

# **Sustainability and Chemistry**

## **CH5106: L11**

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## Chemicals That May Disrupt Your Endocrine System

According to the Endocrine Society, there are nearly 85,000 human-made chemicals in the world, and 1,000 or more of those could be endocrine disruptors, based on their unique properties. The following are among the most common and well-studied.

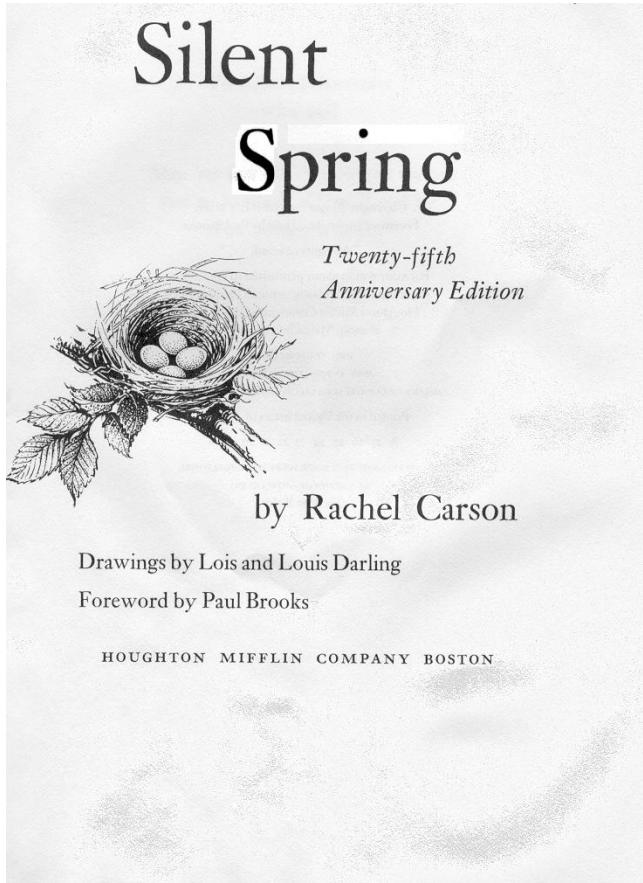
- **Atrazine** (commonly applied herbicides)
- **Bisphenol A (BPA)** is used to make polycarbonate plastics and epoxy resins. BPA based polymers and resins.
- **Dioxins** (byproduct of certain manufacturing processes) Also released into the air from waste burning and wildfires.
- **Perchlorate** (Used in explosives, and fireworks)
- **Per- and polyfluoroalkyl substances (PFAS)** (firefighting foam, nonstick pans, paper, and textile coatings, etc).
- **Phthalates** (liquid plasticizers, food packaging, cosmetics, fragrances, children's toys, and medical device tubing, Cosmetics (nail polish, hair spray, aftershave lotion, cleanser, and shampoo).
- **Polychlorinated biphenyls (PCBs)** (electrical equipment, such as transformers, and are in hydraulic fluids, heat transfer fluids, lubricants, and plasticizers) were banned in 1979.

# Rachel Carson Biography

Born, May 27, 1907, Springdale PA

Educated at Pennsylvania Women's College, Pittsburgh and MA  
in zoology from Johns Hopkins University in 1932

Employment at Marine Biological Laboratory, Woods hole, MA,  
Bureau of Fisheries

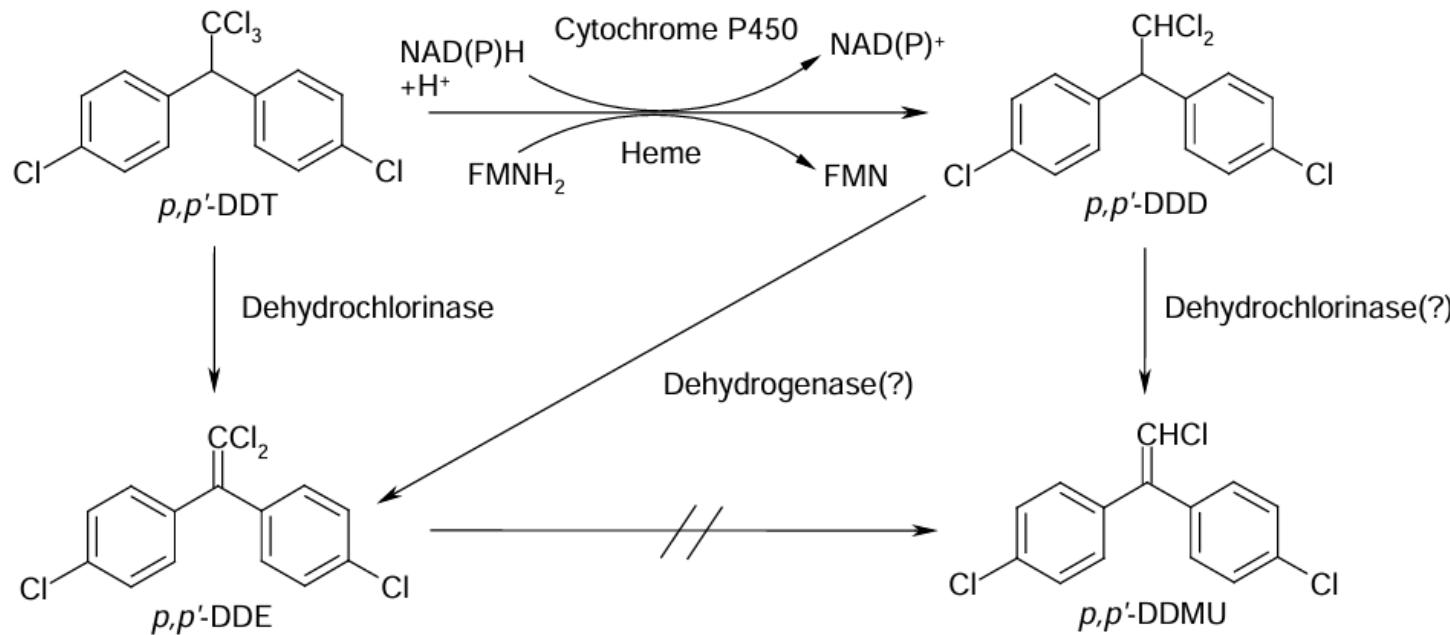


“Only within the moment of time represented by the present century has one species—man—acquired significant power to alter the nature of his world.”

## Early problems with DDT

During the summer of 1949 studies were conducted at Princeton, New Jersey, to determine the effects on wildlife of DDT used in the control of Dutch elm disease. An intensive search for dead birds determined direct mortality after spraying.

Population declines during the 1950s–1970s were largely driven by a combination of reproductive failure due to eggshell-thinning, egg breakage and embryonic death attributable to DDT and its metabolites [Journal of Raptor Research, 2017, 51(2):95-106]



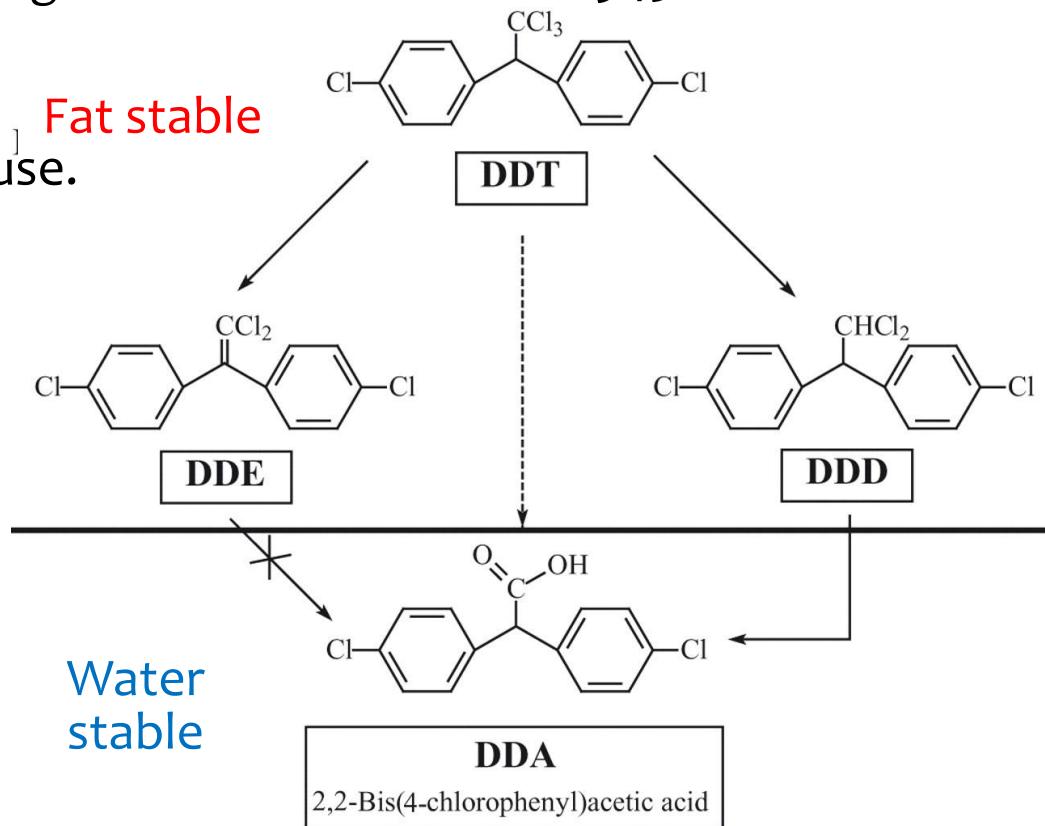
Dichlorodiphenyltrichloroethane (DDT): First synthesized in 1857 [Othmar Zeidler]

Insecticide action: Paul Muller (1939) [Nobel Prize in Physiology or Medicine, 1948]

DDT as an insecticide: First used as an agricultural insecticide in 1945.

Banned in the USA: 1972

Banned in India: 1989 for agricultural use.

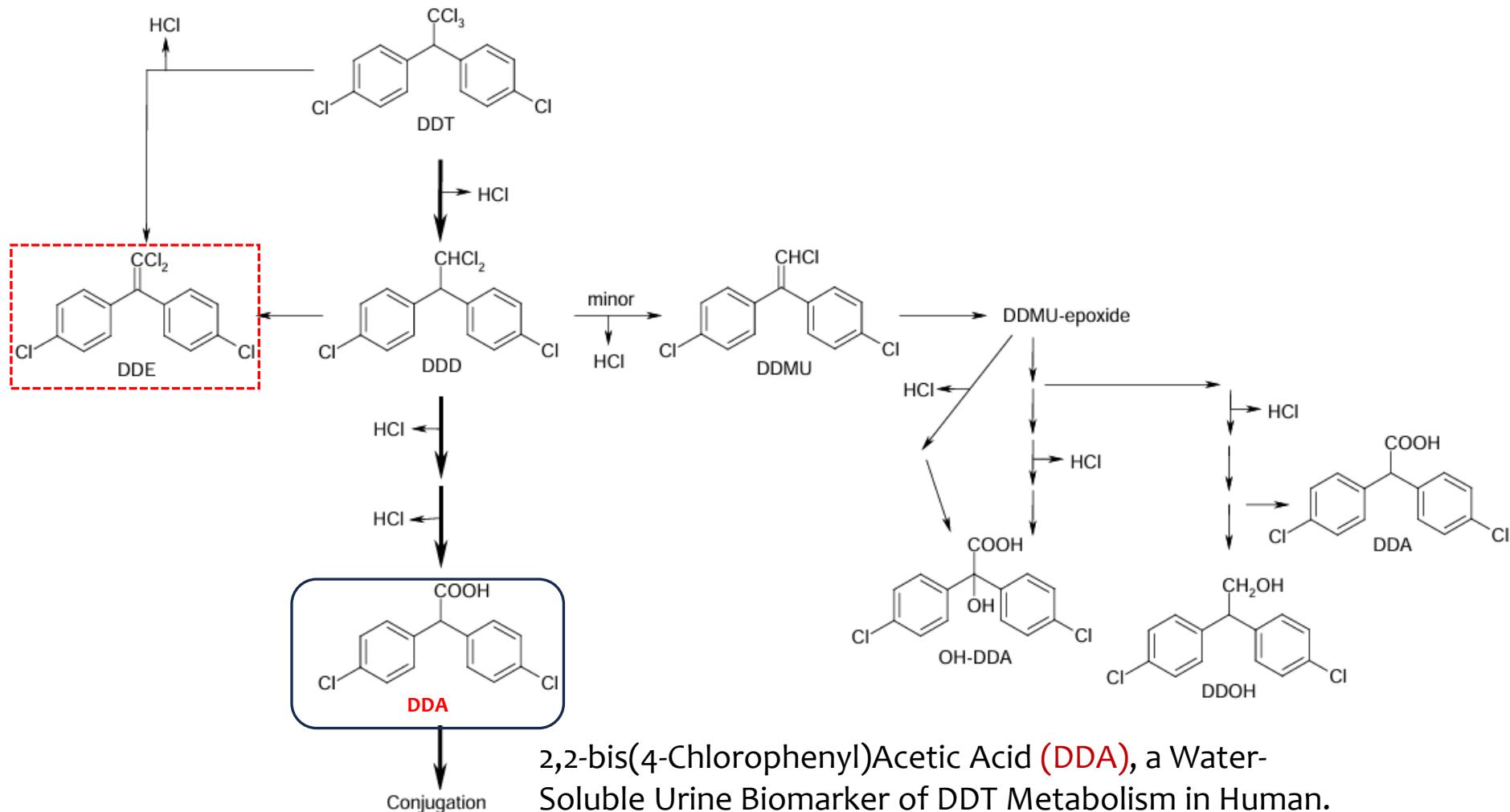


DDT metabolism in humans forms DDA, a stable, water-soluble metabolite that is a useful urine biomarker of active DDT exposure and ideal for DDT exposure monitoring and surveillance.

International Journal of Toxicology  
28(6) 528-533 <sup>a</sup>The Author(s) 2009

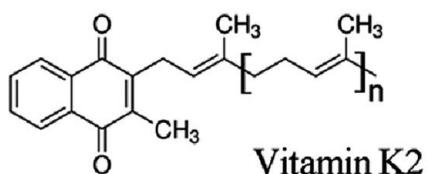
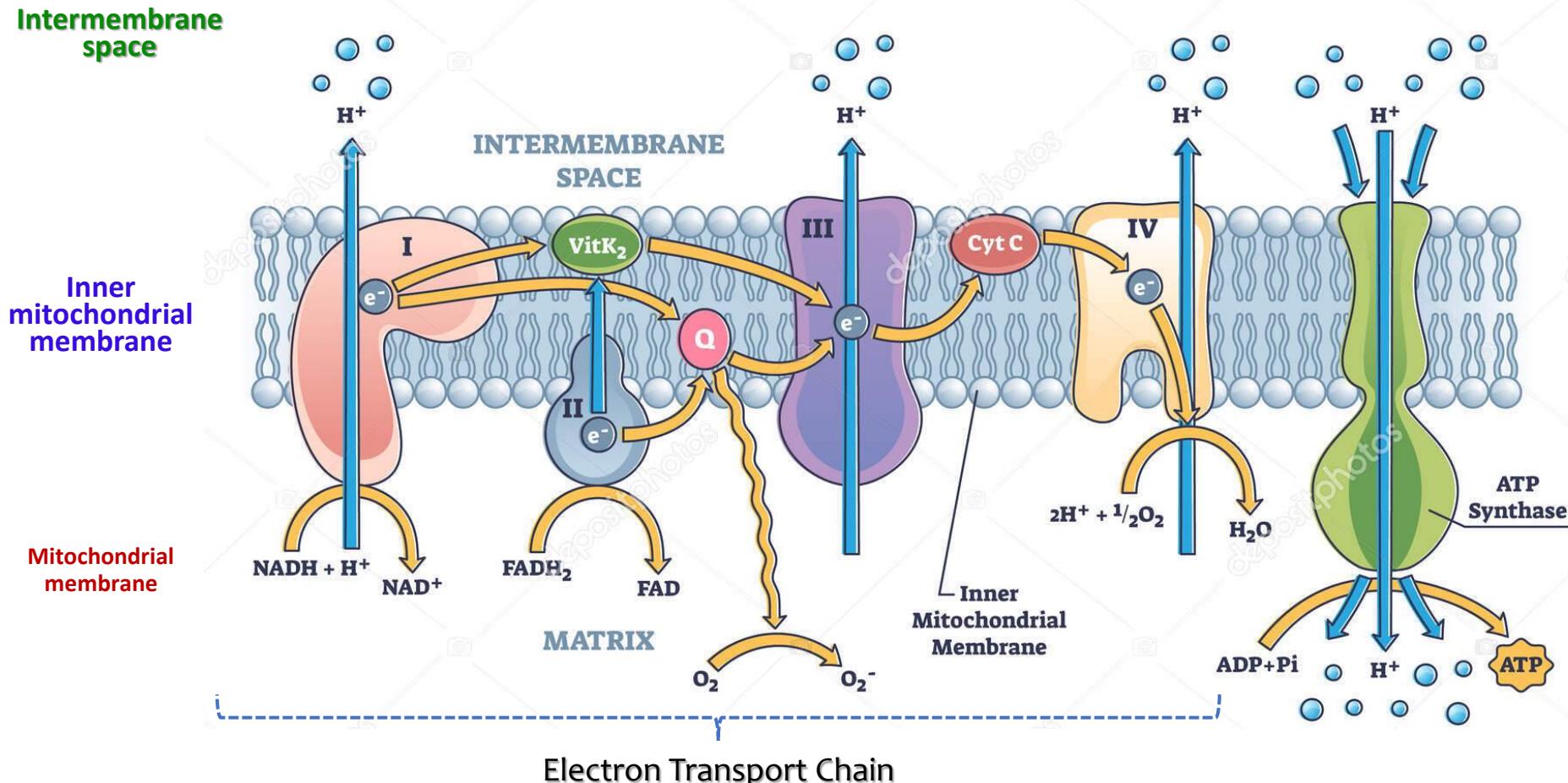
# Proposed metabolic scheme converting DDT to DDA, the principal metabolite excreted in Rat Urine

<https://www.atsdr.cdc.gov/toxprofiles/tp35-c3.pdf>



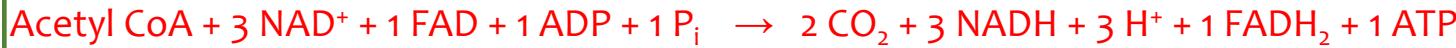
2,2-bis(4-Chlorophenyl)Acetic Acid (**DDA**), a Water-Soluble Urine Biomarker of DDT Metabolism in Human.  
<http://ijt.sagepub.com/cgi/content/abstract/28/6/528>

## Role of NADH and FADH<sub>2</sub> in the Electron Transport Chain

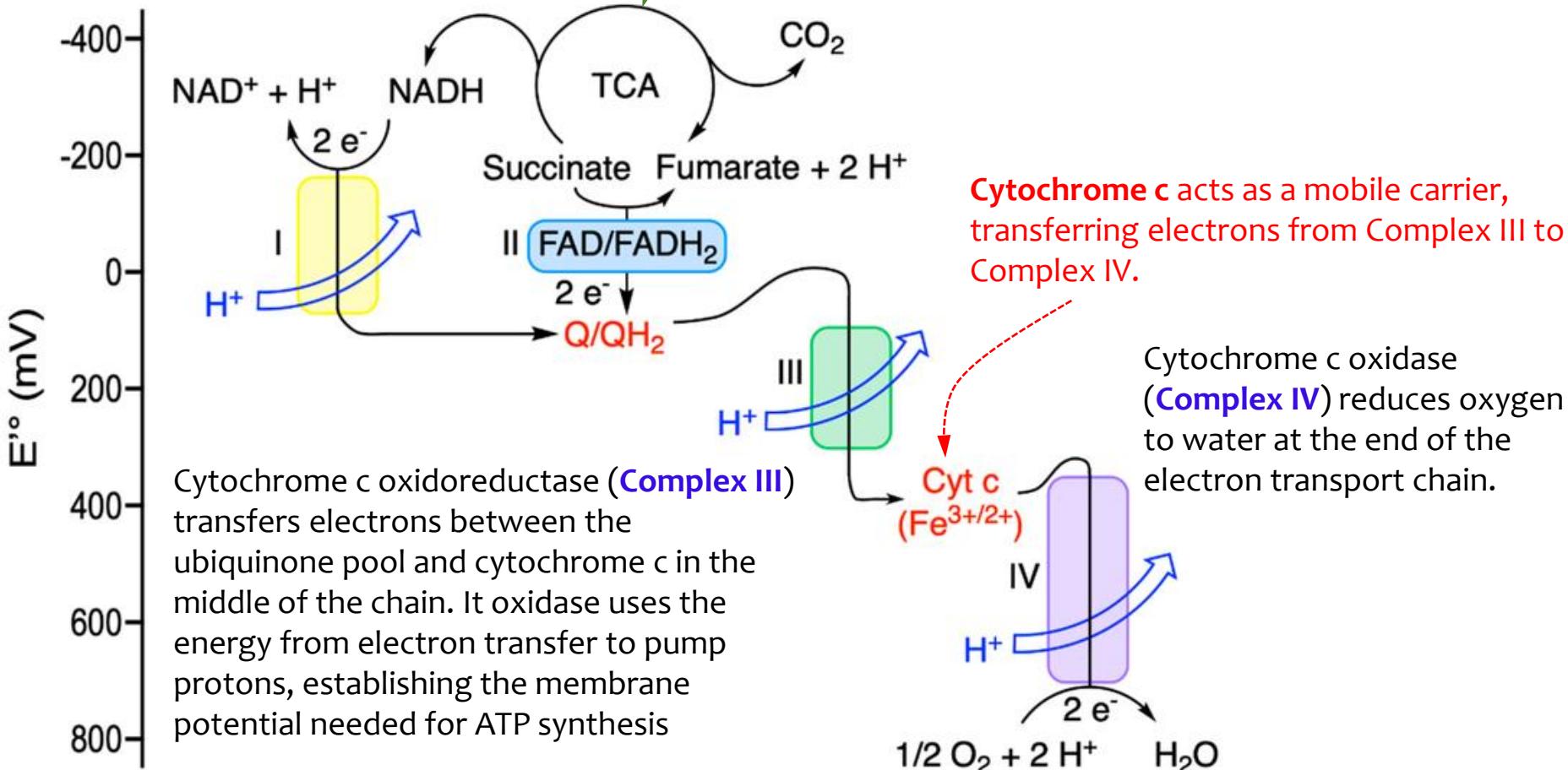


Author: Vector Mine  
<https://depositphotos.com/vector/electron-transport-chain-as-respiratory-embedded-transporters-outline-diagram-530772006.html>

The overall reaction/ equation of the TCA (tricarboxylic acid) cycle is:



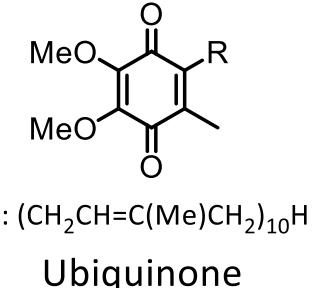
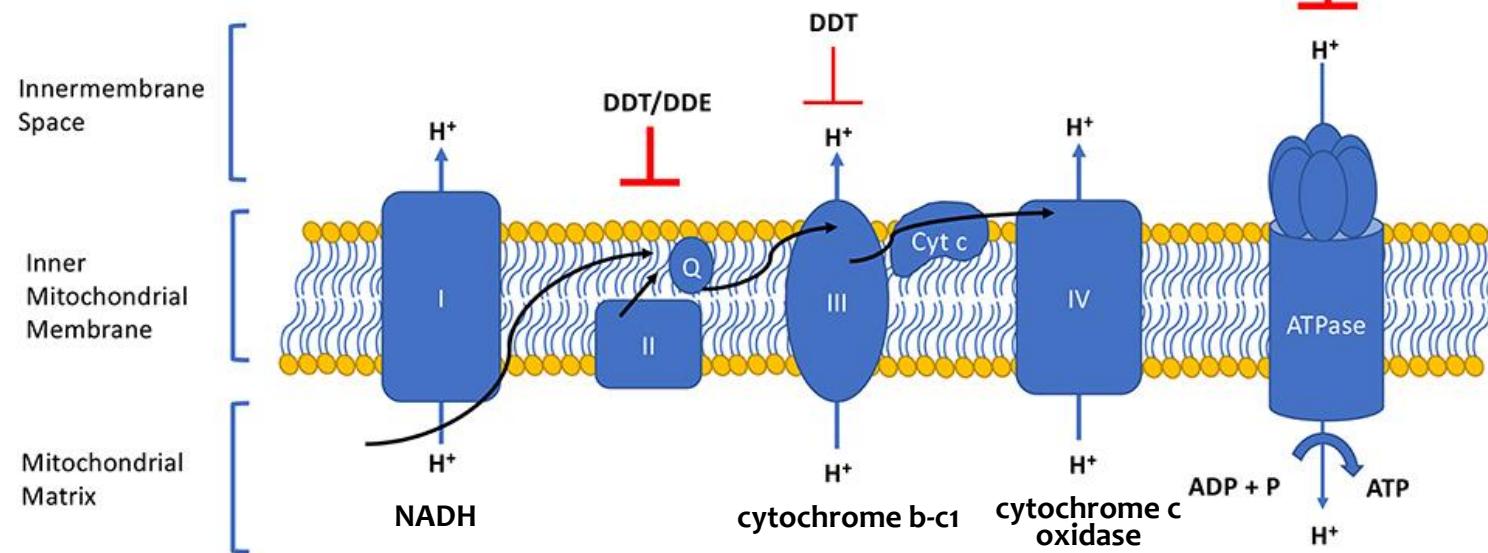
CoA: A coenzyme: Its main function is to deliver the acetyl group to the citric acid cycle (Krebs cycle) to be oxidized for energy production.



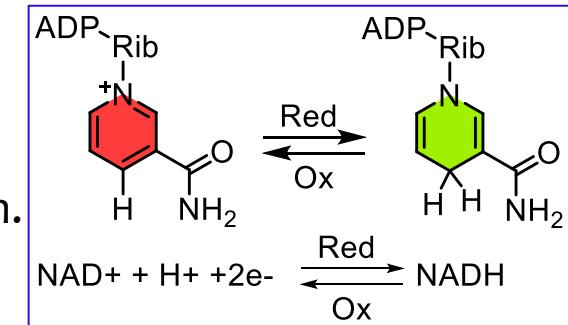
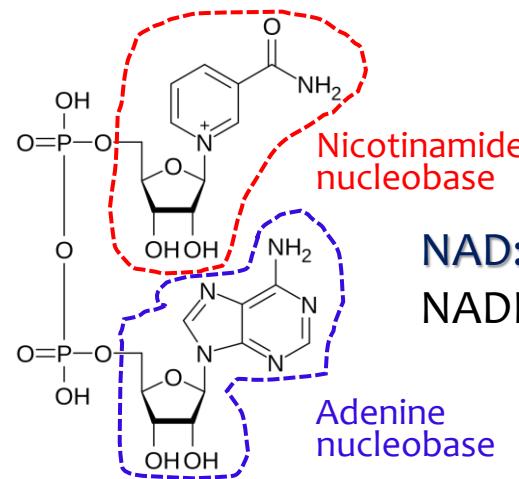
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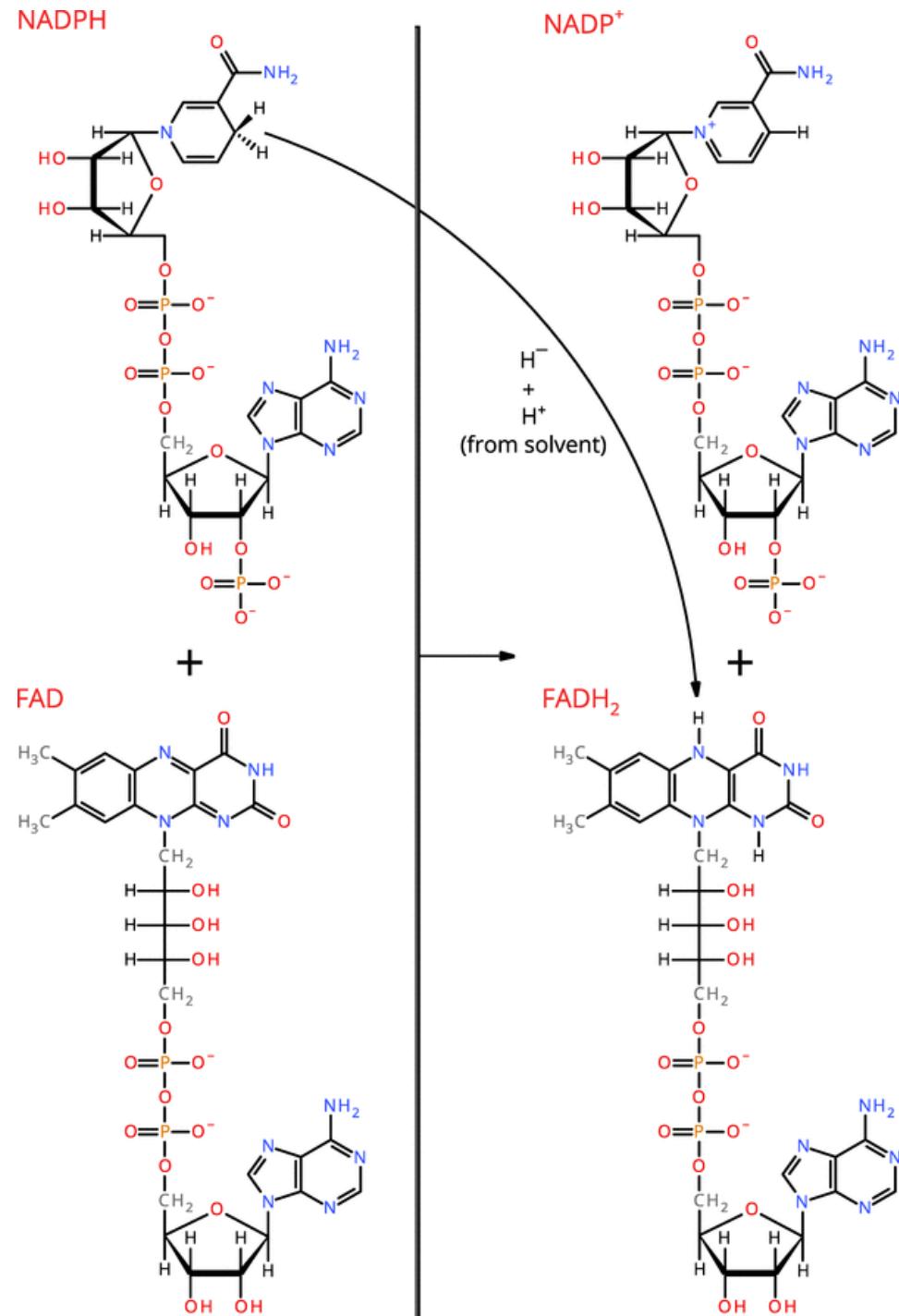
Strong evidence of impairment

Some evidence of impairment



**Oxidative phosphorylation occurs in the inner mitochondrial membrane.** It couples the oxidation of NADH and  $\text{FADH}_2$  (generated in glycolysis, TCA cycle, and  $\beta$ -oxidation) to the production of ATP via the electron transport chain (ETC) and ATP synthase (Complex V).





Reduction of FAD by NADPH. The nicotinamide group of NADPH transfers a hydride ion ( $H^-$ ) to the isoalloxazine ring of the FAD, forming  $FADH^-$ . After reaction with an additional  $H^+$  from the solvent,  $FADH^-$  becomes  $FADH_2$

J. Mol. Evol. 2017, 85(5-6)  
DOI: 10.1007/s00239-017-9821-9

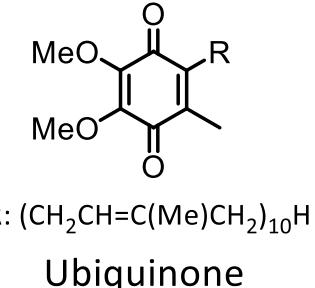
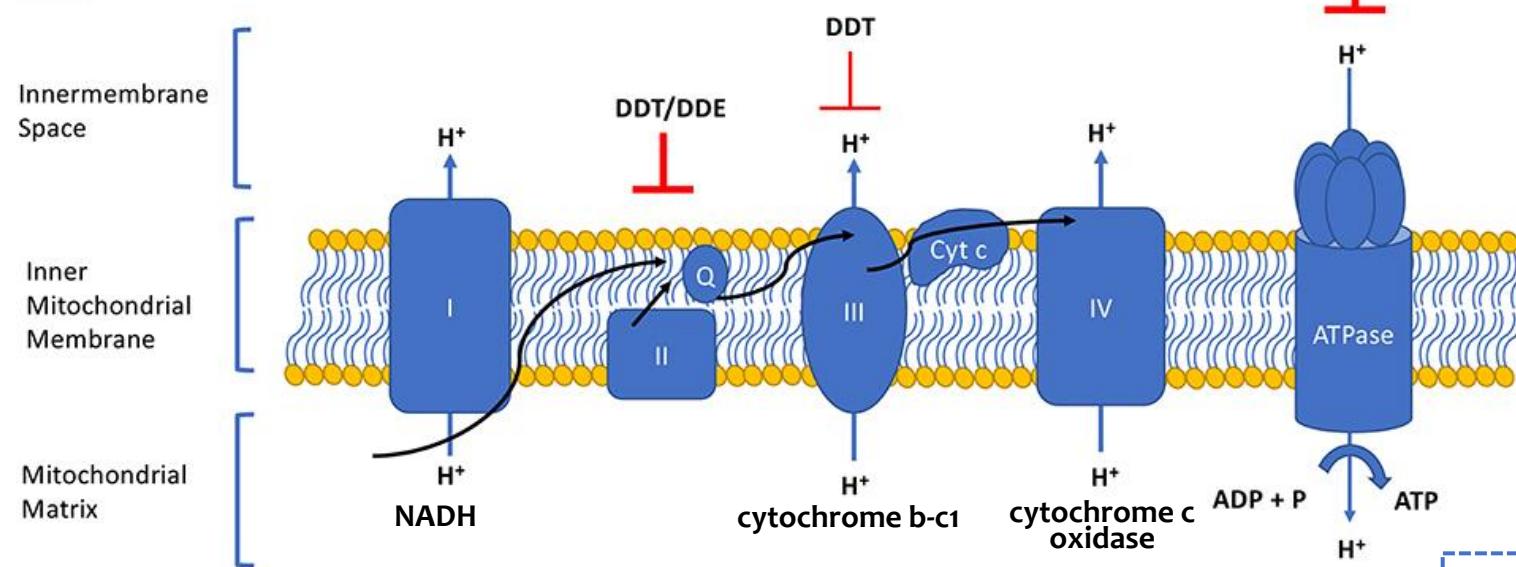
$FADH_2$  is the reduced form of FAD (flavin adenine dinucleotide): Flavin-N (5)-oxide, quinone, semiquinone, and hydroquinone are the four, redox forms of FAD. Quinone is the fully-oxidized form while hydroquinone or  $FADH_2$  is the fully-reduced form, which has accepted two electrons ( $2e^-$ ) and two protons ( $2H^+$ ). FAD, along with proteins, form flavoproteins.

<https://pediaa.com/difference-between-nadh-and-fadh2/>

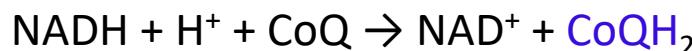
Key:

#### **Strong evidence of impairment**

#### | Some evidence of impairment



## **Complex I – NADH:Ubiquinone Oxidoreductase (Coenzyme Q: CoQ)**



## NAD: Nicotinamide Adenine Dinucleotide

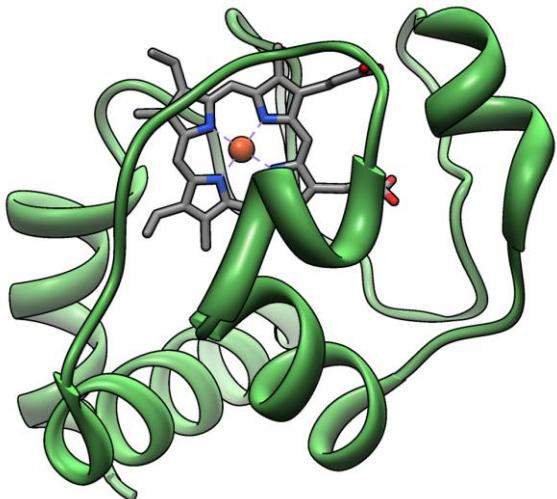
**Complex II – Succinate Dehydrogenase**       $\text{Succinate} + \text{CoQ} \rightarrow \text{Fumarate} + \text{CoQH}_2$

### **Complex III: cytochrome bc<sub>1</sub> complex or ubiquinol–cytochrome c oxidoreductase**

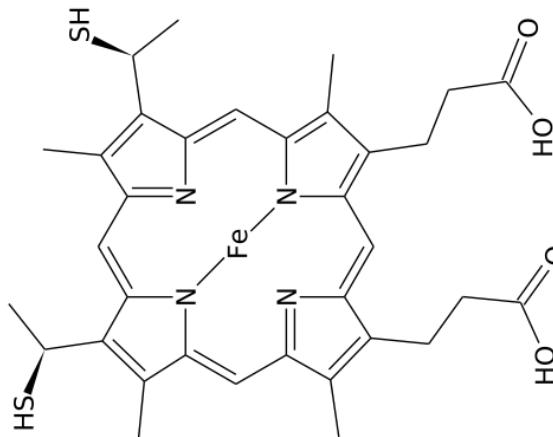
Transfers electrons from **ubiquinol (CoQH<sub>2</sub>)** to **cytochrome c**, while **pumping protons (H<sup>+</sup>)** into the intermembrane space to help build the **proton motive force** used for ATP synthesis.

Overall reaction:  $\text{CoQH}_2 + 2\text{Cyt c}(\text{Fe}^{3+}) \rightarrow \text{CoQ} + 2\text{Cyt c}(\text{Fe}^{2+}) + 4\text{H}^+$  (intermembrane space)

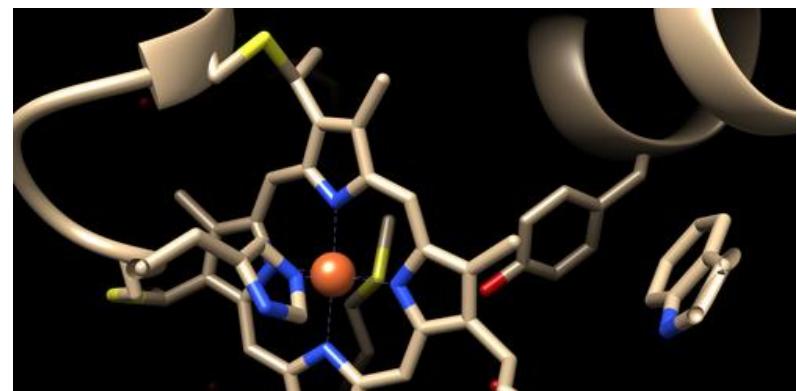
**Complex IV:** cytochrome c oxidase, is the segment where  $4e^-$  are removed from four molecules of cytochrome c and transferred to oxygen to produce two water molecules.



# High-resolution three-dimensional structure of horse heart cytochrome c.” J Mol Biol. 1990 Jul 20;214(2):585-95



Heme prosthetic group of cytochrome c, consisting of a rigid porphyrin ring coordinated with an iron atom.



The cytochrome complex, or cyt c, is a **small hemeprotein found loosely associated with the inner membrane of the mitochondrion**. It transfers electrons between Complexes III (Coenzyme Q – Cyt c reductase) and IV (Cyt c oxidase). It is capable of undergoing oxidation and reduction as its iron atom converts between the ferrous and ferric forms, but does not bind oxygen. In humans, cytochrome c is encoded by the CYCS gene.

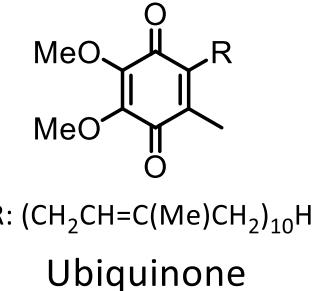
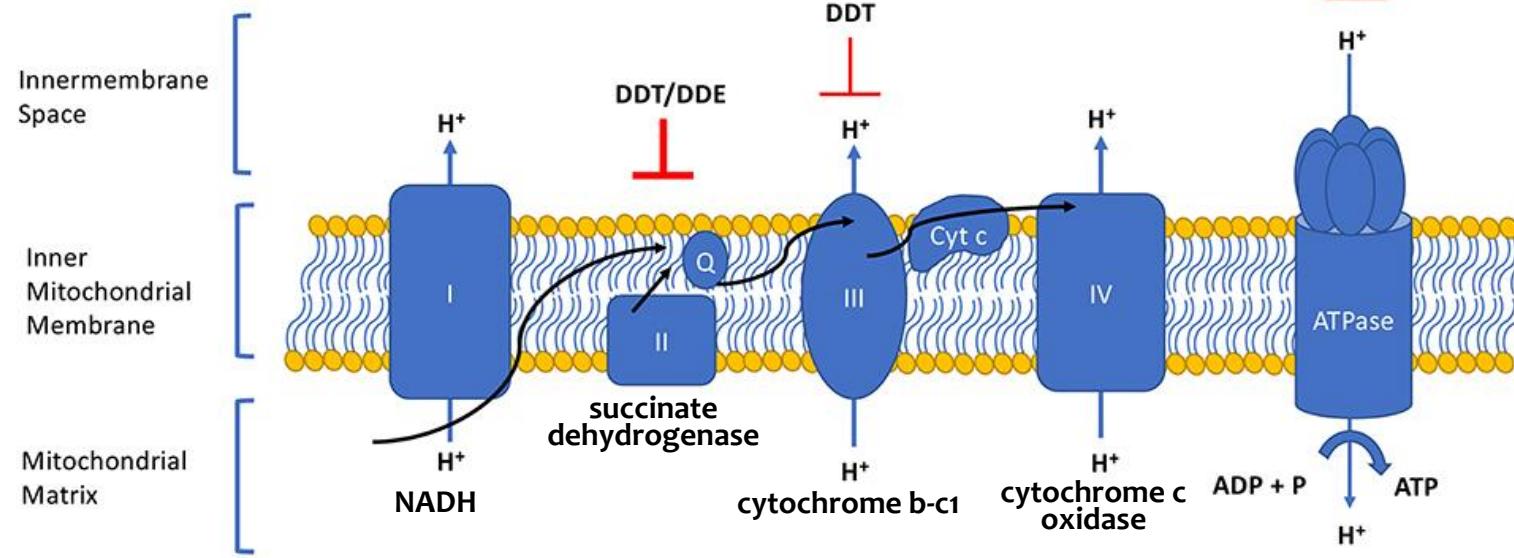
[[https://en.wikipedia.org/wiki/Cytochrome\\_c](https://en.wikipedia.org/wiki/Cytochrome_c)]

**Key:**

Strong evidence of impairment

Some evidence of impairment

## Oxidative Phosphorylation Impairment by DDT and DDE



**Summary of DDT and DDE effects on the electron transport chain and oxidative phosphorylation process.**  
Arrows indicate the direction of the electron flow.

A cyclic flow of these electron carriers occurs within the whole respiratory system in the mitochondrial inner membrane. Thus, starting upstream in the redox potential gradient, the oxidised UQ is reduced upon interaction with Complex I or II, proceeding via an intermediary, the semiquinone UQH, on either complex to become the fully reduced ubiquinol (UQH<sub>2</sub>), which is then released to carry electrons to Complex III, where UQH<sub>2</sub> is re-oxidised by releasing its protons and transferring its electrons to Complex III, before returning for repeated cycles.

Complex IV: cytochrome c oxidase, is the segment where 4e<sup>-</sup> are removed from four molecules of cytochrome c and transferred to oxygen to produce two water molecules. Simultaneously, protons are moved from the mitochondrial matrix to the inner membrane thus contributing to the mitochondrial proton gradient.

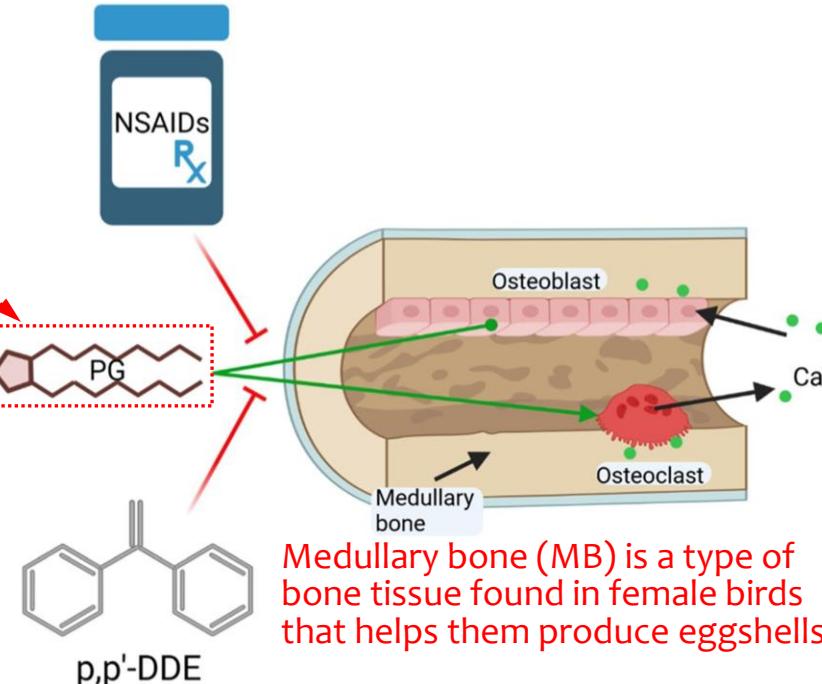
Osteoblasts and osteoclasts are special cells that help your bones grow and develop. Osteoblasts form new bones and add growth to existing bone tissue. Osteoclasts dissolve old and damaged bone tissue so it can be replaced with new, healthier cells created by osteoblasts.

Osteoblasts and osteoclasts work together to maintain healthy bones through two key processes—bone formation and bone resorption.

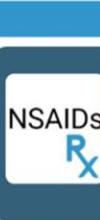
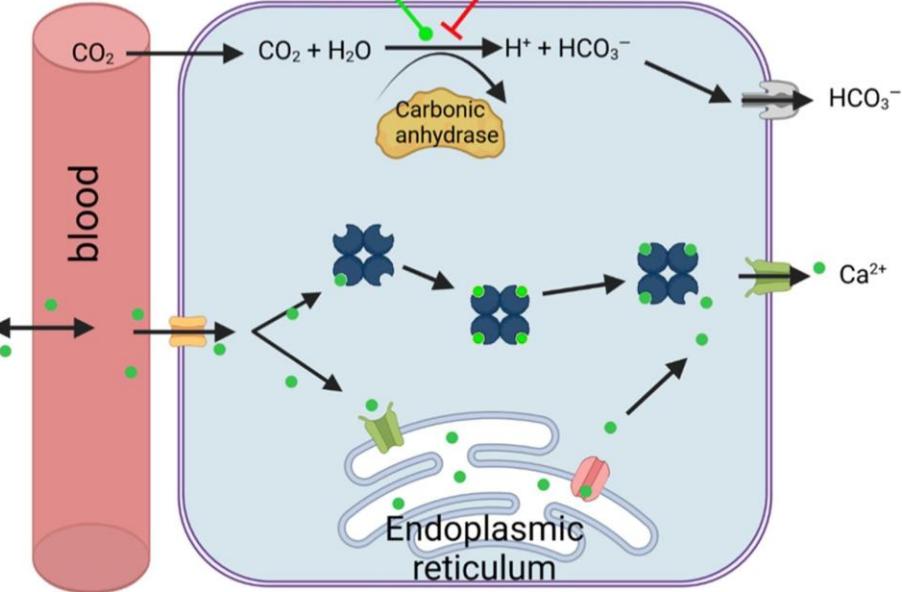
- Bone formation: Osteoblasts are responsible for producing new bone tissue. They secrete collagen and other proteins that form the bone matrix, which later hardens as minerals like calcium and phosphate are deposited. Osteoblasts are triggered by chemical reactions or hormones when a bone grows or changes. They create and release (secrete) a mix of proteins called bone matrix. Bone matrix is made of proteins like collagen mixed with calcium, phosphate and other minerals.
- Bone resorption: Osteoclasts dissolve and remove old or damaged bone by releasing acids and enzymes that break down the mineralised matrix. Osteoclasts release enzymes that break down old bone. They trigger chemical reactions on the surface of old bone tissue that dissolve it and create space for newer, stronger tissue to form in its place.

Prostaglandins (PGs) act on the COX enzyme and inhibit the synthesis of its metabolites, such as PGE<sub>2</sub>. NSAIDs have an adverse effect on bone, inhibiting osteoblast growth.

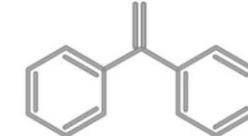
[Osteoarthritis Cartilage, 1999, 7, 419-21]



**Medullary bone (MB)** is a type of bone tissue found in female birds that helps them produce eggshells.

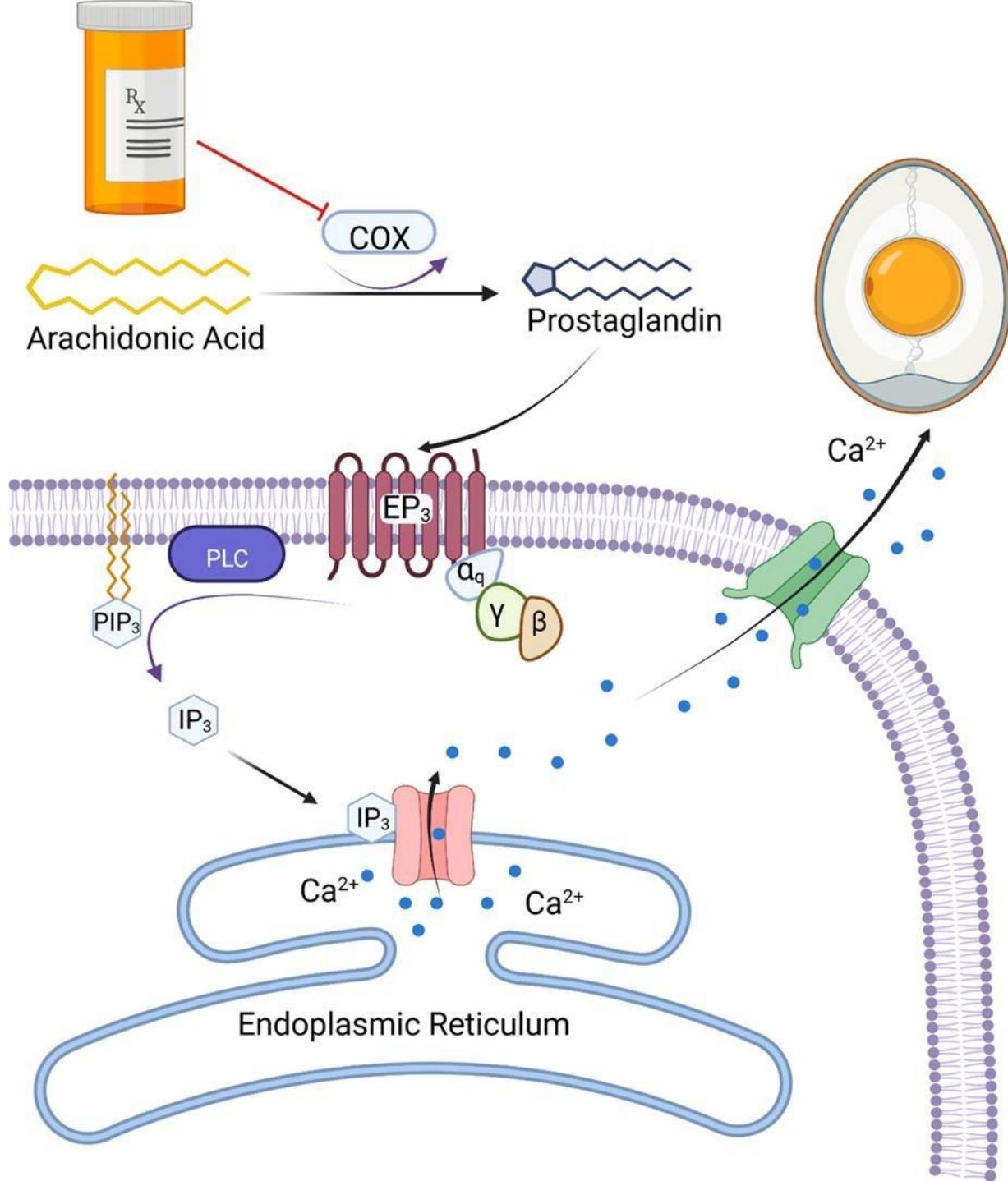


p,p'-DDE



Role of Non-steroidal anti-inflammatory drugs (NSAIDs) and p,p'-DDE in regulating osteocytes (osteoblasts and osteoclasts) through suppression of prostaglandin, and the regulation of long-term, calcium (Ca<sup>2+</sup>) stores from medullary bone, as a source of Ca<sup>2+</sup> for epithelial cells in the shell gland for the eggshell formation.

[The hormone calcitonin **decreases blood calcium levels** by **inhibiting osteoclasts**, **stimulating osteoblasts**, and calcium excretion by the kidneys]



How does p,p'-DDE cause thin-shelled egg?



**Affects medullary bone.**

**Carbonic anhydrase inhibition**

**Inhibition of CaATPase**

Calcium ATPase (CaATPase) is a pump that moves calcium across a membrane, often against a concentration gradient. It uses the energy of adenosine triphosphate (ATP) to do this.

Inhibition of prostaglandin synthetase: inhibits prostaglandin synthesis in the eggshell gland mucosa of sensitive bird species, which can lead to eggshell thinning.

There is evidence that prostaglandin (PG)F-2a decreases blood flow to the ovary or corpus luteum but this does not occur in the guinea pig. [J. Reprod. Fert. 1982, 64, 227](#).

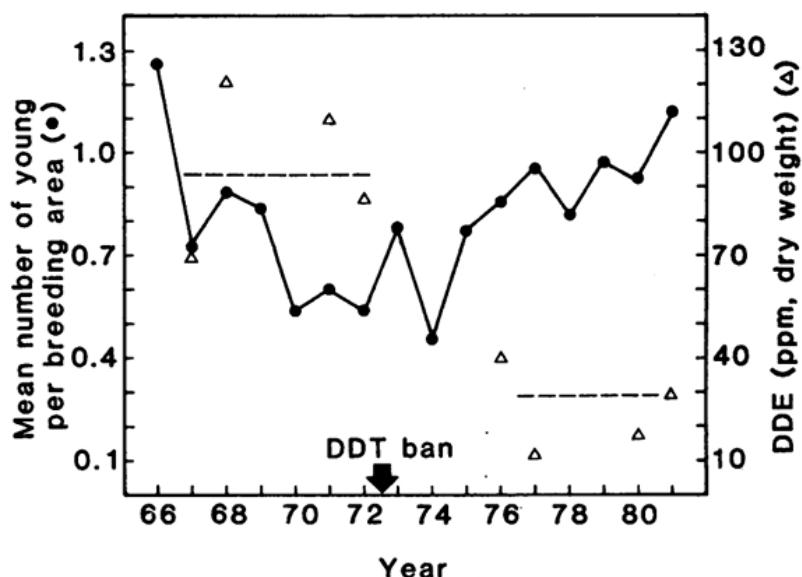
Eggshell development is a crucial and complex reproductive event achieved through a sequence of steps relying on an array of hormones, signalling molecules, enzymes, organic compounds, and minerals. Mineralization begins during the egg's travel from the ovary to the uterus when it enters the isthmus. **The eggshell consists of approximately 95% inorganic minerals, mostly calcite ( $\text{CaCO}_3$ ), and ~3.5% organic matrix, with the remaining portion consisting of water.** The unshelled egg contains two uncalcified protein layers that enter the shell gland (i.e., uterus), **increasing prostaglandin E2 (PGE2) levels.**

- ✓ Simultaneous with the influx of PGE2, the uterine lining (epithelium) floods the intrauterine fluid with calcium ( $\text{Ca}^{2+}$ ) and bicarbonate ( $\text{HCO}_3^-$ ) ions primarily through uterine glandular cells. These spontaneously precipitate into calcite and are deposited onto the outer organic eggshell membranes, forming the hard eggshell.
- ✓ The calcified egg contains numerous pores that allow water and gas to be exchanged during embryonic development.
- ✓ Calcium needed to form eggshells is obtained from the diet and continuously replenishes in the blood.
- ✓ Excess calcium is stored in the medullary bone, an estrogen-dependent, specialized tissue produced only in female laying birds, and which serves as a long-term calcium repository. The medullary bone acts as a labile source of calcium when demands exceed dietary supplies.

[Environment International 171 (2023) 107638]

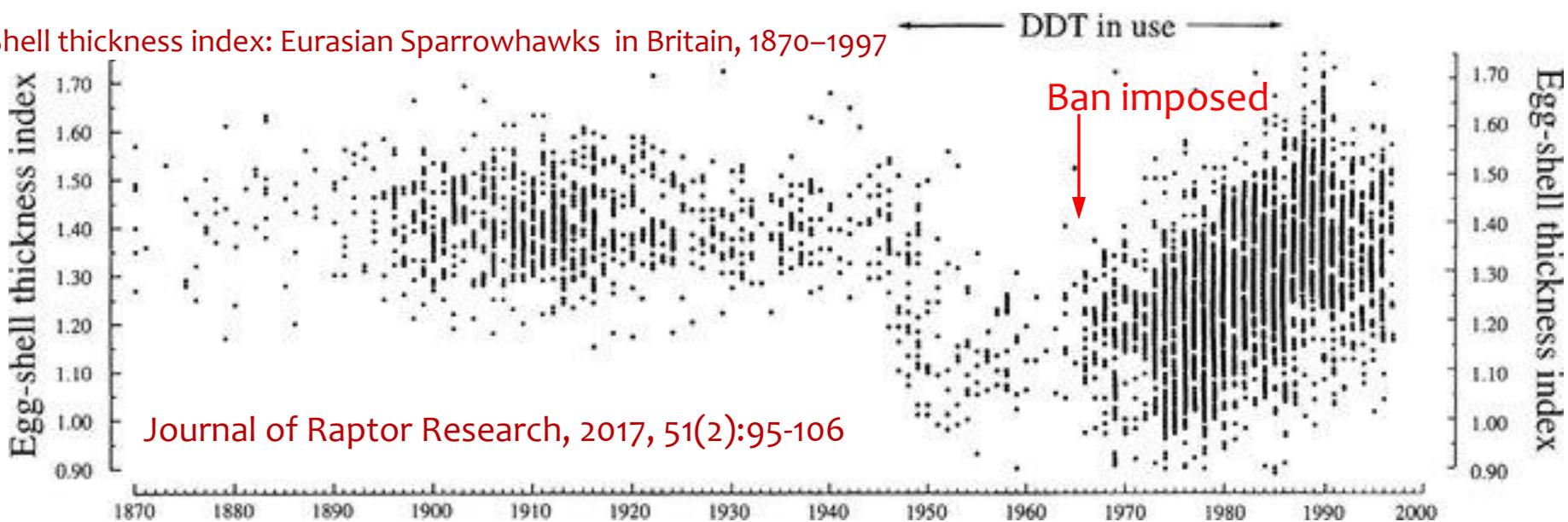
Laboratory experiments showed that DDE could cause eggshell thinning. Field studies showed that field exposures to DDE, a metabolite of DDT, were sufficient to cause effects in many species of birds based on the stressor-response relationship

Science, 1982, 218, 1232-1235



Summary of average annual bald eagle reproduction and DDE residues in addled eggs in northwestern Ontario, 1966 to 1981. Dashed lines indicate weighted mean concentrations of DDE residues in clutches before (94 ppm) and after (29 ppm) the ban of DDT. Means for the 16-year period are 57 ppm DDE (weighted mean) and 0.82 young per breeding area

Shell thickness index: Eurasian Sparrowhawks in Britain, 1870–1997



Journal of Raptor Research, 2017, 51(2):95-106

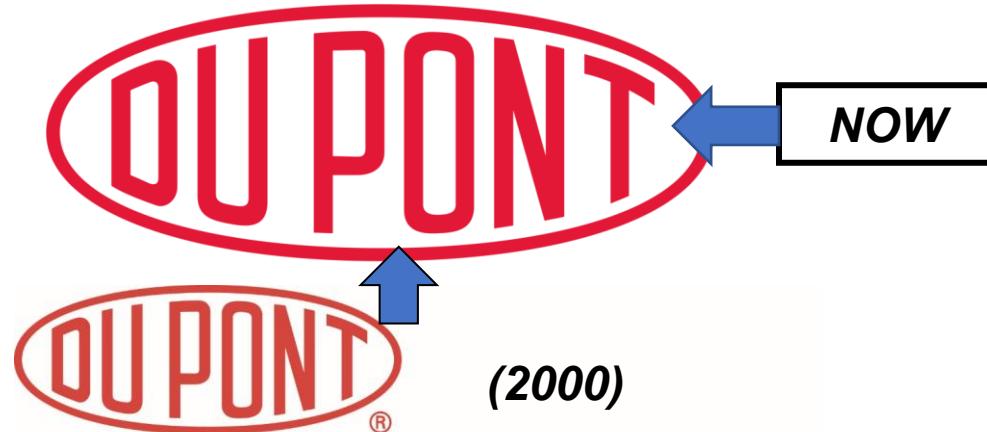
Environmental groups that had previously shown no interest in malaria, such as the World Wildlife Fund, started to profess expertise in alternatives to DDT use—any alternative, as long as it was not DDT. Between 1997 and 2000, member states of the United Nations Environment Program negotiated

the Stockholm Treaty on Persistent Organic Pollutants, with DDT as one of the “dirty dozen” chemicals targeted. Green groups wanted the chemical banned and set 2007 as the year for its demise. Ironically, because of the disastrous surge in malaria cases in South Africa, coupled with Johannesburg being chosen as the final negotiating location in December 2000, DDT was not banned; instead, it was to be phased out when “cost-effective alternatives” were available. In 2000, the South African Department of Health reintroduced DDT. In just one year, malaria cases fell nearly 80% in KwaZulu-Natal province, which had been hit worst by the epidemic. In 2006, malaria cases in the province were approximately 97 below the previous high of 41,786 in 2000. DDT remains an essential part of South Africa’s malaria control program, and the success of its use in that country has encouraged other countries in the region to follow suit.

## The 12 initial POPs under the Stockholm Convention [2024]

Initially, twelve POPs have been recognized as causing adverse effects on humans and the ecosystem and these can be placed in 3 categories:

- Pesticides: aldrin, chlordane, DDT, dieldrin, endrin, heptachlor, hexachlorobenzene, mirex, toxaphene;
- Industrial chemicals: hexachlorobenzene, polychlorinated biphenyls (PCBs); and
- By-products: hexachlorobenzene; polychlorinated dibenzo-p-dioxins and polychlorinated dibenzofurans (PCDD/PCDF), and polychlorinated biphenyls (PCBs).



*The miracles of science*™

**Better Things for Better Living**  
(1985)

**Better Things for Better Living through Chemistry**  
(1935)

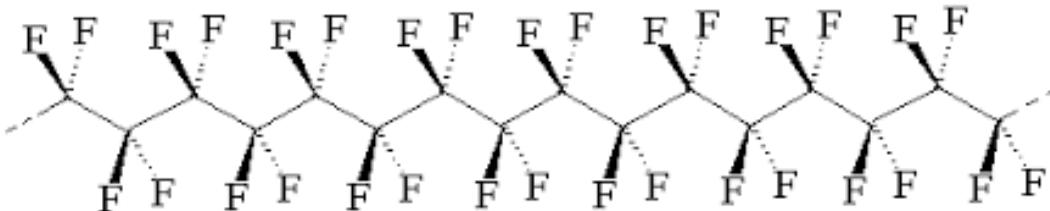
## Du Pont and Nylon:

Nylon was first introduced by DuPont around 1939 and was in extremely high demand in the United States, with up to 4 million pairs of stockings bought in one day. During World War II, nylon was used extensively for parachutes and other war materials, such as airplane cords and ropes and the supply of nylon consumer goods was curtailed.

During World War II, Japan stopped using supplies made out of silk, and so the United States had difficulty importing silk from Japan. Eventually, the U.S was unable to import any silk. So, Du Pont thought of an idea to convince the army that nylon is a much more effective material than silk. Du Pont was able to convince the army, and nylon fabric became increasingly popular because of its elasticity and shrink-proof, moth-proof material.

Nylon stockings became increasingly popular on the black market and sold for up to \$20 per pair. Because nylon stockings were so widely sought-after, they also became the target of crime. In Louisiana, one household was robbed of 18 pairs of nylons. Similarly, robbery was ruled out as the motive of murder in Chicago because the nylons were untouched.

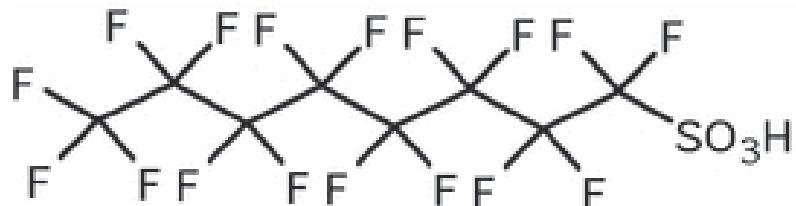
# Du Pont and Teflon



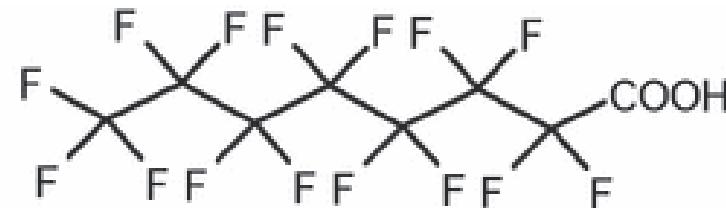
## "Teflon"

The story of Teflon™ began April 6, 1938, at the Chemours Jackson Laboratory (by Dr. Roy J. Plunkett) in New Jersey discovery of Polytetrafluoroethylene (PTFE) in 1938 while working with gases related to Freon™ refrigerants.

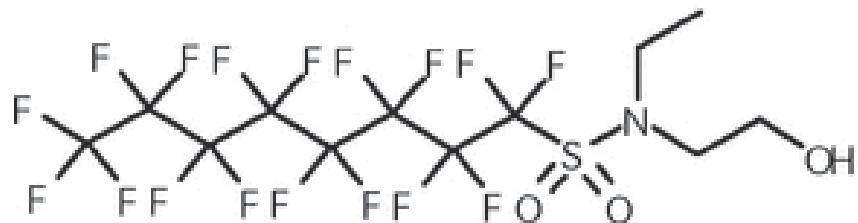
Teflon is the trade name was coined by Chemours (a company created by DuPont) for Polytetrafluoroethylene (PTFE) in 1945. PTFE is inert to virtually all chemicals. Teflon, a product best known for its use in non-stick cookware, but also widely used in a variety of other consumer products, including waterproof clothing and furniture, food packaging, self-cleaning ovens, airplanes and cars.



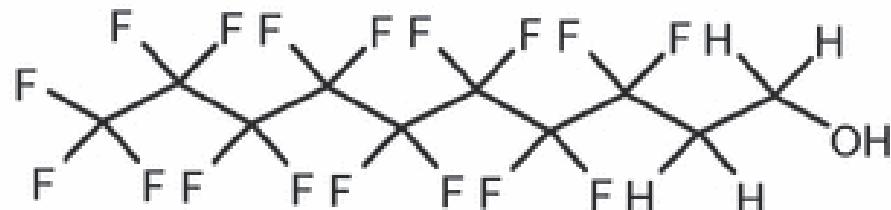
PFOS, perfluorooctane sulfonic acid,  $\text{C}_8\text{HF}_{17}\text{SO}_3$



PFOA, perfluorooctanoic acid,  $\text{C}_8\text{HF}_{15}\text{O}_2$



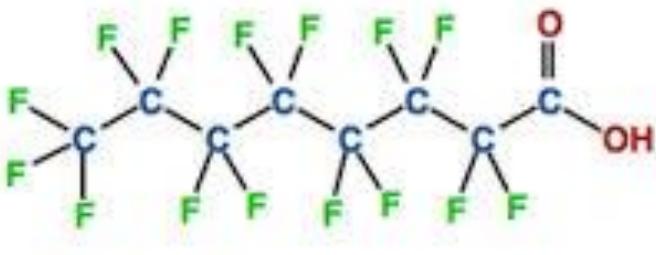
N-Ethylperfluorooctane sulfonamidoethanol (EtFOSE)



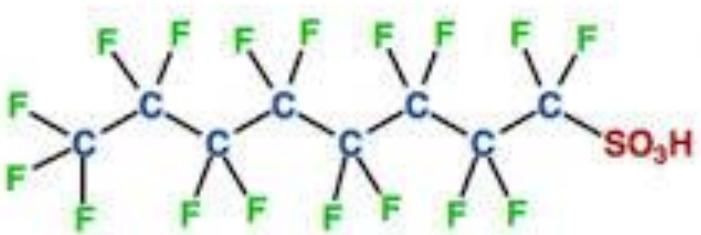
Fluorotelomer alcohol 8:2 FTOH (1H,1H,2H,2H-Perfluorodecanol)

One of the key ingredients in DuPont's Teflon was C8, a toxic, man-made chemical developed by Minnesota Mining and Manufacturing Company (3M). The chemical, also known as **PFOS or PFOA**, is what gave Teflon its non-stick properties.

Perfluoroctanoic acid ( $C_7F_{15}COOH$ , PFOA) is an aqueous anionic surfactant and a persistent organic pollutant.



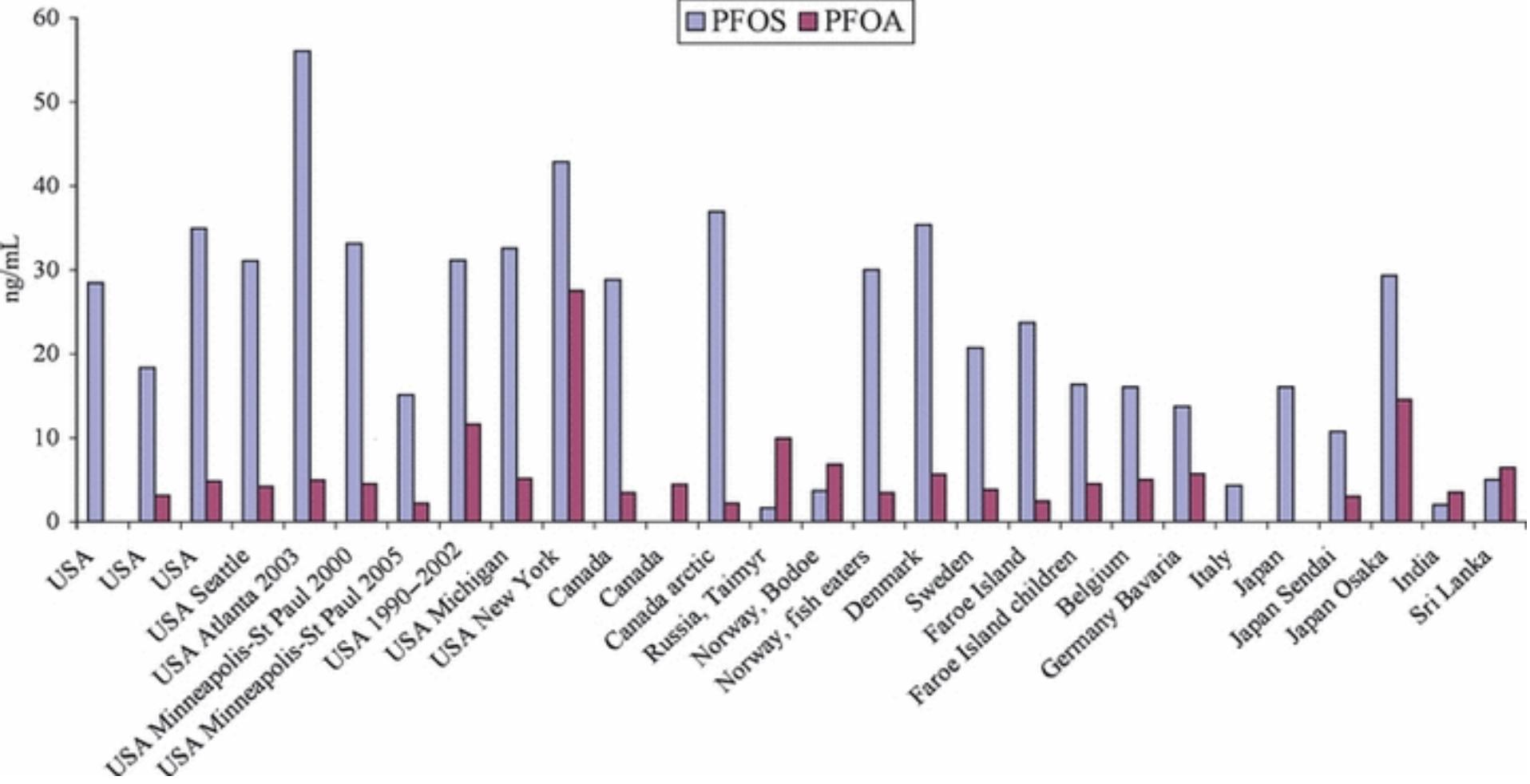
PFOA - perfluoroctanoic acid



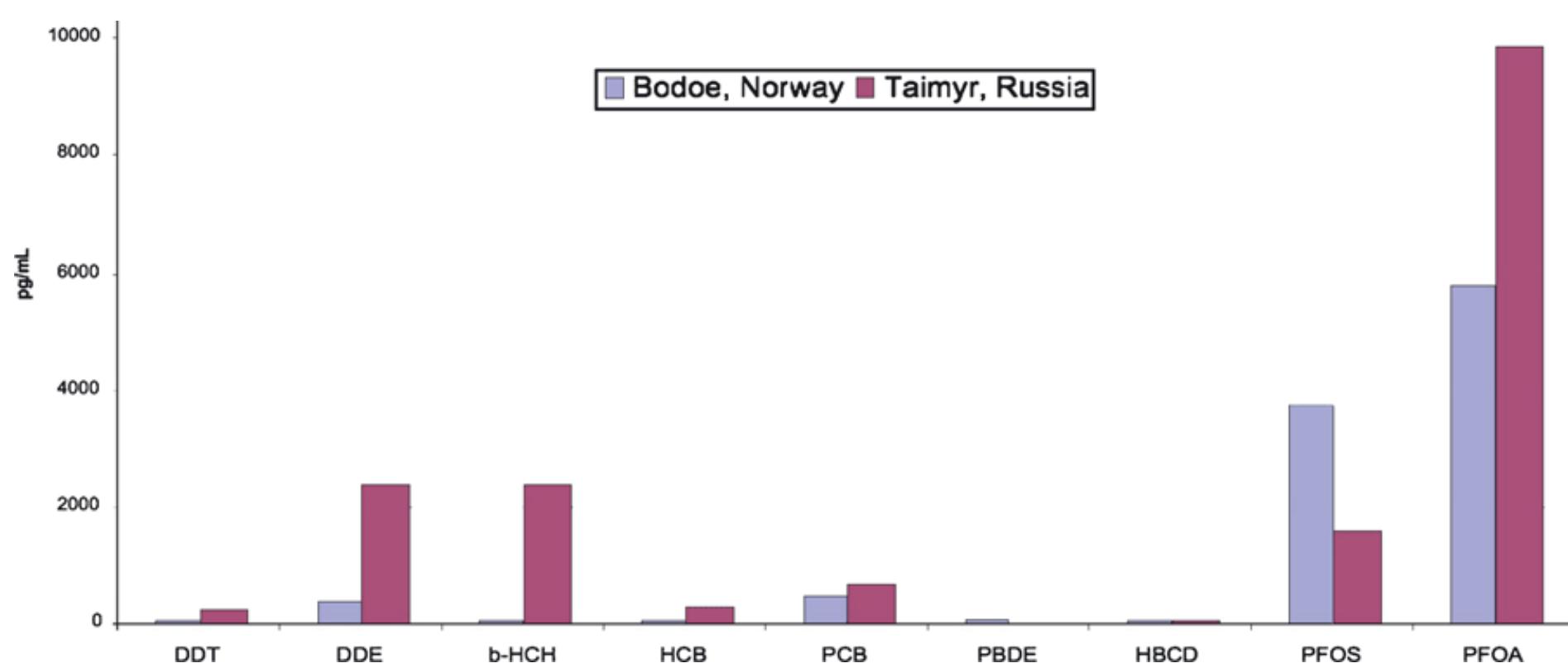
PFOS - perfluorooctanesulfonic acid

PFOA is found in the blood of an estimated 99.7 % of Americans. The eight main fluoropolymer manufacturers, including DuPont, participate in the U.S. Environmental Protection Agency's 2010/2015 PFOA Stewardship Program, which seeks to eliminate PFOA and related chemicals from products and factory emissions by 2015.

Exposure to C8 in drinking water is linked to six different diseases: kidney cancer, testicular cancer, ulcerative colitis, thyroid disease, preeclampsia and high cholesterol.



Typical average concentrations of perfluorooctane sulfonic acid and perfluorooctanoic acid in blood (serum/plasma) from various countries [Int. Jr. Andrology, 2007, 31, 161–169 and refe. Therein]



Persistent organic pollutants in blood plasma from pregnant women living in Norwegian and Russian Arctic [Int. Jr. Andrology, 2007, 31, 161–169 and refe. Therein]

The effects on hormone levels in rodents are reflected in changes in the exposure to perfluorooctanoate and results in Leydig cell hyperplasia and eventually the development of Leydig cell adenomas. A study with adult rats exposed to  $\geq 5$  mg perfluorododecanoic acid/kg bw daily for 2 weeks also showed a reduced gene expression of many genes involved in a reduced serum testosterone level, which accounts for the compromised fertility in the adults.

Leydig cell hyperplasia is common among infertile men who, as a group, also show lower testosterone levels than comparable normal controls. [Int. Jr. Andrology, 2007, 31, 161–169 and refe. Therein]

The international awareness and concern is increasing. In 2000, the main producer (3M Company), voluntarily stopped the production of one of the chemicals (PFOS), and a ban of some fluorotelomers has been introduced in Canada. In Europe, the EU countries will ban PFOS and its derivatives from the summer of 2008. However, PFOS is only a small part of the problem. The family of PFCs consists of several hundreds other unrestricted chemicals. Because the exposure to polyfluorinated substances is so considerable, and uses seem to increase, there is an urgent need to resolve, what effect such exposure has on humans. [Int. Jr. Andrology, 2007, 31, 161–169 and refe. Therein]

Rob Bilott was a corporate defense attorney for eight years. Then he took on an environmental suit that would upend his entire career, and expose a decades-long history of chemical pollution. In March 2001, Robert Bilott embarked on an ambitious plan to force DuPont to come clean — to tell what it knew about C8 and, he hoped, eliminate the chemical from the water consumed by the large section of the population of the country.

### Possibly the first whistleblower:

The farmer, Wilbur Tennant of West Virginia, said that his cows were dying. He believed that the DuPont chemical company, which until recently operated a site in that region was responsible. Till that time, Bilott worked almost exclusively for large corporate clients. His specialty was defending chemical companies. Several times, Bilott had even worked on cases with DuPont lawyers.

In his law suit he presented documents showing that DuPont, which since the early 1950s had used C8 to manufacture Teflon and other products in its Parkersburg plant, had known for years that C8 posed health dangers and had spread beyond the company's West Virginia plant into local sources of drinking water.

By some measures, Bilott has in fact been successful in slamming DuPont, but 14 years after he sent his evidence to the EPA, the company has managed to avoid a full reckoning for its actions. And C8, which is in the bloodstream of 99.7 percent of Americans, remains unregulated at the national level. Although Bilott and his clients eventually prevailed in a ground-breaking class-action lawsuit filed the same year he approached the EPA, that settlement had limited applicability. Action by the EPA could hold DuPont accountable nationally.

Environmental Health Perspectives, 2013, volume 121, number 11-12, A 340  
Toxicology and Applied Pharmacology, 2017.07.001, 330, (9-21); 10.1016/j.taap.  
Environ. Sci. Technol. 2018, 52, 14, 8005–8015  
Encyclopedia of Toxicology, 3<sup>rd</sup> Edn. 2014 Elsevier, Inc.

<https://theintercept.com/2015/08/20/teflon-toxin-dupont-slipped-past-epa/>

# A Timeline of DuPont and C8

<https://theintercept.com/2015/08/20/teflon-toxin-dupont-slipped-past-epa/>

DuPont registers the Teflon trademark.

3M and DuPont become aware that C8 is accumulating in workers' blood and body tissues, causing elevated liver enzyme; several Rhesus monkeys deteriorate and die after being fed C8 in a 3M study.

3M decides to stop making C8; Bernard Reilly warns his DuPont colleagues that C8 communications may be subject to discovery.

DuPont agrees to phase out its use of C8 by 2015

DuPont becomes aware of C8's possible toxicity, the same year a French engineer first applied Teflon to a pan.

DuPont monitors local drinking water for C8 contamination; concludes that reducing C8 emissions is not "economically attractive."

The EPA initiates a priority review of C8.

1945 1951 1954 1961 1978 1981 1984 1999 2000 2001 2002 2005 2006

DuPont begins using C8 in the manufacture of Teflon at its West Virginia plant.

3M releases rat study finding birth defects; DuPont employee Sue Bailey's child Bucky born with birth defects.

DuPont settles with Tennant for an undisclosed sum; attorney Robert Bilott files class action suit against DuPont and provides the EPA with DuPont's internal documents on C8

DuPont researchers confirm that C8 is toxic.

Wilbur Tennant's cows die after drinking water contaminated with C8 and he files suit against DuPont.

DuPont settles \$343 million class action lawsuit and agrees to fund C8 health project to study the chemical's health affects; EPA fines DuPont \$10.25 million for failing to report "substantial risk of injury to human health" from C8 (PFOA).

## Endocrine disruption of vitamin D activity by PFOA.

Perfluorooctanoic acid (PFOA) induces severe health consequences, such as neonatal mortality, neurotoxicity, and immunotoxicity.

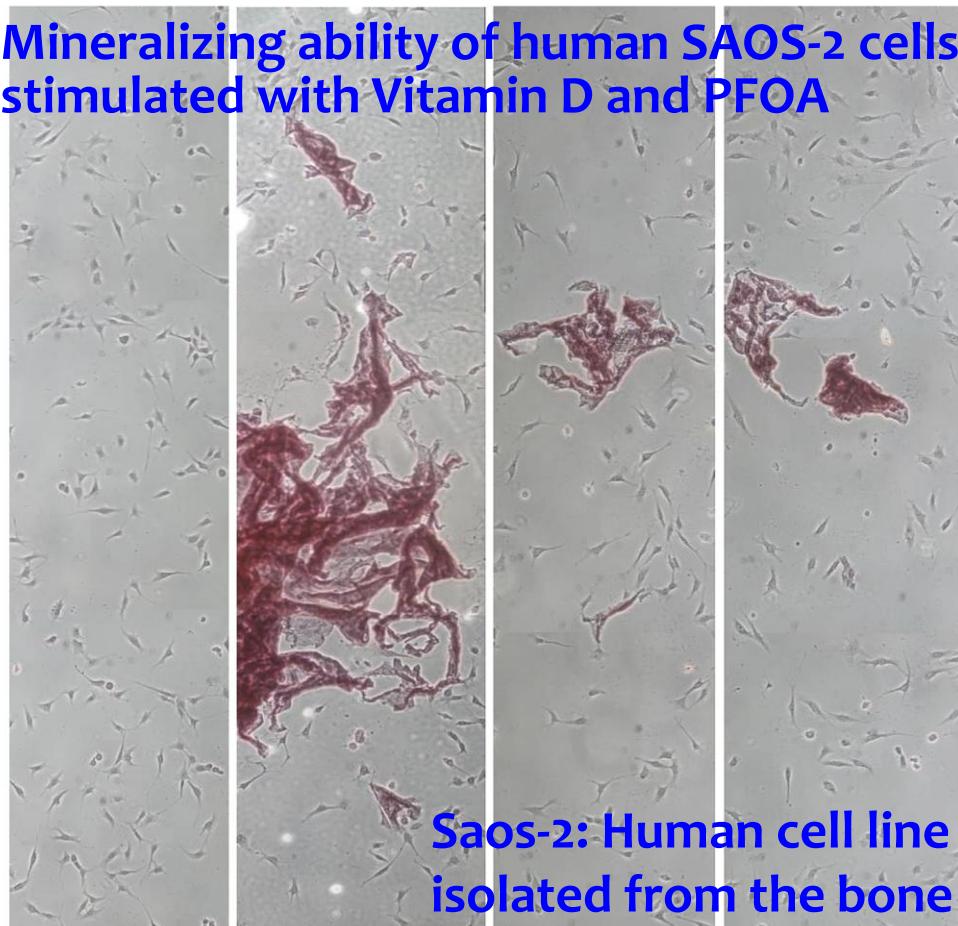
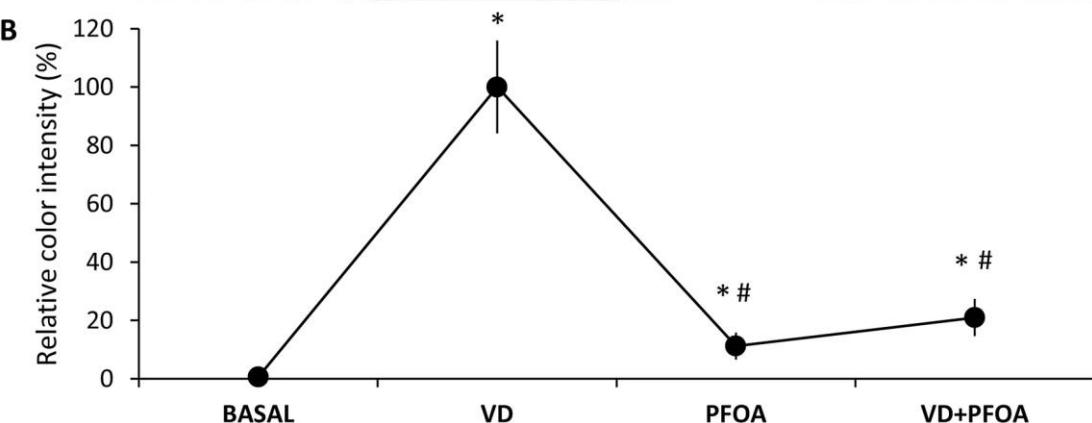
PFAS accumulates in bone tissues and causes altered bone development.

Epidemiological studies have reported an inverse relationship between PFAS and bone health, however, the associated mechanisms are still unexplored.

Interference of PFOA on vitamin D (VD) is established. **First**, PFOA competes with calcitriol on the same binding site of the VD receptor, leading to an alteration of the structural flexibility. **Second**, this causes an altered response of VD-responsive genes in two cellular targets of this hormone, osteoblasts and epithelial cells of the colorectal tract. **Third**, mineralization in human osteoblasts is reduced upon co-incubation of PFOA with VD. **Finally**, in a small cohort of young healthy men, parathyroid hormone (PTH) levels were higher in the exposed group, but VD levels were comparable. These results provide evidence of endocrine disruption by PFOA on VD pathway by competition on its receptor and subsequent inhibition of VD-responsive genes in target cells. [Sci Rep 10, 16789 (2020). <https://doi.org/10.1038/s41598-020-74026-8>]

**A**

Mineralized nodule formation  
detected by **Alizarin red-S staining**

**B**

1: PFOA competes with calcitriol on the same binding site of the vitamin D receptor (VDR).

2: this interference leads to an altered response of vitamin D-responsive genes in two cellular targets of this hormone, osteoblasts and epithelial cells of the colorectal tract.

3: mineralization in human osteoblasts is reduced upon co-incubation of PFOA with calcitriol.

4: VD was not decreased in the exposed group, but PTH levels were higher in association with PFAS exposure, suggesting a compensatory mechanism in response to functional hypovitaminosis D.

[Sci Rep 10, 16789 (2020).]

## Associations of PFASs and their alternatives with bone mineral density levels and osteoporosis prevalence

**Legacy PFASs:**

PFOA、PFOS、  
PFHxS, etc.

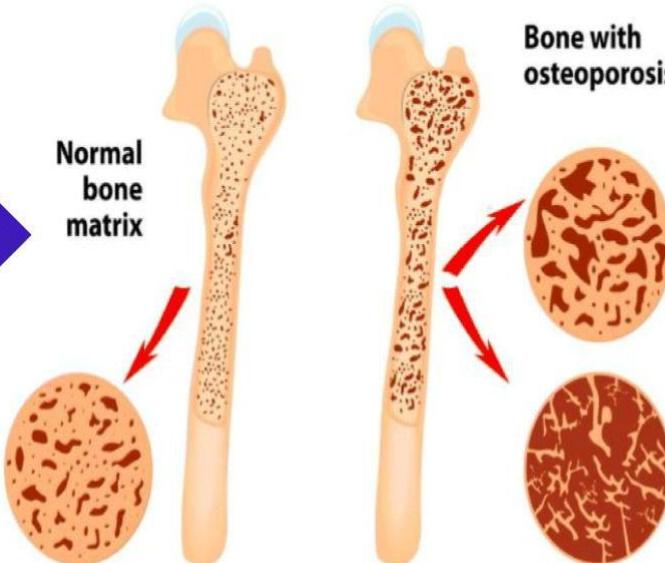
**PFAS isomers:**

branched PFHxS、  
branched PFOS, etc.

**PFAS alternatives:**

6:2 Cl-PFESA, etc.

### Osteoporosis



### Findings:

- Eleven PFASs were inversely associated with bone mineral density levels.
- Greater PFHpA levels were associated with an increased odds of osteoporosis.
- Associations between PFASs and bone mineral density were stronger in women and younger people.

## **The Human Predicament:**

Conflict of Socio-economic development and Human welling/Environment

"Everybody knows everybody's business," Higgs said, but nobody talked about C8. It was a matter of "not wanting to bite the hand that fed you."

Higgs, now an emergency room physician living in Richmond, Virginia

A lasting legacy: DuPont, C8 contamination and the community of Parkersburg left to grapple with the consequences. [Environmental Health News, Jan. 2020]

<https://www.ehn.org/dupont-c8-parkersburg-2644262065.html>