DDT

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DDT (from its trivial name, **D**ichloro-**D**iphenyl-**T**richloroethane) is one of the best known synthetic pesticides. It is a chemical with a long, unique, and controversial history.

First synthesized in 1874, DDT's insecticidal properties were not discovered until 1939. In the early years of World War II, DDT was used with great effect to control mosquitoes spreading malaria, typhus, and other insect-borne diseases among both military and civilian populations. The Swiss chemist Paul Hermann Müller of Geigy Pharmaceutical was awarded the Nobel Prize in Physiology or Medicine in 1948 "for his discovery of the high efficiency of DDT as a contact poison against several arthropods."[2] After the war, DDT was made available for use as an agricultural insecticide, and soon its production and use skyrocketed.[3]

In 1962, *Silent Spring* by American biologist Rachel Carson was published. The book catalogued the environmental impacts of the indiscriminate spraying of DDT in the US and questioned the logic of releasing large amounts of chemicals into the environment without fully understanding their effects on ecology or human health. The book suggested that DDT and other pesticides may cause cancer and that their agricultural use was a threat to wildlife, particularly birds. Its publication was one of the signature events in the birth of the environmental movement. *Silent Spring* resulted in a large public outcry that eventually led to most uses of DDT being banned in the US in 1972.[4] DDT was subsequently banned for agricultural use worldwide under the Stockholm Convention, but its limited use in disease vector control continues to this day in certain parts of the world and remains controversial.[5]

Along with the passage of the Endangered Species Act, the US ban on DDT is cited by scientists as a major factor in the comeback of the bald eagle in the contiguous US.[6]

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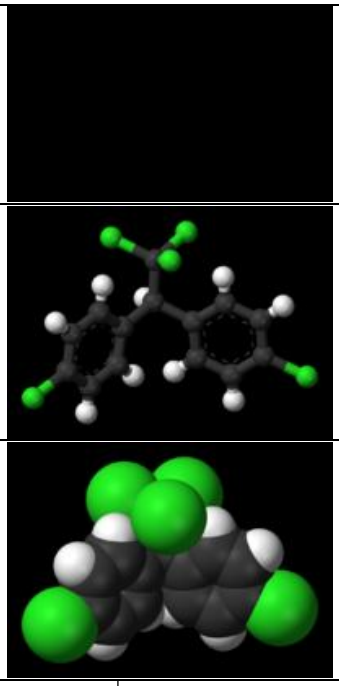


IUPAC name	4,4'-(2,2,2-trichloroethane-1,1-diyl)bis(chlorobenzene)
Identifiers	
CAS number	[50-29-3]
SMILES	[show]
Properties	
Molecular formula	$C_{14}H_9Cl_5$
Molar mass	354.49 g/mol
Density	0.99 g/cm³ [1]
Melting point	109 °C [1]
Boiling point	decomp. [1]
Hazards	
EU classification	Yes
Main hazards	T, N
R-phrases	R25 R40 R48/25 R50/53
S-phrases	(S1/2) S22 S36/37 S45 S60 S61
LD_{50}	113 mg/kg (rat)

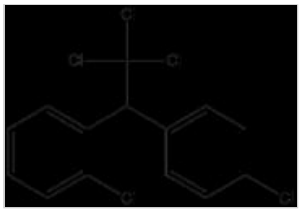
Except where noted otherwise, data are given for materials in their standard state (at 25 °C, 100 kPa)
Infobox references

Properties and chemistry

DDT is an organochlorine insecticide, similar in structure to the pesticides dicofol and methoxychlor. It is a highly hydrophobic, colorless, crystalline solid with a weak, chemical odor. It is nearly insoluble in water but has a good solubility in most organic solvents, fats, and oils. DDT does not occur naturally, but is produced by the reaction of chloral (CCl_3CHO) with chlorobenzene (C_6H_5Cl) in the presence of sulfuric acid, which acts as a catalyst. Trade names that DDT has been marketed under include Anofex, Cezarex, Chlorophenothane, Clofenotane, Dicophane, Dinocide, Gesarol, Guesapon, Guesarol, Gyron, Ixodex, Neocid, Neocidol, and Zerdane.[3]

Isomers and Related Compounds

Commercial DDT is actually a mixture of several closely related compounds. The major component (77%) is the *p*,*p* isomer which is pictured at the top of this article. The *o*,*p'* isomer (pictured to the right) is also present in significant amounts (15%). Dichlorodiphenyldichloroethylene (DDE) and dichlorodiphenyldichloroethane (DDD) make up the balance. DDE and DDD are also the major metabolites and breakdown products of DDT in the environment.[3] The term "**total DDT**" is often used to refer to the sum of all DDT related compounds (*p*, *p*-DDT, *o*, *p*-DDT, DDE, and DDD) in a sample.



o,*p'* -DDT, a minor component in commercial DDT.

Production and use statistics

From 1950 to 1980, when DDT was extensively used in agriculture, more than 40,000 tonnes were used each year worldwide,[7] and it has been estimated that a total of 1.8 million tonnes of DDT have been produced globally since the 1940s.[1] In the U.S., where it was manufactured by Ciba,[8] Montrose Chemical Company and Velsicol Chemical Corporation,[9] production peaked in 1963 at 82,000 tonnes per year.[3] More than 600,000 tonnes (1.35 billion lbs) were applied in the U.S. before the 1972 ban, with usage peaking in 1959 with about 36,000 tonnes applied that year.[10]

Currently about 1,000 tonnes of DDT are used annually worldwide in disease and insect vector control.[7] India and China are the only countries still producing and exporting it.[11]

Mechanism of action

DDT is moderately toxic, with a rat LD_{50} of 113 mg/kg,[12]. It has potent insecticidal properties, where it kills by opening sodium ion channels in the neurons, causing them to fire spontaneously leading to spasms and eventual death. Insects with certain mutations in their sodium channel gene are resistant to DDT and other similar insecticides. DDT resistance is also conferred by up-regulation of genes expressing cytochrome P450 in some insect species.[13]

History

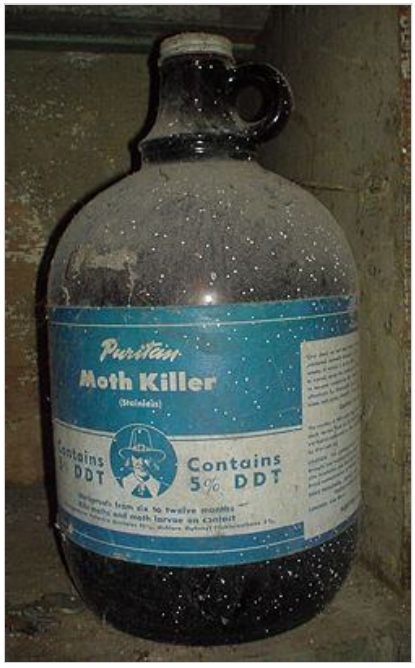
First synthesized in 1874 by Othmar Zeidler,[3] DDT's insecticidal properties were not discovered until 1939 by the Swiss scientist Paul Hermann Müller, who was awarded the 1948 Nobel Prize in Physiology and Medicine for his efforts.[2]

Use in the 1940s and 1950s

DDT is the best-known of a number of chlorine-containing pesticides used in the 1940s and 1950s. It was used extensively during World War II by the Allies to control the insect vectors of typhus—nearly eliminating the disease—and malaria. Entire cities in Italy were dusted to control typhus-transmitting lice. DDT also sharply reduced the incidence of biting midges in Great Britain. After 1945, it was made available to farmers as an agricultural insecticide.[3]

DDT played a small role in the final elimination of malaria in Europe and North America, as malaria had already been eliminated

from much of the developed world before the advent of DDT through the use of a range of public health measures and generally increasing health and living standards.[5] One CDC physician involved in the United States' DDT spraying campaign said of the effort that "we kicked a dying dog."[14] But in countries without these advances, it was critical in their eradication of the disease.



Commercial product containing 5% DDT

In 1955, the World Health Organization commenced a program to eradicate malaria worldwide, relying largely on DDT. The program was initially highly successful, eliminating the disease in "Taiwan, much of the Caribbean, the Balkans, parts of northern Africa, the northern region of Australia, and a large swath of the South Pacific" and dramatically reducing mortality in Sri Lanka and India.[15] However resistance soon emerged in many insect populations as a consequence of widespread agricultural use of DDT. In many areas, early victories against malaria were partially or completely reversed, and in some cases rates of transmission even increased.[16] The program was successful in eliminating malaria only in areas with "high socio-economic status, well-organized healthcare systems, and relatively less intensive or seasonal malaria transmission".[17]

DDT was less effective in tropical regions due to the continuous life cycle of mosquitoes and poor infrastructure. It was not pursued at all in sub-Saharan Africa due to these perceived difficulties, with the result that mortality rates in the area were never reduced to the same dramatic extent, and now constitute the bulk of malarial deaths worldwide, especially following the resurgence of the disease as a result of microbe resistance to drug treatments and the spread of the deadly malarial variant caused by *Plasmodium falciparum*. The goal of eradication was abandoned in 1969, and attention was focused on controlling and treating the disease. Spraying programs (especially using DDT) were curtailed due to concerns over safety and environmental effects, as well as problems in administrative, managerial and financial implementation, but mostly because mosquitoes were developing resistance to DDT.[16] Efforts were shifted from spraying to the use of bednets impregnated with insecticides and other interventions.[18][17]

Silent Spring and the U.S. ban

As early as the 1940s, scientists had begun expressing concern over possible hazards associated with DDT, and in the 1950s the government began tightening some of the regulations governing its use.[10] However, these early events received little attention, and it was not until 1957 when the *New York Times* reported an unsuccessful struggle to restrict DDT use in Nassau County, New York that the issue came to the attention of the popular naturalist-author, Rachel Carson. William Shawn, editor of *The New Yorker*, urged her to write a piece on the subject, which developed into her famous book *Silent Spring*, published in 1962. The book argued that pesticides, including DDT, were poisoning both wildlife and the environment and were also endangering human health. [4]

Silent Spring was a best seller, and public reaction to it launched the modern environmental movement in the United States. The year after it appeared, President Kennedy ordered his Science Advisory Committee to investigate Carson's claims. The report the committee issued "add[ed] up to a fairly thorough-going vindication of Rachel Carson's Silent Spring thesis," in the words of the journal *Science*,[19] and recommended a phaseout of "persistent toxic pesticides".[20] DDT became a prime target of the growing anti-chemical and anti-pesticide movements, and in 1967 a group of scientists and lawyers founded the Environmental Defense Fund (EDF) with the specific goal of winning a ban on DDT. Victor Yannacone, Charles Wurster, Art Cooley and others associated with inception of EDF had all witnessed bird kills or declines in bird populations and suspected that DDT was the cause. In their campaign against the chemical, EDF petitioned the government for a ban and filed a series of lawsuits.[21] Around this time, toxicologist David Peakall was measuring DDE levels in the eggs of peregrine falcons and California condors and finding that increased levels corresponded with thinner shells.

In response to an EDF suit, the U.S. District Court of Appeals in 1971 ordered the EPA to begin the de-registration procedure for DDT. After an initial six-month review process, William Ruckelshaus, the Agency's first Administrator rejected an immediate suspension of DDT's registration, citing studies from the EPA's internal staff stating that DDT was not an imminent danger to human health and wildlife.[10] However, the findings of these staff members were criticized, as they were performed mostly by economic entomologists inherited from the United States Department of Agriculture, whom many environmentalists felt were biased towards agribusiness and tended to minimize concerns about human health and wildlife. The decision not to ban thus created public controversy.

The EPA then held seven months of hearings in 1971-1972, with scientists giving evidence both for and against the use of DDT. In the summer of 1972, Ruckelshaus announced the cancellation of most uses of DDT—an exemption allowed for public health uses under some conditions.[10] Despite the ban on its domestic use, DDT continued to be produced in the US for foreign markets until as late as 1985, when over 300 tonnes were exported.[1] Immediately after the cancellation was announced, both EDF and the DDT manufactures filed suit against the EPA, with the industry seeking to overturn the ban, and EDF seeking a comprehensive ban. The cases were consolidated, and in 1973 the U.S. Court of Appeals for the District of Columbia ruled that the EPA had acted properly in banning DDT.[10]

The U.S. DDT ban took place amid a climate of growing public mistrust of industry, with the Surgeon General issuing a report on smoking in 1964, the Cuyahoga River catching fire in 1969, the fiasco surrounding the use of diethylstilbestrol (DES), and the well-publicized decline in the bald eagle population.[20]

Restrictions on usage

In the 1970s and 1980s, agricultural use of DDT was banned in most developed countries. DDT was first banned in Hungary in 1968[22] then in Norway and Sweden in 1970 and the US in 1972, but was not banned in the United Kingdom until 1984. The use of DDT in vector control has not been banned, but it has been largely replaced by less persistent, and more expensive, alternative insecticides.

The Stockholm Convention, ratified in 2001 and effective as of 17 May 2004, outlawed several persistent organic pollutants, and restricted the use of DDT to vector control. The Convention was signed by 98 countries and is endorsed by most environmental groups. Recognizing that a total elimination of DDT use in many malaria-prone countries is currently unfeasible because there are few affordable or effective alternatives, the public health use of DDT was exempted from the ban until alternatives are developed. The Malaria Foundation International states:

> The outcome of the treaty is arguably better than the status quo going into the negotiations…For the first time, there is now an insecticide which is restricted to vector control only, meaning that the selection of resistant mosquitoes will be slower than before. [23]

Despite the worldwide ban on agricultural use of DDT, some farmers in India still use it in crop production.[24]

About 1,000 tonnes of DDT per year is still used today in some countries where malaria is a serious health problem.[25] In this context, DDT is applied to the inside walls of homes to kill or repel mosquitos entering the home. This intervention, called indoor residual spraying (IRS), greatly reduces environmental damage compared to the earlier widespread use of DDT in agriculture. It also reduces the risk of resistance to DDT.[26] This use only requires a small fraction of that previously used in agriculture; for example, the amount of DDT that might have been used on 100 acres (0.4 km²) of cotton during a typical growing season in the U.S. is estimated to be enough to treat roughly 1,700 homes.[27]

Environmental impact

DDT is a persistent organic pollutant with a half life of 2-15 years. It is extremely hydrophobic and is immobile in soils. In aquatic ecosystem it has a half life of between 28 and 56 days depending on the turnover time of the system. Routes of loss and degradation include runoff, volatilization, photolysis and aerobic and anaerobic biodegradation. Its breakdown products and metabolites, DDE and DDD, are also highly persistent and have similar chemical and physical properties.[28] These products together are known as "total DDT". DDT and its breakdown products are transported from warmer regions of the world to the Arctic by the phenomenon of global distillation, where they then accumulate in the region's food web.[29]

DDT, DDE, and DDD magnify through the food chain, with apex predators such as raptors having a higher concentration of the chemicals than other animals sharing the same environment. They are stored mainly in body fat. In the United States, human blood and fat tissue samples collected in the early 1970s showed detectable levels in all samples. A study conducted in the late 1970s after the U.S. DDT ban found that blood levels were declining, but DDT or metabolites were still found in a high proportion of samples. Biomonitoring conducted by the Centers for Disease Control as recently as 2002 shows that more than half of subjects tested had detectable levels of DDT or metabolites in their blood,[30] and of the 700+ milk samples tested by the USDA in 2005, 85% had detectable levels of DDE.[31]

DDT is a toxicant across a range of phyla. DDT was a major reason for the decline of the bald eagle in North America in the 1950s and 1960s[32][6] as well as the brown pelican[33] and the peregrine falcon. DDT and its breakdown products are toxic to embryos and disrupts calcium absorption, thereby impairing eggshell quality.[34] Studies in the 1960s and 1970s failed to find a mechanism for the hypothesized thinning.[35] However, more recent studies in the 1990s and 2000s have laid the blame at the

feet of DDE.[36][37] Some studies have shown that although DDE levels have fallen dramatically, eggshell thickness remains 10–12 percent thinner than before DDT was first used.[38] DDT is also highly toxic to aquatic life, including crayfish, daphnids, sea shrimp and many species of fish. DDT may be moderately toxic to some amphibian species, especially in the larval stages.

Effects on human health

The effects of DDT on human health are disputed since studies have yielded conflicting results.

Toxicity

Acute

- DDT is classified as "moderately toxic" by the US National Toxicological Program[39] and "moderately hazardous" by WHO, based on the rat oral LD_{50} of 113 mg/kg.[12] It is not considered to be acutely toxic, and in fact it has been applied directly to clothes or used in soap.[40] DDT has on rare occasions been administered orally as a treatment for barbiturate poisoning.[41]

Chronic

- Occupational exposure to DDT was associated with reduced verbal attention, visuomotor speed, sequencing, and with increased neuropsychological and psychiatric symptoms in a dose-response pattern (ie, per year of DDT application) in retired workers aged 55–70 years in Costa Rica. DDT or DDE concentrations were not determined in this study.[42]
- Farmers exposed to DDT occupationally have an increased incidence of non-allergic asthma. [43]
- Organochlorine compounds in general and DDE specifically have been linked to diabetes.[44] A study of Native Americans exposed to DDE primarily from eating contaminated fish found that elevated blood DDE levels were associated with an increased incidence of diabetes. These results are consistent with previous studies on diabetes incidence and organochlorine exposure.[45] A recent study of Mexican Americans yielded similar results.[46]

Cancer

- The United States National Toxicology Program classified DDT as "reasonably anticipated to be a human carcinogen", and the EPA classifies DDT, DDE, and DDD as a class B2 "probable" human carcinogens. The International Agency for Research on Cancer classifies a Group 2B, "possible" human carcinogen. These evaluations are based mainly on the results for animal studies.[1]
- A study of malaria workers who handled DDT occupationally found an elevated risk of cancers of the liver and biliary tract. Another study has found a correlation between DDE and liver cancer in white men, but not for women or black men. An association between DDT exposure and pancreatic cancer has been demonstrated in a few studies, but other studies have found no association. Several studies have looked for associations between DDT and multiple myeloma, and testicular, prostate, endometrial, and colorectal cancers, but none conclusively demonstrated any association.[18]
- A Canadian study from 2007 found a positive association between DDE and non-Hodgkin Lymphoma.[47]
- A recent study in the Journal of the National Cancer Institute concluded that DDE exposure to may be associated with testicular cancer. The incidence of seminoma in men with the highest blood levels of DDE was almost double that of men with the lowest levels of DDE.[48][49]

Breast cancer

The question of whether DDT or its metabolites can cause breast cancer has been the subject of numerous investigations. While individual studies have come to conflicting conclusions, the most recent review of all the evidence concludes that exposure to DDT before puberty increases the risk of breast cancer later in life.[50] Until recently, almost all studies measured DDT or DDE blood levels at the time of breast cancer diagnosis or after. This study design has been criticized, since the levels of DDT or DDE at diagnosis do not necessarily correspond to the levels present in a woman's body at the time when her cancer first started.[51] Such studies have thus yielded conflicting results and taken as a whole "do not support the hypothesis that exposure to DDT is an important risk factor for breast cancer."[52] The studies of this design have been extensively reviewed.[53][18][54]

In contrast to studies which measured DDT or DDE late in life, a recent study was able to assess DDT exposure early in life and track the breast cancer status of the women later in life. This study found a strong association between exposure to the *p, p*-isomer of DDT early in life and breast cancer later in life. Exposure to the *o, p'*-isomer was negatively correlated with breast cancer (*i.e.* a protective effect was observed), and no association was observed for DDE. Unlike previous studies, this was prospective cohort study in which blood samples were collected from young mothers in the 1960s while DDT was still in use, and their breast cancer status was then monitored. In addition to suggesting that exposure to the *p, p*-isomer of DDT is the more

significant risk factor of breast cancer, the study also suggests that the timing of exposure is critical. For the subset of women born more than 14 years prior to the introduction of DDT into US agriculture, there was no association between DDT levels and breast cancer. However, for women born more recently—and thus exposed earlier in life—the most *p, p*-DDT exposed third had a fivefold increase in breast cancer incidence over the least exposed third, after correcting for the protective effect of *o, p*-DDT. [52][55]

Developmental and reproductive toxicity

DDT and its breakdown product DDE, like other organochlorines, have been shown to have xenoestrogenic activity; meaning they are chemically similar enough to estrogens to trigger hormonal responses in animals. This endocrine disrupting activity has been observed when DDT is used in laboratory studies involving mice and rats as test subjects, and available epidemiological evidence indicates that these effects may be occurring in humans as a result of DDT exposure. In areas where DDT is used for malaria control, infants can be exposed via breastmilk in levels that exceed the W.H.O's acceptable daily intake value for DDT. [56] [57]

- A review article in *The Lancet* concludes that, "research has shown that exposure to DDT at amounts that would be needed in malaria control might cause preterm birth and early weaning … toxicological evidence shows endocrine-disrupting properties; human data also indicate possible disruption in semen quality, menstruation, gestational length, and duration of lactation."[18]
- Human epidemiological studies suggest that DDT exposure is a risk factor for premature birth and low birth weight, and may harm a mother's ability to breast feed.[58] Some researchers argue that these effects may cause increases in infant deaths in areas where DDT is used for malaria control, and thus offset any benefit derived from its anti-malarial effects.[59] [60][61] A recent study, however, failed to confirm the association between exposure and difficulty breastfeeding.[62]
- Several recent studies demonstrate a link between *in utero* exposure to DDT or DDE and developmental neurotoxicity in humans. For example, a 2006 study conducted by the University of California, Berkeley suggests children who have been exposed to DDT while in the womb have a greater chance of experiencing development problems,[63] and other studies have found that even low-levels of DDT or DDE in umbilical cord serum at birth are associated with decreased attention at infancy[64] and decreased cognitive skills at 4 years of age.[65] Similarly, Mexican researchers have demonstrated a link between DDE exposure in the first trimester of pregnancy and retarded psychomotor development.[66]
- A 2007 study documented decreases in semen quality among South African men from communities where DDT is used to combat endemic malaria. The researchers found statistically significant correlations between increased levels of DDT or DDE in blood plasma and decreases in several measures of semen quality including ejaculate volume, certain motility parameters, and sperm count.[67] The same researchers reported similar results in 2006 from a study of men in Mexico.[68] A review of earlier studies noted that "Studies of populations with a much lower exposure than that seen in current malaria-endemic areas have shown only weak, inconsistent associations between DDE and testosterone amounts, semen quality, and sperm DNA damage."[18]
- One recent study suggests that women exposed to DDT while in the womb have more difficulty getting pregnant as adults than non-exposed women. On the other hand, prenatal DDE exposure increased the probability of pregnancy.[69]
- DDT exposure is associated with early pregnancy loss, a type of miscarriage. A prospective cohort study of Chinese textile workers found "a positive, monotonic, exposure-response association between preconception serum total DDT and the risk of subsequent early pregnancy losses." [70] The median serum DDE level of study group was lower than that typically observed in women living in homes sprayed with DDT, suggesting that these finding are relevant to the debate about DDT and malaria control. [71]
- A case-control study of congenital hypothyroidism in Japan concluded that *in utero* DDT exposure may affect thyroid hormone levels and "play an important role in the incidence and/or causation of cretinism."[72] Other studies have also found the DDT or DDE interfere with proper thyroid function.[73][74]

DDT use against malaria

Malaria remains a major public health challenge in many parts of the world. The World Health Organization estimates there are 250 million cases of malaria every year, resulting in almost 1 million deaths. About 90% of these deaths occur in Africa, and mostly to children under the age of 5.[75]

The spraying DDT is but one of many public health interventions that have historically been used to control malaria, and one of many still in use today. Before the advent of DDT, aggressive campaigns to eliminate mosquito breeding grounds by drainage or

poisoning with Paris green or pyrethrum were used, sometimes successfully, to fight the disease. In many parts of the world, rising standards living resulted in the elimination of malaria as a collateral benefit of the introduction of window screens and improved sanitation.[15] Today, a variety of interventions are used, and usually many are used simultaneously. These include the use of antimalarial drugs to prevent or treat malaria infections; improvements in public health infrastructure to quickly diagnose, sequester, and treat infected individuals; the distribution of bednets and other methods intended to keep mosquitos from biting humans; and vector control strategies.[75] These include larvaciding with appropriate insecticides, ecological controls such as draining mosquito breeding grounds or introducing fish to eat larva, and indoor residual spraying (IRS) with DDT or other insecticides. IRS involves the treatment of all interior walls and ceilings with insecticides, and is particularly effective against mosquitoes, since many species will rest on an indoor wall before or after feeding. The contemporary DDT debate revolves around how much of a role the chemical should play in the mix of malaria control strategies.

Once the mainstay of anti-malaria campaigns, as of 2006 only 13 countries were still using DDT, including India and some southern African states.[75] The WHO's anti-malaria campaign in the 1950's and 60's relied heavily on the chemical and initially the results were promising, though short lived. Experts tie the resurgence of malaria to numerous factors, including poor leadership and management of malaria control programs, a chronic lack of funds in the countries worst hit by malaria, and the resistance of the malaria parasite itself to the drugs traditionally used to treat the illness.[76][77] According to Richard Tren, "Malaria surged through Africa in the 1990s, fueled by resistance to chloroquine and other historically effective drugs."[78] Resistance of mosquitoes to DDT has also been a factor, which was exacerbated by the often unrestricted use of DDT in agriculture. This, coupled with the awareness that DDT may be harmful both to humans and the environment led governments to restrict or curtail the use of DDT in vector control.[16]

The WHO has always included DDT in its list of insecticides recommend for IRS. Since the appointment of Arata Kochi as head of its anti-malaria division, its policy has shifted from recommending IRS only in areas of seasonal or episodic transmission of malaria, to advocating it in areas of continuous, intense transmission of the disease as well.[79] In 2007, the WHO clarified its position, saying it is "very much concerned with health consequences from use of DDT" and reaffirmed its commitment to phasing out the use of DDT.[80]

Overall effectiveness of DDT against malaria

In the period from 1934-1955 there were 1.5 million cases of malaria in Sri Lanka, resulting in 80,000 deaths. After the country invested in an extensive anti-mosquito program with DDT, there were only 17 cases reported in 1963. Thereafter the program was halted, and malaria in Sri Lanka rebounded to 600,000 cases in 1968 and the first quarter of 1969. Although the country resumed spraying with DDT, many of the local mosquitoes had acquired resistance to DDT in the interim, presumably because of the continued use of DDT for crop protection, so the program was not nearly as effective as it had been before. Switching to the more-expensive malathion in 1977 reduced the malaria infection rate to 3,000 by 2004. A recent study notes, "DDT and Malathion are no longer recommended since *An. culicifacies* and *An. subpictus* has been found resistant."[81]

A 2004 editorial in the *British Medical Journal* argues that the campaign against malaria is failing, that funding of malaria control should therefore be increased, and that use of DDT should be considered since DDT has "a remarkable safety record when used in small quantities for indoor spraying in endemic regions."[82]

One insecticide supply company states on its website:

> *DDT is still one of the first and most commonly used insecticides for residual spraying, because of its low cost, high effectiveness, persistence and relative safety to humans. [...] In the past several years, we supplied DDT 75% WDP to Madagascar, Ethiopia, Eritrea, Sudan, South Africa, Namibia, Solomon Island, Papua New Guinea, Algeria, Thailand, and Myanmar for Malaria Control project, and won a good reputation from WHO and relevant countries' government.*[83]

According to DDT advocate Donald Roberts, malaria cases increased in South America after countries in that continent stopped using DDT.[27] Other mosquito-borne diseases are also on the rise. Roger Bate claims that until the 1970s, DDT was used to eradicate the *Aedes aegypti* mosquito from most tropical regions of the Americas. The reinvasion of *Aedes aegypti* since has brought devastating outbreaks of dengue fever, dengue hemorrhagic fever, and a renewed threat of urban yellow fever.[84]

Mosquito resistance to DDT

Although the publication of *Silent Spring* undoubtedly influenced the U.S. ban on DDT in 1972, the reduced usage of DDT in malaria eradication began the decade before because of the emergence of DDT-resistant mosquitoes. Paul Russell, a former head of the Allied Anti-Malaria campaign, observed in 1956 that eradication programs had to be wary of relying on DDT for too long as "resistance has appeared [after] six or seven years."[15]

In some areas DDT has lost much of its effectiveness, especially in areas such as India where outdoor transmission is the predominant form. According to one article by V.P. Sharma, "The declining effectiveness of DDT is a result of several factors which frequently operate in tandem. The first and the most important factor is vector resistance to DDT. All populations of the main vector, *An. culicifacies* have become resistant to DDT." In India, with its outdoor sleeping habits and frequent night duties, "the excito-repellent effect of DDT, often reported useful in other countries, actually promotes outdoor transmission."[85]

Due to this DDT resistance, in Sri Lanka, parts of India, Pakistan, Turkey and Central America, DDT has already been replaced by organophosphate or carbamate insecticides, *e.g.* malathion or bendiocarb. [86]

According to a pesticide industry newsletter, DDT is obsolete for malarial prevention in India not only owing to concerns over its toxicity, but because it has largely lost its effectiveness. Use of DDT for agricultural purposes was banned in India in 1989, and its use for anti-malarial purposes has been declining. Use of DDT in urban areas of India has halted completely. Food supplies and eggshells of large predator birds still show high DDT levels.[87] Parasitology journal articles confirm that malarial vector mosquitoes have become resistant to DDT and HCH in most parts of India.[88] Nevertheless, DDT is still manufactured and used in India.[89] One study concludes "The overall results of the study revealed that DDT is still a viable insecticide in indoor residual spraying owing to its effectivity in well supervised spray operation and high excito-repellency factor."[90]

The initial appearance of this resistance was largely due to the much greater quantity of DDT which had been used for agricultural spraying, rather than the relatively insignificant amounts used for disease prevention. According to one study which attempted to quantify the lives saved due to banning agricultural use of DDT and thereby slowing the spread of DDT resistance: "Correlating the use of DDT in El Salvador with renewed malaria transmission, it can be estimated that at current rates each kilo of insecticide added to the environment will generate 105 new cases of malaria."[16]

Advocates for continuing use of DDT against malaria state that "Limited use of DDT for public health has continued to be effective in areas where it is used inside homes. As DDT's chief property is repellency, mosquitoes often avoid the DDT treated homes altogether. In so doing, they avoid the exposure that promotes resistance as well. DDT resistance exists in West Africa and in other malarial areas, such as India. Isolated occurrences of DDT resistance have occurred in South Africa, and South Africa continues to monitor for resistance. As the various Departments of Health that use it carefully control DDT use, it is unlikely that resistance will emerge as a major problem."[91]

Studies of malaria-vector mosquitoes trapped while exiting windows in KwaZulu-Natal Province, South Africa found susceptibility to 4% DDT (the WHO susceptibility standard), in 63% of the samples, compared to the average of 86.5% in the same species caught in the open. The authors concluded that "Finding DDT resistance in the vector *An. arabiensis*, close to the area where we previously reported pyrethroid-resistance in the vector *An. funestus* Giles, indicates an urgent need to develop a strategy of insecticide resistance management for the malaria control programmes of southern Africa." [92]

The avoidance of DDT-sprayed walls by mosquitoes is sometimes touted as a beneficial aspect of DDT.[90] For example, a 2007 study published in PLoS ONE reported that DDT-resistant mosquitoes still avoided DDT-treated huts, while entering huts treated with other insecticides to which they were not resistant. The researchers argued that DDT was the best pesticide for use in IRS (even though it did not afford the most protection from mosquitos out of the three test chemicals) because the others pesticides worked primarily by killing or irritating mosquitoes—modes of action the authors presume mosquitoes will develop resistance to.[93] Others have argued that the avoidance of DDT sprayed walls by mosquitoes is detrimental to the actual eradication of the disease.[94] Unlike other insecticides such as pyrethroids, DDT requires a long period of contact before mosquitoes pick up a lethal dose; however its irritant property makes them fly off before this occurs. "For these reasons, when comparisons have been made, better malaria control has generally been achieved with pyrethroids than with DDT." [86]

Residents' resistance to use of DDT

In areas where resistance from residents prevents a high percentage of the homes being effectively sprayed, the effectiveness of the intervention is greatly reduced.[86][15] Many residents resist spraying of DDT for various reasons. For instance, the smell lingers,[95] and DDT leaves a stain on the walls.[96][94][86][95][97] While that stain makes it easier to check whether the room has been sprayed it causes some villagers to avoid spraying of their homes [15][97][98][86] or to resurface the wall, which eliminates the residual insecticidal effect of the spraying.[94][97][98] "Pyrethroids such as deltamethrin and lambda-cyhalothrin are … much more acceptable to householders because they leave no visible deposit on walls… therefore rates of refusal of spraying by householders are lower with pyrethroids than with DDT."[86]

In addition, DDT is not suitable for this type of spraying in Western-style plastered or painted walls, only traditional dwellings with unpainted walls made of mud, sticks, dung, thatch, clay, or cement.[92][95][98][97]As rural areas of South Africa become more prosperous, there is a shift towards Western style housing, leaving fewer homes suitable for DDT spraying, and

necessitating the use of alternative insecticides.[98]

Other villagers object to DDT spraying because it does not kill cockroaches[86] or bedbugs;[94] rather, it excites such pests making them more active,[95][98][97][96][15] so that often use of another insecticide is additionally required.[98] Pyrethroids such as deltamethrin and lambdacyhalothrin, on the other hand, are more acceptable to residents because they kill these nuisance insects as well as mosquitoes.[86] DDT has also been known to kill beneficial insects, such as wasps that kill caterpillars that, unchecked, destroy thatched roofs.[15]

As a result, says Dr. Avertino Barreto, chief of infectious disease control in Mozambique, resistance to DDT spraying is "homegrown", not due to "pressure from environmentalists". "They only want us to use DDT on poor, rural black people," he says. "So whoever suggests DDT use, I say, 'Fine, I'll start spraying in your house first.' "[95]

Human exposure associated with DDT spraying for disease vectors

In the low income areas where malaria eradication is necessary, it is almost impossible to ensure that DDT intended for disease prevention does not get diverted to use on crops, on a totally unregulated basis. "The consequent insecticidal residues in crops at levels unacceptable for the export trade have been an important factor in recent bans of DDT for malaria control in several tropical countries".[86] Adding to this problem is a lack of skilled personnel and supervision.[94]

Evidence for exposure to DDT is seen in South Africa[99][100], where in contrast to areas where DDT use has ceased (even where it was used heavily), in areas where DDT is currently in use ostensibly in small amounts for malaria prevention only, DDT levels in men and women were significantly higher than the allowable daily intake.[97] Breast milk from regions where DDT is used for malaria control contains enough DDT to greatly exceed the allowable daily intake of breast feeding infants.[101][57] These levels have been associated with neurological abnormalities in babies ingesting relatively large quantities of DDT in their milk[86] although toxicity via this mode of intake has not been proved.[97]

Some researchers have suggested that the negative health effects of exposure to DDT might outweigh the health benefits afforded by anti-malarial properties. For example, scientists with the US National Institute of Environmental Health Sciences argued in *The Lancet* that "Although DDT is generally not toxic to human beings and was banned mainly for ecological reasons, subsequent research has shown that exposure to DDT at amounts that would be needed in malaria control might cause preterm birth and early weaning, abrogating the benefit of reducing infant mortality from malaria...DDT might be useful in controlling malaria, but the evidence of its adverse effects on human health needs appropriate research on whether it achieves a favourable balance of risk versus benefit."[18]

Criticism of restrictions on DDT use

There are claims that restrictions on the use of DDT in vector control have resulted in substantial numbers of unnecessary deaths due to malaria. Estimates for the number of deaths that have been caused by an alleged lack of availability of DDT range from hundreds of thousands, according to Nicholas Kristof,[102] to much higher figures. Robert Gwadz of the National Institutes of Health said in 2007 that "The ban on DDT may have killed 20 million children."[103] Paul Driessen, author of *Eco-Imperialism: Green Power, Black Death*,[104] argues that the epidemic of malaria in Africa not only takes the lives of 2 million people a year, but leaves those who survive malaria unable to contribute to the economy while sick and more vulnerable to subsequent diseases that might kill them.

These arguments have been called "outrageous" by former WHO scientist Socrates Litsios, and May Berenbaum, a professor of entomology at the University of Illinois at Urbana-Champaign, says that "to blame environmentalists who oppose DDT for more deaths than Hitler is worse than irresponsible."[105] In May 2008 article in *Prospect*, John Quiggin and Tim Lambert write that "the most striking feature of the claim against Carson is the ease with which it can be refuted."[106]

It has been suggested that DDT treatments were used long enough to eliminate insect-borne diseases in the West, but now that it is only needed in poorer nations in Africa, Asia and elsewhere, it has been banned or otherwise restricted. Some environmental groups have been strongly criticized for trying to ban all use of DDT. According to Amir Attaran, many environmentalist groups fought against the public health exception of DDT in the 2001 Stockholm Convention, against the objections of third world governments and many malaria researchers. "Greenpeace, World Wildlife Fund, Physicians for Social Responsibility and over 300 other environmental organizations advocated for a total DDT ban, starting as early as 2007 in some cases."[107] In an opinion piece in *Nature Medicine* he strongly objected to what would have been a de facto ban and stated: "Environmentalists in rich, developed countries gain nothing from DDT, and thus small risks felt at home loom larger than health benefits for the poor tropics. More than 200 environmental groups, including Greenpeace, Physicians for Social Responsibility and the World Wildlife Fund, actively condemn DDT for being "a current source of significant injury to...humans."[108]

Criticisms of a ban on DDT often refer specifically to the 1972 US ban (with the implication that this constituted a worldwide ban), while ignoring that DDT has not been banned for public health use in most areas of the world where malaria is endemic.[109] Reference is also often made to Rachel Carson's *Silent Spring* even though she never pushed for a ban on DDT. In fact, she devoted a page of the book to consideration of the relationship between DDT and malarial mosquitoes, with cognizance of the evolution of resistance in the mosquito, concluding:

> It is more sensible in some cases to take a small amount of damage in preference to having none for a time but paying for it in the long run by losing the very means of fighting [is the advice given in Holland by Dr Briejer in his capacity as director of the Plant Protection Service]. Practical advice should be "Spray as little as you possibly can" rather than "Spray to the limit of your capacity."

In addition, developing nations are typically heavily dependent on aid from agencies that made the aid contingent upon non-usage of DDT. The *British Medical Journal* of March 11, 2000, reports that the use of DDT in Mozambique "was stopped several decades ago, because 80% of the country's health budget came from donor funds, and donors refused to allow the use of DDT."[110] For instance, the pro-DDT advocacy group Africa Fighting Malaria (AFM) maintains that USAID and some other international donor organizations have refused to fund public health DDT programs.[111] Roger Bate of AFM asserts that "many countries have been coming under pressure from international health and environment agencies to give up DDT or face losing aid grants: Belize and Bolivia are on record admitting they gave in to pressure on this issue from [USAID]."[112]

However, according to the USAID website, "USAID has never had a 'policy' as such either 'for' or 'against' DDT for IRS. The real change in the past two years [2006/07] has been a new interest and emphasis on the use of IRS in general—with DDT or any other insecticide—as an effective malaria prevention strategy in tropical Africa."[113] USAID's Kent R. Hill states that the agency has been misrepresented: "USAID strongly supports spraying as a preventative measure for malaria and will support the use of DDT when it is scientifically sound and warranted."[114] The agency's website explains that in many cases alternative malaria control measures were judged to be more cost-effective that DDT spraying, and so were funded instead.[115]

Alternatives to DDT

DDT versus other insecticides

Those who advocate for increased use of DDT claim that the alternatives to DDT are generally more expensive, more toxic to humans and not always as effective at controlling malaria and insect-borne diseases, and that the petrochemical companies which patent those alternatives push(ed) for DDT's ban simply for their own profits; DDT had entered the public domain, their patented insecticides have not. Actual data on the cost-effectiveness of DDT versus other insecticides and/or means of fighting malaria is, in fact, lacking. One complicating factor is that the relative costs of various measures vary, depending on geographical location and ease of access, the habits of the particular mosquitoes prevalent in each area, the degrees of resistance to various pesticides exhibited by the mosquitoes, and the habits and compliance of the population, among other factors.

Organophosphate or carbamate insecticides, *e.g.* malathion or bendiocarb, are considerably more expensive than DDT, and malathion requires more frequent respraying. Pyrethroids such as deltamethrin and lambdacyhalothrin are also more expensive than DDT, but due to their much greater coverage per unit weight, the net cost per house is about the same.[86]

There are some insecticide alternatives to DDT, including methoxychlor and pyrethroids. The environmental and health effects of alternatives are also under scrutiny. Under the Stockholm Convention, these are issues to be addressed when investigating and promoting alternative chemicals. A recent study has found that DDT as well as pyrethroid residues, such as permethrin and deltamethrin, were present in breast milk from a malaria controlled area in South Africa. The DDT was derived from malaria control, but the pattern of pyrethoid pollution indicated exposure via agricultural use, where mothers frequently work in cotton fields, as well as from domestic use of insecticide dusts in vegetable gardens.[116]

DDT versus non-chemical vector control

Before DDT, malaria was successfully eradicated or curtailed in several tropical areas by removing or poisoning the breeding grounds of the mosquitoes or the aquatic habitats of the larva stages, for example by filling or applying oil to places with standing water. These methods have seen little application in Africa for more than half a century.[117]

The relative effectiveness of IRS (with DDT or alternative insecticides) versus other malaria control techniques (e.g. bednets or prompt access to anti-malarial drugs) varies greatly and is highly dependent on local conditions.[17]

A study by the World Health Organization released in January 2008 found that mass distribution of insecticide-treated mosquito

nets and artemisinin based drugs cut malaria deaths in half in Rwanda and Ethiopia, countries with very high malaria burdens. IRS with DDT was determined to not have played an important role in the reduction of mortality.[118]

Vietnam is an example of a country that has seen a continued decline in malaria cases after switching in 1991 from a poorly funded DDT-based campaign to a program based on prompt treatment, bednets, and the use of pyrethroid group insecticides. Deaths from malaria dropped by 97%.[119]

In Mexico, the use of a range of effective and affordable chemical and non-chemical strategies against malaria has been so successful that the Mexican DDT manufacturing plant ceased production voluntarily, due to lack of demand.[120] Furthermore, while the increased numbers of malaria victims since DDT usage fell out of favor would, at first glance, suggest a 1:1 correlation, many other factors are known to have contributed to the rise in cases.

A review of fourteen studies on the subject in sub-Saharan Africa, covering insecticide-treated nets, residual spraying, chemoprophylaxis for children, chemoprophylaxis or intermittent treatment for pregnant women, a hypothetical vaccine, and changing the first line drug for treatment, found decision making limited by the gross lack of information on the costs and effects of many interventions, the very small number of cost-effectiveness analyses available, the lack of evidence on the costs and effects of packages of measures, and the problems in generalizing or comparing studies that relate to specific settings and use different methodologies and outcome measures. The two cost-effectiveness estimates of DDT residual spraying examined were not found to provide an accurate estimate of the cost-effectiveness of DDT spraying; furthermore, the resulting estimates may not be good predictors of cost-effectiveness in current programmes.[121]

However, a study in Thailand found the cost per malaria case prevented of DDT spraying ($1.87 US) to be 21% greater than the cost per case prevented of lambdacyhalothrin-treated nets ($1.54 US),[122] at very least casting some doubt on the unexamined assumption that DDT was the most cost-effective measure to use in all cases. The director of Mexico's malaria control program finds similar results, declaring that it is 25% cheaper for Mexico to spray a house with synthetic pyrethroids than with DDT.[120] However, another study in South Africa found generally lower costs for DDT spraying than for impregnated nets.[123]

A more comprehensive approach to measuring cost-effectiveness or efficacy of malarial control would not only measure the cost in dollars of the project, as well as the number of people saved, but would also take into account the negative aspects of insecticide use on human health and ecological damage. One preliminary study regarding the effect of DDT found that it is likely the detriment to human health approaches or exceeds the beneficial reductions in malarial cases, except perhaps in malarial epidemic situations. It is similar to the earlier mentioned study regarding estimated theoretical infant mortality caused by DDT and subject to the criticism also mentioned earlier.[124]

A study in the Solomon Islands found that "although impregnated bed nets cannot entirely replace DDT spraying without substantial increase in incidence, their use permits reduced DDT spraying."[125]

A comparison of four successful programs against malaria in Brazil, India, Eritrea, and Vietnam does not endorse any single strategy but instead states "Common success factors included conducive country conditions, a targeted technical approach using a package of effective tools, data-driven decision-making, active leadership at all levels of government, involvement of communities, decentralized implementation and control of finances, skilled technical and managerial capacity at national and sub-national levels, hands-on technical and programmatic support from partner agencies, and sufficient and flexible financing."[126]

DDT resistant mosquitoes have generally proved susceptible to pyrethroids. Thus far, pyrethroid resistance in *Anopheles* has not been a major problem.[86]

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External links

US Government

- A Persistent Controversy, a Still Valid Warning - May Berenbaum, head of the entomology department at University of Illinois, Urbana-Champaign
- EPA press release - December 31, 1972
- EPA on DDT

Toxicity

- DDT Technical Fact Sheet - National Pesticide Information Center
- DDT General Fact Sheet - National Pesticide Information Center
- Agency for Toxic Substances and Disease Registry: ToxFAQs for DDT, DDE and DDD
- EXTOXNET: Pesticide Information Profiles—DDT
- Scorecard: The Pollution Information Site—DDT
- Interview with Barbara Cohn, PhD about DDT and breast cancer

Environmental impact

- Microbial Degradation of Pesticides
- US Fish and Wildlife Service Historic News Releases - DDT
- DDT and its Derivatives - Environmental Aspects
- Aerobic pathway of DDT metabolization
- Anaerobic pathway of DDT metabolization
- Pesticide residues in food 2000 : DDT
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- Environmental Fate Evaluation of DDT, Chlordane and Lindane
- EPA: Pesticides and Public Health

Politics and DDT

- DDT, Eggshells, and Me Article from Reason magazine
- DDT: The Bald Eagle Lie Article from FrontPageMag.com
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Malaria and DDT

- "If Malaria's the Problem, DDT's Not the Only Answer", a *Washington Post* column by entomologist May Berenbaum
- 'Andrew Spielman, Harvard School of Public Health, discusses environmentally friendly control of Malaria and uses of DDT Freeview video provided by the Vega Science Trust
- The DDT ban myth
- Malaria and the DDT Story
- Malaria and DDT
- Putting Myths to Bed
- The Kill Malarial Mosquitoes NOW! coalition, a project of the international NGO Africa Fighting Malaria
- Nets for fighting malaria
- Ugandan farmers push for DDT ban. Dated 31 May 2008 ABC News