

## <Further Development 14.11>

### DDT as Endocrine Disruptor

*Silent Spring* was one of the most influential books of the twentieth century. Its author, fisheries biologist Rachel Carson, warned that pesticides were destroying wildlife, that DDT in particular appeared to be exterminating shorebird populations, and that pesticides were becoming a staple of the American diet. For this she was reviled by the agricultural chemicals industry and called a fanatic, a Communist, and worse (see Lear 1998; Orlando 2002; Stouder 2012). But subsequent research bore out Carson's claims and revealed the first evidence of endocrine disruption due to exposure to environmental chemicals.

The chemical components of DDT (dichloro–diphenyl–trichloroethane) cannot be broken down and eliminated by vertebrate organisms; it remains in their bodies and builds up, becoming especially concentrated in organisms that feed on the DDT–containing tissues of other animals. This persistence, along with its solubility in lipids, results in tremendous **bioaccumulation** such that even though DDT has not been legally used in the United States since 1972, most of us still have this chemical in our bodies. Indeed, it is so resistant to metabolic degradation, and so much was manufactured, that it remains not only in humans and other terrestrial animals but also in fishes, marine mammals, and seabirds. It has an environmental half–life of about 15 years, which means it can take 100 years or more for the concentration of DDT in the soil to fall below active levels.

Bioaccumulation of DDT was especially pronounced in some birds of prey living at the top of the food chain. Peregrine falcons and bald eagles became endangered because of DDT–induced fragility of their eggshells (Cooke 1973). Even seabirds were affected when DDT in runoff

accumulated in the fish they fed on. Fragile eggshells resulted in high mortality as the developing bird embryos became desiccated, were easily preyed upon, and often were not able to withstand even minor physical forces.

Discovering why DDT contamination results in thin eggshells was a formidable research challenge. It turns out that DDT acts as an estrogenic compound (see the next section), while its chief metabolic product, DDE (which lacks one of DDT's chlorine atoms), inhibits androgens such as testosterone from binding to the androgen receptor (Davis et al. 1993; Kelce et al. 1995; Xu et al. 2006). Eggshell thinning is caused by several actions of DDT and DDE. Hens with high DDT levels had poorly developed shell glands, with capillaries deficient in carbonic anhydrase—an enzyme critical for the deposition of shell-strengthening calcium carbonate in the egg (Holm et al. 2006). High DDE levels in the shell gland also prevent calcium carbonate deposition by downregulating the synthesis of prostaglandins (a group of fatty acid derivatives that regulates many vertebrate physiological processes). In birds, one of these prostaglandins is critical for the transport of calcium ions through the shell gland for use in shell formation (Lundholm 1997; Guillette 2006).

DDT use has been banned in the United States since 1972, and is also banned in most of Europe. The Stockholm Convention of 2001, which attempts a worldwide ban on the use of several dangerously persistent organic chemicals, limits the use of DDT to the control of disease-carrying insects (notably mosquitoes), and only in those countries where there is no affordable and/or comparably effective alternative for managing a serious public health threat (primarily malaria).

Banning DDT turned out to be an excellent idea. The birds were indeed the "canaries in the coal mine." What wasn't known in 1972 was that women exposed to DDT before age 14 would

have over a five-fold increase in their incidence of breast cancers when they grew up. Using a remarkable database of American patients studied for over fifty years, Cohn (2011) concluded that DDT exposure after adolescence might not lead to major health risks; but exposure to this endocrine disruptor in utero or at an early age can make a person susceptible to get breast cancer later in life.

Moreover, prenatal DDT exposure in humans has been linked to abnormalities of male genitalia development, lower embryo implantation rate into the uterus, and ovarian dysfunction. The reason for this appears to be the ability of DDT to disrupt the ability of chorionic gonadotropin and luteinizing hormone to stimulate Leydig cells (in the testes) and granulosa cells (in the ovaries) to produce steroid hormones (Munier et al 2021).

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