CHAPTER V

DISCUSSION AND CONCLUSION

The present study is the case-control study to assess the carcinogenic risk of chlorinated hydrocarbon insecticides exposure in humans by determining their blood levels in normal and cancer subjects. All subjects are Thai people who visited the National Cancer Institute, the largest cancer center in Thailand, during the period of June to December 1992. The studied population consists of 62 cancer and 62 normal subjects.The case (cancer) and control (normal) are matched by sex, age and geographic area of residence. The cancer population has the following characteristics: the large proportion are female (table 4), live in central part of Thailand (table 5), have age in the range 46-65 years (table 6), are agriculturists (table 7) and have no family history of cancer (table 8).

Analysis of blood samples from cancer and normal subjects by gas liquid chromatography revealed only the presence of organochlorine insecticides in the DDT group, specifically DDD and DDE. DDT was imported into Thailand in quantity much greater than other chlorinated hydrocarbon insecticides since it was used in agriculture as well as in public health (14). Thus,exposure to DDT presumably

occurred at a greater extent and more frequent than other insecticides.This fact may, at least partly, explain why other organochlorine insecticides cannot be detected in the blood samples.However, agricultural use of DDT was banned by the Thai government in the year 1983 (14). Since then additional exposure to DDT in Thai population can be expected to be minimum. It has been shown in experimental animals that DDT is metabolized to DDD and DDE (38). Because the ban on the use of DDT minimizes additional exposure but metabolism can proceed as usual, the body burden of DDT should drastically decrease with time due to its metabolism to DDD and DDE. These explanations could account for the finding that DDD and DDE but not DDT were detected in the blood samples. Other studies are in agreement with this conclusion. Hayes et al. (39) studied the ingestion of technical or p,p'-DDT during 21.5 months in human volunteers. The concentration in adipose tissue after administration of technical DDT at a dose of 35 mg /man/day rose from a pre-exposure level of 4.1 ppm to 280.5 ppm after 21.5 months. After a recovery period of 37.8 months, 56.8 ppm DDT were still found to be present. The concentration of DDE amounted to 8-11% of the total DDT in adipose tissue during the dosing period; its proportional concentration relative to that of DDT increased during the recovery phase and represented 47% at the end of this period. Thus, this study demonstrated that tissue concentration of DDE rose after DDT exposure was terminated, most likely as a result of metabolic conversion. A higher

percentage of DDT is also stored as DDE in the general population (40).

Generally, the concentration of total DDT in female human adipose tissue is lower than that in males of the general population of the same geographic area and age group (41). In one study involving 919 subjects, the mean level of serum DDT is about 6% higher among men than women (42). In accordance with these reports, the present study shows that the male blood DDT level tend to be higher than the female although the difference of blood DDT level between male and female populations is not statistically significant (table 11).

There is sufficient evidence for the carcinogenicity of DDT and its metabolites, DDD and DDE, in laboratory animals; however, results with human study remain equivocal (25). In this investigation, significantly higher blood DDT level was observed in cancer patients compared with normal controls (table 15). The data provide indirect evidence supporting the postulation that DDT and related compounds may be carcinogenic or at least present a carcinogenic risk to humans. Furthermore, the large proportion (42%) of cancer cases are agriculturists (table 7); and, with the exception of the hirling, agriculturists is the population having highest blood DDT level (table 13). The highest blood DDT level observed with the hirling was due to the very high blood DDT concentration-321 ppb, detected in one cancer patient in this occupation category. If this patient was excluded from the present study, the

blood DDT level in agriculturists was the highest. Since farmers are occupationally exposed to DDT,these data give additional support to the proposed carcinogenic potential of this insecticide. Other case-control studies measuring DDT or DDE levels in blood and tissue have also been reported. Caldwell et al. (43) compared serum levels of DDT in 10 children with colorectal cancer diagnosed between 1974-1976 and 24 controls without a malignancy who had visited a health clinic. The cases were aged 14-19 years and the controls, 5-18 years. One case was deleted because no information on exposure could be found. The mean serum level of DDT was 65.6 ppb for the remaining cases and 28.3 ppb for the 24 controls. When two cases with very high levels (in excess of 200 ppb) were excluded, the mean level was 22.9 ppb. Unger et al.(44) measured DDE in breast fat tissue obtained from 14 patients with breast cancer and 21 patients with other breast disorders who were undergoing breast surgery. Mean DDE levels were similar in the cancer cases (1-23 ppm) and the controls (1-25 ppm).Unger et al. (45) determined DDE levels in adipose tissue obtained post mortem from 51 cancer cases and 63 non-cancer cases between 1978-1980. Ten of the patients had died from cancer of the gut, 13 from lung cancer and the remainder from various other types. Eleven of controls had died of apoplexy, 28 of coronary or vascular disease and the remainder of various other diseases. Mean levels of DDE were higher(5.5 ppm) among the cancer cases than among the controls (3.4 ppm). Thus, the issue whether cancer patients have higher blood

levels of DDT and related compounds than that of controls remains unsettled.

The possibility that higher blood DDT level is associated with certain type of cancer have also been investigated in the present study (table 16). Cancer patients were grouped by cancer type and their blood DDT levels compared with controls. Patients with buccal cavity, liver, nasopharyngeal, lung, breast and skin cancer had higher whereas patients with cancer of the digestive system, lymphnode, and thyroid gland had lower blood DDT level than controls. However, in all instances the differences in blood DDT level between case and control groups were insignificant statistically. Nevertheless, there is a trend for patients with liver and lung cancer to have significantly higher blood DDT level than controls since the P values are very close to 0.05 (the P values for liver and lung cancer categories are 0.06 and 0.07 respectively). As the numbers of subjects having liver (n=5) and lung (n=6) cancer in this study were small, it is suggested that further investigation to correlate blood DDT level with hepatic and lung cancer be conducted with larger population. It should be noted in this connection that DDT and its metabolites, DDD and DDE, have been shown to produce or increase the incidence of liver and lung cancer following oral administration in rodents (25).

In conclusion, the present retrospective case-control study has demonstrated significantly higher blood

DDT level in cancer patients as compared to normal controls. The major proportion of cancer patients are agriculturists, which also have greater blood DDT concentration. The results support the hypothesis that the DDT group of organochlorine insecticides present carcinogenic risk to humans.