## DDT Risk Assessments

Two recent articles in *EHP* (*1*,*2*) and the latest Agency for Toxic Substances and Disease Registry toxicologic profile for DDT (*3*) make repeated references to DDT risks. These statements of risk, like so many others, are one-sided and give no consideration to colossal increases in diseases previously controlled with DDT. Behind disease statistics are grievous human tragedies, as with the case of a little girl who died of an infection that could have been prevented if her house had been sprayed with DDT. She lived in a village in the Andes and was 8 years old in 1998 when she died of bartonellosis. Bartonellosis was previously controlled through malaria house-spray programs, but without DDT, the disease returned.

One-sided and narrowly focused risk assessments form the bedrock of anti-DDT advocacy (*4*,*5*), but advocacy for global elimination of DDT through United Nations Environment Programme (UNEP) treaty negotiations failed (*6*). Countries can continue using DDT for disease control, and DDT is not listed for global elimination. This outcome was possible only through efforts of hundreds of scientists on behalf of hundreds of millions of people at risk of illness and death from malaria (*7*).

Environmental activists who still want DDT eliminated and who are surprised by the lack of cost-effective alternatives should understand that global vilification of DDT eliminated almost all research on public health insecticides. Lack of research support persists and contrasts sharply with the richness of funds for research on adverse health effects of DDT; 29 major projects are presently funded by the National Institutes of Health (National Institute of Environmental Health Sciences, National Cancer Institute, National Institute of General Medical Sciences, and the National Institute of Child Health and Human Development) (*3*).

The evidence of DDT efficacy in controlling diseases is irrefutable. In just 3 years, house spraying in Guyana reduced maternal and infant mortalities by 56% and 39%, respectively, and reduced malaria cases by 99% (*8*). Similar evidence from other geographic areas persuaded delegates to UNEP treaty negotiations that DDT is still needed. Yet, and in spite of all contrary evidence, the UN program to phase out DDT is unabated (*9*,*10*). The current "phase-out" program by the World Health Organization's Roll Back Malaria initiative and the Global Environment Facility (Washington, DC) includes no publicized disease control performance standards and does not include appropriate on-site studies or tests to determine, under varying epidemiologic and environmental conditions, that DDT alternatives will provide adequate and sustained protection of rural populations. After years of successful efforts, the modus operandi of DDT elimination remains the same: apply political and economic pressures, convince country politicians that DDT is not needed, pass laws banning its use, and let impoverished rural populations quietly suffer spiraling increases in disease rates (*11*,*12*). Even short-term commitments of funds for purchasing the more expensive and less effective DDT alternatives are a continuation of past practices: in the end, disease rates will increase.

The Andean girl's death is one of millions of preventable deaths that occurred as national and international regulations, trade barriers, international policies, and UN resolutions were applied to stop public health uses of DDT (*13*). With absolute certainty, the best measures of success in the anti-DDT campaign are increases in disease and death from malaria, leishmaniasis, bartonellosis, dengue fever, and dengue hemorrhagic fever. We can add to this list the renewed threat that urban yellow fever will once again ravage populations of the Americas. Even this emerging threat is linked to past failures to continue appropriate public health uses of DDT. The Andean girl's unrecognized but precious stake in the DDT issue was her life, now lost. How many millions more must die because of hypothetical risks from minute quantities of DDT sprayed on internal house walls?

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### References and Notes

1. Lindhe, O, Lund BO, Bergman A, Brandt I. Irreversible binding and adrenocorticolytic activity of the DDT metabolite 3-methylsolfonyl-DDE examined in tissue-slice culture. Environ Health Perspect 109:105–110 (2001).
2. Ulrich EM, Caperell-Grant A, Jung SH, Hites RA, Bigsby RM. Environmentally relevant xenoestrogen tissue concentrations correlated to biological responses in mice. Environ Health Perspect 108:973–977.
3. ATSDR. Toxicological Profile for DDT/DDD/DDE (update; released for public comment). Atlanta, GA:Agency for Toxic Substances and Disease Registry, 2000.
4. World Wildlife Fund. Resolving the DDT Dilemma: Protecting Biodiversity and Human Health. Washington, DC:World Wildlife Fund, 1998.
5. Physicians for Social Responsibility. The Modern Malaria Control Handbook. PSR Guide to Sources and Strategies. Washington, DC:Physicians for Social Responsibility, 1999.
6. Booker SM. Pulling the plug on POPs. Environ Health Perspect 109:A17 (2001).
7. Malaria Foundation International. DDT-Malaria: Open Letter. Available: http://www.malaria.org/DDT_signatures.html [cited 8 June 2001].
8. Giglioli G. Eradication of *Anopheles darlingi* from the inhabited areas of British Guiana by DDT residual spraying. J Nat Mal Soc 10:142–161 (1951).
9. World Health Organization. DDT Use in Malaria Prevention and Control. Note for the press 15, 28 November 2000. Available: http://www.who.int/inf-pr-2000/en/note2000-15.html [cited 8 June 2001].
10. World Health Organization. INC5 delegates seek exemption for DDT. RBM News 2:5 (2000).
11. Roberts DR, Manguin S, Mouchet J. DDT house spraying and re-emerging malaria. Lancet 356:330–332 (2000).
12. Attaran A, Roberts DR, Curtis CF, Kilama WL. Balancing risks on the backs of the poor. Nature Med 6(7):729–731 (2000).
13. Roberts DR. DDT and the global threat of re-emerging malaria. Pesticide Safety News 2(4):4–5 (1999).

## DDT Risk Assessments: Response

Donald Roberts contends that organizations such as the World Wildlife Fund (WWF) failed in efforts to eliminate DDT under the recently negotiated persistent organic pollutants (POPs) treaty.

To the contrary, the WWF strongly supports the treaty's language on DDT. Throughout the negotiations, the WWF recognized that DDT should not be banned immediately and that uncertainties about the cost and effectiveness of alternatives required flexibility in treaty language (*1*,*2*). Reflecting this, the new treaty proclaims ultimate elimination of DDT as a goal while establishing a mechanism for reducing reliance on DDT and promoting alternatives (*3*). As a result of the treaty, new funds are being provided by the Global Environment Facility to develop malaria control programs that reduce use of DDT.

Roberts has been an outspoken defender of DDT. He has prolifically and passionately downplayed the toxicologic risks of DDT while emphasizing its effectiveness for malaria control (*4*–*6*). He frequently argues that external political pressures drive poorer nations to abandon DDT, thereby endangering millions of the world's most impoverished people.

Malaria-endemic countries have had ample scientific justification for seeking alternatives. For example, in the mid-1990s, Mexican public health researchers expressed concern about high human exposures to DDT as a result of malaria control operations (*7*,*8*). Mexico has since eliminated DDT while successfully combating malaria. South Africa also sought to reduce use of DDT in the mid-1990s because of concern about elevated levels in mothers' milk (*9*). One species of mosquito was resistant to alternative sprays, so South Africa resumed using DDT. South Africa concluded that the hazards from malaria outweigh those

associated with DDT exposure. South Africa's experience underscores the importance of the flexibility provided by the POPs treaty.

Brazil and India offer important lessons about limits to DDT's effectiveness. During the late 1980s and early 1990s, malaria rates in Brazil went up even as spraying of houses with DDT increased, but dropped after Brazil shifted strategies (*10*). With assistance from the World Bank, India is reducing its reliance on DDT. The main rural malaria vector (responsible for 65% of India's malaria) is resistant to DDT (*11*). Indian researchers found elevated levels of DDT in buffalo milk, soil, water, and human blood where DDT had been sprayed to control malaria (*12*,*13*).

The ATSDR's 2000 update of its toxicologic profile for DDT/DDE (*14*) reflects major concerns raised by the WWF and other environmental and public health groups during the POPs negotiations. In contrast to the previous profile published in the early 1990s, the update contains a large section, "Health Effects in Wildlife Potentially Relevant to Human Health," reminding readers that animals are sentinels for health effects in humans. A new section captioned "Children's Susceptibility" reiterates a central message from the U.S. National Academy of Sciences' landmark 1993 report on pesticides in the diets of infants and children (*15*): children are not little adults, but may be uniquely susceptible and exposed to pesticides.

The data in the toxicologic profile support the logic of the POPs treaty: DDT can be valuable for controlling malaria, but it is prudent to reduce human exposures. Recent studies on humans, too late to be included in the toxicologic profile, further support such caution. For example, Longnecker et al. (*16*) found that DDE concentrations in mothers are associated with increased risk of pre-term delivery and lowered birth weight.

Roberts takes *EHP*'s contributors to task for their "one-sided" references to DDT's risks and their failures to account for DDT's benefits. Roberts' encomium to DDT is itself one-sided. Why expose humans to hazards from DDT when less risky strategies might be employed? The POPs treaty encourages development of alternatives and provides a new funding mechanism to support malaria control.

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**REFERENCES AND NOTES**

1. Liroff RA. Commentary: Reduction and elimination of DDT should proceed slowly. Br Med J 321:1404–1405 (2000).
2. Liroff RA. Beyond the DDT controversy: a search for common ground. Presented at the 66th Annual Meeting, American Mosquito Control Association, 13 March 2000, Atlantic City, NJ.
3. United Nations Environment Programme. Text of the Stockholm Convention on Persistent Organic Pollutants for Adoption by the Conference of Plenipotentiaries. UNEP/POPS/CONF/2. Available: http://irptc.unep.ch/pops/POPS_Inc/dipcon/meetingdocs/conf2/en/conf-2e.pdf [cited 3 July 2001].
4. Roberts DR, Manguin S, Mouchet J. DDT house spraying and re-emerging malaria. Lancet 356:330–332 (2000)
5. The DDT question. Lancet 356:1189–1191 (2000).
6. Roberts DR. DDT and the global threat of re-emerging malaria. Pesticide Safety News 2(4):4–5 (1999).
7. López-Carrillo L, Torres-Arreola L, Torres-Sánchez L, Espinosa-Torres F, Jiménez C, Cebrián M, Waliszewski S, Saldate 0. Is DDT use a public health problem in Mexico? Environ Health Perspect 104:584–588 (1996).
8. Waliszewski SM, Pardio Sedas VGT, Chantiri JN, Infanzon RM, Rivera J. Organochlorine pesticide residues in human breast milk from tropical areas in Mexico. Bull Environ Contam Toxicol 57:22–28 (1996).
9. Bouwman H. Malaria control and the paradox of DDT. Africa—Environment and Wildlife 8:54–56 (2000).
10. Gusmao R. The control of malaria in Brazil. Presented at the International Workshop on the Contextual Determinants of Malaria, 14–18 May 2000, Lausanne, Switzerland.
11. Sharma VP. Current scenario of malaria in India. Parassitologia 41:349–353 (1999).
12. Battu RS, Singh PP, Joia BS, Kalra RL. Contamination of bovine milk from indoor use of DDT and HCH in malaria control programmes. Sci Total Environ 86:281–287 (1989).
13. Dua VK, Pant CS, Sharma VP. Determination of levels of HCH and DDT in soil, water and whole blood from bioenvironmental and insecticide-sprayed areas of malaria control. Indian J Malariology 33:7–15 (1996).
14. ATSDR. Toxicological profile for DDT/DDD/DDE (update; released for public comment). Atlanta, GA:Agency for Toxic Substances and Disease Registry, 2000.
15. National Research Council. Pesticides in the Diets of Infants and Children. Washington, DC:National Academy Press, 1993.
16. Longnecker MP, Klepaboff MA, Brock JA, Zhou H. DDE is associated with increased risk of preterm delivery and small-for-gestational-age birthweight in humans. Organohalogen Compounds 48:161–162 (2000).

## Mercury and Autistic Gut Disease

We are challenged to consider the possible role of environmental toxins in autism and other childhood behavioral disorders (*1*), and creative research in this area surely is warranted (*2*). Perhaps particular scrutiny should be given to mercury and autism. Many signs and symptoms of mercury exposure correspond to autism (*3*), and pink disease (acrodynia) from inorganic mercurial teething powders and autism bear strong behavioral resemblance.

Gut disease with inflammation is becoming increasingly evident in autism. Enterocolitis and lymphonodular hyperplasia are found in nearly 90% of regressed autistic children (*4*). Widespread inflammatory changes with poor intestinal digestive enzyme activity (*5*), abnormal intestinal permeability (*6*), and malabsorption (*7*) have been reported in various autistic subgroups. It would be logical to consider toxins known to cause gut injury when we look for causes of autism.

Inorganic mercurial compounds are notorious for gut injury in humans. In animals, chronic low-nanomolar exposure injures intestinal mucosa (*8*) and 30-min micromolar exposure injures the colon (*9*). Also, desposits of antibody in the intestine have resulted from chronic exposure to inorganic mercury (*10*).

Although systemic passage may be poor, inorganic mercury enjoys avid uptake by the small and large intestines (*11*). Organic and vapor forms are known to transit membranes quickly and distribute throughout the body, but their excretion is primarily fecal and significantly inorganic, which may affect intestinal residence.

Biliary mercury excretion, predominant in adults, is not achieved in suckling animals and may not exist in infants (*12*). Ligation of the bile duct of adult animals results in retograde movement of systemic mercury to the feces, emphasizing an excretory role for the intestine (*13*). Poor biliary excretion in infants might be expected to increase intestinal exposure to mercury. In suckling animals, two-thirds of total ingested inorganic mercury is recoverable after 6 days from gut tissue, particularly the ileum (*14*).

Worrisome levels of inorganic mercury exist in domestic water supplies (*15*) and in industrial emissions and municipal sludge widely used as fertilizer on crops (*16*). Up to 40% of mercury emissions from hydrocarbon combustion and 60% from incinerators is in the inorganic form (*17*), and mercurial "fall-out" may exceed 1 ppm in soil (*18*). Individual inorganic mercury ingestion can vary widely and may be greater than expected (*19*).

Some specifics about autism should heighten interest in mercury. A long clinical tradition has evolved in the use of vitamin $B_6$, and its activating enzyme ($B_6$-kinase) is totally inhibited in the intestine at nanomolar concentrations *in vitro* (*20*). Organic forms of mercury such as methyl mercury from fish and ethyl mercury as a vaccine preservative (thimersol) may also inflict gut injury. Methyl mercury in primates produces histologic abnormality of one intestinal cell line: Paneth cells are enlarged and packed with secretory granules (*21*), also specifically reported in autistic children (*5*).

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### References and Notes

1. May M. Disturbing behavior: neurotoxic effects in children. Environ Health Perspect 108:A262–A267 (2000).
2. Olden K, Guthrie J. Children's health: a mixed review [Editorial]. Environ Health Perspect 108:A250–251 (2000).
3. Bernard S, Enayati A, Redwood L, Roger H, Binstock T. Autism: a novel form of mercury poisoning. Med Hypoth 56(4):462–471 (2001).
4. Furlano RI, Anthony A, Day R, Brown A, McGarvey L, Thomson MA, Davies SE, Berelowitz M, Forbes A, Wakefield AJ, et al. Colonic CD8 and gamma delta T-cell infiltration with epithelial damage in children with autism. J Pediatr 138:366–372 (2001).
5. Horvath K, Papadimitriou JC, Rabsztyn A, Drachenberg C, Tildon JT. Gastrointestinal abnormalities in children with autistic disorder. J Pediatr 135:559–563 (1999).
6. D'Eufemia P, Celli M, Finocchiaro R, Pacifico L, Viozzi L, Zaccagnini M, Cardi E, Giardini O. Abnormal intestinal permeability in children with autism. Acta Paediatr 85:1076–1079 (1996).
7. Goodwin MS, Cowen MA, Goodwin TC. Malabsorption and cerebral dysfunction: a multivariate and comparative study of autistic children. J Autism Child Schizophr 1:48–62 (1971).
8. Banerjee S, Bhattacharya S. Histopathological changes induced by chronic nonlethal levels of elsan, mercury, and ammonia in the small intestine of *Channa punctatus* (Bloch). Ecotoxicol Environ Saf 31:62–68 (1995).
9. Bohme M, Diener M, Mestres P, Rummel W. Direct and indirect actions of $HgCl_2$ and methyl mercury chloride on permeability and chloride secretion across the rat colonic mucosa. Toxicol Appl Pharmacol 114:285–294 (1992).
10. Andres P. IgA-IgG disease in the intestine of Brown-Norway rats ingesting mercuric chloride. Clin Immunol Immunopath 30:488–494 (1984).
11. Sasser LB, Jarboe GE, Walter BK, Kelman BJ. Absorption of mercury from ligated segments of the rat gastrointestinal tract. Proc Soc Exp Biol Med 157:57–60 (1978).
12. Clarkson TW. Personal communication.
13. Zalups RK. Intestinal handling of mercury in the rat: implications of intestinal secretion of inorganic mercury following biliary ligation or cannulation. J Toxicol Environ Health 53:615–636 (1998).
14. Kostial K, Kargacin B, Landeka M. Gut retention of metals in rats. Biol Trace Elem Res 21:213–218 (1989).
15. Mumma RO, Raupach DC, Waldman JP, Tong SS, Jacobs ML, Babish JG, Hotchkiss JH, Wszolek PC, Gutenman WH, Bache CA, et al. National survey of elements and other constituents in municipal sewage sludges. Arch Environ Contamin Toxicol 13:75–83 (1984).
16. Wang R, ed. Water Contamination and Health. New York:Marcel Dekker, 1994.
17. Chang LW, ed. Toxicology of Metals. Boca Raton, FL:CRC Lewis Press, 1996.
18. Windom H. Personal communication.
19. Fergusson JE. The Heavy Metals: Chemistry, Environmental Impact, and Health Effects. Oxford, UK:Pergamon Press, 1990.
20. Srikantaiah MV, Radhakrishnan AN. Studies on the metabolism of vitamin B6 in the small intestine: Part III—purification and properties of monkey intestinal pyridoxal kinase. Indian J Biochem 7:151–156 (1970).
21. Chen W, Body RL, Mottet NK. Biochemical and morphological studies of monkeys chronically exposed to methylmercury. J Toxicol Environ Health 12:407–416 (1983).


## Corrections and Clarifications

Toussaint et al. discovered an error in a spreadsheet formula that affected some of the results in their paper [Chronic Toxicity of Chloroform to Japanese Medaka Fish. Environmental Health Perspectives 109:35–40 (2001)]. The intrahepatic level of chloroform at the 0.151 mg/L aquaria concentration was erroneously reported at 33 and 133 mg chloroform/g fish liver; the correct concentrations of chloroform in these two fish livers were 0.8 and 3.3 mg chloroform/kg fish liver. At the 1.463 mg/L aquaria chloroform concentration, the intrahepatic concentrations were incorrectly reported as 23, 26, 35, 41, 128, 144, 159, 194, and 219 mg/g fish liver. The correct intrahepatic concentrations for the 1.463 mg/L fish are 0.50, 0.58, 0.65, 1.03, 3.19, 3.59, 3.98, 4.84, and 5.48 mg chloroform/kg fish liver. Additionally, the chloroform peak in Figure 3 was incorrectly labeled; it should read 0.50 mg $CHCl_3$/kg fish liver (see correct figure below).
The authors regret the error.

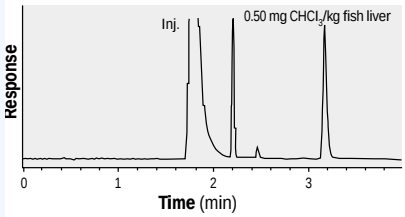


**Figure 3.** Chromatogram of a fish liver sample used to determine intrahepatic chloroform concentration in medaka fish exposed to 1.463 mg/L chloroform for 9 months. Peaks include the injection peak, two unknown peaks, and the chloroform peak, respectively. Instrumental detection limits of chloroform were 0.001 mg/L.

In the Editorial by Axelrod et al. [It's Time to Rethink Dose: The Case for Combining Cancer and Birth and Developmental Defects. Environ Health Perspect 109:A246–A249 (2001)], two references were reversed in the "References and Notes." The correct references are as follows:


22. Staessen JA, Gasowski J, Wang JG, Thijs L, Hond ED, Boissel JP, Coope J, Ekbom T, Gueyffier F, Liu L, et al. Renal function, cytogenetic measurements, and sexual development in adolescents in relation to environmental pollutants: a feasibility study of biomarkers. Lancet 357:1660–1669 (2001).
23. Sharpe RM, Skakkeback NE. Are oestrogens involved in falling sperm counts and disorders of the male reproductive tract? Lancet 341:1392–1395 (2000).


In "Examination of the Melatonin Hypothesis in Women Exposed at Night to EMF or Bright Light" by Graham et al. [Environ Health Perspect 109:501–507 (2001)], the keys in Figures 4 and 5 are incorrect. The corrected figures are shown below. *EHP* regrets the error.

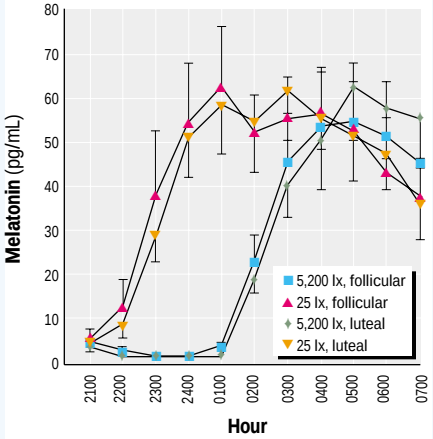


**Figure 4.** Mean (± SE) melatonin levels are plotted from 2100 hr to 0700 hr for eight women in the follicular menstrual phase (days 3–8) initially exposed for 4 hr to bright (5,200 lx) light or to dim (25 lx) light (study 3). Similar data are shown for eight women in the luteal phase (days 18–23) exposed to the same bright and dim light conditions. Bright light reduced the total amount of melatonin secreted ($p < 0.0001$) and delayed peak blood concentrations by 4 hr.

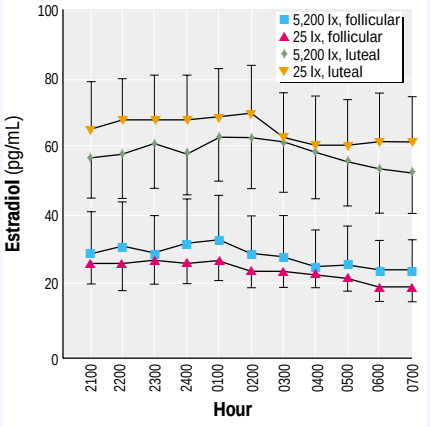


**Figure 5.** Mean (± SE) estradiol levels are plotted from 2100 hr to 0700 hr for the luteal group ($n = 8$) initially exposed for 4 hr to bright (5,200 lx) light or to dim (25 lx) light (study 3). Similar data are presented for the follicular group ($n = 8$) exposed to the bright and dim light conditions. Unlike the profound changes observed in melatonin (Figure 4), no alterations in point-by-point matching measures of estradiol were found in either phase of the menstrual cycle.