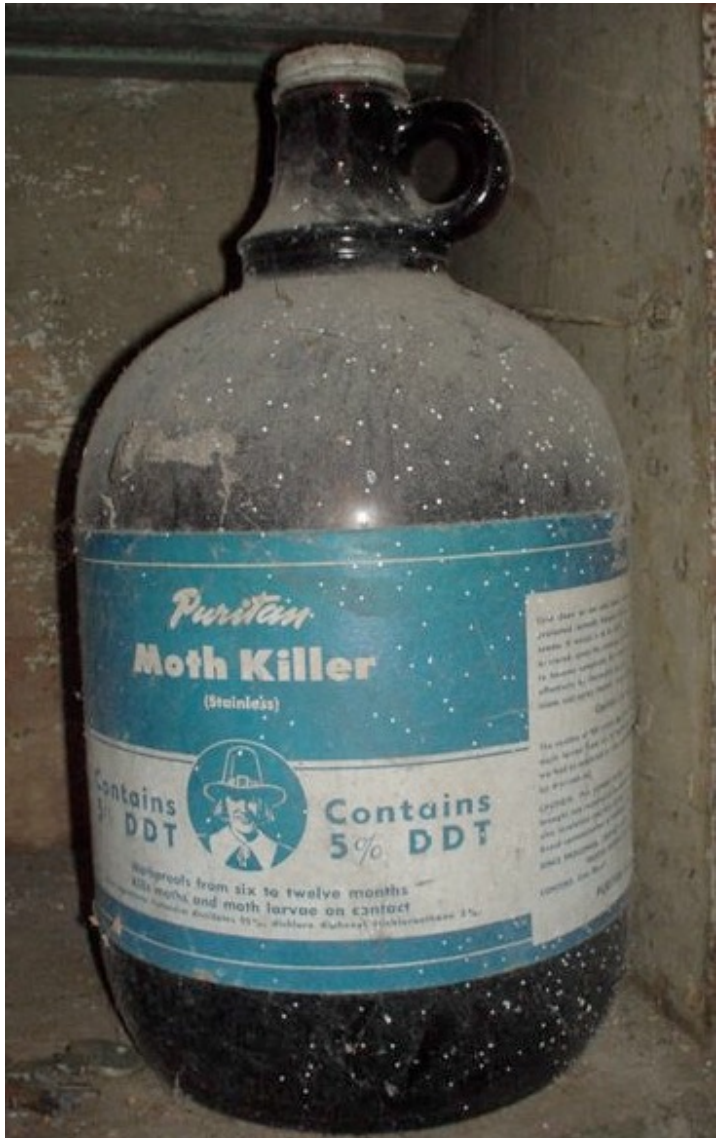
Endocrine Disruptors

Rachel Carson
(1907-1964)
Pittsburgh-Silverspring
Fisheries biologist

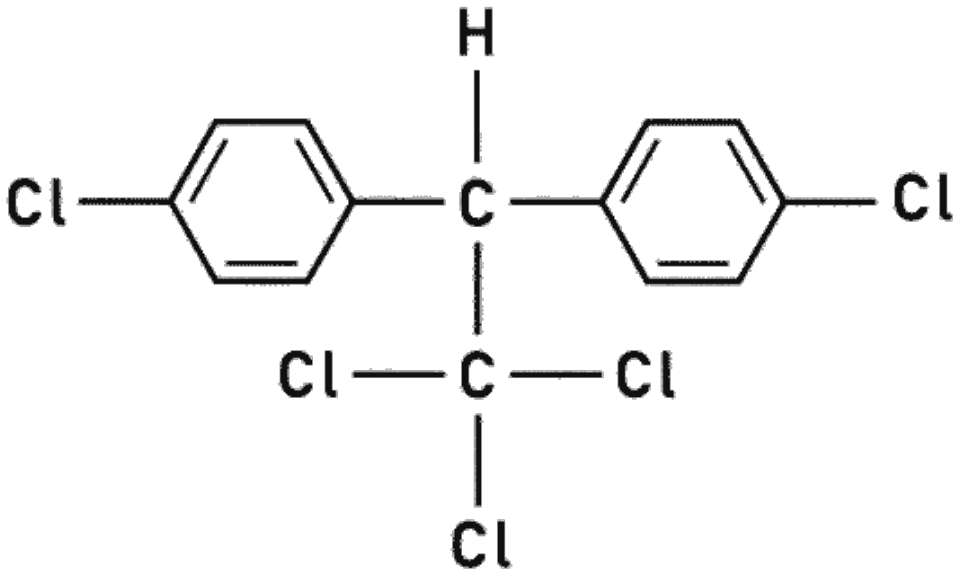
Paul Hermann Müller
(1899-1965)
Olten-Basel
Chemist

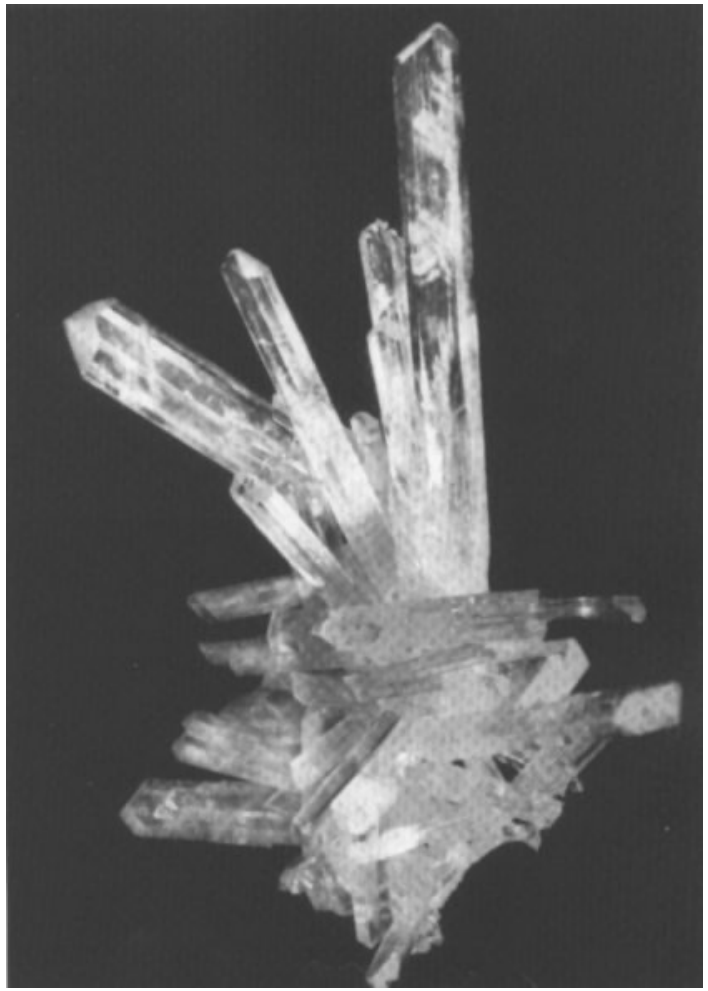
Dichloro-Diphenyl-Trichloroethane (DDT)




The Success Story

DDT:
Dichlordiphenyltrichlorethan

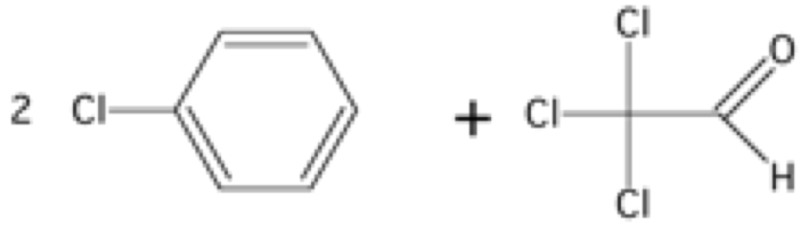




Organochlorine, highly hydrophobic

colorless, crystalline solid with a weak, chemical odor

1874 : DDT-Synthesis

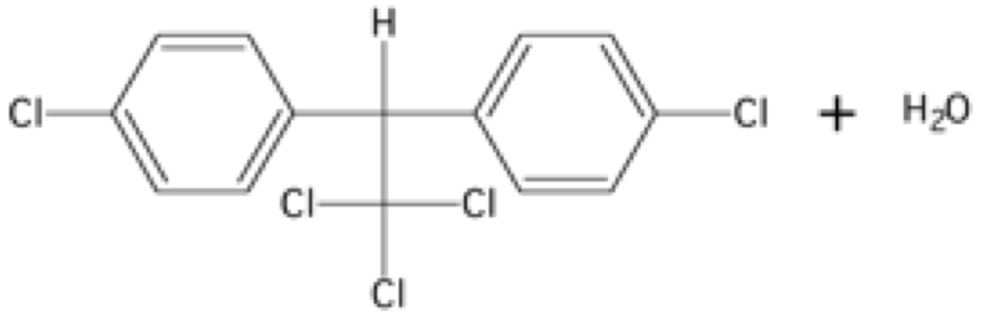


Chlorbenzol

H_2O / H_2SO_4

Chloral

DDT



Othmar Zeidler
1850-1911
Vienna

Paul Hermann Müller

- Chemist at Geigy since 1925
- Discovered the mechanism of action of DDT in 1939
- Nobelprize 1948
- First chemist to obtain a Nobelprize in Medicine and Physiology

DDT

- has potent insecticidal properties:
- Is poorly absorbed through mammalian skin, but easily absorbed through an insect's exoskeleton
- kills by opening sodium ion channels in insect neurons, causing the neuron to fire spontaneously. This leads to spasms and eventual death.
- Resistance mechanisms:
  - certain mutations in the sodium channel gene may provide resistance to DDT and other similar insecticides.
  - up-regulation of genes expressing cytochrome P450 in some insect species leads to resistance

Insects as pests

- transmit disease
- feeding damage
- parasites

anopheles

DDT: the ideal pesticide:

- ✓High toxicity against insects
- ✓Quick toxic effects
- ✓No toxicity for plants and warm blooded animals
- ✓Not an irritant, no unpleasant smell
- ✓Efficient on all arthropods
- ✓Long-lasting effects
- ✓Low cost

DDT: the war hero

- used by military during World War II
- To control:
  - malaria
  - typhus
  - body lice
  - bubonic plague

- 1943/44 typhus epidemic, Italy, Germany;
  - vector: lice
- 1944 malaria Italy, US
  - vector: anopheles

1942: DDT on the Swiss market

Extinction campaigns

- „Maikäferkrieg“ CH 1949-1957
- Elm bark beetle (USA)
- Red fire ant (USA)

cockchafer

elm bark beetle

red fire ant

DDT hype, 1950

- UNO: „To each developing country its DDT production plant“
- Global application
  - Protection from flies in cow stable
  - Moth balls
  - Rat poison
  - Plant protection: beans, cotton, soybeans, sweet potatoes, peanuts, cabbage, tomatoes, caulifower, corn, brussel sprouts, etc
  - Pest control in buildings

DDT

- 1955 WHO commenced a program to eradicate malaria worldwide relying largely on DDT.

-initially highly successful but resistance emerged

-DDT was less effective in tropical regions due to the continuous life cycle of mosquitoes and poor infrastructure

-1963 Peak production in the US 188 million pounds

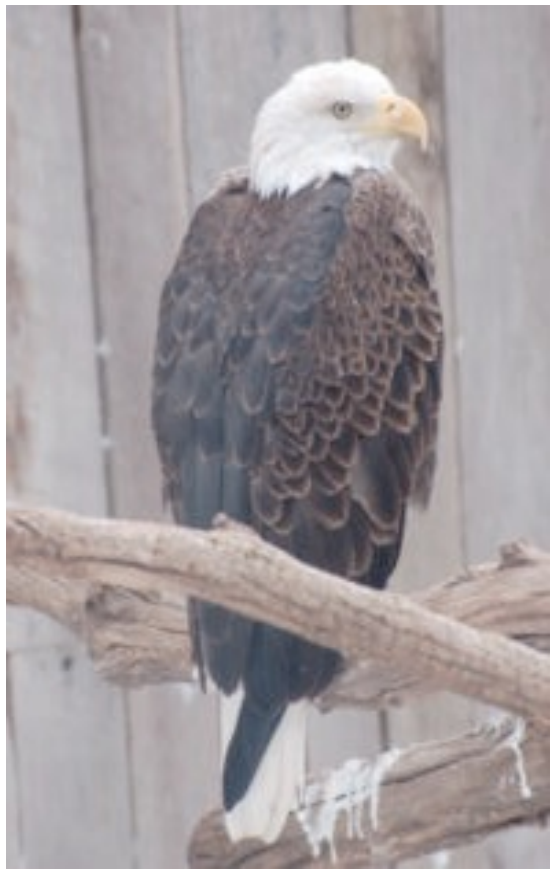
-1969: the goal of eradication was abandoned and attention was focused on controlling and treating the disease.

DDT: End to Euphoria

- Resistance of target insects: increase the dose!
- Some insects, like the house fly, develop the ability to quickly metabolize the DDT into the lower tocixity breakdown product DDE
- 1972 canceled by the US Environmental Protection Agency


SILENT
SPRING
RACHEL
CARSON

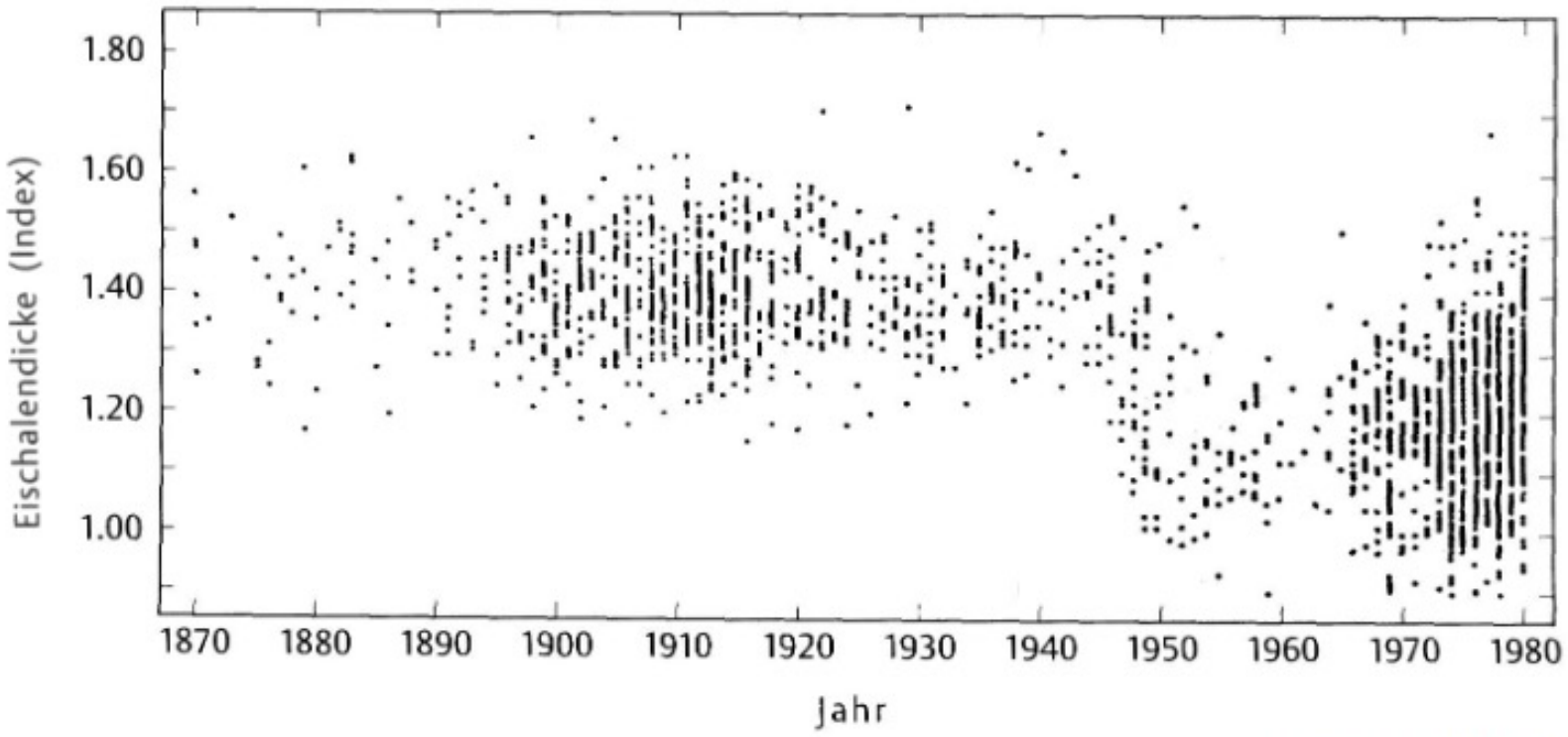
1952, Gulf Coast, Florida



- bald eagles
- 1947 decline in the number of eaglet observed
- bizarre behaviour
- no interest in mating

Proofs:

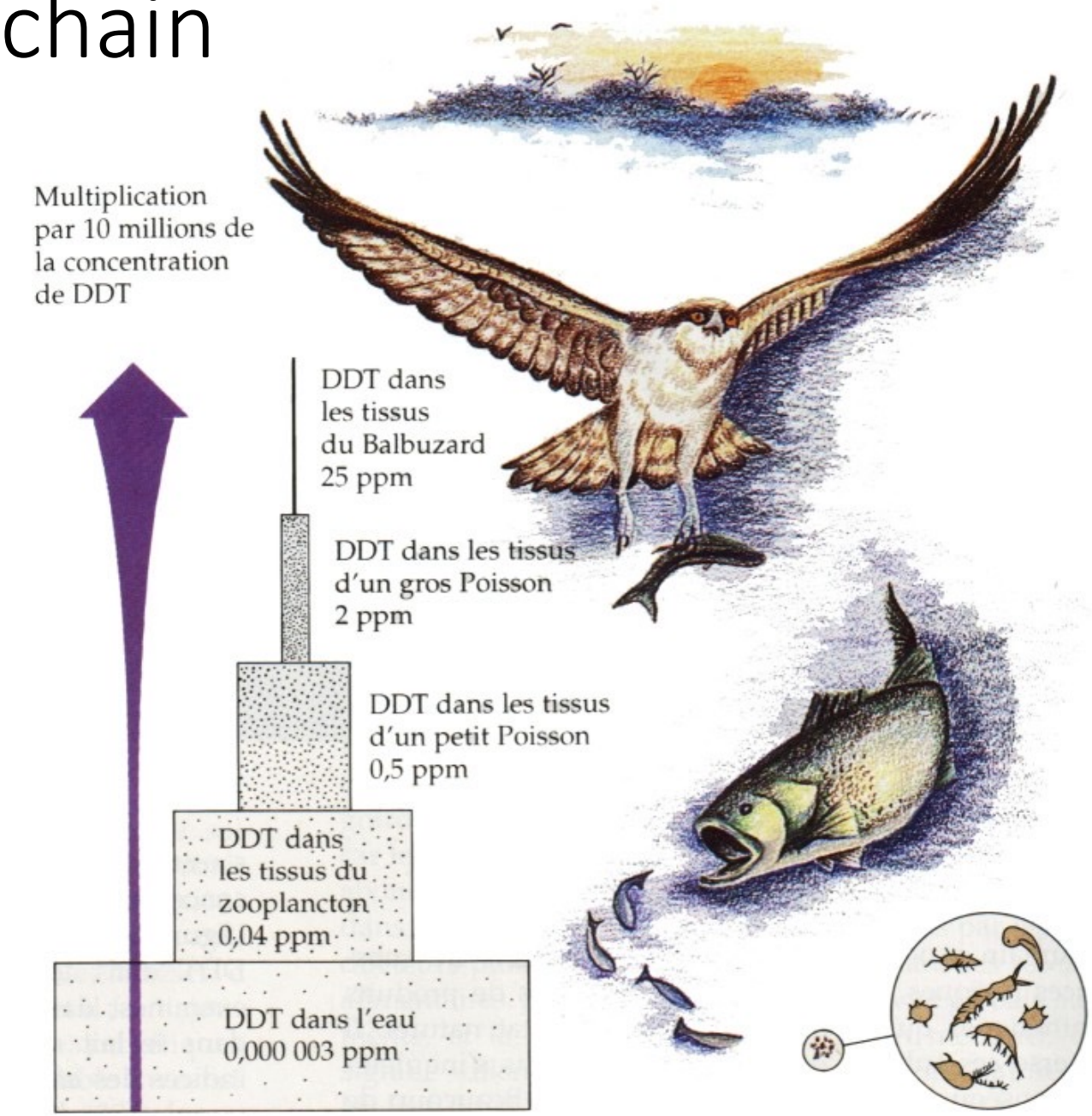
- 1955: abnormal number of broken bird eggs
- 1962: thickness of eggshell depends on DDE concentration
- 1967: comparison of eggs in museums



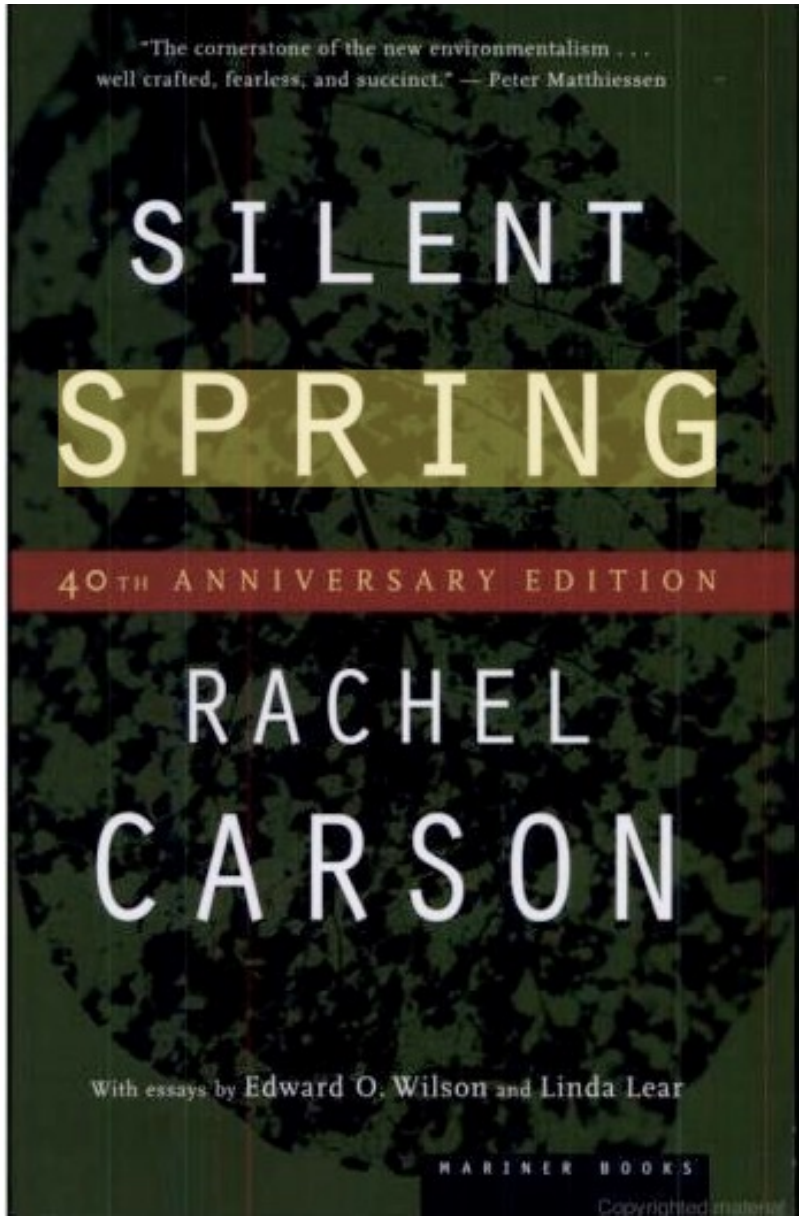
(nach Fendt 1998, 220)

DDT in the Foodchain

- strong bonds, difficult to degrade
- Non polar, lipophilic
- Ingested by insects and fish
- Adipose tissue:
  - insulation
  - energy reserve
- enrichment in higher organisms



1962



- catalogued the environmental impacts of the indiscriminate spraying of pesticides—most notably DDT—in the US
- questioned the logic of releasing large amounts of these chemicals into the environment without fully understanding their effects on ecology and human health
- suggested that DDT and other pesticides may cause cancer
- one of the signature events in the birth of the environmental movement environmental movement.
- 1967 activists launched a wider campaign against DDT

Ban on DDT

- 1970s and 1980s: agricultural use of DDT was banned in most developed countries

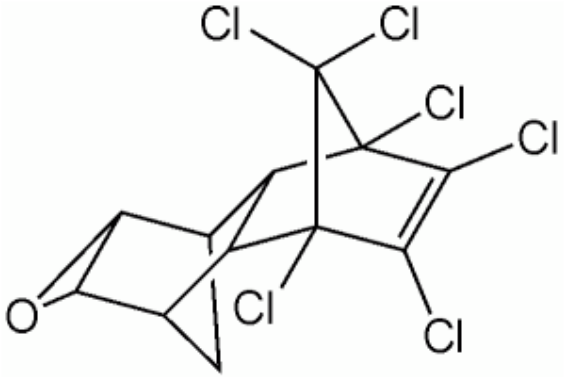
- As of 2006 , DDT continues to be used in other (primarily tropical) countries where mosquito-borne malaria and typhus are serious health problems. Use of DDT in public health to control mosquitoes is primarily done inside buildings and through inclusion in household products and selective spraying; this greatly reduces environmental damage compared to the earlier widespread use of DDT in agriculture. It also reduces the risk of resistance to DDT

Omnipresence of DDT

- Improved detection methods
- DDT detected in
  - Fat of penguins in Antartica
  - Mothers‘ milk
  - Emmentaler

Late 1950s, England

- Otters disappear
- dieldrin suspected
  - Insecticide widely used in 1950ies and 1970ies



Mid 1960s, Lake Michigan

- minks (domesticated)
- fewer pups, sterile
  - except those fed on fish from California
- linked to PCBs
  - Insulation of electrical equipment

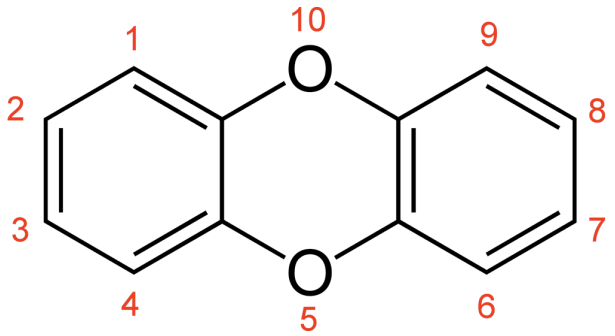
1970, Lake Ontario

- Herring gull
- 80% of the chicks dies before hatching
- multiple malformations

Dioxins suspected

by-product of several manufacturing processes such as paper production

and pesticide formulation



1980s, Lake Apopka, Florida

- Alligators
- less than 20% of eggs hatched
- 50% of the babies died within 10 days
- 60% of alligators had abnormally small penises
- previously: spillage from a chemical factory

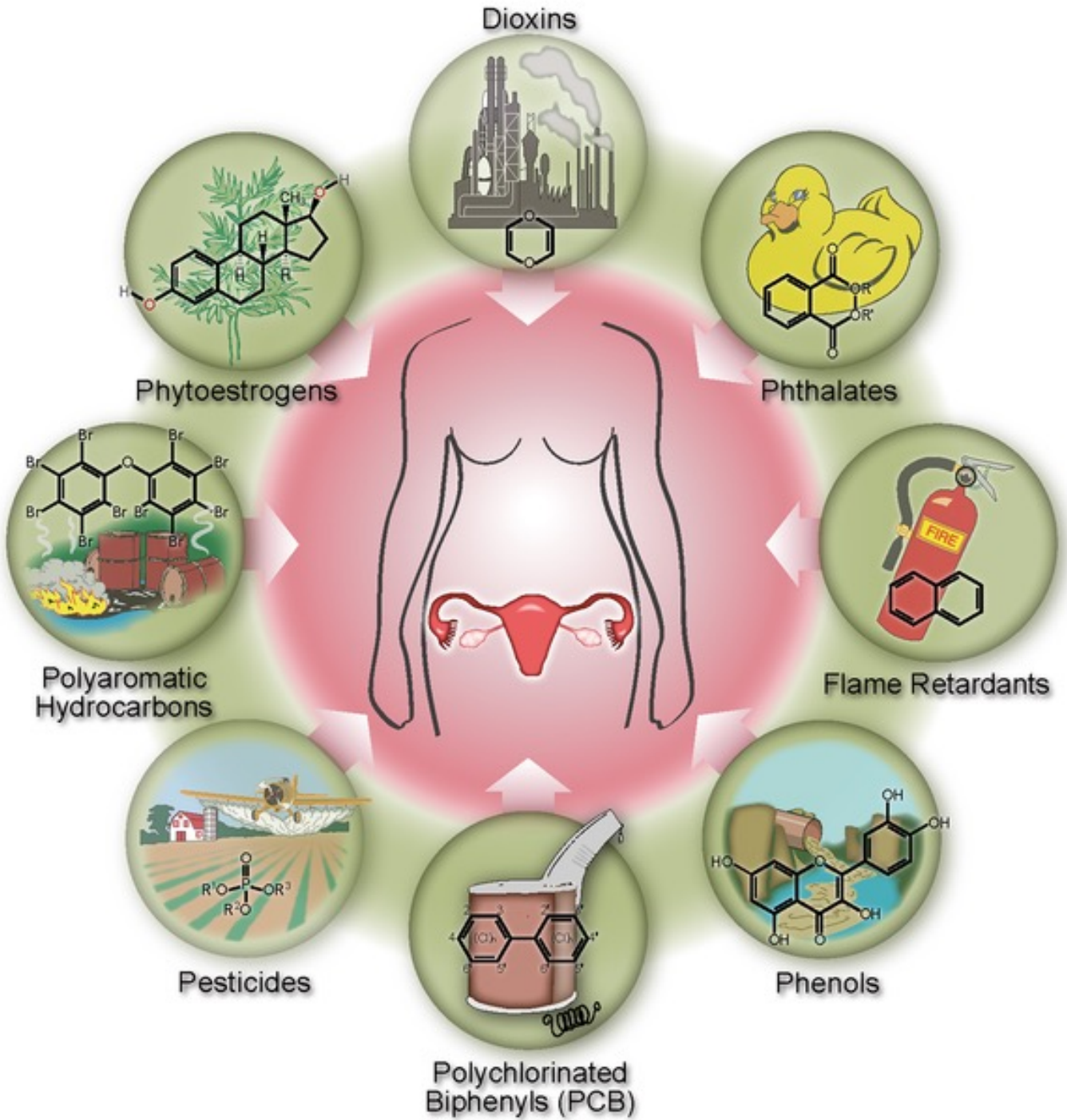
1988, Northern Europe

Island of Anholt in the Kattegat (between SE & DK)

- Seals
- aborted pups
- dead older seals
- all over Northern Europe
- symptoms of immune suppression

Early 1990s, The Mediterranean

- striped dolphins
- 11 000 deaths due to viral epidemic
- dead older seals
- high PCB levels in affected dolphins


Dioxins
Phytoestrogens
Phthalates
Polyaromatic Hydrocarbons
Flame Retardants
Pesticides
Phenols
Polychlorinated Biphenyls (PCB)

Lethal Dose LD50/lethal concentration LC50

- Common measure of toxicity
- LD50 dose which causes death resulting from a single or limited exposure (mg/kg of bodyweight)
- LC mg/volume of medium i.e. air or water the organism is exposed to

What is an Endocrine Disruptor?

- Any chemical agent in the environment that can alter normal endocrine system actions leading to deleterious effects on an organism or its progeny.

US Environmental Protection Agency:

"Exogenous agents that interfere with the synthesis, secretion, transport, binding, action or elimination of natural hormones in the body that are responsible for the maintenance of homeostasis, reproduction, development, and/or behavior"

Mechanisms of endocrine disruptors

Agonist:

DES: ERα antagonist

Antagonist:

DDE (metabolic product of DDT) and Vinclozoline (dicarboximide fungizide) are androgen receptor antagonists

Modify hormone synthesis:

Atrazine (herbizide): induces aromatase activity thereby increasing estrogen levels

Modify hormone elimination or transport:

Polychlorinated biphenyls (PCBs) interfere with the elimination and degradation of thyroid hormone

Exposure to endocrine disruptors during critical periods of mammalian development can interfere with normal DNA methylation patterns, leading to atypical gene expression