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Author(s)	Thompson, Lesa Angela
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学位論文内容の要旨
Abstract of the dissertation

博士の専攻分野の名称：博士（獣医学）　　氏名：Lesa Thompson
Name

学位論文題名
The title of the doctoral dissertation

Health risk assessment and molecular biological characteristics associated with organochlorine insecticides sprayed for control of pests and vector-borne diseases: One Health aspects

(有機塩素系殺虫剤散布による病原性媒介生物および疾患のコントロールが及ぼす分子生物学的特徴と健康リスク評価に関する研究)

Dichloro-diphenyl-trichloroethane (DDT) use in indoor residual spraying programs in many countries is a cost-effective method of controlling malaria vectors to reduce disease cases and fatalities. However, the hidden health costs relating to exposure to this persistent organic pollutant in humans, animals and the environment are difficult to quantify. A literature review revealed extensive contamination of food products in many countries across the African continent by DDT and other organochlorine pesticides (OCPs). Vegetables, meat and dairy products (including processed foods) contained OCPs. Contamination levels were also reported in human serum and breast milk.

Sampling of marine fish from Maputo Bay, Mozambique, and free-ranging chicken products from KwaZulu-Natal, South Africa, confirmed contamination of these. Estimated human health risks associated with consumption showed that chicken eggs carry a much greater potential health risk than chicken meat, which is again greater than fish meat. This information should be used by policy-makers as they plan their malaria control programs, and as they advise residents on how to minimize health risks from contamination with DDT and its metabolites (DDTs).

Although no clinical toxic effects were detected, molecular analysis showed significant genetic changes associated with DDTs exposure in free-ranging chickens. Notably, there was significant down-regulation of several immune-related genes and up-regulation of metabolism genes in birds with higher DDTs. Chicken immunity may be affected, and metabolic irregularities may result. In human MCF-7 cell culture exposed to *p,p'*-DDT, xenobiotic metabolism genes were significantly up-regulated. Changes detected across phase I, phase II and phase III enzymes suggest that this xenobiotic is metabolized by multiple pathways. Significant up-regulation was also seen in a number of oxidative stress and inflammatory markers, particularly at high concentrations. Growth-related genes were significantly down-regulated in this *in vitro* model. These effects on chicken and human immunity and metabolism have implications for disease causation and susceptibility.

An increased identification of adverse effects, and understanding of mechanisms by which DDTs result in these, should improve our capabilities to alleviate health problems in future generations of people, their livestock, and wildlife.