Invited Commentary

Invited Commentary: Why DDT Matters Now

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Abbreviations: CI, confidence interval; DDE, 1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene; DDT, 1,1,1-trichloro-2,2-bis(4-chlorophenyl)ethane.

The insecticide 1,1,1-trichloro-2,2-bis(4-chlorophenyl)ethane (DDT) has been banned in the United States since 1972, and serum levels in the general population have fallen substantially. Why then would the Journal bother to publish two articles on DDT and health in the present issue (1, 2)? The authors of the papers allude to the significance of their contributions, but their explanations merit elaboration.

In many countries, policy towards DDT for malaria vector control is being reevaluated or changing. In Uganda, whether to use DDT is now being sharply debated (3, 4). In Madagascar, South Africa, and Zambia, recent reintroduction of DDT has coincided with marked reductions in malaria morbidity and, in all likelihood, mortality (5–7). In accord with an international treaty, other countries have registered as potential users of DDT (8), but few utilize it because other methods are effective in the particular setting or because of reluctance. The reluctance to use DDT is based on concern for wildlife and humans (9)—the same reasons that led to the ban in the United States and other developed countries.

About 1 million malaria deaths occur annually worldwide, and the incidence is increasing (10). The increase is due mainly to drug-resistant Plasmodium, but in some cases it may be due to reticence to use indoor residual spraying of homes with DDT when it is the best option for disease vector control. The indoor residual spraying with pyrethroids failed in South Africa because the mosquitoes became resistant. Mosquitoes can also become resistant to DDT’s toxicity, but they are still repelled by it (11).

DDT was once used worldwide, nearly all of it for agriculture. The relatively small amounts used for control of infectious disease, however, contributed significantly to the eradication of malaria in many countries and to a substantial reduction of morbidity and mortality elsewhere (12). Whether much of the DDT used for indoor residual spraying is released into the surrounding environment is unclear. Furthermore, almost no data are available on the health effects of DDT exposure at the levels experienced by those living in sprayed homes. The data available on the potential health effects of DDT and its degradation products suggest that there may be no serious consequences of exposure at levels somewhat lower than those encountered by inhabitants of homes sprayed with DDT, though some associations require further inquiry (13). For example, animal experiments clearly indicate that neurodevelopmental effects of early life exposure to DDT are among the most sensitive outcomes (14). Several human studies that address neurodevelopment suggest there may be effects even at relatively low doses (15–17). Several early and relatively crude human studies also suggested adverse reproductive effects. The recent resurgence of interest in health effects has paralleled the recognition that DDT remains useful in selected settings.

The two studies on DDT and health reported in this issue of the Journal were remarkably well done. In both, exposure was assessed by measurement of DDT and 1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene (DDE), which is the primary degradation product of DDT. The half-life of DDT in humans is more than 4 years; for DDE, it is probably longer, for example, 10 years (14, 18, 19). Farhang et al. (1) examined DDT and DDE during pregnancy in relation to preterm and small-for-gestational-age birth, as well as related outcomes, among 420 US women who delivered boys in the...
The subjects in both studies had unusually high exposure levels. The median DDE serum level in the subjects from China in the 1990s was 26 μg/liter (2) and, among those from the United States in the 1960s, the median was 43 μg/liter (1). In the United States now, the median is less than 2 μg/liter (20). By comparison, among people living in houses sprayed with DDT for malaria control in Africa, the median level of DDE was about 80 μg/liter (21). With data on DDT health effects among those dwelling in homes treated with indoor residual spraying being nearly nonexistent, these two new studies are important contributions.

The study by Farhang et al. (1) comes in the wake of a similar but larger one (22), in which the adjusted odds ratio for preterm birth per interquartile range increase in DDE was 1.33 (95 percent confidence interval (CI): 1.17, 1.52) and for small-for-gestational-age birth was 1.15 (95 percent CI: 0.98, 1.35). For preterm birth, the odds ratio from the study by Farhang et al. was 1.28 (95 percent CI: 0.73, 2.23) per interquartile range increase—not all that different, though the precision was lower; for small-for-gestational-age birth, no increase was found (odds ratio = 0.75, 95 percent CI: 0.44, 1.26). The study by Farhang et al. was nested in the Child Health and Development Study cohort. A second study that was nested in the same cohort and of similar size and scope was not supportive of an association of DDE with either outcome (23). The Child Health and Development Study results are important because, compared with most studies on the topic, they not only had relatively high levels of exposure but also were prospective and nicely designed and analyzed. Therefore, the absence of convincing associations of DDE with preterm birth and size at birth in these studies weighs heavily against the hypothesis of such effects. MacMahon’s comments on data addressing an earlier question about DDT are apropos: “As if we needed it, the Journal [Journal of the National Cancer Institute] brings another reminder of the caution with which the results of a single epidemiologic study, or even a handful of them, should be regarded” (24, p. 572).

That caveat notwithstanding, the result from the paper by Venners et al. (2) suggests that, among studies with subjects exposed at higher levels, the evidence consistently supports a relation of DDE with pregnancy loss. In that study, compared with those in the lowest tertile of exposure, those in the highest tertile had an adjusted odds ratio of early loss of 2.1 (95 percent CI: 1.3, 3.6). For clinical loss, the analogous odds ratio was 1.3 (95 percent CI: 0.5, 3.1). One large, recent study of DDE and clinical loss showed a monotonic dose-response relation except among the most highly exposed—a pattern that could be accounted for by increased risk of early loss among those most exposed (25). While the consistency of the DDE–pregnancy loss results is provocative, one would expect that, if DDE caused early loss, the time to pregnancy would be increased. Another recent report, however, suggests that time to pregnancy is not related to DDE (26). The relation of DDE to pregnancy loss is unlikely to be as tidy as it appears on first glance. In animal experiments on the reproductive toxicity of DDT and related compounds (14), adverse effects, when found, were seen at doses that were much higher than for those who live in DDT-sprayed homes. Nonetheless, the possibility that DDT use causes early pregnancy loss is disturbing. Even if mortality could be accurately ascertained in areas where homes are sprayed with DDT (generally not the case), an effect on early pregnancy would remain occult. Early pregnancy loss can be detected only in prospective studies. Pursuing this finding among women living in DDT-treated homes will be a challenge.

The DDT mixture applied to homes comprises mainly DDT and related compounds but contains little DDE. The DDE in people who live in homes that are sprayed arises from their own metabolism of DDT and from ingestion of DDE that has been produced by metabolism in the food chain or photodegradation. The DDT/DDE ratio of 0.36 among dwellers in sprayed homes is higher than the ratio among nondwellers (e.g., 0.26 in the paper by Farhang et al. (1); 0.05 in the paper by Venners et al. (2)). The toxic effects of these compounds are quite different. In both studies in this issue of the Journal, the possibility of confounding or interaction between DDT and DDE was probably not important. However, as potential health effects are explored among those dwelling in DDT-sprayed homes, these issues will need greater attention.

An efficacious vaccine for malaria is at least 10 years off. Where indoor residual spraying is a key component of malaria control, increasing resistance to pyrethroids means that questions about DDT, health, and the environment will require resolution. Data that address these issues have the potential to influence the health of large numbers of people on short order.

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REFERENCES