e.g. toys, floor tiles and furniture upholstery, wall coverings), food packaging, blood storage bags and medical devices	Hepatocellular carcinoma, testicular toxicity, anovulation, teratogenic at high doses, affects fetal growth

Hauser et al, 2005

PESTICIDE

- 105 substante sunt pe lista pesticidelor

INSECTICIDE
46%

IERBICIDE
21%

FUNGICIDE
31%

PESTICIDE:
mecanism de actiune

- AGONIST RECEPTOR

E Rc

A Rc

Aryllhydrocarbon Rc

- ANTAGONIST RECEPTOR AND INTERFERING WITH:

SYNTHESIS

TRANSPORT

METABOLISM

} H

PESTICIDE: efecte

- reproductive and sexual development
- gametogenesis
- early development of the fetus
- intellectual function
- CNS function

PESTICIDE

- Residential proximity to agricultural activity→ low birth weight, fetal death, and childhood cancers (Xiang et al. 2000, Bell et al. 2001, Reynolds et al. 2002)
- Higher prevalence of cryptorchidism and hypospadias was found in areas with extensive farming and pesticide use and in sons of women working as gardeners (Kristensen et al. 1997, Carbone et al. 2006, Weidner et al. 1998)

PESTICIDE

CONCLUZII

- Expunerea la disruptorii endocrini este frecvent intalnita, dar consecintele asupra populatiei si adaptarea la expunerea cronica au cam fost ignorate.

- Impactul pe care-l au disruptorii endocrini asupra mecanismelor fiziopatologice sunt complexe si acestia interfera de obicei cu mai multe mecanisme, ceea ce face aproape imposibil anticiparea efectelor toxice asupra animalelor si oamenilor.

- Influentele pe care le exercita asupra procesului de reproducere, dezvoltare si comportament sexual fac din acesti disruptori endocrini niste substante extrem de periculoase pentru sanatate.

“Every man sitting in this room today is half the man his grandfather was, and the question is, are our children going to be half the men we are?”

1993 - Lou Guillette to US Congress referring to the perceived decrease in human sperm counts.