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Plasma levels of DDT/DDE and liver function in malaria control personnel prior to DDT in-door residual spray in Northern Uganda, 2008

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Abstract

Where 20 million Ugandans are debilitated by malaria in a year, there is continued need of dichlorodiphenyltrichloroethane (DDT) for vector control while further research is implemented to clarify the health impact of the use of DDT in in-door residual spray (IRS). The aim of the study was to determine plasma levels of DDT/DDE and liver function as base line values in malaria control personnel prior to IRS of DDT in Northern Uganda. The study design was a cross sectional prospective laboratory-centred. The sites were districts of Apac, Kitgum, Oyam and Pader in Northern Uganda. The volunteer participants were clinically examined and blood samples were taken in heparinised tubes for pre-spray screening for DDT/DDE and plasma ALT, AST, and GGTenzyme activity levels as measures of liver function. DDT/DDE was extracted with methanol from plasma and assayed using ELISA kits from Abraxis,USA while plasma enzyme activity levels were analyzed using routine clinical chemistry automated methods of Konelab^{TM}. All the 109 plasma samples collected before IRS contained DDT/DDE in a range of 39-108 and a mean (SD) of 63 (19) ppb. All the 95 plasma samples analysed for enzyme activity concentrations of ALT, AST, and GGT showed no abnormal function of the liver: ALT mean (SD) was 10.22 (4.89) u/L, within reference range of up to 40 u/L; AST mean(SD) was 19.91 (8.93) u/L within reference range of up to 40 u/L; GGT mean(SD) was 65.58 (12.05) within substrate-inducible range of the enzyme. In conclusion none of the study participants was DDT-naïve before the chemical was used for IRS
in Northern Uganda. The plasma DDT/DDE levels encountered had no deleterious effect on ALT, AST, or GGT enzyme activities as screening measures of liver function.

Key words: DDT spraying, plasma levels, liver function**,**

Introduction

Based on the available scientific, technical, environmental, and economic information, there is a continued need of dichloro diphenyl trichloroethane (DDT) for disease vector control under WHO recommendations and guidelines while further research is implemented to clarify the health impact of the use of DDT in in-door residual spray (IRS) (1).

It is government policy that in disease control, the application of the insecticide dichloro diphenyl trichloroethane (DDT) should follow a scheme that allows the assessment of its accumulation in the environment and evaluation of its possible deleterious effects on man and the food chain. Prior to the intervention however, it was necessary to register the general state of health and the background amounts of the insecticide accumulated by documented or other sources. This provided back-ground values for reference in subsequent studies.

Although DDT/DDE is reported a possible carcinogen in animal models, no such effects had been reported even in people with excessive exposure to DDT (2). However, controversy exists concerning the liver: whereas Guzelian P.S (1985) reported impaired liver function (3), yet other studies reported that the only effect noted in epidemiological studies of workers exposed to DDT was an increase in activity of liver enzymes (4). This could be a serious matter effect incase of liver diseases such as hepatoma or where there is usual enzyme activity induction typical of alcohol and aromatic medications, usually with no actual liver disease (5).

This study therefore was set out to check the naivety to DDT of sprayers before they came in contact with DDT and to document background levels of the sprayers activity concentrations of the plasma enzymes routinely used to monitor liver disease. The study was therefore destined to determine the concentration of DDT/DDE in plasma samples from the spray team before the IRS of DDT in Northern Uganda, 2008 in order to establish the sprayers` naivity to DDT. In addition, the study also determined plasma levels of biochemical markers of liver disease in blood from the spray team before exposure to DDT in order to document the background reference state.

Methodology

The covered study was done in Apac, Kitgum, Oyam and Pader districts in Northern Uganda(Fig 1). A clinician from the Ministry of Health Malaria Control Program did the field examination in the DDT sprayer recruitment and collected heparinized blood samples in circumstances where the laboratory staff were not available to collect the samples. The specimens were cooled and delivered to the Department of Pathology, College of Health Sciences, Makerere University, for analysis for DDT/DDE and biochemical screening markers of liver disease in plasma.

The DDT in plasma was extracted with methanol and analyzed using enzyme linked immunosorbent assay (ELISA) kits supplied by Abraxis, USA (6). The samples were processed according to the manufacturer's standard operating procedures and quality assurance instructions: during the reactions, color that was inversely proportional to the concentration of dichloro diphenyl ethane (DDE), the principle derivative of DDT in the sample, developed; its intensity was translated and converted into concentration by comparing with that produced by the standards and controls supplied with the DDT reagent kits; the concentrations were read at 450 and 630 *nm* and printed automatically by the ELISA plate-reader – the Stat Fax^{Reg}303 Plus (7)

In assaying for biochemical markers of disease, automated routine Clinical Chemistry methods (8) were used for the activity concentration values of the following enzymes: ALT, AST, and GGT as biochemical screening markers of liver disease.

Results

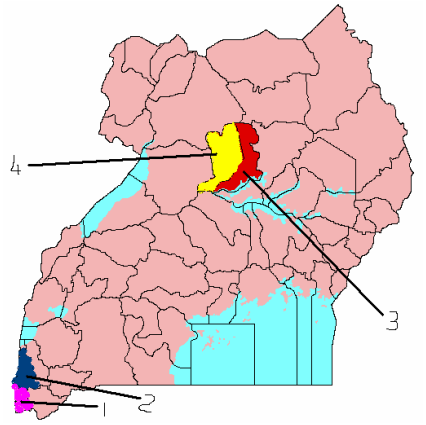
The DDT concentration in pre-spray plasma among the spray participants were as shown in Fig.2. All the pre-spray plasma samples had some DDT/DDE in them: the concentration ranged from 39 to 108 ppb; with mean (SD) of 63 (19) ppb, the distribution was leptokurtic and positively skewed. Surprisingly, no single pre-spray plasma sample was void of DDT/DDE: this means that no single participant was actually DDT/DDE-naïve before DDT was officially sprayed in Nothern Uganda in the malaria control IRS program of 2008.

Visual inspection of the plasma samples showed clear normochromic samples particularly without turbidity, haemolysis, jaundice or chylosis. Of 95 plasma samples analyzed for Alanine amino transferase enzyme activity the concentration ranged from 3.50 to 33.60 u/L and the distibution was as shown in Fig. 3 below.

With mean (SD) of 10.22 (4.89) u/L, the distribution of ALT enzyme activity concentration in pre-spray plasma from Northern Uganda was leptokurtic and positively skewed: the spread lay entirely within the reference range of up to 40 u/L; there was no indication for hepato-cellular damage detected by ALT in the pre-spray plasma

Of 95 plasma samples analyzed for aspartate amino transferase enzyme activity the concentration ranged from 6.30 to 64.10 with mean (SD) of 19.91 (8.93) u/L as shown in Fig.4.

Fig.1 Districts of Uganda reffered to in connection with DDT use



Key
1=Kisoro, 2= Kanungu, 3=Apac, 4= Oyam

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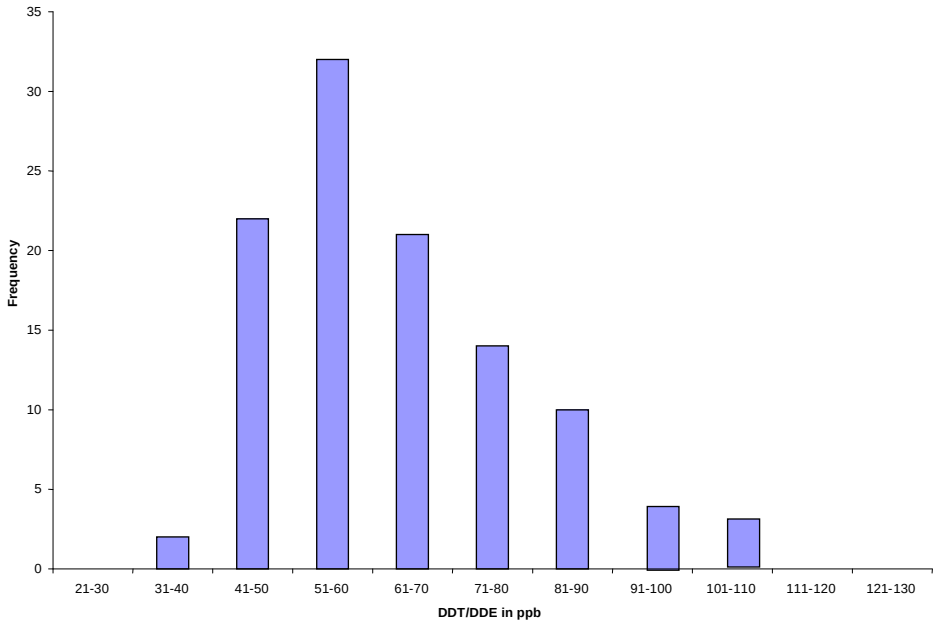

Fig2: The DDT/DDE concentration in pre-spray plasma among 109 particpants

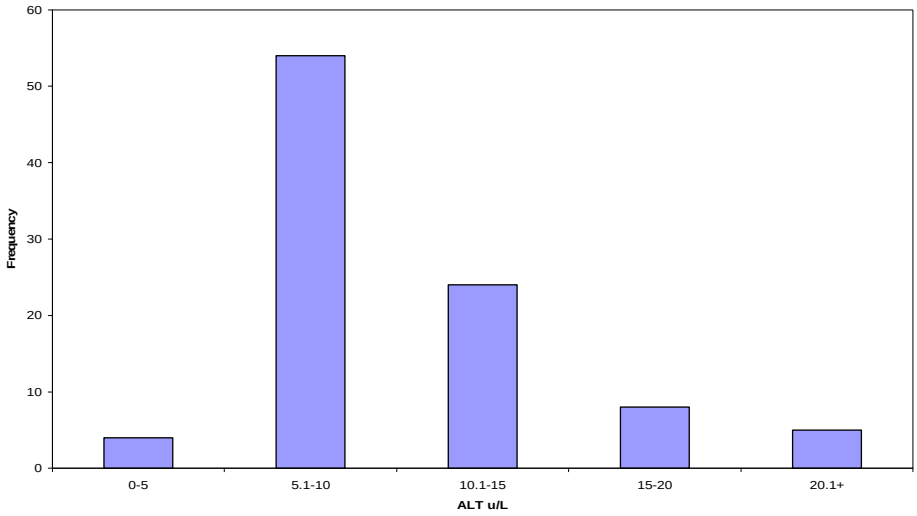

Fig3: The Alanine amino transferase (ALT) enzyme activity concentration in pre-spray plasma

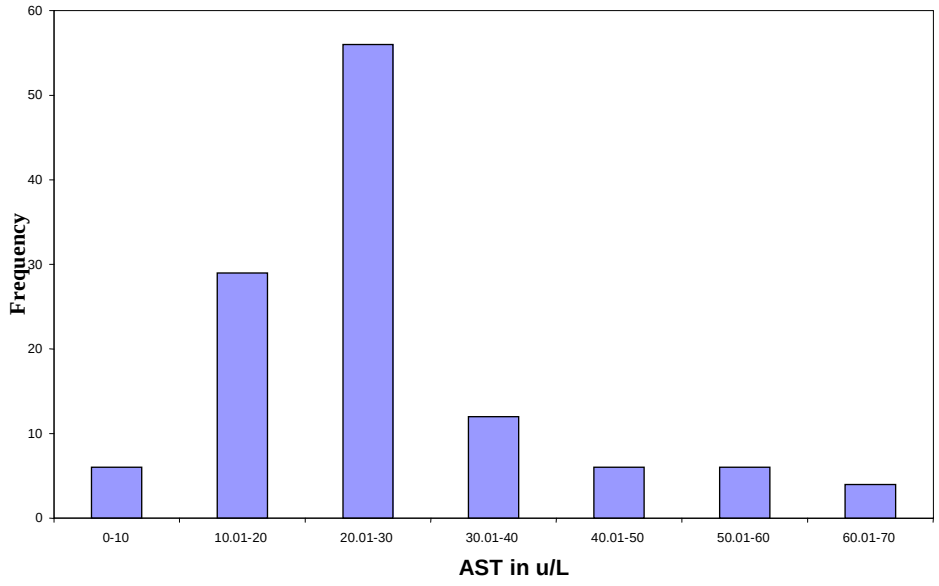

Fig.4 The aspartate amino transferase (AST) enzyme activity concentration in pre-spray plasma

The distribution was typically leptokurtic and positively skewed; the majority were within the reference range of up to 40 u/L; 12 samples had enzyme activities above the upper normal limit but within the enzyme inducible range of 1.5 fold the upper normal limit; the enzyme distribution indicated no hepatocellar or (heart) muscle damage.

Of the 95 plasma samples analyzed, the gamma-glutamyltrasferase (GGT) enzyme concentration ranged from 7.00 to 198.00 u/L with mean (SD) of 65.58 (12.05). The concentration distribution were as shown in Fig. 5. The distribution was leptokurtic and positively skewed. There was a polymodal distribution with 85% of the results within the reference range of up to 60 u/L; 16% of the results were above the normal range but within the drug- inducible range of below 1.5-fold the upper reference limit; there was no liver or biliary tract disease detected by GGT in the pre-spray plasma.

Discussion

It was shown that the population had healthy liver functions with inherent plasma levels of DDE to the average tune of 63 ppb. It was further discerned that chronic internal exposure of DDT/DDE of the order of up to 108 ppb in plasma had no deleterious effect on person in general and on the liver in particular. Also people in Northern Uganda who had no history of physical contact with DDT had up to more than 100 ppb of DDE circulating in their blood without ill effects. These findings therefore support the use of small quantities of DDT in IRS program to control the deadly non-compromising malaria that ravages Northern Uganda.

These results supported the notion of current ubiquity of DDT/DDE (9). The finding of an average plasma DDE of 63 ppb in the people of Northern Uganda before DDT was sprayed for malaria control meant that the people were not DDT- naïve to begin with, and since no DDT had been sprayed in the area during the participants` life time, the DDE found in their blood must have been obtained not through contact absorption or inhalation but most probably through the food chain. This finding agreed with the environmentalists assertion that exposure to DDT, DDE and DDD happens mostly from eating contaminated foods (2). Furthermore, our findings supported the speculation that on this planet today there is no single living organism that does not contain DDT (10). These results confirmed that people live apparently healthy with stores of DDT/DDE in their bodies as was found in each of the 14 European ministers of governments tested for DDT(11) in 2004, meaning that DDT/DDE was now every where and it was so far harmless to human beings and, ergo, it could be safely used in control of human diseases, like the pernicious malaria in Northern Uganda.

Our study used plasma enzyme activity concentration of ALT, AST and GGT to document background state of the liver in the pre-spray population. These are the tests used to measure extent of liver damage. They usually used to assess patients and monitor progression of liver disease (12). These tests are inexpensive, readily available and understood by the general practioner and the specialist alike and when available to the clinician who is making the examination, they are likely to direct his questions and subsequent investigations more (13).

When samples for this study were taken, a general healthy state of the individual was assessed. The findings agree with a healthy status of individuals during recruitment. The findings of this study agree with the healthy state of the individual and the healthy liver function found coexistent with low levels of circulating plasma DDE among people formerly protected with DDT in Kihiihi sub-county of Kanungu District and in people formerly thought DDT-naïve in Nyarusiza subcounty of Kisoro District, both districts being in South Western Uganda (14). These findings also agree with those done by Sharp *et al.* (2002) (15). These results could be used as reference values for the effects of DDT on liver as an organ in an individual with circulating plasma DDE among the people and sprayers in Northern Uganda in subsequent studies after DDT application in IRS program of 2008.

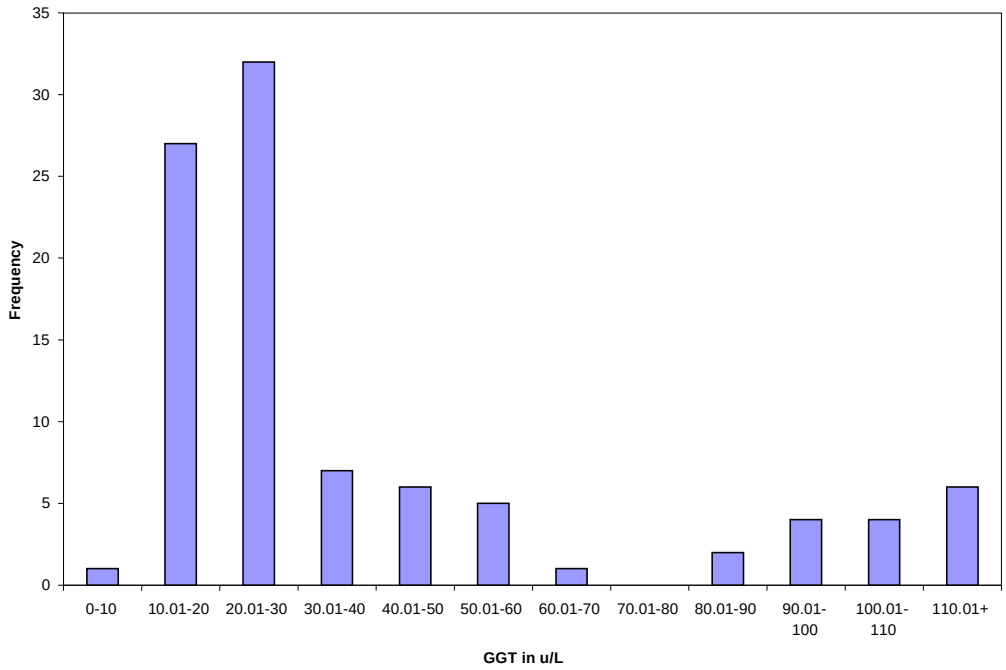

Fig. 5: The gamma-glutamyltrasferase (GGT) enzyme activity concentration in pre-spray plasma

References

1. **UNEP, 2008.** Report of the expert group on the assessment of the production and use of DDT and its alternatives for disease vector control to the conference of the parties of the Stockholm Convention to the Conference of the Stockholm Convention at its third meeting UNEP/POPS/EGDDT .2/5, Geneva,18 Nov. 2008.
2. **ASTDR, 2002**. Agency for Toxic Substances and Disease Registry Toxicological Profile for DDT, DDE, and DDD http:// WWW.astdr.cdc.gov/toxprofiles/tp.35html.
3. **Guzelian P.S. 1985.** Clinical evaluation of liver structure and function in humans exposed to halogenated hydrocarbons . *Environ Health Prospect*, 60: 159-164.
5 **DDE/Technology Transfer Network**. Air Toxics Web Site/ US EPA http:// www.epa.gov/ttn/atw/hlthef/dde.html .
4. **Sharp, B.L., Ngxongo, S., Botha M.J., Ridl, F., Le Seur, D. 1988**. An analysis of 10 years of retrospective malaria data from the Kwa-Zulu area of Natal. *South African Journal of Science* 84:102-106.
5. **Johnson, D.E. 1999.** Special considerations in interpreting liver function tests. American Family Physician. http://www.aafp.org/afp/990415ap/2223.html.
6. **Abraxis, L.L.C.** 54 Steamwhistle Drive, Warmister, PA 18974 USA info@abraxiskits.com.

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7. **Stat Fax^{Reg}303** Plus, Awareness Technology, Inc, Palm City, FL (1987-2001).
8. **Konelab^{TM} 2003.** Thermo Electronic Corporation Thermo Clinical Labsystems Og. Ratastie 2, P.O.Box 100 Fin 0 01620 Vantaa Finland http://www.thermoclinical.com.
9. **Moy, G. 1996.** DDT residues in foodstuffs from various nations GEMS/food database. Letter by Dr Gerald Moy, GEMS/food cordinator of WHO, Geneva, 12 July 1996. unpublished.
10. **Vladimir, T., Valery, R. and Lorenzo, T. 2002.** Dichlorodiphenyl trichloethane (DDT): Ubiquity. Persistance, and Risks. *Environmental Health Perspective*, 110 (2): 125-128.
11. **WWF, 2004.** Bad Blood? A survey of chemicals in the blood of European ministers,WWWDetox Campaign.
12. **Salaspuro, M. 1989.** Characteristics of laboratory markers of alcohol related organ damage. *Scand. J. Gastroenterol.* 24: 769-80.
13. **Tredger, J.M. and Sherwood, R. A. 1997.** The live: new functional, prognostic and diagnostic tests. *Ann. Clin. Biochem*. 34: 121-141.
14. **Bimenya, G.S., Byarugaba, W., Byarugaba B.B., Lugemwa M. and Okwi, A.L. 2007.** The case for spraying with DDT as a strategy against malaria. Malaria Control and Prevention, Forum for Health & Nutrition, Uganda National Academy of Sciences 2007; pp83-96.
15. **Sharp B., Van Wyk, P., Sikasote, J.B., Banda P, Kleinschmidt, I. 2002.** Malaria control residual insecticide spraying in Chililabombwe, Copperbelt Province, Zambia. *Tropical Medicine and International Health,* 7(9): 732-36.

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