Chapter - 5

Summary & Conclusion
5. Summary and Conclusions

Physicians have described longer term effects of malathion exposure in humans. An older man suffered acute kidney failure after malathion exposure. In laboratory animals, malathion exposure has caused stomach ulcers, testicular atrophy, chronic kidney disease increased liver and kidney weights, adverse effect gastrointestinal tract and changes in the adrenal glands, liver, and blood sugar levels. Technical formulations of malathion contain over 11 contaminants and analogues that increase the toxicity of malathion. These occur as a result of the pesticide production process, and their formation and concentration is affected by secret ‘inert’ ingredients and pesticide storage conditions. These contaminants act to increase the toxicity of technical malathion up to ten-fold. Although the concentration of contaminants in commercial formulations is usually less than five percent, environmental conditions can increase the concentration during storage. In 1976, an epidemic of malathion poisoning occurred among 7500 Pakistani spray applicators. After hand spraying malathion to control mosquitoes, five workers died and 2800 became ill due to exposure to the analogue isomalathion in the pesticide. Storage of malathion at high temperatures increased its toxicity by increasing the percentage of isomalathion and other contaminants in the product.

Other studies have also shown similar effects during storage. Malathion
stored at 40°C for six months was 33 percent more toxic to mice than unstored malathion. Exposure of malathion to sunlight high relative humidity during storage and formulation with certain clays and surfactants, can increase contaminant formation in malathion. Some contaminants directly inhibit AChE activity and exposure to large doses causes symptoms similar to organophosphate poisoning. At low doses (down to 15 mg/kg) some impurities cause a characteristic ‘delayed toxic’ effect in laboratory animals, with death occurring slowly days or weeks after exposure. In several studies, rats appear normal except for weight loss from the time of pesticide exposure up until the time of death. Some have reported complications from mammalian exposure to contaminants or analogues include lung damage and bacterial pneumonia, liver damage kidney damage and prolonged blood clotting time. The use of malathion in combination with other pesticides can increase its toxicity to mammals. These synergistic effects are important because pesticides are often applied in combination rather than alone. In rats single low doses of malathion and carbaryl (a carbamate insecticide) increased certain enzymes that are indicative of cellular damage in the liver. The same combination of pesticides reduced the number of live fetuses in pregnant rats and also reduced maternal weight gain. Combinations of malathion and endosulfan (an organochlorine insecticide) are more toxic than malathion alone because the combination interferes with malathion
detoxification.

A considerable work has been done on different organophosphate toxicity to reproductive organs but the malathion interference in adrenal and gonadal functioning and changes observed after cholesterol administration was undertaken for the present study in albino rats.

**Experiments were done by following pattern:**

- **Group I** - Intact + Control
- **Group II** - Intact + malathion (16ml / 5000 ml)
- **Group III** - Malathion + Cholesterol (400 mg / Kg body wt.)

**A. Body and Organ Weight Relationship:**

a. Body weight was significantly reduced after treated by malathion in both male and female but slight increase in body weight after malathion + cholesterol (400 kg/ body weight) feeding.

b. Weight of testes in male and ovary in female and other sex accessories that is epididymis, seminal vesicle, ventral prostate, vas deferens in male and uterus, vagina in female was decreased by malathion treatment while slight increase was observed after malathion + cholesterol concentrated diet.

c. Weight of adrenal was decreased by malathion feeding but after malathion
plus cholesterol concentrated diet, remarkable increase in weight was observed. The decreased weights of testes, ovaries, adrenals and other sex accessories after malathion treatment is suggestive of interference of malathion in steroidogenesis while increase in weights of all these organs after cholesterol diet suggest the role of cholesterol in steroidogenesis by increasing the uptake of total lipids i.e. LDL, HDL, VLDL by adrenal.

B. Sperm Dynamics and Fertility Tests:

a. The motility of sperm in cauda epididymis was significantly reduced in malathion treated groups while it is slightly increases in malathion + cholesterol treated groups.

b. Sperm count was decreased in malathion treated groups and it was nearly equal to the control rats.

c. Decreased sperm density was observed in testes in malathion treated groups while it nearly equal to the control rats when treated by malathion + cholesterol.

d. Fertility was reduced in malathion treated groups while it was increased in malathion plus cholesterol treated groups.

Changes in sperm dynamics and reduced fertility is due to the damage to the testes and decreased androgen synthesis.

C. Haematology:

Haematological studies showed that giving malathion concentrated diet
and then malathion + cholesterol concentrated diet makes no remarkable changes in haematological parameters like RBC, WBC, haemoglobin, hematocrit in both male and female rats. It showed that malathion has no toxic effect to general metabolism.

D. Serum Biochemistry:

a. Serum protein level decreases after giving malathion concentrated food and increases nearly equal to the control after cholesterol with malathion concentrated diet.

b. Serum cholesterol was significantly reduced in malathion treated group rats while remarkably increases in malathion + cholesterol treated rats.

c. HDL, VLDL, LDL and phospholipids concentration were significantly decreased by malathion while it is significantly increases after malathion + cholesterol administration.

d. Serum triglycerides and serum transaminase (SGOT, SGPT) activity significantly decreased by malathion and increases after giving malathion + cholesterol concentrated food.

E. Tissue Biochemistry:

a. Protein and sialic acid contents of testes and sex accessory organs were significantly reduced by malathion but increases slightly in malathion + cholesterol treated groups.
b. Adrenal ascorbic acid was depleted in malathion treated rats while it increases in malathion + cholesterol treated rats. Similar changes was observed in fructose content of seminal vesicle.

c. Cholesterol treatment increases the testicular and adrenal cholesterol.

Depletion in the adrenal ascorbic acid also suggest the impaired androgen synthesis and reduced fructose, protein and sialic acid levels suggest the decreased level of androgen, since these parameters are androgen dependent.

F. Histopathology:

Malathion diet treatments have remarkably altered the histoarchitecture of testes. Spermatogenesis was inhibited at spermatocyte stage. Lumen of vas deferentia were devoid of sperms. Epididymes showed the reduced number of spermatozoa. The secretary activities of seminal vesicle and ventricular prostate were also altered while there was no effect on reproductive organ of female rats. Malathion treated animals reflect a change in sertoli cells. The testicular toxicity of malathion implicate the sertoli cells as the probable target for the toxic actions of this compound in the testes.

G. Hormone Estimation:

Estimation of hormone like FSH, LH, Cortisol, PRL and testosterone after only malathion treated groups showed that peak of increase in concentration in 12th and 18th day but the estimations of 24th day showed the hormone
concentration is nearly equal to the control group rat that means the effect of malathion is greater in early days of treatment while its effect was nullified after some days.

Early increase in serum testosterone concentration may be explained by the fact that treatment causes an increase in serum LH concentration.

H. Electron Microscopic Study :-

Electron microscopic studies revealed that the cells are more affected by malathion treatment for 15 days than the treatment for 30 days.

More changes were observed in Zona fasciculata and zona reticularis of adrenal, vacuolations, shrinked and ruptured mitochondrias were mainly observed as the effect of malathion.

In the cells of the ovary, vacuolations was seen in malathion treated groups and increase lipid droplets in the theca interna cells of ovary after cholesterol administration. Thus in the present work treatment by malathion resulted in decreased testicular mass. The testicular toxicity of malathion implicate the sertoli cells as the probable target for the toxic actions.

Alterations were recorded in the histoarchitecture of the testes, ovaries and adrenal by affecting adrenal steroidogenesis but the administration of cholesterol reestablished the impaired steroidogenesis by increasing the uptake of HDL, LDL and VLDL by the adrenal. Further research is needed for studying the importance of adrenal in reproduction.