Premature Ovarian Insufficiency and Tobacco smoking: a review

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Premature ovarian insufficiency (POI)

- The Pivotal Role of Ovaries in Reproductive health
- Definition: according to European Society of Human Reproduction and Embryology Guidelines
- Stages of POI
- Premature ovarian failure (POF)
- Other Problems arisen from POI

Aetiologies for POI

- 25% Known causes
- Autoimmune Diseases
- Hereditary factors
- Environmental Factors
- Toxic Compounds: Phthalates, Bisphenol A, Pesticides, Tobacco
- Iatrogenic Factors: Chemotherapy, Radiotherapy, Surgery
- Mitochondrial Abnormalities

Pathogeny

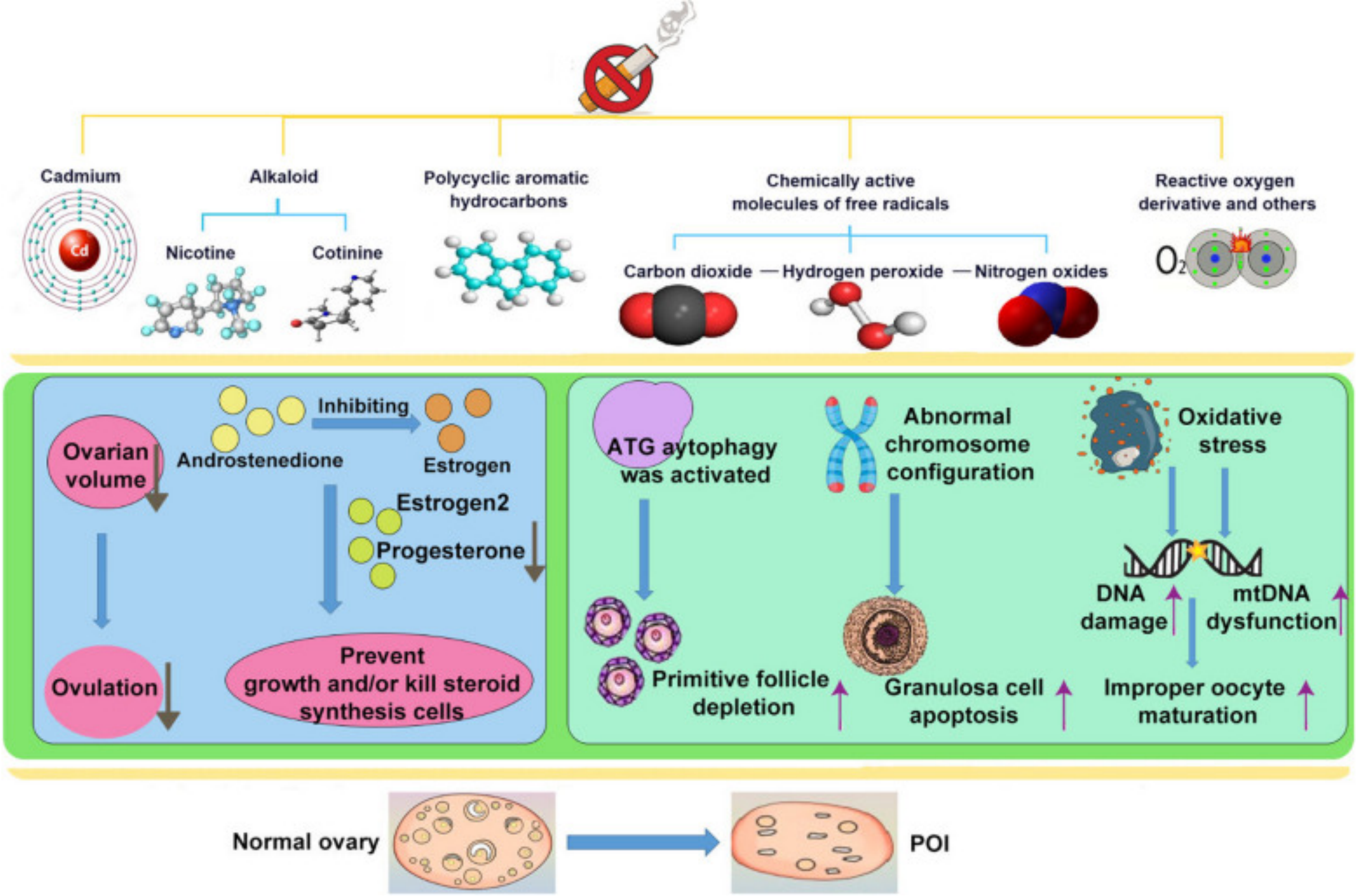
- Autoimmune diseases
- Genetic factors
- Environmental factors
- Iatrogenic factors (eg. chemotherapy, radiotherapy, surgery)
- Mitochondrial abnormalities

Premature ovarian insufficiency

Age
<40 years

Clinical manifestation

- Menopausal symptoms
- Infertility
- Cognition/Emotional health
- Bone disease Osteoprosisi
- Metabolic and cardiovascular disease


Cadmium
Alkaloid
Nicotine
Cotinine
Polycyclic aromatic hydrocarbons
Chemically active molecules of free radicals
Carbon dioxide
Hydrogen peroxide
Nitrogen oxides
Reactive oxygen derivative and others
Ovarian volume
Androstenedione
Inhibiting
Estrogen
Estrogen2
Progesterone
Ovulation
Prevent growth and/or kill steroid synthesis cells
ATG aytophagy was activated
Abnormal chromosome configuration
Oxidative stress
DNA damage
mtDNA dysfunction
Primitive follicle depletion
Granulosa cell apoptosis
Improper oocyte maturation
Normal ovary
POI

Cigarette smoke and POI

- Folliculogenesis disruption
- Autophagy & Apoptosis
- DNA damage
- reduced production of estradiol and progesterone
- persistent oxidative stress in Mitochondrium

Pollutants and POI

- Research has shown that various pollutants can impact all gametogenesis processes and may have adverse effects on ovarian function in women post-birth
- Second hand Cigarette exporsure and POI

Toxic Substances in Cigarettes

- PAHs
- Heavy Metals
- Alkaloids (nicotine, Cotinine)
- Benzopyrene
- Aromatic Amines

Cadmium Effects on POI

- Steroid Hormone Production inhibition
- Follicular atresia
- Ovulation failure
- Implantation disorder
- Spontaneous abortion
- Birth defect

The effect of benzo[a]pyrene on ovarian development

- Negatively correlated with the level of E2
- E2 acts through ERalpha and ERbeta. Granulosa interact through ERbeta
- B[a]P is more concentrated in the follicular fluid compared to serum, suggesting that it may be preferentially accumulated in the ovary, leading to ovarian toxicity and selective destruction of preantral follicles

The effect of alkaloids in Ovarian development

- a certain degree of anti-estrogenic effects
- Activation of the sympathetic adrenal system, and subsequently HPA and HPT pathways, resulting in elevated cortisol and T3,T4 levels.
- nicotine and its metabolites cause human luteal insufficiency by regulating the prostaglandin (PG) system, severely inhibiting progesterone release.

The effects of polycyclic aromatic hydrocarbons on ovarian development

- lower pregnancy rates per menstrual cycle
- induced ovarian tumorigenesis
- increase the expression of Bcl-2
- fetal germ cell apoptosis by directly stimulating Bax expression

Other toxic substances in Tobacco

- carbon dioxide, hydrogen peroxide, and nitrogen oxides, containing reactive oxygen derivatives and free radicals
- Leading to marked increase in cell apoptosis in follicles
- an increase in the thickness of the transparent zone, which could reduce fertilization ability
- Both enzymatic and non-enzymatic antioxidants were found to be reduced in smokers. The study also revealed that the antioxidant capacity of follicular fluid is generally low
- Treatment with different concentrations of melatonin in smokers

Complications of POI

- psychological burden
- Cardiovascular disease and stroke
- cognitive decline
- Bone mineral density

Treatment of POI

- Hormone replacement therapy
- stem cell activation
- in vitro activation (IVA)
- mitochondrial activation
- exosome therapy
- biomaterial strategies
- intraovarian perfusion of platelet-rich plasma (PRP)

Conclusion

- POI can manifest through various mechanisms, including reduced peak follicle quantity, accelerated follicle depletion due to apoptosis, or follicle dysfunction