



ASSOCIATION OF  
PHYSICIAN ASSOCIATES IN  
OBSTETRICS & GYNECOLOGY

## Ovaries Beware:

Endocrine Disruptors and Their Role in Gynecology

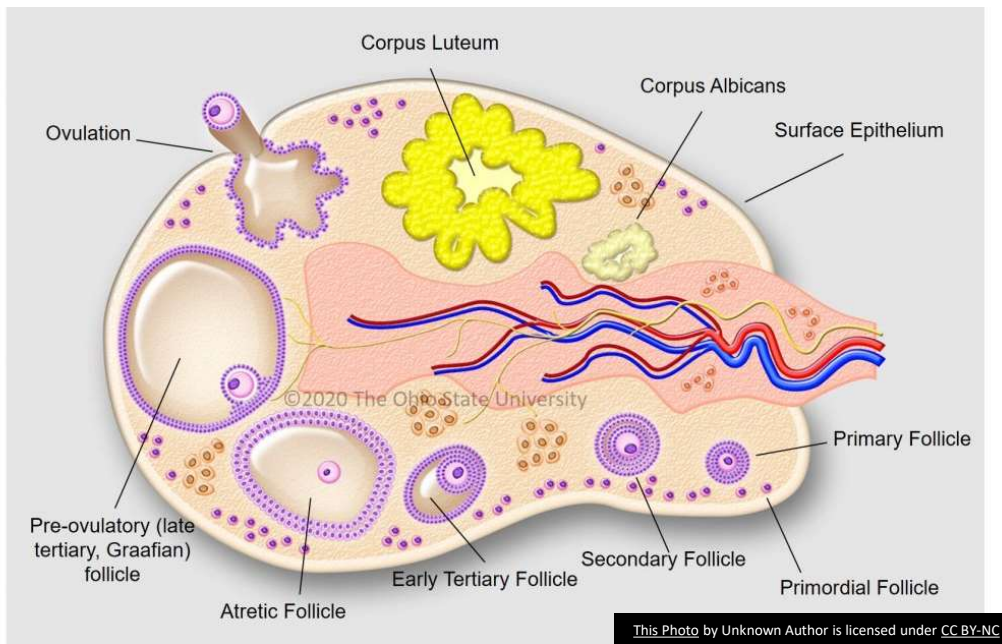
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# Objectives

- Review normal physiology
- Identify the endocrine disruptors involved in the hypothalamic-pituitary-ovarian axis
- Describe the physiological process involved with the disruption of the HPOA
- Identify ways to prevent and resolve the harmful effects of these chemicals

# The Ovarian Cycle Impacts



Hypothalamic-pituitary functions

Neurotransmitters

Hormones

Oviducts

Uterus

Cervix

Adipocytes

Vascular cells

Immune cells

Responds to environmental factors

## The hypothalamic–pituitary–ovarian axis

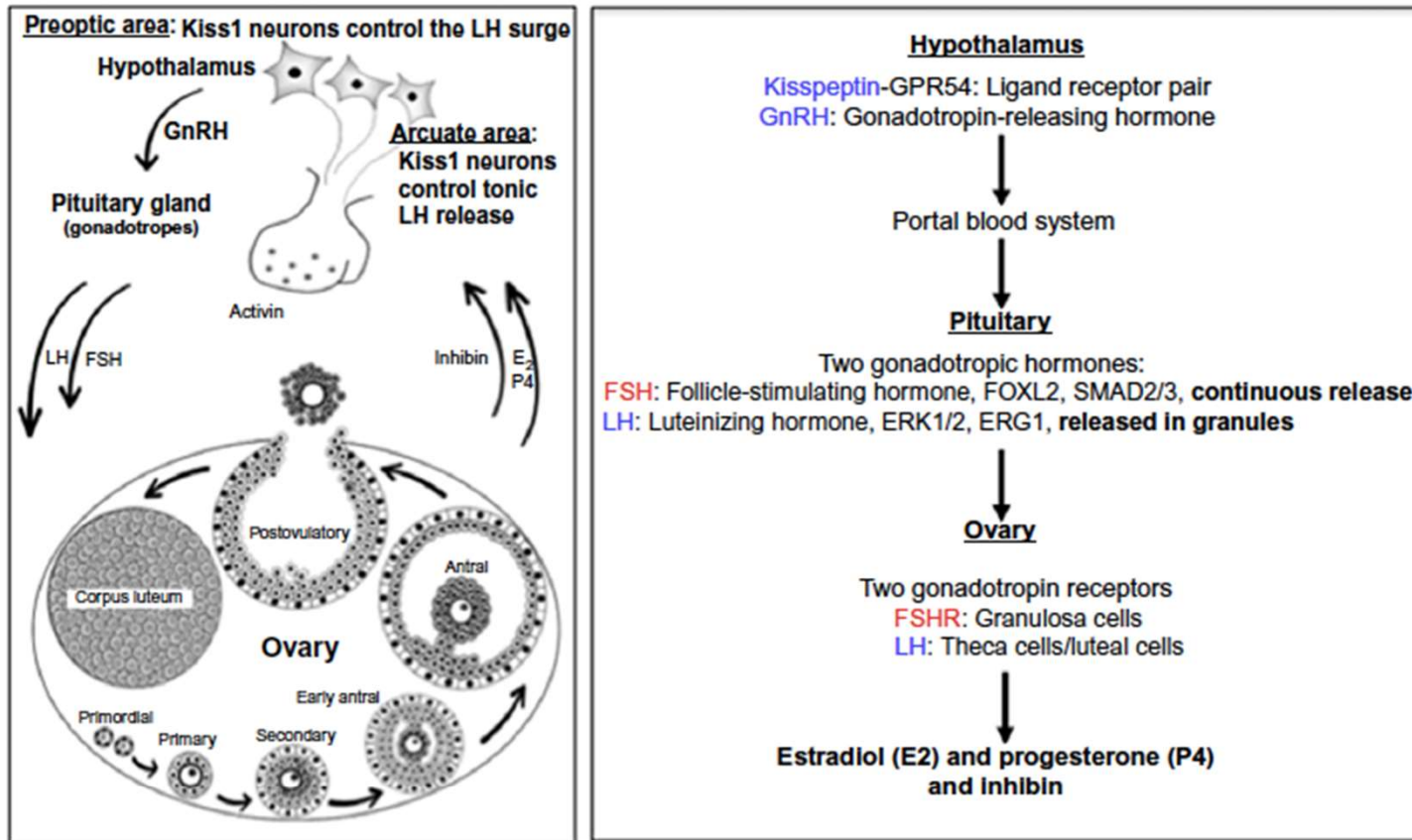
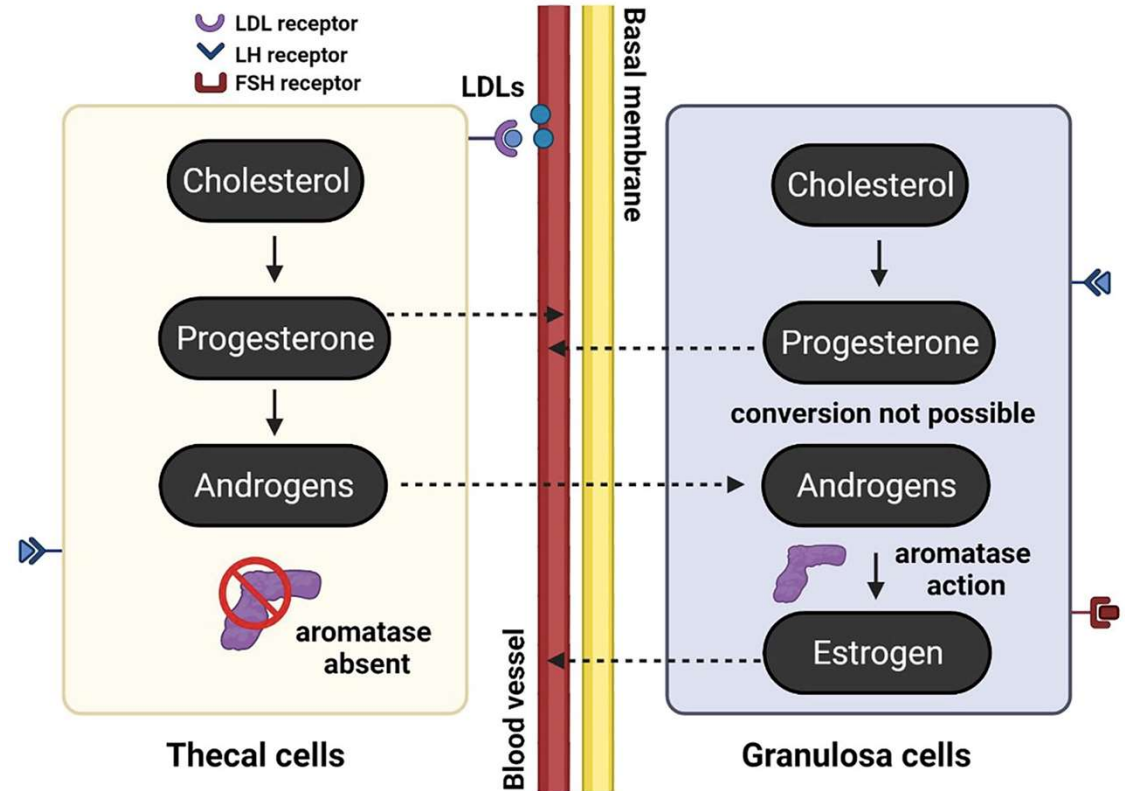


Fig. 2 Schematic and text describing the hypothalamic, pituitary, and ovarian events that occur during the ovarian cycle. Adapted from Monsivais, D., Matzuk, M.M., & Pangas, S.A. (2017). *The TGF- $\beta$  family in the reproductive tract*. Cold Spring Harbor Perspectives in Biology, 9, a022251, PMID: 28193725.

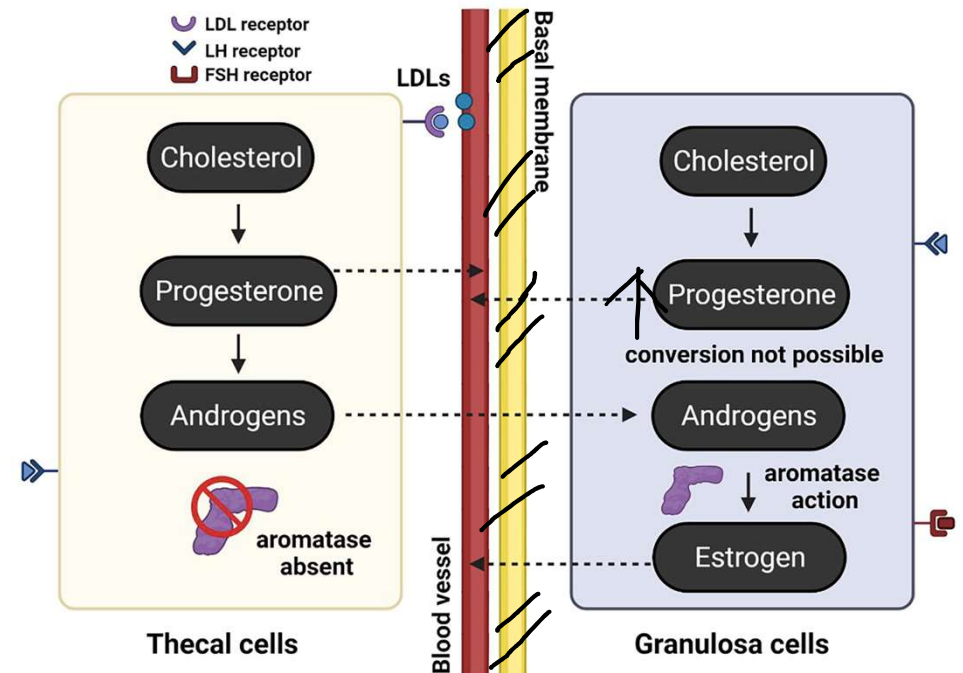
# Secondary Follicle

- Cholesterol is the precursor of all steroid hormones classified into mineralocorticoid, glucocorticoids, and gonadocorticoids (or sex hormones).
- Thecal and granulosa cells produce estrogen, progesterone, and testosterone.
- Androgens:
  1. Dihydrotestosterone (DHT),
  2. Dehydroepiandrosterone (DHEA),
  3. DHEA sulfate (DHEAS),
  4. Androstenedione, and
  5. Testosterone



# After Ovulation

- The granulosa cells also have LH receptors but cannot pick up LDLs from the blood; LDLs cannot easily move past the basal membrane.
- When the follicle ruptures during ovulation, the membrane is destroyed enabling LDL absorption and progesterone production.
- However, the cells do lack the enzymes needed to convert progesterone into androgens.
- Thus, the majority of the progesterone diffuses into the blood, which explains the rapid rise in its level post-ovulation.
- After ovulation, both cells produce progesterone and, to a lesser extent, androgens.



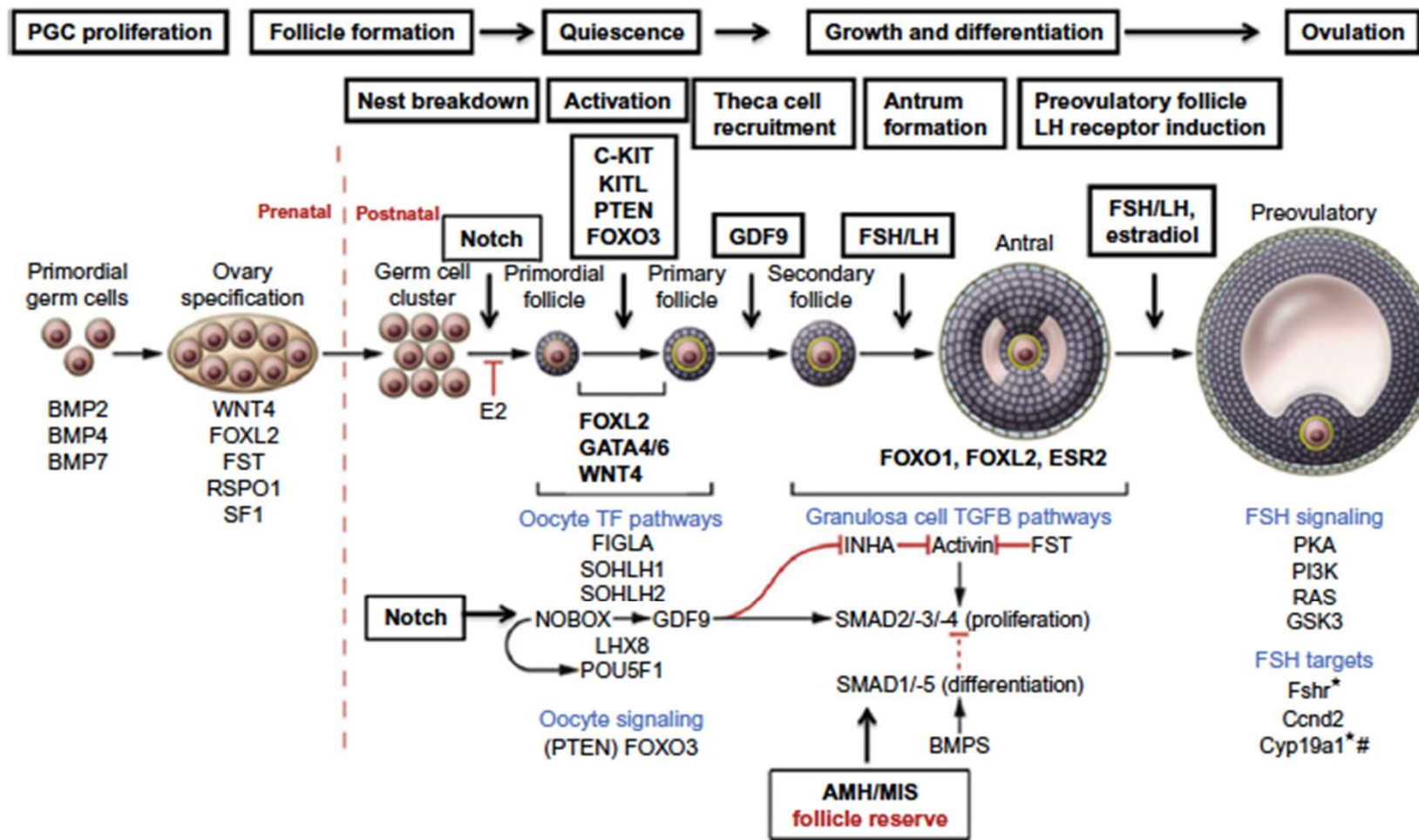
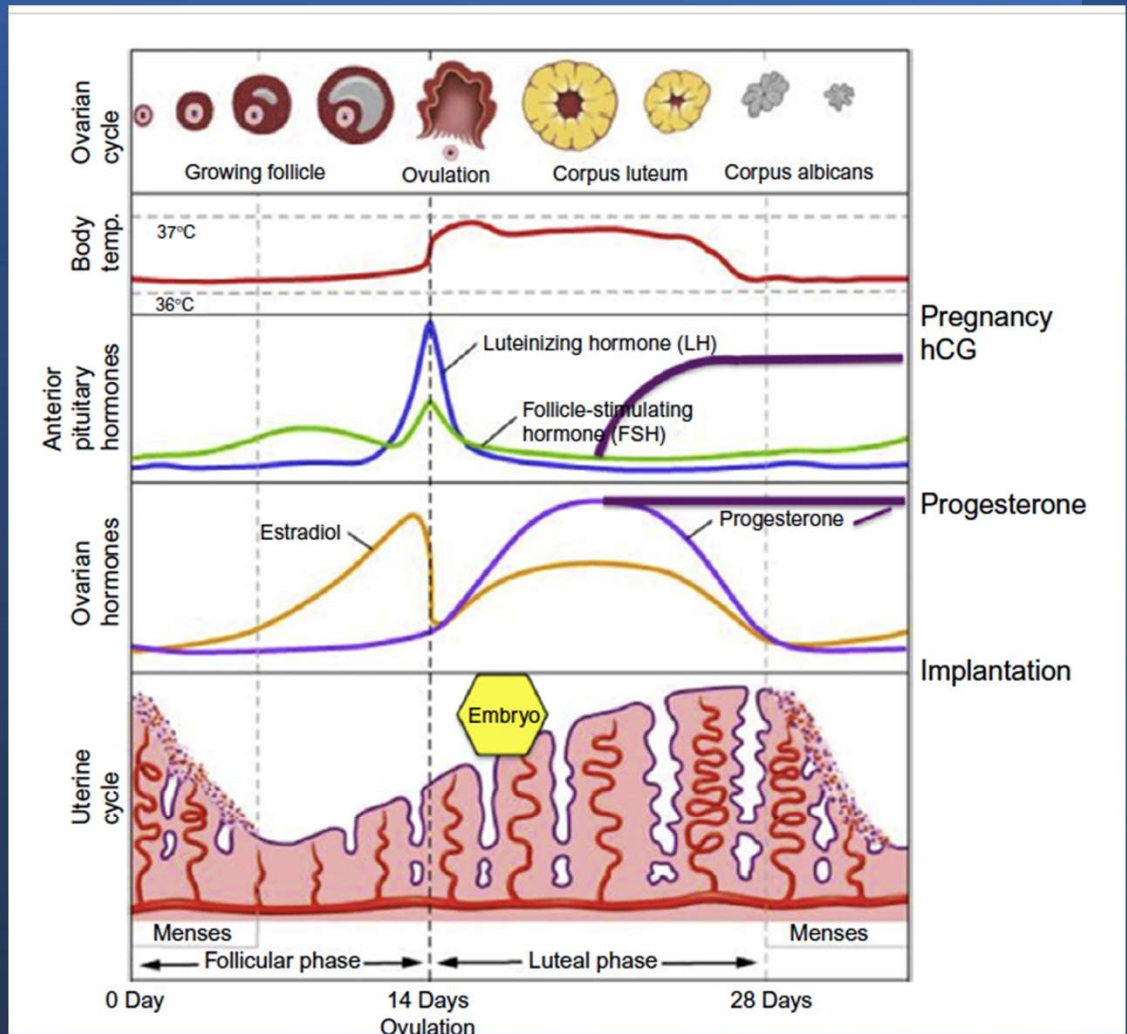


Fig. 3 Schematic of events and factors that regulate ovarian follicular formation, development and ovulation. Adapted from Richards, J. S. & Danneberg, S. A. (2010). The ovary:





## Oviducts

- Estradiol from preovulatory follicles induces cilia formation in ciliated cells and mucin secretion from the glandular cells.
  - critical for promoting the movement of the ovulated egg and embryo (if fertilization occurs) down the oviduct

## Endometrium

- Estradiol and progesterone act on luminal epithelial cells and/or stromal cells to control the window of receptivity, embryo attachment, implantation, decidualization, and parturition



## Lifestyle and Environmental Contributions to Ovulatory Dysfunction in Women with PCOS

- 2,217 infertile women diagnosed with PCOS recruited
- Frequencies of snoring, smoking, plastic tableware usage, and indoor decoration were highest in the PCOS- oligo-anovulation group (OA).
  - This group also preferred a meat favorable diet compared to non-OA group
  - No differences between exercise, insomnia, and alcohol consumption
- Conclusion: snoring, smoking, plastic tableware usage, and indoor decoration were associated with an increased risk for ovulatory dysfunction in women with PCOS
- But why?



# Endocrine Disruptors

- Our environment is filled with chemicals, pesticides, pharmaceuticals, and artificial lighting that disrupt our system
- Exposed via air, water, soil, food, and consumer products
- Interfere with the production, secretion, transport, metabolism, binding action, or elimination of the body's natural hormones
- Mimic naturally occurring hormones (i.e., estrogen, TSH, androgens)
- Bind receptors which prevent the natural hormone from binding which disrupts the normal signaling
- Wreak havoc



## Endocrine Disruptors

- *Women's Voices for the Earth*
  - Household cleaning products contain reproductive toxins such as toluene and phthalates as well as hormone disrupting synthetic musk
- Linked to estrogen dominance, early puberty, infertility, increased risk of breast and thyroid cancers
- The European Union has banned 1,300 chemicals from cosmetics.
- The U.S. has banned 30 according to Credo Beauty
- According to *Environmental Research*, switching to organic foods reduced urinary output of pesticides by 90% in 7 days

# Bisphenols

- A group of highly produced chemicals used as plasticizers in polycarbonate plastics, the epoxy resin in aluminum cans, and in cosmetic and personal care products
- Bisphenol A (BPA) is the most studied
- BPA exposure in women is associated with anovulation, lower antral follicle counts, disrupted menstrual cycle length, poor IVF outcomes (decreased total and mature eggs collected, fertilization rates, embryonic quality, and implantation rates), and infertility
- Newer analogues (BPFA, BPB, BPF, BPM, BPS, BPTMC) all pose similar risks

## BPA

- Plasticizer used commonly in many consumer products
  - Food and drink containers
  - Epoxy resin
  - Plastics
  - Baby bottles
  - Thermal receipts
  - Dental sealants!!!
- Measured in serum, plasma, urine, sweat, breast milk, amniotic fluid, placental tissue, fetal serum, and umbilical cords.
- BPA exposure has been associated with female reduced fertility, pcos, and endometriosis
  
- In women undergoing fertility treatment, urine BPA levels have been associated with decreased antral follicle counts and a reduction in the number of oocytes retrieved.
- Lead to premature ovarian failure
- Disturb the estrous cycle
- Disrupt steroidogenesis
- Follicle atresia
  - Increased expression of the proapoptotic factor BCL2-associated X protein (Bax)
- Associated with decreased oocyte quality

# BPA ban

- **Summary of FDA's Current Perspective on BPA in Food Contact Applications**
- FDA's current perspective, based on its most recent safety assessment, is that BPA is safe at the current levels occurring in foods. Based on FDA's ongoing safety review of scientific evidence, the available information continues to support the safety of BPA for the currently approved uses in food containers and packaging.
- **Food Additive Regulations Amended to No Longer Provide for the Use of BPA-Based Materials in Baby Bottles, Sippy Cups, and Infant Formula Packaging**



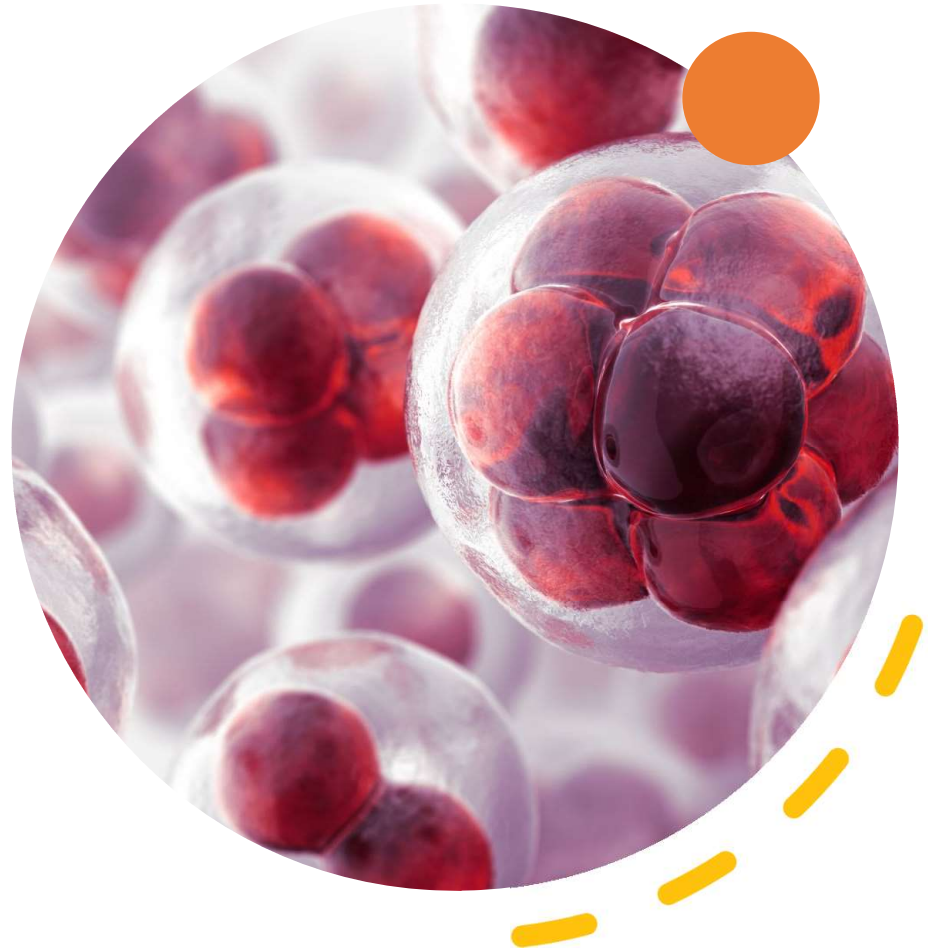
# Methoxychlor (MXR)

- Organochlorine pesticide used against insects
- Discontinued production in the US but we receive imported agricultural products from countries that still use it
- Present in food and water samples
- 35% of agricultural commodities contain pesticide residues [13]
- Several studies show interference with folliculogenesis
  - Treatment with 100mg/kg in vivo inhibits folliculogenesis
  - Treatment with 1-100microg/ml in vitro inhibits growth of isolated antral follicles
  - MXR exposure in vivo induces oxidative stress in mouse ovaries
  - Inhibits ovarian steroidogenesis [67]



## 2,3,7,8-TETRACHLORODIBENZO- p-DIOXIN (TCDD)

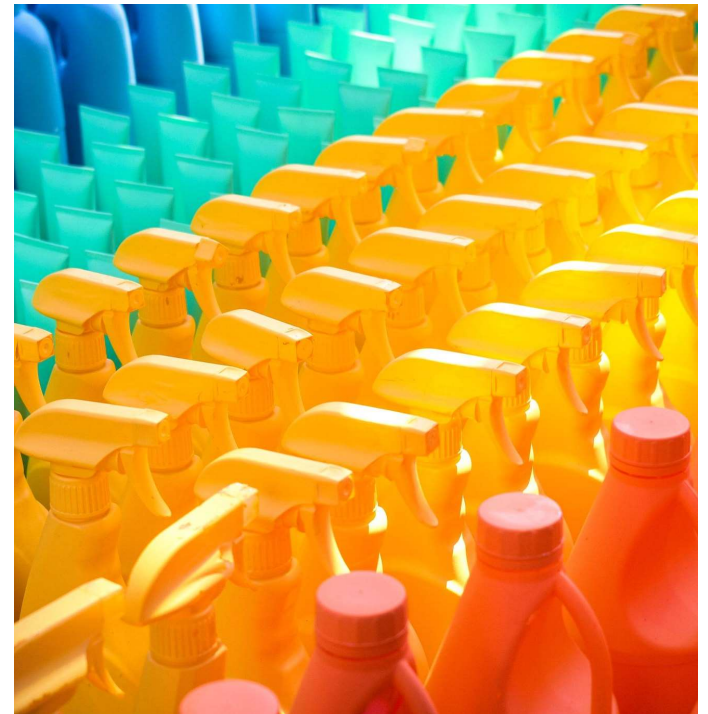
- A persistent environmental contaminant inadvertently produced as a by-product of herbicide and pesticide manufacturing, bleaching process at tree pulp and paper mills, and burning of municipal solid waste [77–79].
- TCDD is the most toxic member of the dioxin class of chemicals.
- It also has a long environmental half-life, accumulates in the food chain [18], and is found in human fat tissue [18], blood serum [18, 80], breast milk [81], and ovarian follicular fluid [82].
- TCDD exposure targets the ovary and leads to altered folliculogenesis



# Phthalates

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- Synthetic chemicals found ubiquitously in the environment
- More than 18 billion pounds of phthalates are used each year, predominantly as plasticizers in polyvinyl chloride (PVC) products such as
  - upholstery
  - tablecloths
  - shower curtains
  - pesticides
  - solvents
  - infant toys
  - personal care/cosmetic products
- Used to impart flexibility to plastics but leach from plastic products into the environment over time due to their noncovalent bonds
- Also be found in air, sediments, agricultural and urban soil, wastewater, and natural bodies of water



# DEHP: Di-(2-ethylhexyl) phthalate

Plasticizer most used for PVC and is approved for use in medical devices such as tubing, blood bags, and dialysis equipment

It is also used to manufacture disposable medical examination and sterile surgical vinyl gloves

Dibutyl phthalate (DBP), butyl benzyl phthalate (BBP), and diethyl phthalate (DEP) are also produced in high volumes and are commonly used in consumer products

# Phthalates & the Ovary

Alter follicle development and growth

Impair follicle function

May lead to acceleration of primordial follicle recruitment in mice

- Specifically, DEHP in vivo for 10-30 days

Adversely affect follicular health

- increased atretic follicles with DEHP
- oxidative stress with MEHP

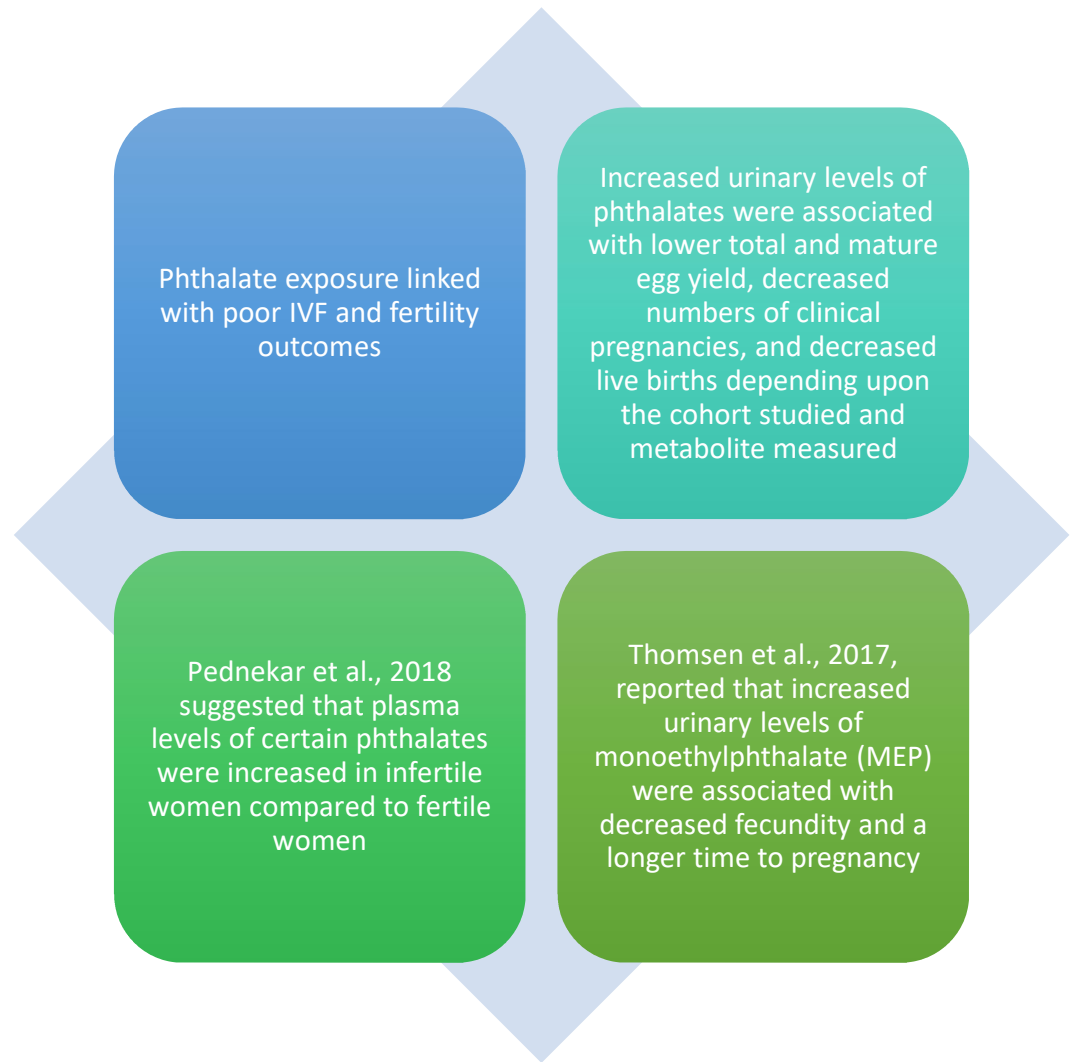
Alter steroidogenesis

Antiandrogenic and antiestrogenic properties

Weak affinity for estrogen receptors and peroxisome proliferator-activated receptors

# Phthalates and Infertility

(Begum et al., 2021; Deng et al., 2020; Hauser et al., 2016; Machtinger et al., 2018; Minguez-Alarcón et al., 2019).



# Phthalates and IVF Outcomes

- Hauser et al., 2016, showed that women with increased urinary levels of phthalate metabolites belonging to di(2-ethylhexyl) phthalate (DEHP) had **lower numbers of total and mature eggs retrieved** during IVF, and decreased incidence of clinical pregnancies and live birth
- Same study showed monocarboxyisononyl phthalate, a metabolite of diisononyl phthalate (DiNP), were associated with **decreased total and mature eggs retrieved**
- Increased urinary levels of DEHP metabolites, monobutyl phthalate (MBP), and MEP were associated with **decreased numbers of total and mature eggs collected and decreased numbers of fertilized eggs**, while the DEHP metabolites were additionally associated with **poor quality embryos**
- Mínguez-Alarcón et al., 2019 reported that increased urinary levels of DEHP metabolites were associated with **lower probabilities of implantation, clinical pregnancy, and live birth**



# Genistein

- An isoflavone phytoestrogen found naturally in plant structures such as soybeans, chickpeas, sunflower seeds, and lentils
- Humans are exposed to genistein primarily through consumption of soy-based dietary products such as soy milk, tofu, and soy flour
- Binds to and signals through estrogen receptors, ESR2 >>ESR1
- Alters folliculogenesis, dose dependent, unclear studies as sometimes it accelerates and others it inhibits follicular growth
- Alters progesterone levels, dose dependent, species dependent
  - May be due to dysregulation of steroidogenic enzymes

# Parabens

- Used as antimicrobial agents and preservatives in food products (tortillas, muffins) and cosmetics and lipstick
- Found ubiquitously, exposed daily
- May reduce antral follicle numbers which may contribute to alterations in hormone levels, shortened menstrual cycle length, and reduced fecundity.
- Can alter gene expression including those in breast cancer cells





# Triclosan

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- 5-chloro-2-(2,4-dichlorophenoxy)phenol (triclosan) is a halogenated biphenyl ether that is used as a broad-spectrum antimicrobial agent.
- Triclosan is found in personal care products, hand sanitizer, food packaging, and medical supplies leading to daily oral and dermal exposure
- Banned in certain soap products by the FDA in 2016
- Increased urinary triclosan associated with decreased fecundity, decreased antral follicle counts, and decreased egg yield in IVF

# Perfluoroalkyl and Polyfluoroalkyl Substances (PFAS)

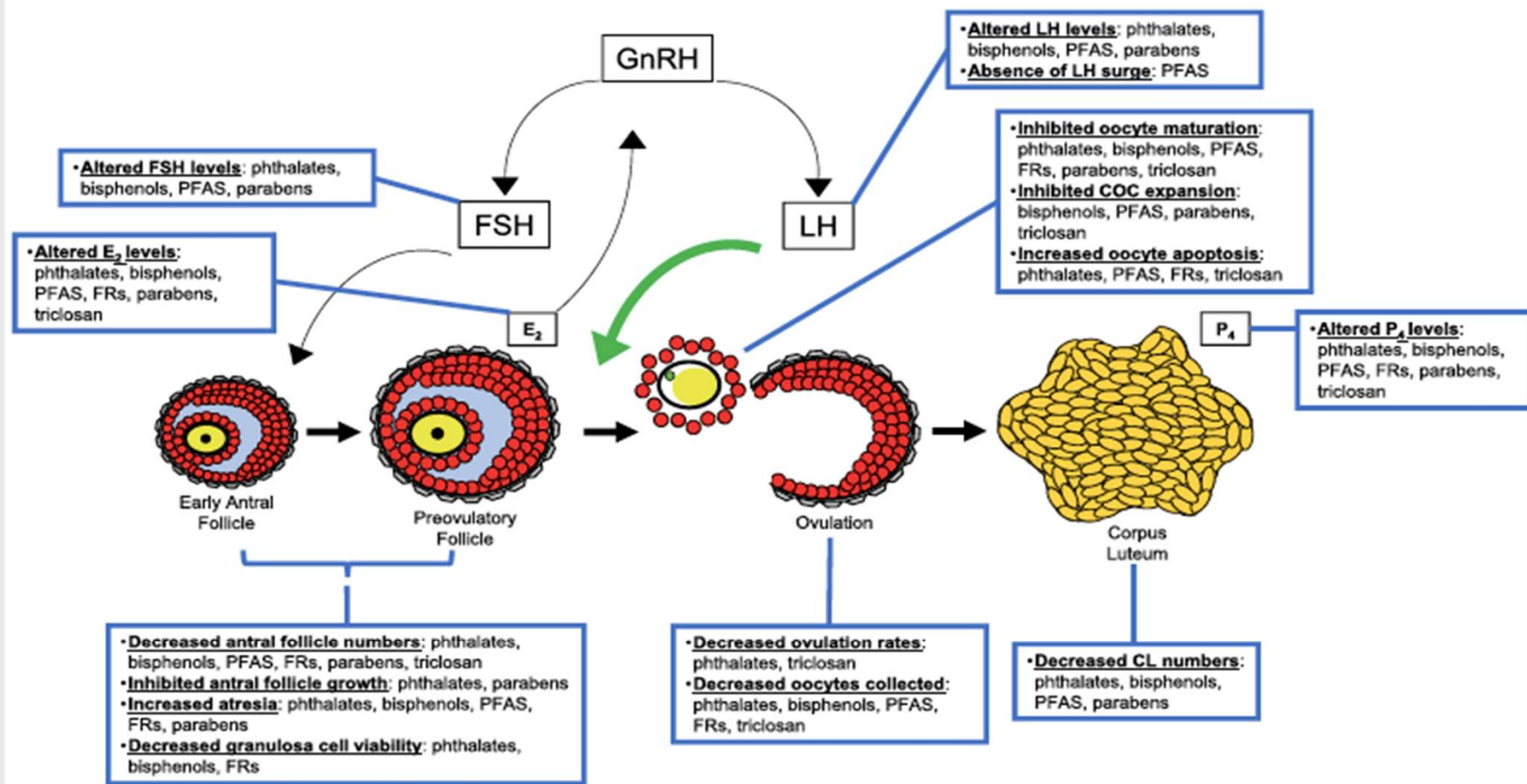
- Dietary sources
  - Fish and shellfish
  - Drinking water
  - Food packaging materials
  - Non-stick cookware
  - Others (dairy, eggs, beverages, vegetables)
- Non-dietary sources
  - Indoor air
  - Indoor dust
  - Soil and sediment
  - Impregnation spray (furniture and carpet)
  - Cosmetics
  - Other (skin waxes, leather samples, outdoor textiles)
- Exhaust the oocyte pool and cause depletion of follicular cells, leading to earlier age at menopause, premature ovarian failure and infertility
- Disrupts the earliest stage of folliculogenesis by altering oocyte development
- Impacts ovarian steroidogenesis
- Delays onset of menarche
- Disrupts menstrual cycle regularity
- Accelerates ovarian aging
- May affect PCOS and ovarian cancer

# EDC & Ovulation

- Exposure to EDCs is a contributing factor to infertility in women
- Defects in ovulation account for 30% of female infertility cases
- EDCs can inhibit the production or decrease the levels of ovulatory mediators, such as P4, prostaglandins, and vascular endothelial growth factors.
- EDCs can alter the number or agonize/antagonize receptors involved in the ovulatory cascade, including P4 receptor and EGF receptor, which can impair downstream ovulatory signaling.
- EDCs can also interfere with the biological processes that facilitate egg release and corpus luteum formation, including cumulus oocyte complex expansion and ECM remodeling.

## EDC & Folliculogenesis

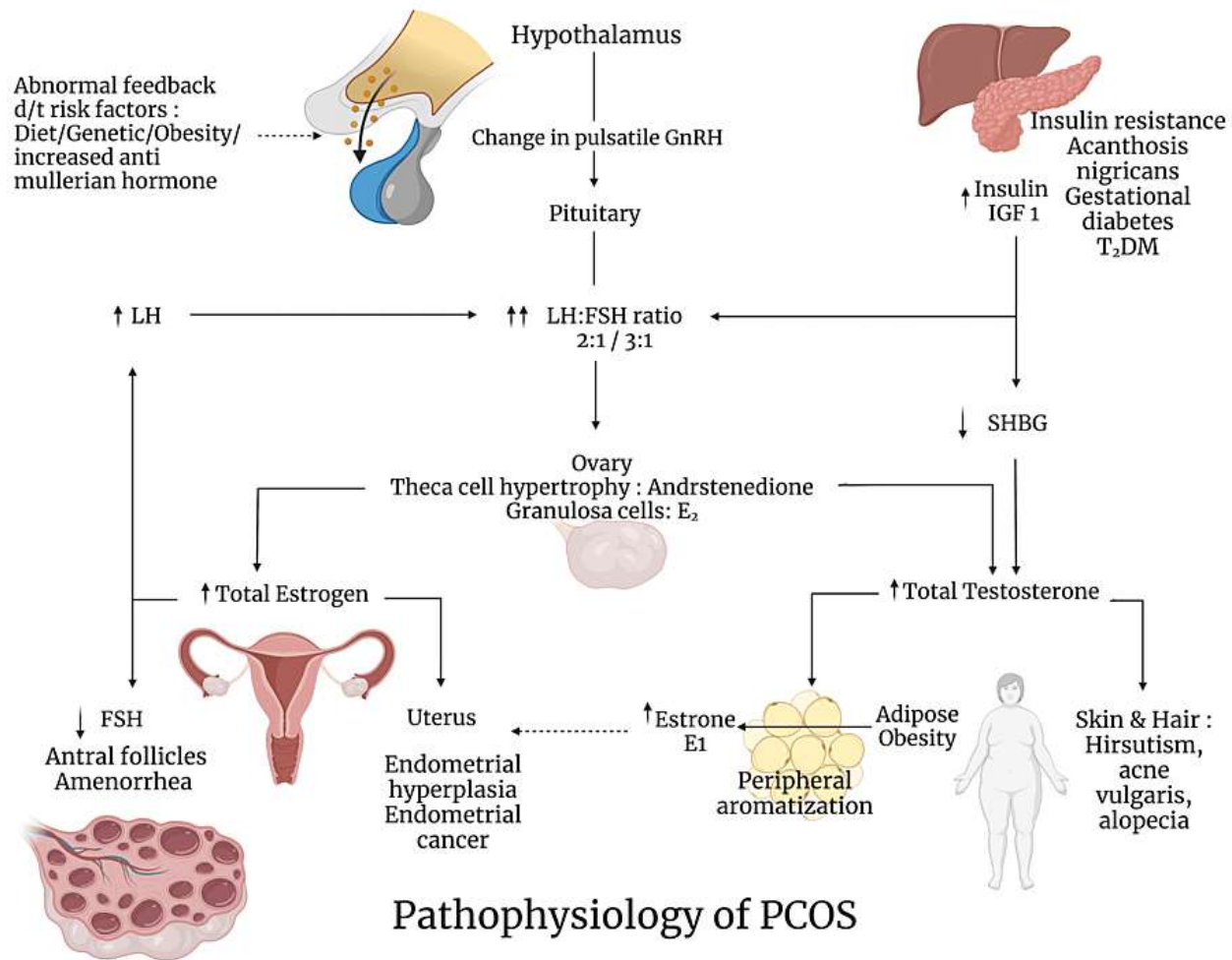
- EDCs can deplete the primordial follicle reserve by causing atresia or premature activation, which would ultimately eliminate the number of follicles that are capable of ovulation.
- EDCs can inhibit FSH-dependent follicle maturation. Inhibition of preantral and early antral follicle growth and development would decrease the necessary levels of E2 and LHCGR to promote ovulation. Increased atresia at these stages would also reduce the population of follicles that could eventually ovulate.
- These direct and indirect effects on the ovulatory process can potentially lead to menstrual cycle irregularity with oligoovulation or anovulation, and ultimately subfertility or complete infertility.



**FIGURE 2** Overview of the effects of EDCs on ovarian- and ovulation-related fertility outcomes. CL, corpora lutea; COC, cumulus oocyte complex; EDCs, endocrine-disrupting chemicals; E<sub>2</sub>, estradiol; FRs, flame retardants; FSH, follicle-stimulating hormone; GnRH, gonadotropin-releasing hormone; LH, luteinizing hormone; PFAS, per- and poly-fluoroalkyl substances; P<sub>4</sub>, progesterone.



# Let's Talk About PCOS



# Environmental Determinants of PCOS

- PCOS: anovulation, hyperandrogenism, polycystic ovaries
- In 1996, the EPA was given a mandate under the Food Quality Protection Act and Safe Drinking Water Act to develop screening tests for specific EDC
- The industrialized (processed) food system recognized as a major contributor to the introduction to toxic chemicals
- Physiology: impaired ability to switch from fat oxidation to carbohydrate oxidation under insulin-stimulated conditions; known as metabolic inflexibility
  - Associated with insulin resistance and hyperandrogenism
- Serum BPA concentrations are higher in those with PCOS
- BPA levels correlated with degree of hyperandrogenemia and insulin resistance \*



# Endometriosis

- Dioxin is known to stimulate the growth of uterine epithelial cells in vitro [70], and lifetime consumption of a soy diet induces key features of endometriosis in rodent models
  - Clinical data is equivocal
  - Bredhult, Backlin, Olovsson. Effects of some endocrine disruptors on the proliferation and viability of human endometrial endothelial cells in vitro. *Reprod Toxicol* 2007; 23:550
  - Smarr, Kannon, Buck Louis. Endocrine disrupting chemicals and endometriosis. *Fertil Steril* 2016; 106:959
  - Sofo, Gotte, Lagana, et al. Correlation between dioxin and endometriosis: an epigenetic route to unravel the pathogenesis of the disease. *Arch Gynecol Obstet* 2015; 292:973

# Uterine Fibroids

- Potential causative link with diethylstilbestrol (DES) and genistein in rodent models. Causes estrogen-responsive genes in the adult myometrium to become hyper-responsive to hormones.
  - Greathouse, Bredfeldt, Everitt, et al. Environmental estrogens differentially engage the histone methyltransferase EZH2 to increase risk of uterine tumorigenesis. *Mol Cancer Res* 2012; 10:546

# Precocious Puberty

- Secondary sexual development younger than age 8yo for girls and 9yo for boys
- Early activation of pulsatile GnRH secretion – central or exogenous
- Attributed to exposure from creams, ointments, and sprays
- Also estrogen exposure in food like phytoestrogens (soy)
- Inadvertant exposure to androgen-containing creams
- Lavender or tea tree oil (both display weak estrogenic and anti-androgenic activities in vitro) associated with premature thelarche in young girls

# Starch-based and dairy foods

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- Found to promote exaggerated insulinogenic responses in PCOS
  - Grains have inherent phytoestrogen production
  - Agricultural pesticides interact with thyroid, androgen, and estrogen paths
  - Dairy from lactating cows affect estrogen and testosterone levels, also insulin resistance from the cow itself or hormones administered to the animal
  - Milk proteins have insulinotropic properties, but the whey component is the predominant influence on insulin secretion
  - Whey protein is an estrogenic endocrine disruptor present in many sports nutritional supplements. The insulinogenic property of whey protein could exacerbate hyperinsulinemia and, subsequently, hyperandrogenism in women with PCOS
  - Avoidance of starch-based foods and dairy can reduce obesity and insulin resistance
  - Vitamin D consumption and myo-inositol derivatives can favorably influence glucose metabolism
- Gluten, also an EDC, increases prolactin in children and adolescents with celiac disease

# Diet

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- High carbohydrate intake is often identified as an exacerbating factor for PCOS, although diet itself is not likely a cause of PCOS.
- Sjaarda et al. found no significant relationships between carbohydrate or any macronutrient intake and hormones such as insulin, antimüllerian hormone, and total and free testosterone, suggesting that no particular macronutrient is responsible for producing a PCOS phenotype in regularly menstruating women. Similarly, dietary composition is not associated with greater indices of insulin resistance in women who have the diagnosis of PCOS compared with control subjects

# Obesity is a symptom, not a cause

- Often report difficulty with losing weight
- Reduced postprandial thermogenesis in PCOS patients related to their reduced insulin sensitivity
  - smaller part of overall energy expenditure
  - reduction could contribute to difficulty in losing weight in women with PCOS.
- Obese women with or without PCOS who desire weight loss may benefit from resistance exercise to increase muscle mass, and thus increase metabolism rate and postprandial thermogenesis





What can help?

# Nutritional Supplements: Inositol

- Potentially beneficial
- Inositols (insulin-sensitizing agents)
  - Myo-inositol promotes glucose uptake
  - Chiro-inositol increases glycogen synthesis
- In the PCOS ovary, myo-inositol promotes glucose uptake and FSH signaling, and chiro-inositol reduces insulin-mediated androgen synthesis
- A 40:1 ratio of myo-inositol:D-chiro-inositol is recommended to improve ovulation and embryo quality (54).
- Myo-inositol supplementation alone of 2–4 g/d is optimal to reduce clinical hyperandrogenism and dyslipidemia through the reduction of insulin plasma levels, with few side effects (52).



# Vitamin D

- PCOS patients with vitamin D deficiency are more likely to have increased fasting glucose and insulin resistance
- Treatment of PCOS women with 20,000–50,000 IU vitamin D3 weekly reduced fasting and stimulated glucose and C-peptide levels along with triglycerides, and improved menstrual regularity in 30%–50% of patients with oligomenorrhea
- Vitamin D3 supplementation is also reported to improve acne and hirsutism, as indicated by the Ferriman-Gallwey score, although the etiology is not clear, because serum testosterone, free testosterone, SHBG, and insulin resistance did not change with treatment

# Other supplements

- Omega-3 fatty acids may improve glucose metabolism but do not appear to promote weight loss in women with PCOS
  - A dose of 1,200 mg/d omega-3 long-chain polyunsaturated fatty acids reduced fasting glucose and insulin but not weight
- Other small trials demonstrate potential benefits of selenium supplements of 200 mg/d in decreasing serum insulin and triglycerides, and of 220 mg/d zinc sulfate in reducing fasting glucose and insulin levels

# Weight Loss & Fertility

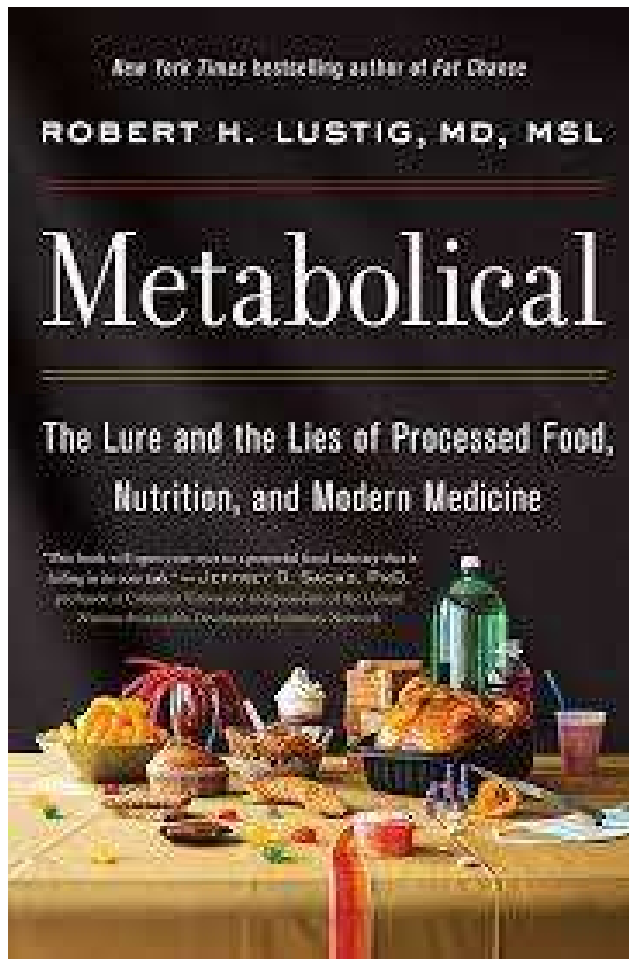
- Weight loss of only 7kg has been found to improve menstrual regularity and ovulation in 44% of patients, with responders having a greater decrease in fasting insulin and insulin resistance compared to nonresponders
- For nonresponders, ovulation induction medication may be considered
- Insulin-sensitizing drugs, such as metformin, may promote weight loss in some women and may increase clinical pregnancy rates, but they do not increase live birth rates when used alone or in combination with clomiphene

# The Microbiome

- Dysbiosis of the gut microbiota has been hypothesized to play a role in increased gastrointestinal permeability, initiating chronic inflammation, insulin resistance (IR) and hyperandrogenism shown to be reversible after interventions aimed at improving diet quality or treatment with probiotics or synbiotics



# Book Reviews

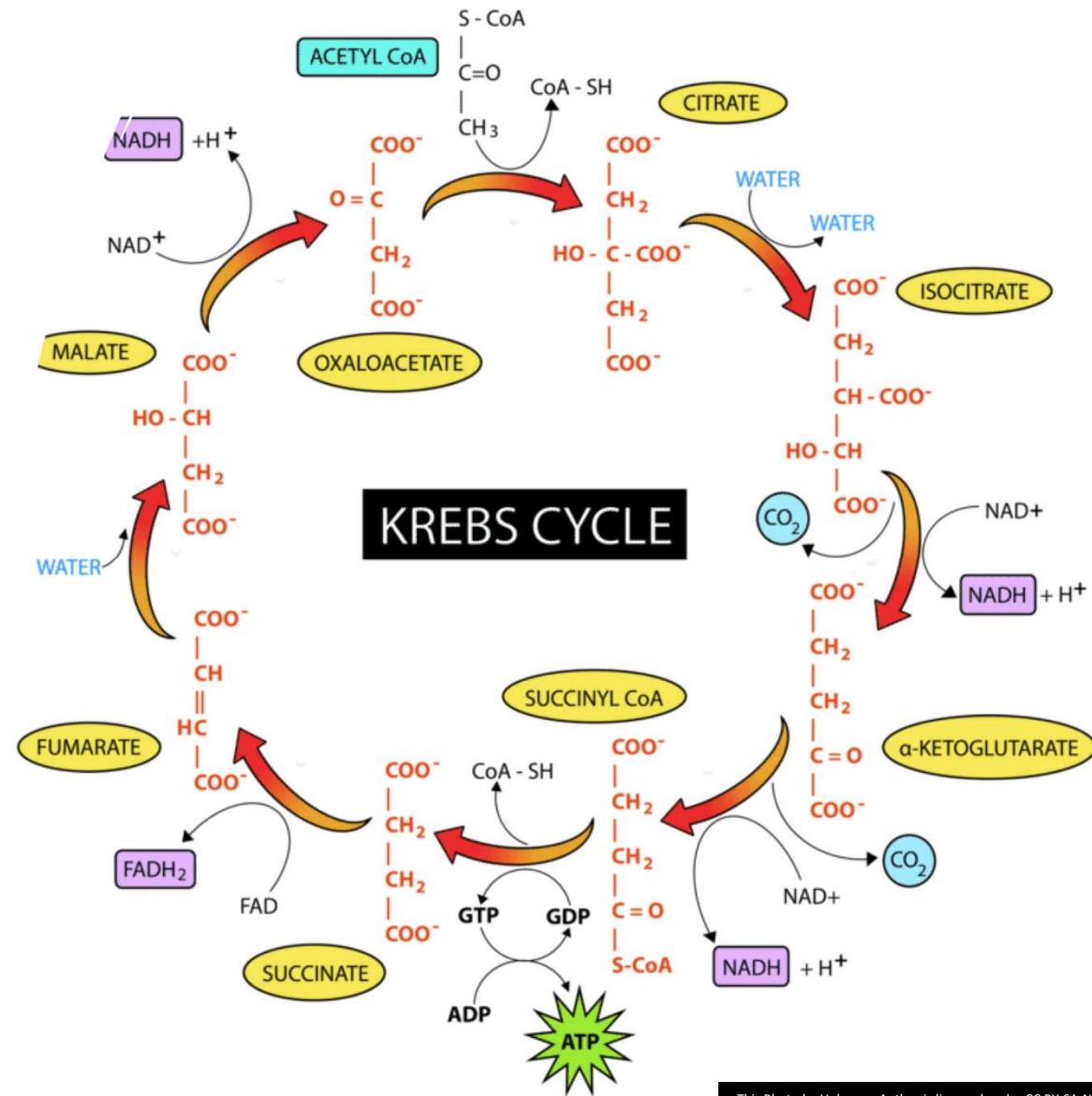



## Metabolical

- Metabolical: The Lure and the Lies of Processed Food, Nutrition, and Modern Medicine by Robert H. Lustig
- The medical model of healing involves treating symptoms
  - not curing disease
- We are taught to identify the symptoms and prescribe a medication
- Big Pharma has a long and entwined history with medical education
- Big Food industry

# Intracellular processes that go awry

1. Glycation
2. Oxidative stress
3. Mitochondrial dysfunction
4. Insulin resistance
5. Membrane integrity
6. Inflammation
7. Epigenetics
8. Autophagy






Processed  
food is  
defined by  
seven  
engineering  
criteria

- Mass produced
- Consistent batch to batch
- Consistent country to country
- Uses specialized ingredients from specialized companies
- Consists of pre-frozen macronutrients
- Must stay emulsified so that the fat and water do not layer out
- Must have a long shelf life or freezer life





# Metabolic Syndrome

- Approximately 88% of Americans have some level of metabolic dysfunction that has likely gone unrecognized
  - fatty liver, HTN, high blood uric acid, hyperlipidemia, or hyperglycemia) → due to insulin resistance
- Three commonalities:
  - Despite all efforts, these diseases are all increasing in incidence, prevalence, and severity at a faster rate than obesity
  - They are all exacerbated by obesity, although not caused by it
  - While there are drugs to treat the symptoms of each one (including obesity), there are no drugs to either treat, cure, or prevent the diseases themselves



# Food adulterations

- Environmental toxins build up in animals, plants and water
- Mercury contamination in fish and shellfish?
  - A byproduct of various tech advances like converting corn into high-fructose corn syrup
- Heavy metal runoff from food processing finds its way to our food supply
- Animals raised on grass (tougher, healthier) vs raised on corn (fatty)
- Omega-6 Fatty acids: pro-inflammatory (prostaglandins, leukotrienes, and thromboxanes); corn and soybean oil processing increases it
- Trans-fat: using an unsaturated fat to fry foods (smoking point) converts cis-bond to trans-bond. Saturated fats has no double bonds, so does not change)
- Hydrocarbons (PAH): from charcoal grilling
- Dietary AGEs are absorbed through the intestine, enter the bloodstream, bind to receptors for AGE (RAGE) on liver cells, tells mitochondria to stop burning and promote fat accumulation. Example: Acrylamide, a byproduct of coffee roasting, is turned into glycidamide, which is a potent carcinogen. One third of cancers tested showed alterations in the cancer genome associated with this compound



# Food subtractions

- Micronutrients not all that tasty and they are metabolically active
  - Exposed to oxygen they either lose potency or turn rancid, or both
- Wheat: originally made stone ground wheat kernels, rustic bread out of pulverized semi-smooth flour, but the flour could not be stored
  - Wheat kernel has three parts: bran (soluble and insoluble fiber), endosperm (pure starch), and the wheat germ (nucleic acids, polyphenols, flavonoids, vitamins, antioxidants, and other micronutrients reside)
  - During milling, separate the fiber and the germ from the starch (white flour) --> without spoilage
- White flour is easily absorbed raising glucose and insulin
- Fiber protects the liver and feeds the gut (microbiome)



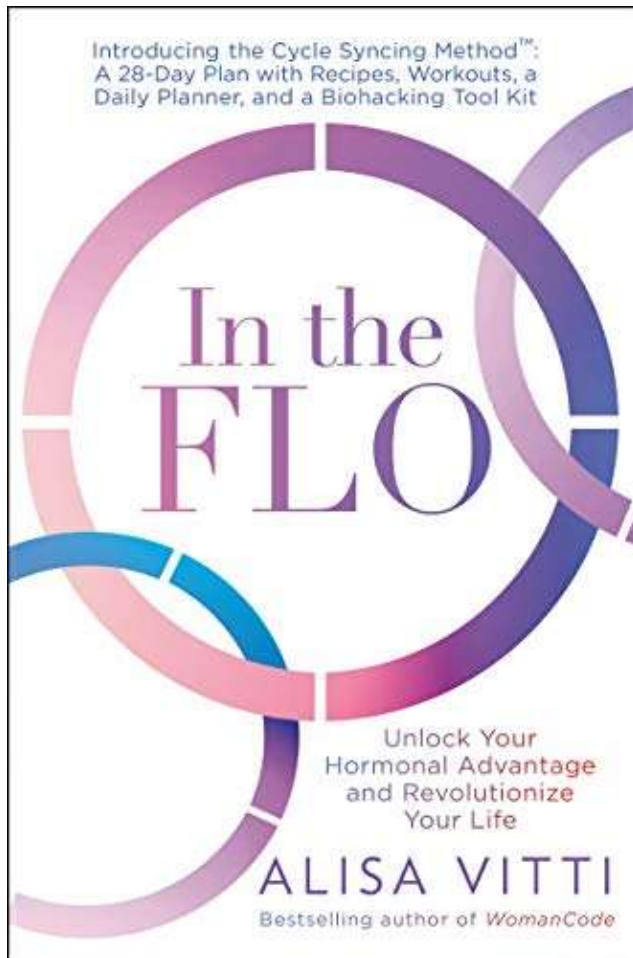
# Food additions

- Antibiotics
- Pesticides (i.e., DDT is estrogenic and promotes cancer)
- Flavor, colors, textures, preservation
- Hormones: bovine growth hormone
  - Dairy and cancer risk
  - Beef and inflammation



# Metabolical Solution

- Real Food
- Removing processed food from your diet
  - “its not what is in the food, but rather what’s been done to the food”
- Fermentation (kimchi, sauerkraut, miso, tempeh, kombucha) produces lactic acid as a natural preservative, and vitamin/mineral availability is greater



# Flo Living Biohacking

- 4 menstrual cycle phases need support
- PCOS caused by several factors
  - Insulin resistance
  - Increased cortisol and testosterone
  - Excess estrogen (EDCs, pesticide-laden food, medications)
  - A sluggish liver
  - An imbalanced gut
  - Chemicals in beauty and cleaning products
- Step 1: stabilize blood sugar to improve metabolism and digestion to clear excess hormones and lose fat
- Step 2: restore adrenals to lower stress and increase energy
- Step 3: support organs of elimination to prevent estrogen build up
- Step 4: synchronize your food and lifestyle each week of your cycle to balance hormones
- Step 5: improve relationship with feminine energy

# Are you exposed to EDCs?

- Do you eat nonorganic foods?
- Do you eat meat that isn't antibiotic-free and hormone-free, or do you eat farmed fish?
- Do you drink from plastic bottles?
- Do you use chemical-laden household cleaning products and detergents?
- Do you use drugstore cosmetics and skincare products?
- Do you use haircare products that aren't all natural?
- Do you use standard nail polish?



# Using food to fight symptoms

- PCOS: high fiber foods (beans, lentils, cooked cruciferous veggies like broccoli, kale, brussels sprouts, cabbage, collard greens, sweet potatoes, almonds)
- Fibroids: eat more flaxseeds (act like natural SERMs); add unprocessed, organic fermented soy (tempeh, miso) for its anti-estrogenic effect on the uterus; Beans (kidney, lentils, mung) provide healthy fiber and protein; high fiber whole grains (oats, brown rice); pears and apples)
- Endometriosis: anti-inflammatory foods (leafy greens, broccoli, salmon, bone broth, blueberries, flaxseeds); high magnesium (almonds, avocados, sunflower seeds, pumpkin seeds, spinach, black beans)



# Key Takeaways

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- “Diet and exercise” is vague advice, we should provide more guidance
- Consider specific recommendations like:
  - Organic foods
  - Fermented foods
  - Grass fed, antibiotic and hormone free meat
  - Wild fish
  - Whole vegetables (avoid smoothies)
  - Unprocessed foods
- Exercise: resistance training
- Other recommendations:
  - Avoid plastic containers/bottles and utensils
  - Avoid chemical-laden products for soaps, detergents, cosmetics, etc.



Thank you





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- Book: *Metabolical: The Lure and the Lies of Processed Food, Nutrition, and Modern Medicine* by Robert H. Lustig, MD, MSL
- Book: *In the Flo: Unlock Your Hormonal Advantage and Revolutionize Your Life* by Alisa Vitti

EDC	Use	Activity
BPA	Epoxy resins are found in many plastic products, including food storage containers	anovulation, lower antral follicle counts, disrupted menstrual cycle length, poor IVF outcomes (decreased total and mature eggs collected, fertilization rates, embryonic quality, and implantation rates), and infertility
Dioxins (2,3,7,8-tetrachlorodibenzo-p-dioxin)	A by-product of herbicide manufacture and paper bleaching, released during the burning of waste and wildfires	Alters folliculogenesis
methoxychlor	Organochlorine pesticide used against insects	Dose dependent -inhibits folliculogenesis -inhibits growth of isolated antral follicles -induces oxidative stress in mouse ovaries -Inhibits ovarian steroidogenesis
Genistein	Food (soy, legumes, grains, nuts)	Alters folliculogenesis, dose dependent, unclear studies as sometimes it accelerates and others it inhibits follicular growth
Parabens	Used as antimicrobial agents and preservatives in food products (tortillas, muffins) and cosmetics and lipstick	May reduce antral follicle numbers which may contribute to alterations in hormone levels, shortened menstrual cycle length, and reduced fecundity.
Per- and polyfluoroalkyl chemicals (PFAS)	Dietary sources Fish and shellfish Drinking water Food packaging materials Non-stick cookware Others (dairy, eggs, beverages, vegetables) Non-dietary sources Indoor air Indoor dust Soil and sediment Impregnation spray (furniture and carpet) Cosmetics Other (skin waxes, leather samples, outdoor textiles)	Exhaust the oocyte pool and cause depletion of follicular cells, leading to earlier age at menopause, premature ovarian failure and infertility Disrupts the earliest stage of folliculogenesis by altering oocyte development Impacts ovarian steroidogenesis Delays onset of menarche Disrupts menstrual cycle regularity Accelerates ovarian aging May affect PCOS and ovarian cancer
Phthalates	Cosmetics, children's toys, food packaging	Alters folliculogenesis, impairs follicle function, accelerated follicle recruitment, adversely affects follicular health, alters steroidogenesis, antiandrogenic and antiestrogenic properties, Weak affinity for estrogen receptors and peroxisome proliferator-activated receptors, poorer IVF outcomes Decrease rates of implantation, higher rates of miscarriage, and decreased viability of neonates  [ Craine, Janssen, Edwards et al. Female Reproductive Disorder: the roles of endocrine disrupting compounds and developmental timing. Fertil Steril 2008; 90:911 ]
Polybrominated diphenyl ethers (PBDE)	Flame retardants	
Polychlorinated biphenyls (PCB)	Electrical equipment like transformers, hydraulic fluids, lubricants, cutting oils, electrical insulators, machinery → exposure through sediment in fatty tissue of seafood and livestock	Longer menstrual cycles, longer time to pregnancy, and high levels correlated to failed pregnancies
Triclosan	personal care products, hand sanitizer, food packaging, and medical supplies leading to daily oral and dermal exposure	Increased urinary triclosan associated with decreased fecundity, decreased antral follicle counts, and decreased egg yield in IVF