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With Compliments of

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U N I V E R S I T Y O F Z A G R E B

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A PROSPECTIVE STUDY ON ASSESSMENT OF PESTICIDE EFFECTS (PARTICULARLY ANTICHOLINESTERASES) ON HEALTH OF EXPOSED WORKERS IN TANZANIA

M A S T E R ' S T H E S I S

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Zagreb, June 1978

This thesis was submitted for assessment to
the School of Public Health "Andrija Stampar",
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FOR ATTAINING AN ACADEMIC TITLE OF

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A C K N O W L E D G E M E N T S

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Supervisor: Associate Professor R. Plešťina

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OBJECTIVES FOR THE STUDY

Bearing in mind that Tanzania is largely an agricultural country, and that a relatively large section of the working population is engaged in farming and involved in handling of pesticide compounds, this study has been conducted with the following objectives:

1. To assess the effects of occupational pesticide exposure. For this purpose, the staff of two agricultural research institutes in Tanzania, who are continuously exposed to different pesticide compounds were selected for this study. Appropriate procedures, including various investigations with clinical examinations and laboratory tests were conducted. My aim was to discuss the findings in the light of present knowledge and experience on implications these chemical compounds have on health;
2. To consider all possible factors known to influence exposure to pesticides, and to find out how these factors can influence the degree of exposure;
3. To try designing a comprehensive methodology for assessing the degree of exposure, which could be further developed into a model for the purpose;
4. To assess how preventive and protective measures applied in the working environments of the exposed subjects could have repercussions on already recognised effects of pesticides on health of the workers;
5. To arouse a sense of awareness to the recognized and unrecognized health hazards and to develop interest on further research in respect of occupational exposure and general exposure of the population at risk as potential sources of ill-health resulting from pesticide poisoning in Tanzania.

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S U M M A R Y

A prospective study was conducted in two agricultural research institutes in Tanzania on 111 workers who were exposed to various groups of pesticide compounds including cholinesterase inhibitors from 19. 3. - 20. 4. 1977. The workers were categorized into A, B, C, D occupational groups, and group E comprised of 54 subjects was selected as a control group.

The objectives for the study were to assess the effects of the pesticide chemical compounds on health of the workers; and to try how to design a methodology for assessing the degree of exposure risk based on external influencing factors. For determination of cholinesterase activity, usually inhibited by some anticholinesteras pesticide compounds Spectrophotometeric and Tintometric methods were used simultaneously, while interviews, questionnaires and clinical examinations were the other objective and subjective methods applied for assessing the clinical pesticide effects.

It was revealed in the study that there was significant inhibition in cholinesterase activity among the exposed subjects particularly in groups A and B who handled cholinesterase inhibitors which correlates with exposure factors and the clinical manifestations observed during the investigations. A proposed model for assessing the degree of exposure risk to anticholinesterases in form of a screening test is also described.

I. LITERATURE REVIEW

I N T R O D U C T I O N

In order to conquer the enemies of his interests, paradoxically, man has introduced undesirable chemical substances into his environment which turn out to be a threat to his own health and welfare.

In recent years, concern over the escalating usage of pesticide compounds for combating diseases and for increasing agricultural productivity has been expressed all over the developing countries, particularly in Europe, North America and Japan. While there is no reason for alarm, there is enough evidence regarding potential hazards to the environment and particularly to human health, demanding corrective measures. The issue becomes more and more actual as we consider that, in addition to the small doses of accumulating pesticide compounds we take into our bodies daily, mainly through the food we eat and water we drink, environmental pollution by other pollutants which accumulate in air, water and soil is a threat to human health now and in future as industrialisation continues to grow day by day.

The problem attached to pesticide usage may not attract the attention of, or alert the developing countries now, in view of multiple social and economic problems confronting them, especially in terms of disease and hunger. But, while the major demand for chemical method of pest-control has until now come from developing countries, the likelihood is that the greatest potential increase in future will be within the developing countries, and that future is at hand!

As the world population continues to increase, especially in countries with poor economic footing, the developing countries, and as long as tropical diseases like malaria continue to persist in some areas as a major cause of morbidity and mortality, the demand for more pesticides is inevitable. In addition to this, the developing countries have a relatively short tradition, if any, in production and pesticide usage, so they are likely to suffer from similar errors formerly committed by developed countries due to inexperience in handling pesticide compounds in which health hazards

are likely to occur. Furthermore, lack of technology and economic power on the side of developing countries is a handicap to developing their own research in order to identify their needs with regard to the best and safest way of making use of pesticides.

There is no rationality in advocating to ban the use of moderately toxic pesticide compounds in view of the great advantages they have contributed to health and welfare of mankind. However, the concern and emphasis should not be spared in pointing out the harmful effects to health of those who by nature of their occupation may happen to be victims of "improved human welfare!" Indeed, occupational pesticide exposure can be a serious health hazard if proper precautions and appropriate protective and preventive measures are overlooked. As FAO and WHO continues to give support to these efforts, it is the responsibility of chemists, entomologists, agriculturalists, toxicologists and physicians to work hand in hand in order to minimize human health hazards which may be contributed by irrationality in pesticide usage, misuse and abuse.

1. 1. History of Pesticide Usage

Different substances and methods have been used to kill insects and to control other pests a long way back in History, as Brooks put it, "the origin of chemical insect control seems to be lost in antiquity" (Brooks, 1974). During the prehistoric era, man defended himself against flies, mosquitoes and other pests by bare hands and smoke. The development of human society has disrupted the biological equilibrium, in a way, by growing plants of its own interests, domesticating animals and establishing organised settlements. This has no doubt created new and favourable conditions for breeding and multiplication of large numbers of parasites, bacteria, virus and other pests. Man, therefore, has been compelled through the ages to defend himself and his interests (food, cattle and other property) from being destroyed by pests. In spite of these defensive efforts, today man is still harvesting only what the pests have left over!

Development of some of the pesticides has evolved through experience, by chance or under influence of certain factors. The oldest pesticides ever known to have been used were natural elements and their salts. As far back as 70 A. D. , Plinius is said to have recommended arsenic compounds for insecticidal purposes. During Homer's era sulphur is mentioned as a means of controlling insects, and in the tenth century, the Chinese are recorded to have used arsenic for the same purposes.

Preparations from the plant sebadilla, containing veratrine alkaloids has been used for centuries as powder against body lice by the natives of South America, while the application of tobacco extracts (nicotine alkaloids) as insecticides dates from the mid-18th century, which was recommended in France to kill aphids. The general toxicity of alkaloids from the South American plant, Rynia speciosa has also been known for a long time, but the insecticidal properties were first reported in 1945. Various oils such as petrolium, kerosine, cresote and turpentine came into use

in the 18th century in Europe, some of which (vinegar and paraffin oil) were applied to the human scalp to control head lice and were poured into cracks in bedsteads and other furnitures to kill bed-bugs.

The 19th century has opened a new era for development of insecticides in terms of variety and intensity. While complex of Paris green (copper arsenate and copper acetate), calcium arsenate, lead arsenated and salts of copper, zinc, thalium, chromium, lead, mercury, selenium and cryolite (sodium fluoraluminate came into use in this century, it also witnessed the birth of organochlorine group of chemical compounds. It was in 1874 when for the first time DDT "the wonder chemical" was synthesized in the laboratory by Zeider (Mellanby, 1967a). Its use was widespread in Africa, Asia, Europe and South America in the Second World War against flies, louseborne typhus and malaria, the diseases which claimed thousands of lives, of inhabitants and soldiers the world over where these diseases were endemic.

According to one source (Mrak Commission, 1969a) pyrethrum, was introduced into Europe from the Far East by Marco Polo and another authority states that the use of pyrethrum as an insecticide by certain Causasian tribes was observed in the early 19th century (O'B rien, 1967). Extracts of the Derris species have long been used by primitive peoples as fish poisons, and it was suggested in 1848 that such extracts might be insecticidal. Cyanide, usually in the form of hydrocyanic gas was extensively used in 1886 onwards in California against cotton cushion scale insect, Icerya purchasi, and human deaths as a result of poisoning have occurred.

As early as 1892, dinitrophenols have been used in Germany, first as insecticides to control the Nun moth, a pest of forest trees, and later as herbicides until the present day. Methyl bromide and carbon sulfide have been used for many years and the use of naphthaline and p-dichlorobenzine dates from the beginning

of the 20th century. A few additional potential insecticides were recognised in the 1930s but there seem to have been few developments of importance before the appearance of DDT. Benzene hexachloride came into use at the end of the Second World War, while dieldrin and related compounds such as cyclodiene group of chlorinated hydrocarbons, - aldrin, heptachlor, endosulfan and endrin which are toxic to mammals and man, have been used since 1948.

Resistence against the "wonder chemical" (DDT) eventually led the way to the introduction of more effective insecticides based on organic phosphate compounds. It is stated in the book "Insecticides and Fungicides Handbook" that parathion was the first organophosphate substance to find insecticidal use, having been introduced in 1944. However, as early as 1820Lassaigne reacted alcohol with phosphoric acid in a reaction analogous to that with sulphuric acid and therewith launched the chemistry of the organophosphorus compounds (Fest and Schmidt, 1973a). TEPP, another organophosphate compound, probably the most poisonous substance ever to be used on farms (1 g could fatally poison about 17 people) is mentioned to have been used as a nicotine substitute in 1939 (Mellanby,. 1967a). Malathion an organophosphorus insecticide widely used today, was introduced in 1950. Since 1950, a number of systemic organophosphorus insecticides have been on the market for protecting sugar-beet from colonisation by aphids which cause a virus disease called sugar-beet yellows. During the past decade another group of anticholinesterase compounds used as pesticides the monomethyl carbamates, have been introduced, and very recently synthetic pyrethroids started to receive special attention as insecticides. However, their toxity is comparatively higher than that of the natural pyrethrum.

1. 2. Definition of Pesticides

Today a pesticide means a chemical substance (which may or may not be mixed with other substances) intended to be used for the destruction of organisms detrimental to man or to his interests (Occupational Health and Safety, 1974). In other words, it is a substance or preparation meant to be used as a protection against damage to property, sanitary advantages etc., caused by herbs, animals, bacteria, birds, virus or any other pests. The term does not apply to drugs or compounds meant to preserve foods or drugs, nor to paint, vanish tar and the like, under certain conditions, neither does it apply to chemicals or drugs which are intended to be absorbed as medicines into the human or beneficial animal body whether systemically or topically.

Pesticide is a term which is derived from two latin expressions, pestis = plague, and caedere = to kill. Literally, the word means a "plague-killer", a perpetual reminder of widespread epidemics of plagues which harassed masses of people in Europe in the 16th century when the term was coined. The word clearly has a very wide meaning, and includes a number of terms (e. g. insecticides, fungicides, herbicides, rodenticides, miticides, nematocides, molluscides) which indicate the organisms or pests a particular chemical or class of chemical agents is designed to kill. Since there are different types of chemical agents used for these general classes, it is usually advisable to indicate the particular category of pesticides. Considering that, about 3/4 of all 800,000 types of living creatures on earth belong to the insect kingdom, it is easy to conceive the consequences of their multiple destructive activities which threaten the welfare of mankind. It is, therefore, not suprising to hear commonly of insecticides, which are widely used in disease-vector control and in agricultural pest control.

1. 3. Classification of Pesticides

There are several classifications of pesticides, depending on the purpose they intend to serve. The following first two classifications have been often adopted and applied by most authors dealing with health aspects of pesticide exposure.

1. The WHO recommended Classification by Hazard (WHO Chronicle, 1975);
2. Classification according to Chemical Groups (Kenaga and End, 1974 REVISION);
3. Classification of Pesticides by Usage (PANS, 1973)
   a) according to the terms which indicate the organism or pests a particular chemical or class of chemical agents designed to kill (e. g. acaricides, fungicides, herbicides, insecticides, molluscides, nematocides, rodenticides etc.)
   b) according to the term describing the effect of pesticide on the organism or pest which is designed to be affected by it, such as attractants and repellents.

The WHO recommended classification of pesticides by hazard is intended to distinguish between the more and the less hazardous forms of each pesticide regardless of it's chemical group. The only criteria for its classification is based on toxicity of the technical compound and on it's formulations. However, even this classification has run short of some aspired expectations, since the hazard referred to in this recommendation is acute risk to health while it gives little consideration for the question of "chronic" pesticide effects, which is a current subject of intensive investigations and discussions by experts in the field of agricultural occupational health.

The classification according to chemical groups is indeed very significant and has had very wide application in literature

on pesticide because of the more or less specific chemical structures and properties and the biochemical effect the pesticide chemical groups have on biological systems in mammals including man. For instance, many organophosphorus compounds and methylcarbamates are known to be cholinesterase inhibitors, while chlorinated hydrocarbons act differently.

2. ASSESSMENT OF RISKS IN PESTICIDE USAGE AS RELATED TO BENEFITS

All living systems are constantly exposed to small doses of pesticides through the contaminated environment in which we live: air, water, food and soil, and since the demand for these chemical compounds is on increase the environment will consequently also continue to be polluted, while at the same time man is also benefiting from this disadvantage, since the use of pesticides has in many instances relieved hunger and reduced vector-borne diseases.

2. 1. Environmental Pollution

Perhaps the most obvious way in which man has contaminated his environment is by polluting the air with smoke from burning coal and oils primarily in cold climate countries, with waste products from industries, and with poisonous gases from combustion of fuel for motor vehicles, the number of which is tremendously increasing. Atmospheric pollution by these substances differ, however, from insecticidal atmospheric pollution in that the later is more or less confined to those areas where agriculture with the use of pesticides is extensive (Mellanby, 1967b). The introduction of pesticides into the environment for the control of insects or unwanted plant growths is most generally accomplished by aerial or surface applications. In all such cases air is the medium through which pesticides move to their intended targets. While in developed countries such as USA aerial spraying by using dusts and aerosols accounts for over 80 % of the total pesticide application, the case is reversed in favour of surface spraying in developing countries for obvious economic reasons. So the degree and extent of air pollution will depend on these factors as well as to other various factors, including wind and thermal conditions (Mrak Commission, 1969b ; Akkesson and Yates, 1964; Quinby, and Doornink, 1965). The potential danger of pesticides to handlers and operators is well known, but there is little information

concerning pesticide exposure to the general public, and some comparative studies in this respect have been conducted over Barbados and La Jolla, California revealing that pesticides are universally present in air (Risebrough et al., 1968) and by the findings of Stanley that contamination by pesticides in the USA was dominated by DDT (Stanley, 1968). There is no doubt that man inhales considerable amounts of pesticides in widely sprayed areas.

While air contains sufficient oxygen to sustain life, water may be greatly depleted of oxygen so that it cannot sustain most kinds of life, when certain pesticide chemical compounds are added into it, or animals and plants can be poisoned by such toxic compounds they take into their body with water. The major pathway of pesticides into the water environment occurs through direct application to surface waters and surface run off. The major recipients of surface run off are streams, lakes and coastal waters. According to Mrak Commission, the ground water is much less affected by quantities normally encountered in agricultural practice, but there may be cases of wells being contaminated by and large through accidental spills and back siphonage of pesticide content when care is not taken with pumps (Mrak Commission, 1969c). Industrial and domestic pollution of many estuaries discussed by Butler indicate that the pesticide chemical compounds can degrade the environment to such an extent that only the most tolerant of organisms can persist (Butler, 1966; Barthel et al., 1969).

Pesticide-laden irrigation waters may be a source of contamination to nearby streams as a result of flooding. Pesticides are applied directly to waters for the control of mosquitoes, obnoxious or undesirable weeds and snails and this could be a potential health hazard if the question of human consumption of water is not considered prior to such application (Smith and Ison, 1967).

Agriculture as the major producer of human food also provides the principle sources of intake for a majority of the pollutants in man. The contaminations of agricultural produce may arise

accidentally through industrial operations close to cultivation areas or through the application of a wide range of chemicals in modern methods of crop production and animal rearing. Crops may absorb pesticides from the soil previously treated, and studies conducted by Bruce and others have indicated that seeds with high fat content such as soybeans and groundnuts contained greater pesticide residues (Bruce et al., 1966). Various foods receive direct exposure to pesticides during growing season, and, depending upon the methods of processing, may contribute considerable pesticide content to the diet of the food consumer.

The fall-out of pesticides following sprayed applications in the direct treatment of soil has led to a build-up in the soil of various amounts of pesticides. Soil residues may, therefore, be a cause for concern since they may reach man by a number of routes: uptake from soil by consumable crops; leaching into water supplies; volatilization into the air and by direct contact with the contaminated soil. The magnitude of the problem is directly related to the amount supplied to the soil and the rates of degradation in the soil. The problem can be minimized by reducing the amounts of pesticides reaching the soil by more effective procedures, by using pesticides that have a low persistence so that once they reach the soil they remain only for short periods or by the use of pesticides of relatively low toxicity.

2. 2. Risks in Humans

It is possible to categorize human pesticide risk into three major exposure circumstances:

- accidental exposures which involve all population groups (several studies indicate that underfive children are a significant vulnerable group in USA (Reigh et al., 1968);
- individuals not occupationally exposed (those who live in agricultural areas) and the general urban population (people whose exposures are largely limited to pesticide traces in food, water and air);
- occupationally exposed workers (agricultural applicators, workers in formulating plants, pest control operators, greenhouse workers and aerial spray pilots).

Accidental exposures to pesticides occur through inhalation, direct consumption of contaminated food and through skin apsorption. The use of pesticides fordomestic purposes has become widespread. Accompanying this increased application is an increased danger of misuse, accidental poisoning and increased contamination of the home environment. Homeowners are seldom acquinted with the scientific rationale of safe application and frequently fail to read and understand the instructions contained in the label. In other circumstances when pesticide contents are stored in containers which are used for storing edibles, such as juice bottles, soft drink containers and the like, this can prove to be a very important source of accidental poisoning, especially in children.

Although individual farmers and cultivators as a group apply the largest quantity of pesticides, the most important population group to be considered comprises those persons subjected to a relatively heavy and prolonged occupational exposure when working as spraymen either in agriculture or in public health programmes. In this vulnerable group, the safe handling of toxic chemicals is a major problem and the greatest concern for pesticide health hazards should be given due consideration.

While pesticide hazards have been considerably identified particularly in acute poisoning, uncertainty prevails about the true extent of pesticide poisoning. The scattered reports in the world literature, drammatic as they are, themselves add up to a relatively small total. The trouble is that in scarcely any country at all is fact finding and incidence reporting systematically conducted. Reliable information on incidence and epidemiology of poisoning among people on the land is scanty all over the world (WHO Regional Office for Europe, 1971) partly because poisoning by pesticides in most areas is not a notifiable disease, so that the acquisition of true incidence is deficient even in the more developed countries (Mrak Commission, 1969a). In those developing areas of the world where facilities for health and vital statistics are almost completely lacking the gap between reported and true incidence of poisoning would be expected to widen (Hayes, 1964).

However, the risk of starvation would certainly tend to minimize the significance of this gap in those areas where agriculture must struggle to meet at least subsistence levels of food production, even if such information was available.

The mortality rate of pesticide poisoning is considered to be about 1 % of the total chemical poisoning prevalence per year, in those countries where medical treatment and antidotes are readily available but it may be higher in other countries (WHO Expert Committee on Pesticides, 1973). In the United States, the mortality rate has been given as 1:1,000,000 and the ratio of fatal and non-fatal poisoning expressed as 1:13 in one study and 1:75 in another study depending upon the criteria of severity (Hayes, 1969). Pesticides contribute a substantial proportion of cases caused by all solids and liquids, a proportion which ranges from 6 - 12% in different years (McCarthy, 1967).

Morbidity data can be extrapolated from areas where reporting of occupational poisoning by pesticides is mandatory. For example, in California (1969) such reports were required if work injury involved the approximately 80 % of employed persons in the state covered by California Workmen Compensation Law (West, and Milby, 1965). Between 1960 - 1963, the number of reports of work injury from pesticides ranged from 827 to 1013 annually, out of approximately 250,000 persons at risk (California Dept. of Public Health, 1960 - 1963). About 1/2 of these reports dealt with skin diseases and about 1/3 with systemic illness. During the same period, pesticides caused 21 deaths in California. Of the total, 5 were associated with occupational exposure, while 16 other deaths, largely of children, were not occupational in origin (West and Milby, 1965). These findings significantly differ from those of one hospital in Algiers, Algeria (one of the developing countries in Africa) over five years, 1966 - 1970, received from a radius of 50 - 80 km, in that, of the 57 patients who suffered from pesticide poisoning nearly always from parathion, 33 were occupational in origin (WHO Regional Office, 1971).

2. 3. Benefits of Pesticide Usage in Crop Protection

In spite of protests emanating very often from those critics who have little or no direct experience in food production or public health care, the use of pesticides throughout has continued to expand, the annual increase probably being of the order of some 10% per annum, all told. This has mainly involved the herbicides and fungicides. As a rule these have lower mammalian toxicity than the insecticides, the use of which has not increased so much. Large amounts of pesticides are used in many countries for the production of food and fiber. World grain such as wheat, maize and others are very dependent on the use of insecticides in the first place in order to increase the yields, and the fruits which supplement for nutritive requirements are all protected by pesticides. This also applies to vegetables which provide relish in the diets. In certain areas of the world it is clear that crop production would have failed entirely without the aid of pesticides. The interrelationships of man and animals have become increasingly complex as human populations have increased. As wildlife habitats have become altered, certain species have established new balances. Thus some species have substancially increased in population density, often creating problems that affect man's interests and welfare. There are numerous situations when control of predators and rodents like rats is essential to protect agricultural and pastoral interests as well as human health and safety. However, it must be emphasized that an escalating tonnage of pesticides will not necessarily be accompanied by burgeoning yields. The temptation to be prodigal with them must be resisted, as much in countries where methods of pest control are already well-established as in those for which they are a novelty (WHO Regional Office for Europe, 1971a). For some years to come, the campaign for general improvement of plant protection services to which FAO is committed, is tantamount to a wider use of Pesticides, subject always to the over-riding consideration of safety. That is why FAO maintains

that in each country, official control should be exercised over the use of pesticides and why in 1963, the Organisation set up a Working Party on this subject which compiled a booklet entitled "A Model Scheme for the Establishment of National Organisations for Official Control of Pesticides", published by FAO in 1970. The same Working Party, in association with WHO, has already propounded a model law for such control and had incorporated this in "Guidelines for Legislation Concerning the Registration for Sale and Marketing of Pesticides", published in 1969. Only by such means, coupled with a programme of technical education, can safe handling be equated with efficient deployment.

2. 4. Advantages in Vector Control

Disease vector control is still a major concern in tropical countries where malaria, schistosomiasis and other similar diseases are still an important contributing factor to morbidity and mortality. In such areas of the world, disease vector control programmes conducted by teams of field technicians, spraymen, and laboratory workers, necessitate the use of large quantities of pesticide compounds such as DDT, malathion, dieldrin, chlorpyrifos etc. Some of these major control programmes have been conducted by many countries in collaboration with the World Health Organisation (Vandekar et al.,1968, Vandekar, 1965). In vector control programmes DDT has been in use for over 30 years. Very large quantities have continued to be used and no reports of serious harmful effects have been recorded among the thousands of people who use it daily in malaria eradication campaigns. It has, therefore, enjoyed the reputation of being an exemplary insecticide with efficacy and low mammalian toxicity. It was a very remarkable achievement to learn that1/5 of world's malaria had been eliminated by use of pesticides (PANS A, 1968). In India, for example, the number of malaria cases dropped from 100 million in 1933 - 35 to 150,000 in 1966, and the loss of economy in the same period reduced from 1,3 billion dollars to 2 million (World Health, 1968). This is of

particular importance in India, Mexico, Brazil, Venezuela, Columbia, Vietnam, Honduras, and Japan, and African Tropical countries. The use of DDT in vector disease control has been extended to include application against simulium fly which transmits onchocerciasis (riverblindness) which is a disease of particular importance in West African states of Nigeria, Ivory Coast, and Upper Volta.

Sleeping sickness (trypanosomiasis) is another disease transmitted by the Tsetse which has been under effective control by the use of DDT in Nigeria and Zambia, but more effective control is obtained with dieldrin, which is widely used in Nigeria, Tanzania, Kenya, Uganda, and Zambia, in an endevour to utilize the 11,520,000 sq. kms of land in Africa which is denied to cattle and horses with consequent improvishment of farming practice. The problem of sleeping sickness was so serious between 1930 and 1946 that half a million cases of patients were reported and treated in Nigeria alone (World Rev. Pest Control, 1966).

DDT has been used against Aedes aegypti, transmitting yellow fever; and gamma BHC and dieldrin have been applied for residual house spraying in Central and South America, particularlyin Venezuela and Brazil against Chagas disease.

While the operations are justifiably intended to promote health to the general public, the pesticides used have on several occassions been a cause of ill-health to the exposed workers. The opinion of the WHO Committee on Pesticides that health authorities are urged to take a realistic view of the hazards presented by the new pesticides intended to replace the ones against which vectors have developed resistance, by sacrificing a few individuals who might be adversely affected in order to effect a substantial improvement in the health of the country as a whole, (WHO Expert Committee on Pesticides, 1967) is a rational one. However, this will be justified, only if all other measures to minimize over-exposure to these victims have been adequately taken.

Note

2. 5. Scheme of Toxicological Testing of Pesticides

Before launching a new chemical on small-scale trials to ascertain potentialities as a pesticide, an understanding is required of its toxicological characteristics. These must be determined initially by definitive and comprehensive studies in animals. It is essential to compare different routes of uptake, e. g. oral, intravenous, peritoneal, respiratory and per cutaneous. Besides assessing the acute lethal dose in a number of species, short-term and long-term animal studies must be conducted. Consideration must also be given to carcinogenicity, embryotoxicity, teratogenicity and mutagenicity. The experimental work involved in building up toxicological dossier of this complexity is labourious, exacting, time-consuming and expensive. There is indeed, no limit to repeated testing that may be required to answer unresolved doubts in the minds of those preoccupied with safety. The WHO Programme for Testing and Evaluating New Insecticides is on the fore front in these efforts by providing for evaluation of candidate insecticides in seven stages of increasing magnitude and complexity and for concurrent investigations of the hazard involved in their application.

Extrapolation of animal findings to human experience presents many problems. The significance of the animal manifestations in terms of human hazards demands experts' interpretation. In recent years, toxicological methodology has involved even more disciplines, embracing refined techniques, not only of classical morbid anatomy, physiology and biochemistry but also for example, those of genetics, immunology, electronmicroscopy and molecular biology. These new skills, coupled with highly sensitive and specific system of analysis, have been adapted to intricate studies of metabolism enzymology and sub-cellular functions, notably of the microsomes and mitochondria. Reactions revealed in this way may point to particular target organs, or tissues, which should then be more closely investigated. The bewildering complexity thus presented by the toxicity testing programme has led authorities in some countries to stipulate a routine system of testing for all pesticide chemicals.

By this means and by reference to a standard classification scheme, they arrived at a toxicity rating by which a chemical may be accepted rejected, or permitted with certain restrictions. Other authorities prefer to adopt a more empirical attitude by having a modium of obligatory tests as a routine. Thereafter, the testing sequence is designed expressedly with the nature of the chemical and its proposed uses in mind, e. g. intrinsic toxicity, operator exposure, likelihood of residues in food. All the diverse findings are subjected to a "judgement of value", in which benefits are equated with risks and in arriving at which the toxicologist does not act alone, but in consultations with experts in, for example, agronomy, nutrition, economics, and so on.

No matter how intricate penetrating and wideranging these investigations in animals may be and no matter how impressive and comprehensive the toxicological dossier so compiled, laboratory exercises never give the final answer on safety. They are simply a preliminary means of predicting the risks to man, a process which is fraught with guess work and uncertainties.Difficult as the task may be, it remains a challenge to the toxicological assessor from which he should not retreat by taking refuge in still more abtruse animal experiments. In this connection, a distinction must be drawn between toxicity, which is a quality intrinsic to the biological activity of the substance and can be demonstrated by animal tests and hazard, which refers to the risk created when the same substance is handled under practical conditions. It is these latter that the expert is asked to anticipate, so that appropriate precautions can be taken. In spite of the above rather pessimistic view, a correlation has been shown to exist between acute toxicity levels as determined in experimental animals and the occupational hazard of pesticides to man based on actual use experience (Hayes, Jr., 1960). Gaines has also presented evidence that there is a closer relationship between acute dermal LD 50 values and the occurrence of occupational poisoning than between oral LD 50 values and occupational poisoning. The predictions of occupational poisoning for man may be improved somewhat by studying the effect of

repeated dermal doses of a pesticide in animals. In pesticide toxicity studies with experimental animals, a number of factors have been found to be important in determining the response of the animal to the toxicant. The factors include differences in the physiological state of the animal (species, age, sex, disease and nutritional status) and environmental variations, light (Pearson and Malkinson, 1965) and temperature (Baetjer and Smith, 1956). Some of these factors have also been noted to have similar effects on pesticide toxicity in man (Funckes et al., 1963a).

3. HUMAN EXPOSURE TO PESTICIDES

The broad classification of human exposure to pesticides has been outlined under RISKS IN HUMANS (2.2). This section will deal with the forms of exposure as well as the routes of exposure in occupational, accidental poisoning, and exposure of the whole population.

There are three major methods applied to assess pesticide exposure with regard to human health: 1) Controlled human exposure; 2) Epidemiological studies involving retrospective or planned prospective investigations of defined human populations exposed to pesticides, and preferably involving also unexposed "control" group by monitoring the effects produced by the biologically active material and by determining the compound and/or its metabolite in blood, urine and tissues; and 3) Clinical case reports, in which one or several human subjects have apparently been made ill as a result of exposure to a single or combination of Pesticides.

Conclusions reached from these forms of evidence vary in validity and reliability, but it appears that evidence based on controlled human exposure is the most reliable of all, although it relates only to the conditions of the study in question and the dosage employed. One of the most difficult tasks still remaining to be tackled in human exposure to pesticides is that of objective assessment of exposure in order for a rational cause-and-effect relationship to be established. The main problem in determining exposure lies in the multiplicity of influencing factors and their entangled interreactions some of which are not clearly understood. However, many epidemiological and biochemical studies in this respect, though fragmented in their approach, have contributed considerably to disentangling the many unknowns.

While external exposure influencing factors give an understanding to what may happen to the body when the chemical compounds enter the body, intrinsic factors play a leading role in the fate of these compounds in the body and the effects they have on the

organism, man. These biochemical aspects will be described later in the MODE OF ACTION under 4.

3. 1. Routes of Entry

Pesticide chemical compounds make their way into the body through the blood-stream, by penetrating the skin, by inhalation, and/or by ingestion. There may, however, be different combinations of these routes of entry, particularly in occupational exposure. While it is true for the general human population that ingestion is the commonest form of pesticide poisoning, skin appears to be the most important route of entry in occupational exposure to a considerable number of pesticides , followed by the respiratory route.

Several studies suggest that during spraying operations, skin deposition of pesticide residues varies between 718 and 1755 µg/hour, rates which are much higher than those obtained for respiratory exposure. Skin exposure seems likely to be significant in pesticide toxicity encountered when workers reenter sprayed fields as well (Mailbach and Feldman, 1974). Continous abundance of sebum containing many lipids enables high affinity for lipid-soluble, water-soluble substances such as pesticides to be absorbed readily through the skin. Considering that the average skin area is about 1700 cm^2, the area which is most likely to be directly exposed, face, neck, "V" chest, forearms and hands constitutes a considerably large area (about 12 1/2 %). Under the specified conditions of study with parathion formulations for example, the dermal route represents a potentially greater source of absorption than the respiratory route for orchard spraymen (Durham et al., 1972), and for mosquito control spraymen applying various pesticides (WHO Expert Committee on Pesticides, 1973). It is regarded also that the most common and important route of industrial exposure to organophosphate compounds is by accidental spillage on the skin where it is rapidly absorbed into the body (Patty, 1963). It has been claimed that for some pesticides, 8 times as much pesticide is absorbed through the skin, and in the tropics skin absorption

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may be influenced by sweating, increased blood flow, and inadequate protective clothing (WHO Expert Committee on Pesticides, 1973). The rate of absorption in damaged skin appears to be 3 times of the normal skin; and so far no biological significant differences of absorption of parathion are found between black and white skin investigated (Maibach and Feldman, 1974). As far as occupational groups are concerned, pesticide formulating plant workers mixing and bagging carbaryl dust were subjected to greater potential dermal and respiratory exposure than were field workers applying the same compound by spraying with air blast machines in orchards (Batchelor and Walker, 1954). However, in carbaryl exposure to dry formulations, the respiratory route takes an increased significance and some other authors consider that occupationally exposed people are at risk of hazardous absorption of pesticides primarily through inhalation of dust or droplets generated during pesticide manufacture, mixing and applying.

The second important route of entry in occupational exposure to pesticides is by inhalation. Pesticides are particularly hazardous for farm workers because oral ingestion is generally not necessary. Most cases of pesticide poisoning occur from inhalation of pesticide dust or vapours of accidental contact with clothing and skin, with subsequent absorption through the skin (Bogden et al., 1975). Some of the highly toxic members of the organophosphorus compounds which are a potential source of poisoning by inhalation, include TEPP, demeton (Systox), parathion and mevinphos (Patty, 1963).

As far as studies to determine potential oral exposure are concerned, it was found out by Amstrong et al., that oral exposure of workers to parathion may amount to only a small fraction of the total potential absorption by the combined oral and respiratory routes during a work day. However, it would be unwise to consider it unimportant, in as much as ingested parathion would be completely absorbed (Amstrong et al,, 1973).

The elimination of most of pesticides and their metabolites

is through urine and in some instances, and with certain pesticides, this fact has been advantageously applied to determine the degree of absorption or for chemical analysis in pesticide poisoning (Durham et al.,, 1972; Mountain et al., 1951).

3. 2. Occupational Exposure

Numerous morbidity surveys have been conducted in workers exposed to a single or a group of pesticides. Thus, for the organophosphate compounds the health effects of occupational exposure for the following pesticides have been described: azinphos-methyl (Simpson,1965),demeton (Kagan et al., 1958), dichlorvos (Gratz et al., 1963; Menz et al., 1974; Funckes et al., 1963b; Stein et al., 1966; Zavon and Kindel, 1966), fenitrothion (Vandekar, 1965), * fenthion (Taylor, 1963), ethion (Palazzolo et al., 1972), malathion (Grech, 1965; Elliot and Barnes, 1963), methyldemeton (Asribekova, 1963), parathion (Brown and Bush, 1950; Ingram, 1951; Wolfe et al., 1975; Kay et al., 1952; Davies et al, 1965; Lieben et al., 1953), thiometon (Rosival and Rajnoha, 1961) and mevinphos (Rider et al., 1975).

For the carbamate compounds: carbaryl (Best and Murray, 1962; Vandekar, 1965; Comer et al, 1975), Carbamult (Vandekar, 1965), propoxur and mobam (WHO Expert Committee on Pesticides, 1973).

For chlorinated hydrocarbons: DDT (Kranyuk, 1964; Ortelee, 1958; Quinby et al., 1965; Law et al., 1967; Edmundson et al., 1969; Brzozowski et al., 1954), chlordane (Alvarez, 1953; Fishbein et al., 1964), dieldrin and related compounds (Fletcher et al., 1959; Hoogendam et al., 1962), p-dichlorobenzene (Pagnotto and Walkley, 1965), dichloroethane (Brzozowski et al., 1954), trichloroethane (Frant and Westendorp, 1950).

For combination of pesticide compounds, the following studies have been described: (Barnes and Davies, 1951; Princi and Spurbeck, 1951; Fowler, 1953; Sumerford et al., 1953; Culver et al., 1956; Brnax, 1957; Hayes et al., 1957; Quinby and Lemon, 1958; Stein, 1964; Wassermann et al., 1969; Ruprich, 1963; Hartwell and

* Summary from WHO Bull (1971); FAO → effect on health of occupational exposure, as above.

Hayes, Jr., 1965; Gershon and Shaw, 1961; Bogden et al., 1975; Sundell and Rehn, 1973; and Zavon, 1964).

Workers' exposure risks extend from processes of manufacturing and formulating pesticide materials, through transportation and storage to application of pesticide chemical preparations. Industrial employees may be exposed to pesticide gases, fumes and dust, and skin contact with these chemicals. Hartwell and Hayes have described hazardous effects of pesticide poisoning through inhalation of airborne contaminants among manufacturing employees in USA, and stressed the effect of personal protective devices and improvement in engineering and measures of reducing health risks (Hartwell and Hayes, 1965). As an example, in California during 1966, 1,347 accidents were attributed to pesticides and other agricultural chemicals (California, State of, Dept. Publ. Hlth, undated). Accidents in the agricultural use of these chemicals numbered 820 while all other occupations accounted for 527 accidents. The number of accidents involving these chemicals in terms of the industry where the accidents occurred and the occupation of the injured persons clearly indicates that in areas where agriculture with the use of pesticide is extensively conducted, occupational exposure to the pesticide chemical compounds is an important health hazard to be considered. Exposure to pesticides from agricultural applications may be experienced by individuals who apply the pesticides or by agriculture workers who work in the fields where pesticides have been applied. Wolfe et al., 1963 studied the health hazard associated with agricultural application of endrin and dieldrin, two of the more toxic chlorinated hydrocarbons. Quinby and Lemmon, 1958, studied the potential exposure of workers engaged in picking, thinning, cultivating, and irrigating various crops to which parathion had been applied. Eleven cases of poisoning involving more than 70 persons occurred from contact with parathion residues. Transport workers may be affected by pesticide contamination if provisions for safe transportation equipments to avoid spills and escape of pesticides are overlooked.

Table 1. EPIDEMICS OF POISONING BY PESTICIDES
Adopted from Mrak Commission, pp.310
1969

Pesticides involved	Material Contaminated	Number of Cases	Number of Deaths	Location	Reference
	Accidental Spillage during Transport and/or Storage				
Endrin	Flour	159	0	Wales	Davies and Lewis, 1956
Endrin	Flour	3	0	Egypt	Coble et al., 1967
Endrin	Flour	691	24	Qatar	Weeks et al., 1967
Endrin	Flour	183	2	S.Arabia	Weeks et al., 1967
Dieldrin	Food	21	0	Shipboard	Przyborowski at al., 1962
Diazinon	Doughnut mix	20	0	U.S.A.	West, 1965
Parathion	Wheat	360	102	India	Karunakaran et al., 1958
Parathion	Barley	38	9	Malaya	Kanagaratnam et al., 1960
Parathion	Flour	200	8	Egypt	Wishashi et al., 1958
Parathion	Flour	600	88	Colombia	Gomez Ulloa et al., 1967
Parathion	Sugar	300	17	Mexico	Marquez Mayaudon et al., 1969
Parathion	Sheets	3	0	Canada	Anderson et al., 1965
Mevinphos	Pants	6	0	U.S.A.	Warren et al., 1963
	Eating Formulations				
Hexachlorobenzene	Seed-grain	3000	[a] 3-11%	Turkey	Cam and Nigogosyan, 1969 Schmid, 1960
Organic mercury	Seed-grain	34	4	West Pakistan	Haq, 1963
Organic mercury	Seed-grain	321	35	Iraq	Jalili and Abbasi, 1961
Organic mercury	Seed-grain	45	20	Guatemala	Ordonez et al., 1966
Warfarin	Bait	14	2	Korea	Lange and Terveer, 1954
	Improper Application				
Toxaphene	Collards	4	0	U.S.A.	McGee et al., 1952
Toxaphene	Chard	3	0	U.S.A.	McGee et al., 1952
Nicotine	Mustard	11	0	U.S.A.	Lemmon, 1956
Parathion [b]		17	15	Iran	Ol Achrafi, 1963

Table 1 EPIDEMICS OF POISONING BY PESTICIDES(Continuation)

Pesticides involved	Material Contaminated	Number of Cases	Number of Deaths	Location	Reference
		Miscellaneous			
Parathion	Crops	400	0	U.S.A.	Quinby and Lemmon,1958
Pentachlorophenol	Nursery linen	20	2	U.S.A.	Amstrong et al., 1969
Parathion	Crops	23	0	U.S.A.	Hatcher and Wiseman, 1969

[a] 3 to 11 annually in different years

[b] Used as a treatment for lice

3. 3. Accidental Poisoning

A large number of accidents from pesticides occur each year. For example, in 1961, 8,5 % of all cases of accidents and poisoning of children younger than 5 years of age in the United States was attributed to pesticides (Cann, 1963). Of the 32,034 reported cases, 16,119 were caused by medicines, 1,726 by petroleum products, and 2,709 by pesticides. Some studies indicate that children who accidentally ingested pesticides in the homes account for a large proportion of the accidental poisonings attributable to pesticides. Accidental exposure to pesticides occur through direct consumption of contaminated food, or drinking the contents of an insecticide stored in an improper container (e. g. Coca-cola bottles) by mistake, or through inhalation and skin absorption. Table 1 has listed some of reported epidemics of pesticide poisoning around the world (- Mrak Commission, 1969). Another problem and a source of poisoning is that of the disposal of used pesticide containers which still contain appreciable amounts of pesticide after use. The practice of using containers for packing foods or the like, as far as possible, should be discouraged. For containers used for household pesticide, it is important that glass, plastic or metal containers be disposed of soon after their contents have been emptied in order that they may not be used as drinking water jugs, for other household purposes or remain available for possible contact with children. Obviously there exists a problem af disposal of these containers because the present method of disposal i. e. incineration or burial in the ground are unsatisfactory in that, even though they minimize the immediate dangers of exposure, they contribute to the build-up of environmental contamination.

In order to prevent accidents of the types listed above, one of the important aspects is that of labelling, colouring, or otherwise clearly marking pesticides in such a manner that will bring to the attention of the users the hazards which exist. It is important that the user of pesticides be thoroughly and forcibly warned of the hazardous nature of the material and the reasons for the pre-

cautions which are recommended. Problems of storage need to be given adequate attention, particularly in relation to storage of household pesticides so as to prevent their availability to children.

The possibility of sales control through appropriate registration of the more hazardous pesticides is an important measure in protecting the public from potential pesticide poisoning.

3. 4. Exposure of the General Population

Apart from exposures encountered under direct circumstances of pesticide usage during manufacturing, formulating, transportation, storage and application of pesticide chemical compounds, the general population is exposed to daily small doses of these environmental chemical contaminants inhaled through the air we breath, and ingested in the water we drink and food we eat. The degree of this indirect exposure will largely depend on the group of compounds used for edible crop protection and the extent of usage of the pesticide chemical compounds in agriculture. Some food products which are subjected to a series of pesticide application are consumed by the public without extensive processing. In some cases, the processing of the food may remove a portion of the pesticide residue while in other cases the food processing method may serve to concentrate and accentuate the pesticide problem in the food product. The total dietary exposure varies from one country to another and also depends upon the dietary habits of the individual or family. Few, if any, foods are completely free from pesticide residue.

The result for a variety of individual staple foods and food groups measured by official laboratories in the United Kingdom at the request of the Advisory Committee on Pesticides and other toxic chemicals are summarised in Table 2. The high contributions of fats and meats to the total dietary consumption of three insecticides from the chlorinated hydrocarbon group, should be especially noted. These two food sources are together responsible for just over 60 % of the DDT and dieldrin consumed in each case and about 55 % of

Table 2. AVERAGE DAILY CONSUMPTION OF CHLORINATED HYDROCARBONS 1966 IN GT. BRITAIN, 1966-7
Adopted from Harries, G. M.: J. Sci. Food Agr. 20: 242, 1969

Food group	% by weight of total consumed food ca 1.7 kg/day	DDT compounds	dieldrin	BHC compounds
Fats	4.9	17.1	1.9	4.9
Meats	14.5	11.8	2.2	3.9
Fruits, preserves	16.8	6.7	0.4	1.4
Cereals	15.9	4.4	0.6	3.5
Root vegetable	16.4	1.6	0.5	1.0
Green vegetables	8.2	1.5	0.3	0.7
Milk	23.3	1.3	0.7	1.1
Total	100	44.4	6.6	16.5

Table 3. ORGANOPHOSPHORUS RESIDUES IN SELECTED FOODS IN GREAT BRITAIN
Adopted from Abbot, D. C.: Pestic. Sci. 1:10, 1970

Food	Organophosphorus residues (ppm)
Bread	140
Imported cheese	700
Pork	1370
Milk	80
Infant food (mild based)	125
Sausages	60
Breakfast sausage or salami	60 - 180
Ham	60
Lettuce	87

the BHC; the importance of fats despite their contributing less than 5 % of the daily dietary, is especially significant. The relatively high concentrations of these pesticides in meat is most, probably due to their presence in the fatty parts of the meat; the chlorinated hydrocarbons are distinguished by their solubility in fats, and it is to be expected that this association will be maintained even after human consumption, metabolism and deposition in the body (Harries, 1969).

There have been considerably fewer analyses for other types of residue including the potentially highly toxic organophosphates which are finding increasing application as replacements for DDT. Their concentrations may be expected to show more variation owing to their more rapid degradation on their application. The results of some analyses on foostuffs from the report of the Joint Survey of Pesticide Residues in Foodstuffs are reproduced in Table 3 (Abbot, 1970).

The exposure of the general population, therefore the impact of pesticides on the health of man, is much greater through the food route than either air or water. Although "market basket" studies indicate that the exposure of the population to pesticides through food over years in the United States in particular has generally not increased up to 1969 when Mrak Commission was issued, particularly for aldrin and dieldrin, further studies are necessary at least for future trends (Mrak Commission, 1969e). At any rate, so far as the health of the gereral population is concerned, the greatest emphasis in pesticide control should be on reducing the concentration in foods.

Table 4 - PESTICIDE MODES OF ACTION
Adopted from Lucas, J.: Our Polluted Food. 2: 36-76, 1975

CHEMICAL CLASS	MODE OF ACTION
Triazins Thiocarbamates Bipyridyls	Inhibition of photosynthesis
Organophosphates Methyl-carbamates	Inhibition of acetylcholine
Chlorinated phenoxyacetic acids	Hormone analogues
Chlorinated hydrocarbons Pyrethrins	Disturbance of nerve conduction Neurotoxicant
Alkyl tin, Orthocresols	Uncouplers

4. MODE OF ACTION AND METABOLISM OF TOXICOLOGICALLY MOST IMPORTANT GROUPS OF PESTICIDES

The harmful effects of any pesticide chemical involve a complex of factors. In addition to the magnitude of the exposure and the rate at which the exposure occurs, any effect will depend on the critical pathways of the foreign substances within the body, on any biotransformation occurring along the pathways, and especially on the target organ in which the original substance or any toxic metabolite is concentrated preferentially or which may be especially sensitive to damage. The state of health enjoyed by the individual and the adequacy of the diet may also be factors in modifying and adapting to toxic effects.

All pesticide chemicals are selected for their biological activity and their ability to be toxic to and hence destructive of some form of pest, insect, fungus or weed. The various classes differ appreciably in their chemical behaviour and mode of action within the organism. These differences are listed in Table 4.

The metabolism of organic pesticide chemical compounds in the human body can be divided into two large distinct biochemical processes: Activation, which is defined as a metabolic reaction or reactions that convert an intrinsically inactive chemical compound to an active compound or an active compound to another one, in the human body; and detoxications is a chemical reaction or reactions that lead toxic substances to non-toxic ones. The mixed function oxidases that require $NADPH_2$ and O_2 are responsible to a large degree for the activation and detoxification processes of insecticides (Fukuto and Metcalf, 1969). The "incubation" period of pesticide intoxication depends on several factors, including the specificity of the compound in terms of its biochemical action in the body mode of entry, absorption rate, length of its action, individual susceptibility etc. which give a variability of toxicity signs, from one individual to another.

4. 1. Anticholinesterases

The effects of both organophosphorus and the carbamates have been related to the inhibition of tissue cholinesterases at synaptic sites and to an accumulation of excessive amounts of acetylcholine in effector organs. The symptoms of intoxication are mostly, if not exclusively, of a cholinergic nature. If the rate at which cholinesterase (ChE) is inhibited is rapid , there tends to be good correlation between the inhibition of blood ChE and the severity of illness. If the rate of ChE inhibition is slow there may be little or no correlation with illness. In fact, the blood enzyme levels may reach a very low activity without occurrence of symptoms or signs.

The duration of symptoms of poisoning depends in part on the rate of reactivation of the inhibited cholinesterase and the rate at which the inhibitor itself is destroyed or removed from the tissues. Both these factors are related to the chemical structure of the compound. Between the two groups of compounds and among the compounds in each group there are both differences and similarities that have to be emphasized. There are common characteristics among carbamates which distinguish them from organophosphorus insecticides in several important aspects. In case of over-exposure to an insecticidal carbamate the signs of poisoning develop rapidly, i. e. during or immediately after exposure; the incapacitating symptoms prevent further exposure, making the operator stop work long before a dangerous dose can be absorbed; recovery is rapid and complete; and chronic or cumulative effects are extremely improbable. Owing to these characteristics there have been no cases of severe poisoning after occupational exposure to carbamates. These differences between carbamates and organic phosphates have been established on experimental animals (Vandekar et al.,, 1965; Vandekar et al.,, 1971).

4. 1. 1. Organophosphorus Compounds

The biochemical mechanism of intoxication is much better understood for organophosphorus compounds than for many other toxic compounds. The association between inhibition of cholinesterase and toxicity by attacking the system of neural transmission in mammals and arthropods has been clearly demonstrated (Fest and Schmidt, 1973b). The inhibiting organophosphorus compounds have an affinity to cholinesterase, and their phosphate radicals form a strong bond with these enzymes which are normally responsible for destroying acetylcholine a few seconds after being released while acting at the active zone of the enzyme (O'Brien, 1969; Namba, 1971). Inhibition leads to an excessive accumulation of the intermediary substances (acetylcholine, butrylcholine, acetyl-beta-methylcholine etc., depending on species) responsible for neural transmission, transmission of nerve impulse, permiability of membranes and local humoral functions (e. g. in the heart), at the axonic and synaptic junctions. The effect of this interference may mimic muscarinic and/or nicotinic action. Acetylcholinesterase (E.C.3.1.1.7 according to IUPAC classification) normally found in the nervous system, vertebrate erythrocyte and electric organs of eels and fishes is the "true" cholinesterase. Plasma or serum cholinesterase (E.C.3.1.1.8) also known as the "pseudo"-cholinesterase which occurs primarily in plasma, brain and other tissues has no known physiological function. However, its usefulness in determination of cholinesterase activity in organophosphorus overexposure is very significant.

Investigations into the nature and effects of various organophosphorus compounds have enabled classification of these compounds, according to the degree of cholinesterase inhibition they produce. The biochemical mechanism of intoxication consists of phosphorylation of the active site of the vital enzyme - acetylcholinesterase. The compound may itself bring about this enzyme inhibition, but in many other instances the compound is first metabolized in the body and converted into the inhibitor. Dichlorvos

is an example of "direct inhibitor", while malathion and fenitrothion are examples of "indirect inhibitors". It has been demonstrated, for example, that in pure state phosphorothionate esters such as parathion are poor innibitors of cholinesterase (O'Brien, 1960; Menzie, 1966; Fukuto, 1957) because of the reactivating effect of the thionate sulfur atom. By contrast, paraoxon , the corresponding oxygen analogue of parathion, is a very potent anticholinesterase; the toxic action of parathion and related compounds is attributable to phosphate ester formed *in vivo* by disulfuration (oxidation) of the thionate ester. In mammals, the liver appears to be the source of phosphorothionate activating tissue. Transformation of phosphorothionate activation has been demonstrated with a wide variety of insecticides including malathion (O'Brien, 1957).

Organophosphorus compounds react with cholinesterase to produce a relatively stable phosphorylated enzyme. This reaction is progressive and temperature-dependent. When an active or free enzyme HE (in equation (1)) reacts with an inhibitor - an organophosphorus compound or a carbamate - AB, the reaction leads to the formation of phosphorylated enzyme EA, and BH is the first leaving product, where k_a is the biomolecular rate constant (Aldridge, 1971). The faster this rate is, the severer the inhibitor. Once the cholinesterase is phosphorylated, it looses its function. A spontaneous reactivation of the phosphorylated enzyme occurs *in vivo*. The rate of reactivation depends on the chemical structure of the phosphoryl group attached to the enzyme and hence on the chemical structure of the insecticide. Thus, the phosphorylated enzyme produced when dimethyl phosphate esters inhibit ChE reactivates spontaneously more rapidly than that produced by diethyl phosphate esters. The reactivation of inhibited enzyme can be considerably accelerated by special compounds (notably oximes) *in vivo* and *in vitro*. Some of these compounds have become important antidotes in the treatment of poisoning. When the phosphorylated enzyme is hydrolised, reactivation results as shown in equation (2). Such an outcome is desirable in the body since the

enzyme (cholinesterase) has an opportunity of reactivating for further reactions.

$$EH + AB \xrightarrow{k_a} EA + BH \qquad (1)$$

$$EA + H_2O \xrightarrow{k_r} EH + AOH \qquad (2)$$

Spontaneous reactivation is not the only reaction that the inhibited enzyme may undergo. It may also be transformed into a state where no spontaneous reactivation occurs and where oximes are no longer capable of reactivating it. This phenomenon is called "aging" and is characterized by removal of one of the alkyl groups from the phosphoryl group attached to the enzyme. The rapidity of "aging" of inhibited ChE is dependent upon the nature of the phosphorylating insecticides. The "aging" of an enzyme is a special characteristic of some potential poisons used in warfare (soman, VX) measured in minutes, while reactivation of phosphorylated enzyme is slight and axtremely slow. There are, however, some organophosphorus insecticides which can phosphorylate cholinesterase in such a way that the phosphorylated enzyme is partially "aged". In such cases it is important to know the relationship in the rate of these two reactions. Understanding of rate constant of phosphorylation (k_a), constant rate of reactivation (k_r) and the constant rate of "aging" (k_o) is the basic condition for assessment of an effect of an insecticide in insects as well as in man.

4. 1. 2. Carbamates

Unlike the organophosphorus insecticides, carbamylation generally leads to detoxication of the molecule. The spontaneous reactivation of carbamylated enzyme is more rapid than that of phosphorylated enzymes. Decarbomylation of inhibited enzyme is so rapid that, unless special precautions are taken, determinations of blood ChE in people or in animals exposed to carbamates are likely to give results that are too high, since the inhibited enzyme is progressively reactivated after collection of specimens.

No "aging" phenomenon has as yet been observed with monomethylcarbamoylated enzyme, either in vitro or in vivo. While inhibition in the early stages is rapid, it is difficult to produce severe degree of inhibition in the case of the carbamates because the rate of reactivation approaches that of inactivation. These differences in behaviour as enzyme inhibitors are important when the toxic effects of carbamates and organophosphorus compounds are compared.

4. 1. 3. Chlorinated Hydrocarbons

Sooner or later after discovery of insecticidal properties of DDT, it was also established that chlorinated hydrocarbons are stored in the human body and animals. The earliest published reports of DDT storage in man is apparently that of Howel (1948). He found DDT-derived material at a concentration of about 7ppm in the fat of a man with occupational exposure for 4 years and a history of eating foods known to bear appreciable residues.

In mammals, including humans, the principal metabolites of DDT is DDA, bis-(p-chlorophenyl) acetic acid (Burns et al.,, 1957; White and Sweeney, 1945).

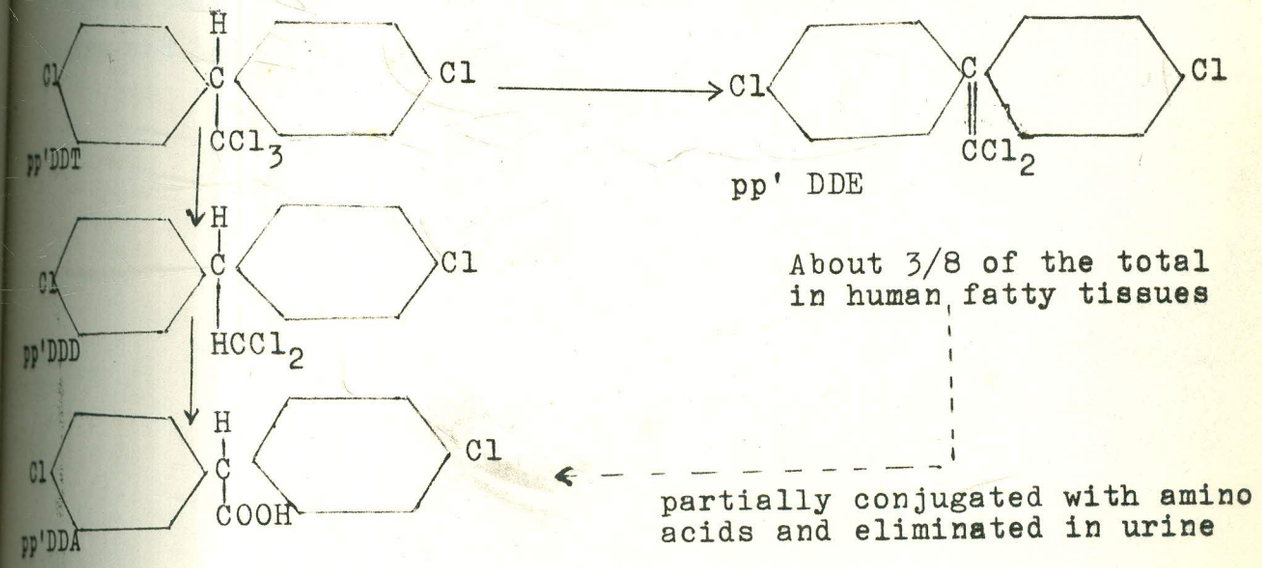


Fig. 1 Metabolites of DDT in Man

The residues of the chlorinated hydrocarbons entering the body in food eaten are absorbed relatively slowly in passing through the intestines and are then transported rapidly to the liver via portal vein. Within the liver they undergo biotransformations quite slowly, mainly owing to the stability of the bond between chlorine atoms and the carbon atoms in the ring structure. They are, therefore, totally foreign substances and the enzymes for breaking down those bonds do not normally exist. They are, however, slowly transformed into a number of metabolites mainly by process involving more vulnerable parts of the molecular structure (Fig. 1). Small quantities of the metabolites may also be secreted via the bile into the small intestine, where they may be recycled through the small intestine or eliminated in feaces. There are evidences that the acute action of chlorinated hydrocarbons, particularly DDT, can be detected under certain conditions in the cerebrum, cerebellum, brainstem, spinal cord, and periferal nerves (Bromiley and Bard, 1949; Shankland, 1964). Thus the acute poisoning effects of these compounds appear to be a diffused nervous system effect thought to be caused by interference with nerve impulse conduction and/or transmission. Acute DDT poisoning is characterized at the onset by marked parasthesiasis of the tongue, lips, and face along with malaise and headache.

5. RECOGNISED AND POSSIBLE EFFECTS OF PESTICIDES IN HUMAN

In order to understand better the aspects of human exposure to pesticides and their effects to the human body functions, it is necessary to review briefly the expressions often used in publications regarding pesticides health hazards. Exposure is described as "acute" or "chronic", "high-level", "over-exposure" or "low-level" and "short-term" or "long-term". The effects on the other hand can be "acute" or "chronic", "transient" or "permanent", and "immediate" or "delayed". The term "acute toxicity" and "chronic toxicity" also deserve elaboration. While "acute toxicity" usually implies overwhelming intoxication with overt illness or death, where often only one pesticide is involved and the diagnosis is relatively clear-cut, the term "chronic toxicity" is as a rule more difficult to interpret, but it may be appropriate to refer it to "illness resulting from long-term exposure".

5. 1. Acute Poisoning, Diagnosis of Major Pesticide Compounds and Treatment

The diagnosis of poisoning with cholinesterase inhibitors and organochlorine compounds depends on careful occupational and disease history, clinical observations and laboratory tests. It may not be too difficult to collect useful information which leads to the right diagnosis in occupational over-exposure, especially if the victim or the exposed subjects are employees in an organised or established institution where it may be easy to trace the source of poisoning. But, in remote areas where knowledge on the effects of pesticide poisoning on the side of medical personnel may be lacking or overlooked, diagnosis may not be established. The diagnostic study of pesticide poisoning whether fatal or surviving should commence with a consideration of social, ethnic and geographical background of individuals, bolstered by community knowledge (Davis et al., 1969). The clinical manifestations are discussed under Symptomatology of Poisoning with the

Table 5. SIGNS AND SYMPTOMS OF ANTICHOLINESTERASE POISONING
Adopted from Holmstedt, B.: Pharmacol. Rev., 11: 567, 1959

Site of action	Signs and symptoms
Following local exposure	
Pupils	Miosis, marked, usually maximal (pin-point), sometimes unequal
Ciliary body	Frontal headache, eye pain on focusing, slight dimness of vision, occassional nausea and vomiting
Conjuctivae	Hyperaemia
Nasal mucous membranes	Rhinorrhorea, hyperaemia
Bronchial tree	Tightness in chest, sometimes with prolonged wheezing expiration suggestive of brocho-constriction or increased secretion, cough
Sweat glands	Sweating at site of exposure to the liquid
Striated muscle	Fasciculations at site of exposure to the liquid
Following systemic absorption	
Bronchial tree	Tightness in chest, with prolonged wheezing expiration suggestive of brochoconstriction or increased bronchial secretion, cough
Gastro-intestinal system	Anorexia, nausea, vomiting, abdominal cramps, epigastric and substernal tightness (?cardio-spasm) with "heartburn" and eructation, diarrhoea, tenesmus, involuntary defecation
Sweat glands	Increased sweating
Salivary glands	Increased salivation
Lachyrymal glands	Increased lachrymation
Heart	Slight bradycardia
Pupils	Slight miosis (occassionally unequal), later more marked
Ciliary body	Blurring of vision
Bladder	Frequent or involuntary micturition
Striated muscle	Easy fatigue, mild weakness, muscular twitching fasciculations, cramps, generalized weakness including muscles of respiration, with dyspnoea and cyanosis
Sympathetic ganglia	Pallor, occassional elevation of blood pressure
Central nervous system	Giddiness; tension; anxiety; jitteriness; restlessness; emotional lability; excessive dreaming; insomnia; nightmares; headache; tremor; apathy; withdrawal and depression; bursts of slow waves of elevated voltage in EEG

P.T.O.

Site of action	Signs and symptoms
Central nervous system	especially on over-ventilation; drowsiness; difficult in concentration; slowness of recal confusion; slurred speech; ataxia; generalized weakness; coma with absence of reflexes; Chyne-Stokes respiration; convulsions; depression of respiratory and circulatory centres with dyspnoea, cyanosis, and fall in blood pressure

respective chemical compounds.

As with the all other types of intoxication, first aid and treatment are based on measures aiming at 1) preventing the additional absorption of the toxicant by removal of unabsorbed material by rapid gastric lavage of the poison was ingested, or by rapidly washing the contaminated parts of the body with water and soap for at least 10 minutes; 2) administering specific antidotes and symptomatic treatment such as suspected artificial respiration. Avoid mouth-to-mouth respiration when it is suspected that the victim had been intoxicated by mouth.

5. 1. 1. Anticholinesterases

The general symptomatology of poisoning with anticholinesterases - both carbamates and organophosphorus compounds - is given in the Table 5. In many cases, only a few of these signs and symptoms are observed and no case can be expected to show all of them.

The local effects commonly seen include unilateral or bilateral miosis lachrymation, conjuctival hyperaemia, spasm of accomodation and dim vision. Other local effects in the respiratory system are excessive bronchial secretion, and bronchospasm, with salivation and nasal discharge, after exposure of the lower and upper portions of the respiratory tract to direct inhibitors.

If the substances are ingested, gastro-intestinal spasm with colic, hypersecretion, vomiting and diarrhoea are common early symptoms.

In the initial picture of poisoning with organophosphorus or carbamate compounds, progression of intoxication can be divided into three main stages: the initial symptoms and signs; cramps or convulsions; and finally, paralysis. Since recovery in carbamate poisoning takes place more rapidly than in organophosphorus poisoning, symptomatology may not necessarily comply with the above sequency of progression.

The initial effect is marked by action on the smooth muscles,

cardial muscle and exocrine glands, generally described as the "muscarinic action" of acetylcholine. It refers to stimulation of the post-ganglionic parasympathetic nerves.The most common signs and symptoms in this stage include a feeling of malaise, salivation, neusea, vomiting, intestinal disturbance (diarrhoea and abdominal pain), headache, blurred vision, miosis, lachrymation and decrease in blood pressure.

If the dose is more powerful, stimulation proceeds to the periferal motor system and to all autonomic ganglia. The effects in this stage resemble those of the action of nicotine, hence the expression "nicotinic action" of acetylcholine, associated with a complexity of toxic action, resulting in neuromuscular and ganglionic blockade, manifested by cramps or convulsions. Lastly, the final stage is referred to as stimulation of somatic, autonomic and central nervous system, accompanied by such signs as involuntary defecation, incontinence and pulmonary oedema. Death often occurs due to paralysis of the respiratory functions.

Diagnosis

Apart from the clinical manifestations already discussed, there are laboratory tests conducted in respect of cholinesterase inhibitors: These biochemical tests for diagnosing and/or for monitoring cholinesterase inhibition in people exposed to the cholinesterase inhibitors are based on determinations of blood cholinesterase activity in blood (whole blood, plasma, or erythrocyte) and/or the metabolites of certain compounds in urine such as parathion.

The Ellman spectrophotometric method is considered adequate for determining plasma and whole blood cholinesterase activity. The reliability of Acholest and Tintometric methods were studied by using the spectrophotometric method as a reference method (Wilhelm and Reiner, 1973). They proved to be as valid as the spectrophotometric method, for measuring plasma cholinesterase activity (Plešting, 1966). The Tintometric method, modified in such

a way that substrate was added to the reaction mixture immediately after addition of blood sample, gave somewhat (2 - 11 %) higher values than did the spectrophotometric method.

It has been shown that with carbamates (e. g. carbaryl), propoxur and mobam), the erythrocyte cholinesterase is inhibited more than the plasma cholinesterase (Vandekar et al., 1971), while with others (e. g. landrin, carbamult, and m-isopropoxy-phenyl-methylcarbamate both enzymes are inhibited similarly (Simeon and Reiner, 1975) and the modification (Wilhelm, 1968) enables erythrocyte determinations as well. The method has been proposed to be developed for a field kit.

While the Tintometric and Acholest methods have been found to be suitable, the Tintometric method proved to be faster and more convenient (Edison, 1958). When enzyme activity is measured under field conditions temperature conversion tables are required, for the Tintometric (Watson and Edison, 1964) and for the Spectrophotometric method (Reiner, 1974) in order for the user to be able to regulate the time of assay according to the ambient temperature.

For monitoring and general diagnostic purposes, the question, which of the two cholinesterases is more diagnostic arises. It is important to consider the fact that plasma cholinesterase may be depressed in early hepatitis, alcoholic cirrhosis, other liver diseases and by some drugs. It is felt that plasma cholinesterase is less specific and too sensitive for routine monitoring (Zavon 1976). It is considered that erythrocyte cholinesterase is a better measure , but if possible both should be determined. Whole blood could be reliably applied for monitoring purposes too.

Some authors have described natural variability like differences between ethnic groups, age and sex. It is considered that the white people have higher cholinesterase values than the blacks; likewise females have higher values than males (Elliot and Barnes, 1963), and that human cholinesterase activity increases with age (Zavon, 1976). Because of natural cholinesterase variability, it

is important that each individual worker should have estimation of plasma and erythrocyte cholinesterase before handling or coming into contact occupationally with organophosphate compounds, as a baseline against subsequent exposures. In the absence of pre-exposure figures, average "normal" cholinesterase determined from a relevant population may have to be accepted.

In several studies conducted in respect of the association between symptomatology and cholinesterase activity level, it is indisputable that the relationship exists between the two variables. However, it has been demonstrated that the mere fact that a cholinesterase value is within the normal range cannot be used to exclude the diagnosis of organic phosphorus or carbamate over-exposure, although it does exclude serious poisoning from that source (Sumerford et al., 1953; Vandekar et al., 1968). On the other hand, some workers can show considerable low cholinesterase values without complaining of any symptoms.

Neuromuscular Conduction Velocity Test. In an effort to develop other methods for biological monitoring in exposure to cholinesterase inhibitors, a test based on neuromuscular conduction velocity has been suggested (Zavon, 1976). There is evidence now that tests in workers who are exposed to organophosphorus compounds for prolonged periods may demonstrate reduction in the conduction velocity in EMG voltage; but the condition returns slowly to normal as soon as the workers cease handling the compounds.

Treatment for Intoxication with Cholinesterase Inhibitors (WHO Expert Committee on Pesticides, 1967):

On signs of systemic absorption, both atropine and reactivators must be given parenterally.

Persons without signs of respiratory insufficiency but with manifested peripheral symptoms should be treated with 2-4mg of atropine sulfate and 1-2g of a soluble salt of pralidoxime or 250mg of obidoxime chloride (adult dose) by slow intravenous injection. More atropine (with or without the reactivators) may be

given depending upon the severity of intoxication and the response to the first dose. After the administration of oximes, less atropine may be required.

Severe intoxicated unconscious persons with respiratory difficulties and convulsions should be given atropine and a reactivator as above. In addition to this, the airways must be kept free and artificial ventilation applied if required. Atropine should not be given to a cyanotic patient until cyanosis has been overcome, since this may lead to ventricular fibrillation.

In these cases of severe intoxication, 4-6mg atropine sulfate should be given initially, followed by repeated doses of 2mg or as much as required to maintain full atropinization. The patient's condition, including respiration, convulsions, blood pressure, pulse rate and salivation should be carefully observed as a guide for further administration of atropine.

If possible, blood samples should be taken for cholinesterase determination before and during treatment. In parathion poisoning, reactivation of the enzyme activity of erythrocytes may be observed within an hour, but if the patient comes late for treatment (after 36 hours) oxime therapy may prove to be less effective. Since symptoms of intoxication with carbamates disappear rapidly compared to organophosphosphates, atropine treatment is often not necessary by the time the patient reaches the place where the antidote is at hand. In case of accidental poisoning or manifest symptoms, 1-2mg of atropine sulfate (adult dose) may be given intramuscularly or even intravenously, and the dose repeated as necessary. Oximes should not be given in cases of poisoning with carbamates.

5. 1. 2. Chlorinated Hydrocarbons

The effects of chlorinated hydrocarbons on the body depend very much on the quantity consumed. Severe acute poisoning and some deaths have occurred as a result of a very few accidental exposures involving endrin and BHC but DDT does not appear to

have been involved in any fatal accidents. They are known to have an effect on the central nervous system leading to serious disorientation in the case of experimental animals. Some comparatively mild adverse reactions have been reported from a few human volunteers receiving a single acute dose of 750 - 1000mg of DDT. Maximum symptoms occurred some 6 hours after dosing and included a general feeling of malaise with some uncertainty of gait, a cool moist skin and increased sensitivity to contact. There were no detectable changes in the reflexes and recovery was complete after 24 hours. A higher consumption of 1500mg of DDT produced a slightly more severer reaction with giddiness, confusion and tremors of the limb extremities after 10 hours but complete recovery again after 24. Single acute exposure, however, do not present in any way the chronic situation affecting the general public from the small exposure received from food over a long period of time.

Diagnosis and Treatment

Blood analysis for organochlorine levels in the blood may be used to confirm the cause of poisoning, but this is at present a lengthy and highly specialized procedure.

The organochlorine levels in the blood may be used to confirm the diagnosis. The organochlorine compounds most commonly causing poisoning are endrin, aldrin and dieldrin. Treatment is aimed at controlling the symptoms, especially hyperactivity and in some instances convulsion. Artificial ventilation may be required. Anticonvulsant treatment with soluble diazepam or paraladehyde could be given in sufficient dosage to calm the patient and prevent convulsions.

5. 1. 3. Cyanides

Cyanides are chemical compounds used as fertilizers and for fumigation in agriculture. The threshold is considered to be 5mg/m^3 of air. In poisoning, the chemicals are absorbed through inhalation, ingestion and through the skin.

Symptoms of the nervous system appear as a result of cytotoxic anoxia (headache dizziness, hyperpnoea, neusea vomiting etc.).

Blood sample of the victim should be taken for determination of cyanide, while increasing excretion of thiocynate in urine in non-smokers can be diagnostic for cyanide. The victim should be removed from exposure immediately, and measures to reduce absorption such as washing the contaminated body areas externally and gastric lavage internally should be performed without delay. Artificial respiration and oxygenation should be administered, and amyl nitrite pearls should be inhaled by the victim every 5 minutes accompanied by intervernous doses of 10cc of 3 % sodium nitrite over a period of 2 minutes, then 50cc of 25 % sodium thiosulfate, repeated possibly at hourly intervals(Plunkett,1966).

5. 1. 4. Methyl Bromide

Methyl bromide or bromomethane, is a colourless irritating gas with chloroform-like odour. It is used in agriculture as an insecticide as well as a fumigant, where occupational over-exposure occurs. It is estimated that the threshold is 20ppm in the air. It enters the body through inhalation, ingestion, or percutanously, and then through the blood-stream it can lead to pulmonary haemorrhage and oedema, cerebral heamorrhage, congestion of liver and renal tubular damage (Plunkett, 1966). Locally, it can cause chemical burn, while systemically it leads to the appearance of psychiatric and neurological symptoms and signs. Convulsions can occur.

Bromide in blood and cerebral fluid are diagnostic tests for poisoning. Treatment should aim at preventing further absorption of the toxicant, administration of oxygen, and sedation.

Preventive measures should include adequate ventilation, hygienic conditions in work areas, the use of chemical goggles, and respirators. If possible, some authors suggest that workers

should work in pairs in order for them to save one another in case of poisoning of either of them. Physical examination of exposed subjects should be conducted every 6 monthswith special attention to the central nervous system, including determinations of bromide in blood. Individuals with psychiatric and neurological disorders as well as those with diseases of skin, lungs, liver and kidneys should be precluded from exposure (Plunkett, 1966).

5. 1. 5. Paraquat

Paraquat is a nitrogen containing pesticide compound. It can cause fatal poisoning if swallowed in sufficiently large amounts. All reported deaths so far have been a result of proliferation of cellular elements in the lung with attendant impairment of ventilation. No systemic poisoning had been reported from its use in agriculture in the United States except local irritation on the skin, eye, or nasal mucosa which have been observed.

The substance is poorly absorbed from the intestines and the fraction absorbed is excreted rapidly in urine; the bulk of it is excreted unchanged within 48 hours. Because of the progressive nature of the pulmonary fibrosis, death was often 3 or more weeks after ingestion (Barnes, 1968). Individual case reports are available for some more detailed description of the clinical picture of Paraquat poisoning (Howe and Wright, 1965; Clark et al., 1966; Mckean, 1968; Almog and Tal, 1967; Manktelow, 1967, Campbell, 1968). Among the many cases that have recovered from Paraquat poisoning have been some manifesting severe hepatic and renal involvement, where steroid therapy was constituted early (Weidenbach, 1969).

5. 1. 6. Pyrethrins

Pyrethrins are chemical compounds extracted from flowers of a plant Chrysanthem cinerariaefolium. Its synonyms include such names as cinerius, pellitory, Persian insect powder, pyrethrolone

esters of Chrysanthem carboxylic acids and pyrethrum insecticides.

The substances enter the body by inhalation or ingestion. Pyrethrum is probably the most widely used insecticide of vegetable origin, which has become an important cash crop in Kenya, Tanzania, and several other tropical and subtropical countries. The most striking feature of this insecticide is that in insects, it gives a remarkably rapid "knockdown", that is, when an insect is treated it is quickly paralysed. It is a most effective insect poison requiring a very low dose to paralyse, and higher dose kill an insect, but still in comparison with other insecticides, a low dose (Plunkett, 1966). It is unfortunately, rather expensive to produce pyrethrum, so it has been used more often in public health work to control disease carrying insects like malarial mosquitoes than in agriculture.

As skin irritant and sensitizers, pyrethrins cause skin irritation and allergic dermatitis. The acute signs and symptoms include asthmatic breathing, headache, tinnitus, neusea and vomiting as well as incoordination of muscles, tremors and convulsions. Anaphylatic reaction can occur. Diagnosis is based on oesinophylia and clinical symptoms (Plunkett, 1966).

Treatment of pyrethrin intoxication is based on preventing further absorption of the toxic chemical compounds externally as well as internally, and administering oxygen or artifical respiration, and barbiturates for sedation, accordingly.

Preventive measures include precluding from exposure those individuals with pulmonary diseases and allergies, as well as removing from any further exposure those individuals that become sensitized. The use of protective clothing and devices is an important measure to be taken.

5. 2. Delayed Effects of Some Pesticide Chemical Compounds

5. 2. 1. Anticholinesterases

The organophosphates, particularly parathion, mevinphos and TEPP are health hazards because of their high toxicity and ease of absorption by ingestion and the dermal or respiratory routes. The disease they produce in workers are chiefly acute poisoning, but may in addition leave sequelae of acute intoxication which are probably anoxic in nature. However, there is an additional hazard to workers which may not be recognised; this is because undue exposure resulting in cholinesterase inhibition from chronic exposure may predispose the worker to poisoning when he/she is exposed subsequently (to an exposure not expected to be noxious) with the resulting of clinical signs of poisoning. Somewhat similar hazards build-up slowly from repeated spraying with residues of organophosphorus compounds to the point that orchard workers are affected gradually by dermal or respiratory contact with plant material (Milby, 1964). Some of the deletarious persistent manifestations produced by some organophosphorus compounds include polyneuropathy (delayed neurotoxicity). One of the first published reports in this respect was demonstrated in the so-called "Ginger jake" paralysis or "Jakeleg" paralysis syndrome in connection with myelin degeneration due to tri-o-cresyl phosphate (TOCP) (Smith and Evolve, 1930). Other persistent manifestations which involve the central nervous system, liver functions and other body systems in man and experimental animals are presented in Table 6.

Cases of carbamate poisoning usually occur where the compounds are more extensively used (Vandekar, 1965). The biochemical effects and clinical picture essentially resemble to those manifested by organophosphorus compounds, but it is characteristic with carbamates that the usually mild symptoms encountered, rapidly subside and recovery is quicker than with organophosphate compounds. There are specific acute effects produced by each carbamate compound but

Table 6 - CLINICAL EFFECTS OF CHOLINESTERASE INHIBITION IN MAN, MAMMALS AND CHICKENS

NAME OF COMPOUND	ANIMAL AFFECTED	PATHOLOGICAL EFFECTS	MANIFESTATIONS
Cholinesterase inhibitors(general) mipafox in particular	man and mammals	damage to myelin sheath, myelin degeneration	flaccid paralysis(Davies,1963 paralysis similar to Jakeleg (Birdstrup et al.,1953)
		cholinergic/adrenergic	slow wave burst.Generalized weakness,confusion,forgetfulness, difficult in thinking, visual difficulty(Gershon & Shaw, 1961; Davies, 1963; Metcalf, 1969)
		eye and vision	Saku disease- constriction of periferal fields(Pleština and Pleština,1978, In Press)
		possible changes in coagulation factors (Namba, 1971)	
		abnormal liver functions	increased serum bilirubin
Mevinphos	man	reduction in the conduction velocity in both fast and slow motor nerve together with reduction in EMG voltage spontaneously returning to normal when handling ceases(Verbeck and Sallè,1977)	increased in Achilles tendon reflex
Parathion	man	decreases rate of tubular reabsorption in chronic exposure(Davies, 1969)	aminoaciduriasis with greater frequency than usual(sugar, keto,acids, phenolic acids, indoles, purines, pyridines, mucopolysaccharides and amino acids

			anxiety, depression, impairment of language function(Rodnitsky et al.,1975), nasal discharge miosis, weakness(Sumerford et al.,1953;Gershon & Shaw,1961)
Parathion with chlordane and Gamma BHC	man	hemotoxicity(validity of claim challenged(Christophers, 1969)	dyscrasiasis(aplastic anaemia thrombocytopenia,leukopenia, erythroid aplasia, haemolytic anaemia.
TOCP, diisopropyl phosphorfluoridate(DFP), diethyl phosphorfluoridate, ENT	chicken rats rabbits	myelin degeneration apparently the lesion is located at the end of the nerve cell affected,confined to the long tracts (Cavanagh, 1964)	paralysis (Davies, 1963; Austin and Dvies, 1954; O'Brien, 1960)
Cholinesterase inhibitors	rats	diminishes pharmacological activity of progesteron and deoxycorticosterone (Conney et al., 1967)	
Trio-cresyl-phosphate	rats	accentuated an EFA (Seward et al., 1966)	

the main toxic effect of carbamine compounds is the effect on endocrine organs. Possibly another effect is allergic reaction in the organism. The present available data suggest that the possible development of delayed effects of carbamine compounds may be the main potential hazard. In certain instances, there is evidence to suggest that the real hazards may be carcinogenic and genetic effects (Medved and Copplestone, 1974).

5. 2. 2. Organochlorine Compounds

DDT studies in occupational exposures have not revealed specific adverse effects. In a study conducted on 400 persons exposed to organochlorinated pesticides, for example, it was suggested that workers experienced a high frequency of cardiovascular diseases than expected, as revealed by abnormalities in their electrocardiograms but the evidence was not conclusively convincing.

The evidence of the feeding trials with DDT and dieldrin already described provides some information about adverse effects at subacute levels of exposure but provides no evidence whatever for any long-term chronic effects which might be expected from exposures continuing at the present levels in food. The evidence for long-term effects is based entirely on animal experiments involving livels of exposure which are still well above food consumption levels and has been thoroughly reviewed by Mrak Commission.

An attempt to summarize their essential findings for long-term carcinogenic, mutagenic, teratogenic and other effects through enzyme interactions is set out in Table 7 (Lucas, 1975). With the Diene group of compounds, - aldrin, dieldrin, endrin etc., among many studies which have been conducted, one of them revealed prevalence of 5 % of workers to be having epileptiform convulsions (Hoogendam et al., 1965), but the incidents were temporary and associated with over-exposure. In one comprehensive epidemiological survey of 826 plant workers exposed to aldrin and dieldrin for a

Table 7 - SOME CHRONIC EFFECTS OF PESTICIDE CHEMICALS IN ANIMALS
Data summarized from Mrak Commission
by Lucas, J.: Our Polluted Food.
2:36-76, 1975

CHEMICAL GROUP	NAME	Mutagenicity Prob.	Mutagenicity Poss.	Carcinogenicity Prob.	Carcinogenicity Poss.	Teratogenicity Prob.	Teratogenicity Poss.	Enzyme Interaction Prob.	Enzyme Interaction Poss.
Chlorinated hydrocarbons:									
	DDT			X				X	
	Dieldrin	X		X		X		X	
	Heptachlor	X		X				X	
	Endosulfan				X			X	
	Endrin	X							
Organo-phosphates:									
	Malathion		X					X	
	Parathion		X				X	X	
Carbamates:	Carbaryl	X				X		X	
Dithio-carbamates:									
	Maneb				X				
	Nabam				X				
	Thiram	X			X		X		
	Ziram	X			X				
Triazines:	Simazine		X		X				
	Atrazine		X		X				
Phenoxy acetic acids:									
	2,4-D				X		X		
	2,4,5-T				X	X			
Bioyridyls:	Diquat	X							
	Paraquat	X							
Miscellaneous:									
	Chlorfenson				X				
	Captan				X		X		
	Folpet						X		

Probable = adequate evidence to suggest comparable human effect; possible = inconclusive evidence

total 1,728 years exposure, it was revealed that hazards of working with pesticides were slight. Lindane has been incriminated directly or indirectly, with 18 cases of blood dyscrasias (West, 1967), but there is an admitted lack of data to confirm the suspicion. Porphyria has been described following ingestion of hexachlorobenzene (Schmid, 1960).

5. 2. 3. Miscellaneous Pesticide Chemicals Compounds

In a factory manufacturing phenoxy (the herbicide 2-4D, 2,4,5T) a number of workers were found to have hyperpigmentation and fragility of the skin, eruptions on exposed areas and acne lesions, porphyria. It was postulated that the disturbed metabolism was due to a toxic action on the liver by one or more different chemicals being used in the factory although no direct relationship between clinical signs and the degree of chemical exposure was demonstrated; the diseases were considered to be the result of individual susceptibility (Bleiberg et al., 1964). Other effects associated with 2,4-D include excessive fatigue, headaches, epigastric pains, anorexia and occassional upper respiratory tract symptoms and impaired sensitivity (Fetison, 1966).

In spite of all the information available on the effects associated with pesticide usage, a review of the published reports on epidemiological studies of human hazards from long-term exposure to pesticides lack definitions of the pathological conditions attributable to the usage of pesticides. However, there is enough evidence of illhealth associated with many aspects of pesticide usage, including the nature of the compounds and the way they are handled. Exposure is found to be essentially universal throughout developed and developing countries,over all social classes, ages (from newborns to all adult ages), and for both sexes. Wide variations of exposure exist with extremely high levels being associated with occupational exposures.

II. PERSONAL STUDY

4. SPECIFIC FEATURES AND HEALTH ASPECTS RELATED TO THE USE OF PESTICIDES IN TANZANIA

4.1. General Geographical feature and Population Structure

The United Republic of Tanzania consists of the former Tanganyika and the islands of Zanzibar and Pemba situated in the Indian Ocean about 40 kilometres off the coast, north of Dar es Salaam. The country lies on the east coast of Africa between 1° and 11° 45' S latitudes and 29° 20' and 40° 38' E longitudes. The total area (about 939,767 sq.km.) can be divided into the following vegetational divisions: arable land and plantations 12 %, permanent pastures, including national parks and game reserves 10 %, uncultivated land 18 %, forests 39 % and the remaining land is about 15 %. Lakes and rivers occupy the rest of the area. Topographically, the altitude rises from the low-lying eastern coastal belt along the Indian Ocean shores, towards the high westcentral plateau and the scattered mountain zones, the southern highlands, and the northern highlands including the highest peak in Africa (Mount Kilimanjaro, 5895 metres above sea-level), which projects on the north-eastern part of the country, at the border with the neighbouring Kenya. Because of the large variations in altitude, the climate displays a great range of temperatures from langurous tropical warmth of the coast to the cool invigorating highlands. The climate in Tanzania can be described broadly according to the following seasons: the warmer dry season from January to March; the first or long rains, from April to May; the cooler dry season, from June to September; and the short rains from November to December. Average temperatures vary from 27° - 32° C. The chief cash crops are coffee, cloves, sisal, cotton, cashew nuts, tobacco and tea, while food crops include cereals, legumes, tropical fruits (including citrus fruits) and vegetables.

Tanzania is mainly an agricultural country and most of the farming was until recently at subsistence level, while the industry is largely concerned with processing of raw materials, either

for export or for local consumption. However, emphasis on some heavy industry has been placed in the 3rd Five-Year Development Plan in order for it to complement the requirements for modern farming.

Assuming that the present occupational population structure in Tanzania has not significantly changed from that of the last census (1967) (Egero and Henin, 1967), and accepting the 1977 population estimates as a base, about 42 % of the total population is engaged in agricultural pursuits, and the agricultural population of about 6,828,780, constitutes nearly 91 % of the total economically active population. Therefore, for many years to come, Tanzania economic development will depend largely on the sweat of the farmer!

1.2. Extent of Pesticide Usage

In the past 20 years, the use of pesticides in agricultural development and public health has tremendously increased in Tanzania. The increase has to a large extend been accelerated by great efforts employed to increase agricultural productivity and to combat vector diseases which are still the major cause of morbidity in Tanzania today.

It is estimated that Tanzania used 86,112 tons of pesticides in 1967 for agricultural and public health purposes (Ministry of Agriculture Personal Communication). Ten years later pesticide usage for the same purposes had nearly trebled. Roughly, 8 % of all pesticides is used for preventive health measures, mainly in malarial control and other disease vector control programmes. The rest of total quantity of pesticides is used mainly in agriculture for crop pest control.

Bearing in mind that about 42 % of the whole population is engaged in agriculture, this information provides valuable insight of the extent of pesticide usage and concealed health hazards of occupational exposure as well as to the rest of the population which comes into contact with the toxic chemical compounds

occassionally or casually.

As far as origin of pesticides used in Tanzania is concerned, USA and the Federal Republic of Germany are the chief manufacturers and exporters of pesticide compounds used in Tanzania. The local industry still in its infancy formulated and manufactures some pesticides under licence from overseas proprietors, but for some years to come Tanzania will still depend on imported pesticides.

It may prove fruitless to trace the historical development of pesticides in most of Africa before the colonial era, because of lack of records. However, there are ample evidences that African peoples used plant extracts and smoke of certain substances such as leaves and roots similar to the account given by Brooks on the South American inhabitants (Brooks, 1974), either to kill or to repel insects. For example, the author observed the use of "unkondo", a perenial plant whose leaves are smashed and poured into a pond as fish poison in fishing, by the "Wanyakyusa" tribe in Tanzania. The same substance is said to be an effective insecticide as well. The "Vaasu" tribe of north-eastern Tanzania as well as some other tribes used to burn cow-dung for controlling house flies vexing their cattles or against mosquitoes in bedrooms at night. These methods may not be very effective, but, in my opinion, may not be totally ineffective either.

Regardless of the extent of exposure to pesticides, exclusive of residual exposure, most of the Tanzania working population coming into contact with pesticide chemical compounds can be grouped and described under the following broad categories:

- Workers in production and formulation plants;
- individual peasants, farmers, husbandry and poultry keepers and private employees who operate small scale pest control schemes against agricultural or domestic pests;
- workers in forestry, agricultural and veterinary institutions such as state farms and ranches, and international or national research institutes;

Table 8a. COMMON PESTICIDE COMPOUNDS USED IN TANZANIA IN 1968
Adopted and modified from Eberhard, B.:
Crop Pests in Tanzania and Their Control. 1968

GROUP OF COMPOUND	PESTICIDE COMPOUND
Organophosphorus	azinphos-methyl, diazinon, dichlorvos, dimethoate, fenitrothion, fenthion, fensulfothion, malathion, omethoate, oxydemeton, parathion, phenamiphos, phosphamidon, trichlorfon
Carbamates	carbaryl
Chlorinated hydrocarbons	aldrin, chlordane, chlorbenzilate, DDT, dieldrin, endosulfan, endrin, heptachlor, dicofol, lindane, lindasan, toxaphene
Plant derivatives	pyrethrins and nicotin
Miscellaneous	ethylene dibromide, oxythioquinox, white oils

Table 8. INSECTICIDES RECOMMENDED FOR SMALL HOLDINGS IN TANZANIA
Compiled from Mshiu, E.: Lyamungu Leaflet
1976

Group of Compounds	Name of Compound
Organophosphorus	fenitrothion, fenthion, dichrotophos, diazinon
Halogenated hydrocarbons	endosulfan, dieldrin
Miscellaneous	methomyl

Table 9. INSECTICIDES RECOMMENDED FOR ESTATES IN TANZANIA
Compiled from Mshiu, E.: Lyamungu Leaflet
1976

Group of Compounds	Name of Compound
Organophosphorus	parathion, dichrotophos, fenitrothion, azinphos-methyl
Chlorinated hydrocarbons	dieldrin
Miscellaneous	methomyl, sulfur compounds

Table 8b. ORAL AND DERMAL TOXICITY OF SOME PESTICIDE COMPOUNDS WITH THEIR ACTIVE INGREDIENTS AND FORMULATIONS USED IN TANZANIA

GROUP, NAME AND SYNONYMS OF PESTICIDE COMPOUNDS	CONCENTR. (%C)	ORAL TOXICITY IN RATS- LD_{50} (MG/KG)	DERMAL TOXICITY IN RATS - LD_{50}
S L I G H T L Y H A Z A R D O U S			
ORGANOPHOSPHORUS:			
pirimiphos-methyl (ACTELLIC)		2050 M1180	>2000
CHLORINATED HYDROCARBONS:			
chlorbenzilate(Acaraben)		700-3200	10200
MISCELLANEOUS COMPOUNDS:			
atrazine		3080	
captan		10,000	
dalapon		6000-9000	
oxythioquinox(FORSTAN)		2500-3000	
prometryne		3750	
simazine		5000	
M O D E R A T E L Y H A Z A D O U S			
ORGANOPHOSPHORUS:			
(Abate, BIOTHION)		1000-3000 M4000	>4000
dimethoate(Rogor, PERFEKTTHION)	40%*	Rb300-500 250-500	>150-1150
fenitrothion(SUMITHION, FOLITHION)	50%*	250-500 M700-900	200->3000
fenthion(Lebaycid, BAYTEX)	50%* 40WDP*	255-298	330
formothion(ANTHIO)	25%*	365-500 Rb420 M190	1680
malathion(Malathon)	50%	885-2800 M720-4060	>4000>4444
phenthoate(Cidial, dimethenthoate)	50%	200-2000 M350-1500	>4000
trichlorfon(chlorfos, NEGUVON)	50%*	M300-500 450-469	>2000 Rb5000
CARBAMATES:			
carbaryl(Sevin)	50%	307-986 Rb710	500- 4000
CHLORINATED HYDROCARBONS:			
benzene hexachloride(BHC)	20%*	600-1200	
chlordane (Velsicol 1068)		283-590	580-1600 Rb780
DDT	75%	87-500	1931-3263

PHENOLS:

dinocap(Karathane)		980-1190 Rb2000	4700 Rb9400
linuron		1500	
MCPA (2,4-D)			

MISCELLANEOUS COMPOUNDS:

ametryne		1750	
dazomet	85% *		
	dust	650	
pyrethrins		200-2000	

H I G H L Y H A Z A R D O U S

ORGANOPHOSPHORUS:

azinophos-methyl(m-Guthion)	25%WDP*	13-16	200 Rb1000-2000
chlorpyrifos(Dursban)	35%*	97-276	Rb2000
demeton(Demeton-S)	50%WDP*	2-12	8-14 Rb24
diazinon (Diazinon)	60%	66-600	379-1200
dichlorvos(DDVP,NUVAN,NOGOS)		25-170	59-900
dioxathion(Delnav)	70%	19-176	53-350
disulfoton (DI-SYSTON)	10%gran*	2-12	20-50
methidathion (Ultracide, Supracide)		25-48 M25-68	Rb375
mevinphos (Phosdrin)	1o%gran*		
monocrotophos (NUVACRON, Azodrin)		21	Rb354
morphothion (Ekatin)		100-120	M105-120
omethoate(FOLIMAT)		50	1400

CARBAMATES:

aminocarb(METACIL)	50%WDP*	30	275
methiocarb (MESUROL)		130-135	2000
propoxur (arprocarb,BAYGON)	50%*	45-104	1000

CHLORINATED HYDROCARBONS:

dieldrin	50%	40-100 M44	80- 200
endosulfan (Thiodan)	35%*	18-110	74-130 Rb36
endrin	50%	3-45 Rb 7-10	12-19 Rb 60-120
isodrin	50%WDP* 25%	12-17	
lindane (Gamma BHC)		76-200 M86	500-1200
heptachlor (Velsicol 104)		40-188 M68	119-320 Rb2000

MISCELLANEOUS COMPOUNDS:

dinoseb acetate (Phenol)	50%*	37-50	80-200
dinitrocresol (DNOC)	20%	26-65	200-600
ethylene dibromide		108-170	VA200
methyl bromide			VA200
nicotine	90% *	50-91 M24	140 Rb50
methomyl (Lannate)	90%gran*	17-24	Rb1000
paraquat compounds	20% sol.	157	
warfarin (coumarin)		58	

ORGANOPHOSPHORUS:			
dicrotophos(CARICRON)	40%	22-75	Rb225
methyl-demeton(Metasystox)		40-180	
fensulfothion (DASANIT)		8-10	3-30
methyl-parathion		9-42 M32	63-72 Rb1270
mevinphos (Phosdrin)	20%	3-7 M8-200	3-90 Rb13-55
paraoxon		3.5	
parathion (BLADAN)	40%	3-30 M6-25	4-200
phenamiphos (NEMACUR)		8-9	72-84
phorate (Thimet)		1-5	2-300
phosphamidon (Dimecron)		15-33 M6-12	125-150
CHLORINATED HYDROCARBONS:			
aldrin	30% *	39-60 M44	65-90 Rb50-80
MISCELLANEOUS COMPOUNDS:			
dicamba		2.9	
piperonyl butoxide (Butacide)		7.5	
schradan (Pestox)	60% *	20-30	

EC = Emulsion Concentration

WDP = Water Dispersible Powder

M = Mouse

Rb = Rabbit

VA = Acute Vapour(ppm)

* Adopted from WHO Chronicle. Recommended Classification of Pesticide by Hazard. 29: 397-401, 1975.

The Dermal and Oral toxicities have been adopted from Kenaga E.E. and End, C.L.: Commercial and Experimental Organic Insecticides, (1974 REVISION).

Table 8c . MISCELLANEOUS COMPOUNDS USED IN TANZANIA

alchlor
amitrole (aminotriazole)
benomyl (Benlate) - Carbamate
bentazone - Organophosphate
bis (Dimethylthiocarbamoyl) disulfide
(Thiram)
carbendazim (Bavistin) - Carbamate
carbensazim (Derosal) - Carbamate
chloramben (amiben)
chlormequat
cyclohexanone (threshold 50ppm of air)
epichlorhydrin (threshold 5 ppm of air)
EPTC (S-ethyl dipropylthiocarbamate) -
Carbamate
ethoxyethylmercuric-hydoxide (Tillex)
ethoxyethylmercury-methyl mecury-citrate (Festix 85)
isoproturon /N-4-isopropyl-N', N' dimethyl urea
lindasan
MCPP (mecoprop) - Phenol
niclosamide (Bayluscide)
oxadiazon - (1, 3, 4-oxadiazoline-5-one)
penoxalin /N-(1-ethylpropyl)-3, 4 dimethyl-2,
6-dinitrobenzen
pentochlorophenol (threshold 0.5mg/cu.m. of air)
2,3,6-TBA
secarol
sevimal

Table 10 - PESTICIDES RECOMMENDED FOR LOWER ALTITUDE CROPS IN TANZANIA

Compiled from Mshiu, E.: Lyamungu Leaflet 1976

GROUP OF PESTICIDE COMPOUNDS	NAME OF PESTICIDE COMPOUND	APPLICATION
Organophosphorus	mevinphos, malathion, dimethoate	For Field Crops: maize and legumes
Chlorinated hydrocarbons	DDT, endosulfan, aldrin	
Organophosphorus	dimethoate	For Fodder Crops: lucerne
Chlorinated hydrocarbons	DDT	
Organophosphorus	malathion, diazinon, trichlorfon dimethoate, phosphamidon, mevinphos	For Vegetable Crops: cauliflower, turnips, tomatoes, onions, egg-plants, carrots pepper, cabbages, okra
Carbamates	carbaryl	
Chlorinated hydrocarbons	endosulfan, DDT	
Organophosphorus	dimethoate	For Fruit Crops: bananas, grape vines, citrus fruits
Chlorinated hydrocarbons	DDT, dieldrin	

Table 11 · PESTICIDES COMMONLY APPLIED FOR DISEASE VECTOR CONTRO
From Ministry of Health, Tanzania, 1977

Type of Vector Control	Pesticide Compounds
Anopheline	malathion, dieldrin, pyrethrins
Culicine	Abate, chlorpyrifos
Tse tse	DNCO, chlorbyrifos
Molluscidal	niclosamide
Rodent	Warfarin, coumachlor, coumatetraetil
Miscellaneous	benzene hexachloride, dichlorvos, diazinon

Table 12 · SOME OF THE MOST FREQUENT CAUSES OF ATTENDANCES AT OUT PATIENT MEDICAL DEPARTMENTS IN TANZANIA MAINLAND 1973 - 74

Adopted from the Ministry of Health
Annual Reports (Tanzania) 1973/74

CAUSES	NO. OF CASES		% OF TOTAL	% OF CASES
	1973	1974	1973	1974
Symptoms of ill-defined conditions	510,094	541,577	8.9	9.1
Malaria	747,170	607,709	13.1	10.3
Accidents, poisoning violence	329,461	354,186	5.8	6.0

- field workers (spraymen) and health technicians who are engaged in small and large scale disease vector control programmes (malarial, schistosomiasis, tse tse etc.)

1. 2. 1. Agricultural Use

The number of different kinds of pesticide compounds for crop protection in Tanzania has continued to increase year after year. While in 1968 the list of 5 groups of commonly used pesticide compounds shown in Table 8a was only handful, the different kinds of pesticides used in the country today probably run to over hundred, since the chemical industry continues to flood its new products into use from day to day. Majority of the compounds used in Tanzania now are presented in Table 8b and 8c.

With the emphases placed on increased agricultural productivity there are clear indications from the recommendations on pesticide usage issued to small holdings and estate farmers (see Tables 8, 9, 10), by the leading national agricultural research institute, Lyamungu(Simon et al., 1976; Mshiu, 1976), that such access to some dangerous toxic compounds may prove to be a source of pesticide health hazards due to possible mishandling. One of the groups of pesticide compounds used to protect or cure coffee crop from coffee berry disease (CBD) is the fungicide group, including the following chemical compounds, most of which are carbamates: benomyl, captafol, carbendazim, carbensazin, cuprous oxide and delan.

The Ministry of Agriculture through the National Milling Corporation based in Dar es Salaam conducts fumigation operations yearly carried out by a team of 55 workers who cater for all regions in the country during harvest season, using mevinphos, malathion, dichlorvos, and methyl-bromide for preservation of harvested crops for storage (Ministry of Agriculture, Personal Communication, 1977). It easy to foresee the pesticide health hazards which may arise during the handling of toxic chemical

compounds, if proper precautions are not taken into consideration (Wagner, 1976).

1. 2. 2. Public Health Use

In order to control the problem of vector diseases, the Ministry of Health established a number of zonal health technicians and auxiliary teams (Ministry of Health, Dar es Salaam, Tanzania, 1977, 1978 - Personal Communication). Since malaria is still a major health problem, these teams conduct malaria control programmes in which even the highly toxic insecticides have to be applied in order to overpower the ever increasing threat of resistence demonstrated by some mosquito species towards some of the pesticides, such as DDT. Table 11 shows types of pesticide compounds commonly used for malarial, rodent and other pest control programmes relevant to public health.

1. 3. Existing Legislation with regard to Pesticide Usage in Tanzania

Apparently, there is no specific legislation in Tanzania yet in respect of pesticide safe handling. As in some other countries, requirements for the control of highly and moderately toxic pesticide compounds are covered under the Poisons Act, but obviously there are so many loopholes in such a legislation that there is a need for clearly defined specifications by the law, for production, transportation, storage, distribution and application of pesticides in Tanzania, as the country embarks on modern farming economical techniques. This is one of the ways to ensure that the public is protected by the law from untoward and imminent health hazards imposed by these toxic substances, especially those who are exposed to them by nature of their occupation.

The need to establish a pesticide controlling body was felt in 1974 by the East African countries including Tanzania, when

the East African Pesticides Control Organization was formed by coordination between representatives from the ministries of agriculture, health and veterinary of Kenya, Tanzania and Uganda Governments (TPRI, Annual Report, 1974). While not so much would be expected so soon in terms of achievements from such an infant organisation because of lack of qualified staff, laboratory facilities and scientific equipments, the organisation has been threatened by the unfortunate overall disintegration of the parent organisation, the East African Community, whose doom now seems inevitable.

1.4. Health Problems and Apparent Pesticide Health Hazards in Tanzania

While the war against pests has to be waged, the battle is not without bilateral victims. People who handle the pesticides in an improper way, or indiscriminate use of these compounds has led to ill-health, and often than usually thought others have ended their lives tragically.

Sporadic reports of pesticide acute poisoning received every year in Tanzania through intentional or accidental ingestion of contaminated food or water, only indicate that the problem exists to some extent but that true incidence is higher and that it may not be revealed at present. One of the reasons for this assumption is that Tanzania has a long way to go before establishing comprehensive reporting and statistical systems in health services. Secondly, there is no established reporting of births and deaths in the rural areas. Although diagnostic facilities and expertise are to be claimed as the impeding factors to this move, this deficiency requires such system to be started, not only in respect of pesticide health hazards but for the benefits it will bring to the overall health services.

The few competent chemical/pathological laboratories available in the country, mainly in Dar es Salaam, Moshi, Mwanza, Tanga and Arusha can not sufficiently cope up with the demand for ana-

lysing all the specimens, including those of other forensic ases, apart from the fact that it sometimes takes too long for the specimens to reach them due to inadequate transportation facilities.

According to the Ministry of Health Annual Reports for 1973 and 1974, the data presented in Table 12 may reflect concealed incidence or prevalence of pesticide poisoning (Ministry of Health, Annual Reports, Tanzania, 1973, 1974). Considering that malaria alone claimed the first place as a single disease cause of out-patient attendances in 1973 and 1974 respectively, it appears that poisoning combined with accident and violent cases occupies a significant fourth position in frequency of overall cause of morbidity in medical units. In addition to that, symptoms of ill-health or ill-defined conditions indicated in the table could as well include some of the symptoms and signs known to occur due to pesticide over-exposure. It should be remembered too that a considerable number of patients, due to one reason or another, do not attend for treatment. Bearing in mind that pesticides are the commonest chemical compounds with minimum controllable access to the rural population, it is justifiable to deduce that poisoning referred to in the annual reports is most likely to be at large attributed to pesticide poisoning. This conclusion could be backed up by the number of specimens analysed by the Central Chemical Laboratory in Dar er Salaam every year. Although there are no systematic studies conducted so far in connection with occupational exposure to pesticides, there are indications that the long-term effects on those who are continuously exposed to the toxic chemical compounds are not so insignificant to be ignored (Ministry of Health, Tanzania, 1977, Personal Communication).

2. MATERIAL AND METHODS

2.1. Population under Study

This study was focussed on spraymen and technical staff handling pesticides in two leading research institutes in Tanzania, the Tropical Pesticide Research Institute (TPRI) formerly operated jointly under the suspices of the East African Community which catered for Kenya, Tanzania, and Uganda; the second is Lyamungu Agricultural Research Institute which primarily serves the interests of Tanzania government in agricultural research and development. The T.P.R.I. is divided into three major divisions: the agricultural entomology and research division, the medical and veterinary research, and the chemical and physics research divisions. The Lyamungu Agricultural Research Institute mainly concentrates on agricultural research, more or less confined to field, fodder, vegetable, fruit and food crops.

A random sample of the group under study was comprised of 165 workers from both research institutes in such a way that either institute contributed part of the 111 exposed subjects as well as the 54 subjects comprising the control group. The control group was composed of adminstrative clerical staff, workers in carpenter and mechanic repair workshops, and watchmen, who were in no way exposed to pesticides at the site of work.

2.2. Occupational and Domestic Exposure to Pesticides

It was not intended to subject the volunteers to any experimental conditions, but to assess the different aspects of exposure which could affect their health in the course of their day to day duties in the institutes. Their duties ranged from experimental laboratory work with soil, water, animals, insects, etc., involving the use of pesticide compounds, to field work, exposing them to a number of different pesticide chemical compounds while mixing and spraying in experimental plots. At the time this study was

Table 13. AGE AND SEX DISTRIBUTION OF EXPOSED AND CONTROL GROUPS

OCCUPATIONAL GROUP	SEX	AGE(YEARS) 15 - 25	26 - 35	36 - 45	46 - 55	56	Total
		NUMBER OF WORKERS					
A	M	4	4	10	2	-	20
	F	-	-	1	-	-	1
B	M	4	19	13	8	2	46
	F	-	-	-	-	-	-
C	M	6	11	6	-	-	23
	F	1	2	-	-	-	3
D	M	3	6	2	1	-	12
	F	4	-	-	-	-	4
E	M	2	15	20	5	1	43
	F	2	6	1	-	-	9
TOTAL	M	19	55	51	16	3	144
	F	7	8	2	-	-	17
						GRAND TOTAL	161

conducted (March/April, 1977), only ground insecticide spraying manually was going on. Since the workers were exposed to pesticides of different chemical groups and toxicity, at various working sites and under varying working conditions, it was deliberately considered appropriate to classify them under the following categories which have been adopted throughout the whole text: Group A (Primarily spraymen from TPRI), Group B (spraymen from Lyamungu Agricutural Research Institute), Group C (Laboratory workers in T.P.R.I), Group D (workers in plant pathology in TPRI), and Group E (the control group as described above). Groups A and B work in agricultural entomology sections of their respective institutes.

Group A and B; Field workers (spraymen) in entomology section constituted the largest single group exposed to similar types of pesticide compounds in this study, and were engaged in spraying operations involving the use of aldrin, benzene hexachloride, carbensazim, chlorpyrifos, copper sulfate, diazinon, DDT, dimethoate, dioxathion, endosulfan, fenitrothion, fenthion, isodrin, phorate, pyriphos_methyl, secarol and trichlorfon.

Group C; Laboratory Workers. This group embraced chemists, physicists, technicians and laboratory attendants in biology, chemistry, and physics laboratories who were exposed to a number of pesticide compounds including aldrin, azodrine, atrazine, DNCO, coumatetratil, benzene hexachloride, endosulfan, monocrotophos, parathion, phosphamidon, pyrethrins, toxaphene, warfarin and others.

Group D; Workers in Botany or Plant Pathology section. At the time this study was conducted, this group of workers was exposed to the following pesticides: alchlor, bentazone, 2,4-Damine 2,4 dichloracetic acid, benomyl, carbendazim, captafol, cuprous oxide,

Table 14. DESIGN FOR ASSESSING DEGREE OF EXPOSURE RISK

GROUP	INFLUENCING OBJECTIVE FACTORS	RANGE OF SCORES
I	ACTIVITIES AND CONDITIONS RELATED TO HIGH RISK OF EXPOSURE Activity, site(indoor or outdoor), mode of application (mixing, spraying/dusting), handling contaminated equipment carelessly, possibility of exposure from other sources (domestic use), environmentl conditions(high tempertures, wind, etc.), nutritional status	0 - 9 0 - 3 =low 4 - 6 =mode 7 - 9 =high
II	OBSERVANCE OF PROTECTIVE AND PRECAUTIONARY MEASURES Lack of training on safe use of pesticides, failure to respect good health habits (washing hands accordingly) and follow instructions, lack of adequate protective clothing and devices	0 - 9 0 - 3 =low 4 - 6 =mode 7 - 9 =high
III	DURATION OF EXPOSURE TO PESTICIDES (ANTICHOLINESTERASES) Consideration for length of occupational pesticide exposure in years, weeks, days, per week, hours per day;persistence of exposure(periodic or continuous, occassional or constant etc.)	0 - 9 0 - 3 =low 4 - 6 =moder 7 - 9 =high
IV	TOXICITY OF PESTICIDES Classes of chemical compounds by hazards, according to formulations, solvents or vehicles; possible route of entry; "aging" of enzyme	0 - 9 0 - 3 4 - 6 7 - 9

Index score = total score for each individual from Groups I, II, III, and IV above

TABLE 14 a. DISTRIBUTION OF SCORES IN THE DESIGN FOR ASSESSMENT OF DEGREE OF EXPOSURE RISK TO PESTICIDES

GROUP			SCORES
I.	ACTIVITY:	Mixing of pesticides	1
		Spraying/dusting	2
		Cleaning containers(contaminated)	1
		Feeding experimental animals	1
	SITE OF APPLICATION:	Indoor (e.g. green-house)	2
		Outdoor(in farms and gardens)	1
	MODE OF APPLICATION:	Manually	2
		By mechanical means (tractors, aerial spraying)	2
	ENVIRONMENTAL CONDITIONS:	Mean daily temperatures over 20°C	1
		Relative humidity over 75%	1
		Wind: Wind speed above 19km/hr	2
		Wind speed above 12km/hr	1
	HEALTH STATUS OF EXPOSED SUBJECTS:	Poor nutritional status	2
		Respiratory, neurological, dermatological conditions, etc.	2
II.	PREVENTIVE AND PROTECTIVE MEASURES:	Lack of training on use of pesticides	1
		Lack of protective clothing and devices	2
		Failure to wash hands, face or to take showers accordingly after coming into contact with pesticides	2
		Failure to undress (contminated) working clothes after work	2
		Eating or drinking during contact with pesticides	1
		Smoking during handling of pesticides	1
III.	DURATION OF EXPOSURE:	Over 8 hours per day	3
		Over 5 hours per day	2
		Over 2 hours per day	1
		over 5 days per week	3
		Over 3 days per week	2
		Up to 3 days per week	1
		Constantly exposed for more than 3 months	3
		Constantly exposed for more than 1 months	2
		Constantly exposed for less than 1 month	1
IV.	TOXICITY OF PESTICIDES:	Extremely toxic	4
		Highly toxic	3
		Moderately toxic	2
		Slightly toxic	1
		Solvents or vehicles(other than H_2O)	2
		Route of Entry: Skin	1
		Inhalation (according to prevalence of absorbtion of pesticide)	1
		"Aging of enzyme" (according to the pesticide)	1

NB. In mutually exclusive items above, the maximum score is taken to add up to the total score of 9 in a group.

In mutually non-exclusive items in the same category, an average is calculated(e.g. if an exposed subject is involved in both manual and mechanical spraying, the resulting score would be 2 + 2 * 4 * 2 = 2.

Total score in group I is divided by 2 in order to bring conformity of total scores of 9 as in the other groups (Refer to Table 14)

TABLE 14b. GROUP SCORES AND TOTAL SCORES FOR EACH INDIVIDUAL SUBJECT IN RESPECT OF DESIGN FOR ASSESSMENT OF DEGREE OF EXPOSURE RISK TO PESTICIDES.

E NO. SUBJECT	GROUPS OF INFLUENCING FACTORS				TOTAL SCORE
	I	II	III	IV	
1	6	5	6	6	23
2	6	3	4	6	19
3	6	3	7	6	22
4	5	2	4	6	17
5	6	4	5	7	22
6	6	3	5	6	20
7	5	4	7	7	23
8	6	4	9	6	26
9	6	5	6	6	23
10	6	5	6	6	23
11	6	1	4	7	18
12	7	4	7	7	25
13	5	3	4	5	17
14	6	1	9	7	23
15	7	4	4	7	22
16	5	3	4	5	17
17	5	3	4	6	18
18	4	3	4	7	18
19	6	2	4	5	17
20	6	3	5	6	20
21	5	3	7	7	22
22	5	3	9	7	24
23	5	5	8	7	25
24	5	5	7	7	24
25	5	3	7	7	22
26	5	5	8	5	23
27	5	5	8	7	25
28	5	4	7	7	23
29	5	3	7	7	22
30	5	5	5	6	21
31	5	5	7	5	22
32	5	5	8	7	25
33	5	5	7	7	24
34	5	3	7	5	20
35	5	5	7	6	23
36	5	5	9	7	26
37	5	5	7	2	19
38	5	6	7	7	25
39	5	5	7	6	23
40	4	5	7	7	23
41	5	3	8	7	23
42	5	4	8	7	24
43	5	3	8	7	23
44	5	3	7	5	20
45	5	3	8	6	22
46	5	5	7	7	24
47	5	5	7	2	19
48	5	3	7	7	22
49	5	5	7	7	24
50	5	5	7	7	24
51	5	5	8	7	25
52	5	5	7	6	23
53	5	5	8	6	24
54	5	4	8	6	23
55	5	3	8	6	22
56	5	6	8	7	26

CODE NO. OF SUBJECT	GROUPS OF INFLUENCING FACTORS				TOTAL SCORE
	I	II	III	IV	
57	5	5	7	7	24
58	5	4	8	7	24
59	5	5	6	5	21
60	4	3	8	7	22
61	5	4	8	7	24
62	4	5	7	7	23
63	5	5	8	7	25
64	4	2	8	6	20
65	5	5	8	5	23
66	5	5	7	7	24
67	5	3	8	7	23
68	-	-	-	-	-
69	3	3	1	3	10
70	0	2	2	1	5
71	6	2	2	2	12
72	2	3	3	3	11
73	5	3	4	2	14
74	2	4	4	2	12
75	-	2	1	1	4
76	0	2	0	0	2
77	3	3	2	2	10
78	2	2	2	1	7
79	2	2	7	4	15
80	2	3	5	3	13
81	3	2	7	4	16
82	-	2	0	-	2
83	2	2	5	3	12
84	3	2	6	3	14
85	3	3	2	3	11
86	3	3	2	3	11
87	3	3	5	3	14
88	3	3	2	3	11
89	4	1	5	3	13
90	4	2	4	3	13
91	7	2	7	3	19
92	4	2	2	3	11
93	4	2	4	4	14
94	5	2	5	2	14
95	5	4	2	5	16
96	5	3	2	4	14
97	5	2	1	3	11
98	6	3	1	4	14
99	5	5	2	4	16
100	3	3	1	5	12
101	6	5	2	4	17
102	5	3	2	4	14
103	5	2	2	5	14
104	5	3	2	3	13
105	6	3	4	4	17
106	5	3	2	4	14
107	6	6	3	3	18
108	4	4	4	5	17
109	5	2	2	5	14
110	6	3	2	4	15
111	5	4	1	5	15

Occupational Group A = Code No. 1 - 21

B = Code No. 22 - 67

dioxathion, carbendazim, isoproturon, MCPA, oxadiazon, and penoxalin, majority of which were carbamates.

2.3. Major Objective Factors Influencing Degree of Exposure Risk

In an attempt to assess the degree of occupational pesticide exposure risk, especially for the anticholinesterases, the author arbitrarily designed a pattern of objective factors known to influence such exposures, by giving negative scores for each corresponding finding on each exposed subject during the handling of pesticides, in such a way that the higher the total score against the corresponding findings of the individual, the higher the risk of exposure. In so doing the author had in mind the idea of using the design as a screening test or as a method of orientation as to the extent of exposure risk encountered by those who are continuously exposed to pesticide chemical compounds. The information for the design was obtained from a special form, the Daily Record Sheet, which was completed by the group supervisor concerned, well instructed on how to fill it on the spot as he watched the activities of the subjects. The form duly completed was submitted to the author at the end of the work session or day. The author who visited the sites of work and supervised the way the procedures were conducted in this respect was satisfied that the procedures were adequately complied with. Table 14 outlines the influencing objective factors which were considered for assessment. In the design, the scores from each group (I - IV) were treated collectively and given a single score, which is not necessarily comparable to that of another group in magnitude. For grading the scores in group IV, the WHO Recommended Classification according to toxicity (or by hazard) was adopted so that those compounds which fall under the categories of extremely hazardous and highly hazardous had scores ranging 7 - 9, those under moderately hazardous 4 - 6, and those under slightly hazardous 0 - 3.

identical categories were applied to the other groups of influencing factors (I - III).

2.4. Clinical Examinations and Laboratory Tests

In view of the fact that many workers were exposed to the organophosphate and carbamate groups of compounds which are of medical concern at present in terms of their recognised biochemical effects, more attention was given to them in terms of the designed questionnaire, clinical examinations and laboratory tests.

2. 4. 1. Personal History

The author designed a questionnaire with the objective of investigating age, sex, social and educational background, anthropometric measurements, medical and occupational histories, subjective (symptoms) factors reflecting the effects of exposure to organophosphate and carbamate chemical compounds, and the working environment as a whole. The main subjective factors taken into consideration were: loss of apetite, nausea, vomiting, abdominal, pain, diarrhoea, dizziness (giddiness), headache, coughing, blurred vision and lachrymation, and excessive sweating.

2. 4. 2. Clinical Examinations

Clinical medical examinations covering head, chest, abdomen and limbs were conducted according to established medical procedures for each individual, in order to exclude any pathological or physiological abnormalities. The neurological tests were intended to involve tests for biceps, quadriceps, pupilary, and abdominal reflexes, tremor, muscle tone etc.

On chest auscultations, murmur of the heart and wheezing were particularly taken into account, while enlargement of the liver and spleen on abdominal palpation was noted.

The Anaeroid sphigmomanometer was used for taking blood pressure, pulse rate was measured by stop-watch. The measurements were taken in the morning in a sitting position after a subject for examination was allowed to rest on a lying position for about 15 minutes.

2. 4. 3. Laboratory Tests

Laboratory tests were conducted in well equiped laboratories at the T.P.R.I., Arusha, under the guidance of a qualified toxicologist, assisted by the author and two other laboratory technicians. Haemoglobin content was measured for each subject in this study in the morning before any activity. Likewise, two methods for determining cholinesterase activity were adopted simultaneously. The Tintometric method was used for determining whole-blood cholinesterase activity, and the Spectrophotometric method for plasma (serum) cholinesterase activity.

2. 4. 3. 1. Haemoglobin Content

A lovibond comparator identical to that used for Tintometric method for determination of cholinesterase activity was adopted for measuring haemoglobin content in percentage for each subject by obtaining a blood sample from a finger-prick. The blood was allowed to ooze between a special blood glass slide and a cover-slip, after which direct reading was taken by facing the Lovibond comparator towards a uniform source of light or sunlight and matching the colour of the blood smear on the slide with that on the standard disc where corresponding readings of haemoglobin content in percentage can be taken.

2. 4. 3. 2. Methods for Determination of Cholinesterase Activity

a) Spectrophotometric Method

The principle of this method for determination of serum cholinesterase activity is based on the reaction between acetylcholine and serum cholinesterase. The substrate used was butyrylthiocholine iodide which is very easily hydrolised by serum cholinesterase, and the indicator, used was 5,5' dithiobis-2-nitrobenzoic acid which is reduced by enzymatically liberated thiocholine to form the yellow-coloured 5-mercapto-2-nitrobenzoate. The rate of colour change (absorbance increase) is measurable photometrically and this is proportional to the pseudocholinesterase (ChE) activity (Merck-1-Test).

Blood samples were obtained from finger-prick of the volunteers, after cleansing the fingers with methylated spirit. The blood was then sucked into sterile heparinized micro-pipettes or glass capillaries) ready for centrifugation. Blood samples for group B and half of group E were first centrifuged immediately after they were obtained from finger-pricks, into heparinized micropipettes. They were then transported to the laboratory for analysis under sterile conditions and at optimum cool temperature, with ice-cubes, and were analysed within 2 hours from the time of taking the samples. As for the other groups analyses were conducted within 45 minutes from the time they were obtained. The Pye-Unicam Spectrophotometer Sp 500 Series 2 with wavelength 185 - 1000 manometers was set at 405 nm Hg with an optic layer thickness of 1 cm. The procedure for measuring the time in which the absorbance increased by 0.100 was conducted systematically as follows: A stop-watch was used to ensure accurate timing. An assistant began pouring the contents of bottle 1 (dilution solution with the serum) into bottle No. 2 (Buffer-substrate mixture) and then immediately shook the contents vigorously and thoroughly for 15 seconds and then poured the mixture quickly into the photometric cuvette. The stop-watch

as then started after 30 seconds and each reading was consequently aken in turn; time in which absorbance increased by 0.100 was recorded for each sample consecutively.

Serum cholinesterase activity was then calculated from the time-readings according to the following formula:

$$\text{ChE activity} = \frac{90.7}{t} \text{ kU/l } (25^{\circ}C) \qquad (3)$$

where t = time (in seconds) required for A_{405} to increase by 0.100

kU/l = kinetic unit (1U) is the activity of the enzyme which is required to convert 1 micromole of substrate in 1 minute. The normal value is considered to be at the range of 3.0 - 8.0 kU/l (butyryl thiocholine, at 25°C, and pH 7.7.

b) Tintometric Method

The Tintometric method for determination of whole-blood cholinesterase activity is based on observations established by Watson and Edson(Edson, 1958; Watson and Edson, 1964) that it is possible to dispense with a timed control sample and to substitute a temperature/time relationship from a reaction of a mixture of blood, indicator and acetylcholine perchlorate, allowed to stand for a fixed time resulting in a change of pH, due to CO_2 liberation, provided that the temperature range involved is not excessive, or the time is subsequently corrected, the modified instructions to be followed exactly. It is, therefore, possible from this principle to determine blood cholinesterase in human subjects. As blood contains enzyme cholinesterases, which liberate acetic acid from acetylcholine, thereby changing the pH, cholinesterase activity level can be measured from the time required for the change of pH to take place. All the instructions for the test were

followed exactly in this study, including preparations of CO_2-free distilled water and the time limits for the indicator-blood dilution was allowed to stand. The substrate was added immediately to the test tubes containing blood samples of individual subjects and 0.5 ml indicator solution (Sodium salt of bromothymol blue), after the reagents were tested by mixing 0.5 ml of indicator with 0.01 ml of finger-prick blood from a selected normal "control" subject, and 0.5 ml of substrate solution accordingly.

Two observers took the readings simultaneously, and in about 95 % of cases there was agreement between their readings. However, where the readings of the two observers differed, a third arbiter's opinion, which was usually in agreement with one of the observer's reading, was accepted as final reading. Shade temperatures under which tests were carried out ranged from 20^0 - 25^0 C. Three to four tests were conducted for each subject in the exposed group as well as in the control group. In addition to this, 46 subjects from the exposed group (agricultural entomology) had one more test on another occassion when blood samples were taken before and after exposure.

2. 4. 3. 3. Miscellaneous Information

From the questionnaire, the author intended to know particulars regarding workers' awareness of the potential health hazards arising from improper handling of pesticide chemical compounds, including first aid in case of acute poisoning. The author was also interested to know whether the examinees had any information on pesticide poisoning cases in their neighbourhood for the past two years.

3. R E S U L T S

3.1. Observations on Population under Study

Of the four groups of 110 exposed subjects, field workers in groups A and B constituted 62 %, while 24 % and 14 % represented groups C and D respectively. Table 13 refers to statistical data on age and sex distribution of all groups.

Out of all exposed subjects examined 69 % were aged between 36 and 45 years, similarly 81 % of the 54 examined in the control group fall under this age group. The youngest workers from the control and exposed groups were 21 and 19 years respectively, likewise the oldest were 60 and 56 years of age. The number of females among the exposed group (7 out of 110) is almost negligible, however, all but one were between 19 and 35 years of age, the reproductive age. Only one female was involved in spraying among the spraymen in groups A and B. Information on age was missing on 5 of the subjects.

In order to find out whether exposure to pesticides elsewhere other than at the site of work influenced significantly the overall effects of pesticide exposure, provisions for this information were provided in the questionnaire.

3.2. Findings on Occupational and Domestic Exposures to Pesticides

As far as length of service in respect of pesticide exposure is concerned, 77 % of the 16 workers in Group D were below a year of service with pesticide exposure and only one had 15 years of service, while two had 5 years' service. Exposure in this group was casual during the study with an average of 8 hours per week, taking about 2 to 3 hours per day, and only periodically the workers were involved in handling pesticides during the month. Ten of the workers used copper sulfate and aldrin for gardening and pyrethrin preparations against insects such as flies, mosquitoes, bedbugs

cockroaches in their homes.

Among the workers from Group C, 42% had exposures ranging between -3 years, but another 34 % had engaged in pesticide handling for to 18 years. During the study, the subjects did not have uni- length of exposure, but it depended on their site of work. average exposure which did not differ much from one section another, however, ranged from 2 - 3 hours per day, for 5 days week, less constant from one week to another. 18 of the workers dled pesticides for either gardening or against disease vector sects in their homes, by using DDT and pyrethrin preparations.

There were distinct differences between Group A and Group B rkers in terms of length of service with pesticide exposure. ile the length of service in group A ranged between 1 and 22 ars, with an average of about 8 hours, that for Group B spray- n had a range of between 1 and 7 years with the exception of e subject who had 16 years of service, and the average length as about 5 years. During the study, Group A spraymen were exposed r an average length of 3 hours per day for five days in a week, ile Group B spraymen had relatively longer exposures per day about 5 hours) and their exposure was more less constant. I was nformed that the exposures were more or less the same through- t the years. Ten of the spraymen in this group applied DDT and alathion for gardening in their homes, and 15 from group A pplied insecticides including DDT, pyrethrins and dieldrin, hile one individual used diazinon for similar purposes.

3. Assessment of Degree of Exposure Risk

As there is no single standard available for assessment of total degree of exposure risk, the author deliberately and arbi- trarily categorized the total obtained negative scores for each individual into low (0 - 12), moderate (13 - 24), and high (25 - 36), according to the design already described in Table 14 . The results of the total scores (sum of scores from Group I, II, III and IV)

Table 15. DISTRIBUTION OF INDIVIDUAL INDEX SCORES FOR ASSESSMENT OF EXPOSURE RISK? ACCORDING TO THE CATEGORIES OF THE EXPOSED SUBJECTS

CATEGORY OF EXPOSURE RISK	OCCUPATIONAL GROUP A	B	C	D	TOTAL
LOW	-	-	11	2	13
MODERATE	19	30	16	15	80
HIGH	2	15	-	-	17
TOTAL	21	45	27	17	110

Table 16. DISTRIBUTION OF INDIVIDUALS FROM GROUPS A AND B IN RESPECT OF SMOKING HABITS AND CHOLINESTERASE ACTIVITY (kU/l)

CHOLINESTERASE ACTIVITY (kU/l)	SMOKING HABITS NON-SMOKERS	UP TO 20 CIGAR.	ABOVE 20 CIGAR.
Significant inhibition (below 2.5)	10	12	2
Insignificant inhibition (above 2.5)	20	16	1
Total	30	28	3

each individual were summed into a single grand total or an dex score for the degree of exposure risk.

The distribution of individual "index" scores of exposure presented in Table 15. From this latter table, we find that % of the 110 exposed workers fall under high exposure risk, ile 73 % and 12 % fall under moderate and low degree of exposure sk, respectively. About all of the 15 % under high degree of posure risk were from Groups A and B, but the majority of them re from Group B. No spraymen either from Group A or Group B were ler the low exposure risk.

4. Results on Clinical Examinations and Laboratory Tests

3. 4. 1. Personal History

As far as medical history is concerned, most of the control oup underwent pre-employment medical examination. About 80 % of oup C and D inclusive, 1/2 of Group B spraymen and about 13 % Group B had undergone similar medical examinations. Practi-lly, there was no monitoring of either cholinesterase activity r those exposed to cholinesterase inhibitors or any other routine dical examination intended to detect ill-effects in respect of sticide exposure.

In order to assess whether social habits such as smoking and inking could in any way be associated to the effects of over-posure, since habitual smokers are likely to fail in refraining om smoking during spraying operations, for example, the author d not find sufficient statistical evidence to associate smoking drinking in Groups A and B with the level of inhibited cholineste-ase activity below 2.5 kU/l,as shown in Table 16 and Table 17. roportionally however, there are more subjects with significantly hibited cholinesterase activity among smokers than among non-okers. It appears that the number is too small for a comprehen-ive statistical analysis. It is to be noted that "significantly hibited cholinesterase activity"in this context means inhibited

Table 17. DISTRIBUTION OF SUBJECTS FROM GROUPS A AND B IN RESPECT OF DRINKING HABITS AND CHOLINESTERASE ACTIVITY (kU/l)

CHOLINESTERASE ACTIVITY(kU/l)	ALCOHOL CONSUMING HABITS		
	ABSTAINERS	OCCASSIONAL	HABITUAL
Significant inhibition (below 2.5)	5	5	15
Insignificant inhibition (above 2.5)	9	12	15
Total	14	17	30

Abstainer in this context signifies a person who does not take alcoholic drinks at all.

Occassional drinking in this context signifies a habit of a person who does not take alcoholic drinks for more than three days per week.

Habitual drinking in this context signifies the habit of taking alcoholic drinks for more than three days per week

cholinesterase activity below 2.5 kU/l, deliberately set by the author in order to acquire more accuracy, while normally it is considered to be below 3.0 kU/l (MERCK-1-TEST).

The 11 subjective factors (symptoms) which were considered to be some of the commonest in workers exposed to anticholinesterases for a long period of time are presented in Table 18. The predominant type of complaints among the exposed group are headache and dizziness, which indicate a comparatively higher frequency in this group than in the control group. As a whole, paired relative frequencies of each type of complaint which are presented in Table 18 indicate that frequencies were comparatively higher in the exposed group. Only five spraymen received what one would consider as "on the spot" training on proper and safe handling of pesticides which lasted for a number of hours to 3 days, all told by the workers themselves in Group A and Group B, while there were 16 with such training from Group D and 22 from Group C.

3. 4. 2. Findings On Clinical Examinations

The clinical examination revealed four cases of abdominal pathological findings. Two of the subjects, one from Group B and the other from Group D, had liver enlargement of 2 to 3 fingers respectively and on palpation the liver of the former was tender. He was referred to hospital for further investigation and treatment accordingly. The other pathological cases were detected among the control group too; one of the subjects had liver enlargement and the other had enlarged spleen. The neurological tests conducted gave a range of responses which were regarded to be within normal limits.

Apart from one case of bronchial asthma from the exposed subjects, there were neither wheezes nor murmurs detected by chest auscultation during the period of this study.

One sprayman from Group A had claimed to have been a victim of overexposure to insecticides and avicide a year back during one

Table 18a .VALUES IN RESPECT OF PULSE RATE OF EXPOSED AND CONTROL GROUPS

GROUP	N	X	S	Range
Exposed	87	77.8	8.9	60-100
Control	46	74	5.9	56-84

N= total number of subjects
X=mean pulse rate
s= standard deviation

Table 18 .ABSOLUTE AND RELATIVE FREQUENCY DISTRIBUTION OF TYPES OF COMPLAINTS BETWEEN EXPOSED GROUP AND CONTROL GROUP

NO. OF A COMPLAINT	TYPE OF COMPLAINT	ABSOLUTE FREQUENCIES EXPOSED	ABSOLUTE FREQUENCIES CONTROL	RELATIVE FREQUENCIES EXPOSED	RELATIVE FREQUENCIES CONTROL
1	Loss of apetite	17	7	15%	13%
2	Excessive salivation	22	3	20	6
3	Vomiting	39	9	35	17
4	Abdominal pain	32	15	29	28
5	Diarrhoea	14	7	13	13
6	Headache	50	9	45	13
7	Dizziness	53	12	48	22
8	Tightness in chest	37	7	33	13
9	Frequent coughing	32	6	29	12
10	Blurred vision and lachrymation	27	2	24	4
11	Excessive sweating	34	4	31	8

the campaigns against crop pest invasions. As a result his eyes were adversely affected to the extent that the left one had been rendered completely blind by corneal opalescence.However, the case was not supported by medical report confirming the claim.

In comparing systolic and diastolic blood pressures between the exposed and control groups respectively and singly, there were no statistically significant differences between them. There were, however, three cases of spraymen who had blood pressures of 150/100, 160/110 and 180/100 respectively which are significantly high.

The difference in pulse rate between exposed and control subjects was statistically significant, being higher in the exposed group. Refer to Table 18a.

3. 4. 3. Results of Laboratory Tests

3. 4. 3. 1. Haemoglobin Content

In analysing haemoglobin content from blood samples of the exposed and control subjects, the mean haemoglobin level for the control group was slightly lower than that for the exposed group, probably due to the larger number of females in this group. However, there was no statistically significant difference in haemoglobin levels between the two groups.

3. 4. 3. 2. Determination of Cholinesterase Activity

A) Spectrophotometric Method

While Group A spraymen were occassionally exposed to several more cholinesterase inhibitors than Group B spraymen, the latter were more constantly exposed to fenthion, carbendazim (a carbamate) for three consecutive weeks and they were only occassionally exposed to parathion and malathion.

The results of cholinesterase determinations on three occassions at average weekly intervals, for all other groups

Table 19. VALUES ON CHOLINESTERASE ACTIVITY OF EXPOSED OCCUPATIONAL GROUPS(A-D) AND THE CONTROL GROUP(E AND E_1) BY SPECTROPHOTOMETRIC METHOD ON THREE OCCASSIONS

DETERMINATIONS		OCCUPATIONAL GROUPS A	B	C	D	E*	E_1*
I	N	21	41	27	16	28	22
	R	1.4 - 4.8	1.1-6.1	1.6 - 7.2	2.3-4.1	2.7-7.0	2.7-7.5
	$\bar{X}$	2.9	2.7	3.5	3.2	4.6	4.7
II	N	19	42	26	14	25	23
	R	1.7 - 4.5	1.1-4.1	1.3-5.5	2.3-5.1	2.3-6.3	2.8-6.0
	$\bar{X}$	3.0	2.4	3.5	3.7	4.9	4.5
III	N	19	40	26	15	27	
	R	2.3-6.9	1.8-4.2	1.7 - 5.3	2.3-4.3	2.6-6.5	
	$\bar{X}$	3.1	2.9	3.4	3.3	4.4	

N = Total number of Subjects in each group

R = Range of Cholinesterase Activity (kU/l)

$\bar{X}$ = Mean Value of Cholinesterase Activity (kU/l)

E* and E_1* above constitute the Control Group

except for Group B spraymen who had determinations on four occassions are shown in Table 19. It is clear that Group B subjects had individually and collectively the lowest values of cholinesterase activity, followed by Group A. The values for Groups C and D were not so remarkable in this respect, and even so much less remarkable were those for the control group.

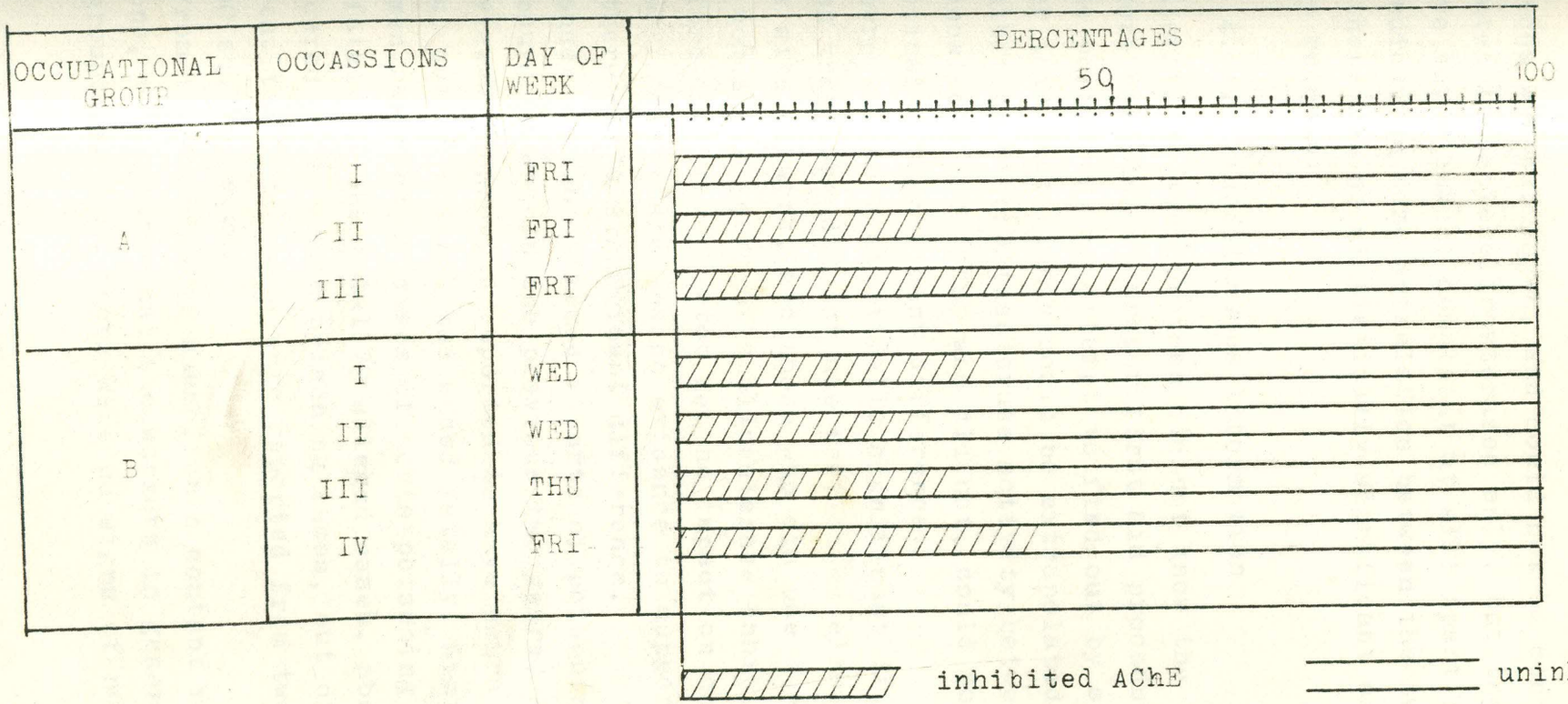
B) Tintometric Method

The percentage of subjects with depressed cholinesterase activity for Group A, mainly at 87.5 % level shows a steady rise, while in Group B the steady rise begins from the second determination; refer to Fig. 2. It is important to mention that in this group, the number of subjects with inhibited activity level considered to be requiring removal from further exposure (75 % and below) rose from 2 cases on first determination 2 on the second and third determinations, to 9 on the fourth determination. It is also interesting to note that of the total occassions recorded on cases of inhibited whole-blood cholinesterase activity below 75 %, corresponding findings of inhibited plasma cholinesterase activity below 2.5kU/l were found in half of them as well.

Frequencies for depressed cholinesterase activity below 100 % for Groups C and D were more or less uniform through the three determinations. The percentage of people with such depressed cholinesterase activity was small.

In spite of the fact that the two methods applied measured principally two different enzymes (erythrocyte and plasma ChE), a very striking evidence of some agreement between the two methods, at least for significant cholinesterase inhibition (apparently below 75 %), was demonstrated by the findings on one subject from the acaricide section in the Group C whose plasma cholinesterase on the three occassions were 1.6, 1.3, and 1.7kU/la for the Spectrophotometric method, and 62.5 %, 62.5 % and 75 % for the Tintometric method. The cause for such severe

Fig. 2 BAR-CHART REPRESENTING RELATIVE FREQUENCY DISTRIBUTION OF CHOLINESTERASE INHIBITION ACCORDING TO TINTOMETRIC METHOD FOR GROUPS A AND B



inhibitons was not known, and could not be convincingly be attributed to anticholinesterases only, but the subject did not have any clinical complaint at all! Apart from this single case indicating some correlation between the two methods, as a whole there was no statistically significant association between the two methods.

3. 4. 4. Miscellaneous Information

Majority of the spraymen did not know the names of pesticides they were handling or proper first aid procedures for acute pesticide poisoning. An attempt to find out by statistical methods whether this defficiency could be extrapolated on the effect on inhibition of cholinesterase activity between those who had such knowledge and those who did not, could not demonstrate statistically significant difference.

There was no statistically significant difference either between those who did not use pesticides elsewhere other than at the site of work, and those who did use some pesticides at their homes (in terms of cholinesterase inhibition). It appears, therefore, that this factor had no impact on cholinesterase activity, or rather there was no evidence to support the hypothesis that there was a significant difference.

Concerning unconfirmed reports of poisoning cases in their neighbourhood within the previous two years, 20 volunteers interviewed in Group A reported to have heard 29 cases of poisoning, out of which 7 had ended fatally. Similarly, Group B spraymen reported 50 cases of acute poisoning out of which 5 were fatal. Of the total 79 alleged cases, about 60 were to be considered as separate poisoning cases, out of which 8 deaths had resulted. The cases were reported from two separate areas of 900 sq. km. each.

From the results of haemoglobin content and physical examinations, it appears that the workers in general were well-fed in all groups and that there were no signs of nutritional deffi-

ciencies. This observation is in agreement with the fact that the area in which the workers live is rich in a variety of foodstuffs.

4. DISCUSSION, RECOMMENDATIONS AND CONCLUSIONS

4. 1. General Discussion

There are still many unknowns prevailing with regard to the adverse effects on health in respect of occupational exposure, although there are circumstances of clear-cut manifestations of pesticide over-exposure. The present objective method of assessing the adverse physiological effects by laboratory tests are surrounded by some uncertainties as to which all factors influence the results of cholinesterase activity, such as age, sex, ethnic characteristics, weather conditions etc. In this respect the question of ethnic differences regarding the normal levels for cholinesterase activity, as an example, still remains unanswered yet. It is even least known what impact various physiological and psychological stresses have on biochemical changes in enzymatic behaviours effected by pesticides, just to mention a few examples.

The other problems one faces in a study like this one, is the variety of chemical compounds the workers were handling simultaneously, which touches the question of interactions implicated among different kinds of pesticide (Mrak Commission, 1969f). In this study, I have deliberately omitted this consideration due to the complexities involved.

Despite all the shortcomings in assessing the effects of high-level of pesticide exposure, I have adopted the methods for laboratory tests and clinical investigations from available knowledge in literature and experiences from other countries, whose characteristics may differ from our population in Tanzania, because practically there is very little or no information available in Tanzania on studies conducted within the country or its neighbours with regard to pesticide occupational exposure. In fact this is the first prospective and systematic study of its kind to be conducted in Tanzania on spraymen continuously exposed to pesticides on whom investigations in this respect

had involved clinical examinations, questionnaire, and the use of Spectrophotometric and Tintometric methods respectively for determination of cholinesterase activity. In addition to that the responses reflected in cholinesterase activity levels and symptoms on subjects in this study indicate that these findings do not essentially differ from results obtained from other parts of the world in repect of exposure to cholinesterase inhibitors. It means that experiences from other countries could serve to predict or to interpret pesticide health hazards in Tanzania at present or in future, if proper precautions on the safe use of pesticides are not taken in time, assuming that the present situation has not assumed proportions of great concern yet.

During the three or four determinations for cholinesterase activity, there was a distinct difference in frequencies of subjects with depressed or inhibited cholinesterase activity among the five groups. This distinction is very apparent between Group A and Group B, which were almost identical in respect of pesticides they handled, the main difference between them largely lying in working conditions, including the length of exposure and protective measures enforced. It would be reasonable to summarize the overall findings of levels of exposure of the groups according to the following ascending order: E, D, C, A, and B, E being of the theoretically zero level of exposure, as a control group. The laboratory findings in Table 19 correspond closely with the frequencies of complaints in the above-mentioned order as well. In other words, there was correlation between average cholinesterase activity levels and the number of complaints(frequencies) and $p<0.05$. Considering all the factors and findings it is justifiable to say that Group B was the most exposed group and that the high-level of exposure in this group had affected their health to such an extent that on one occasion during this study 11 spraymen were taken to hospital for treatment, complaining of severe headache and dizziness. However, as expected, physical examinations did not reveal any patholo-

gical findings except ChE inhibition, which would be directly associated with pesticide high-level of exposure, excluding the single case of alleged eye injury claimed to have resulted from over-exposure. The three cases of high blood pressure and a case of bronchial asthma could as well be attributed to other causes.

In an attempt to analyse the factors which would have contributed to the effects of exposure, the laboratory findings and the symptoms or complaints related to high-level of pesticide exposure, it is important first to compare the findings of the exposed group and those of the control or non-exposed group. It is clear from Table 19 that the exposed group in general had relatively lower cholinesterase activity levels than the control subjects, and this difference was statistically significant, $p < 0.05$.

Similarly there was a statistically significant difference in the number of complaints between the two groups in favour of increased frequencies among the exposed subjects. Since the two groups do not differ essentially in other respects like age, sex, educational and social background, except in the work environment, it is justified to associate the adverse effects with this latter factor. For Group B, the inhibition of cholinesterase activity is associated with the exposure to parathion and malathion on first determination, and on continuous exposure for about 3 weeks to fenthion and carbendazim on the consecutive three determinations which followed. The compounds are known to inhibit cholinesterase activity and in this case there is reason to assume the cause-and-effect relationship.

The other method of assessing the effects of high-level of exposure by subjective responses from the workers, such as complaints, is quite unreliable by itself. While some workers may have genuine reasons to complain, based on established clinical manifestations, others may take the advantage of making false claims and complaints for the sake of winning sympathy

and unwarranted favour, and therefore, distort the objectivity of the investigation. On the other hand, there are several cases reported on individuals whose cholinesterase activity levels were confirmed to be very low beyond all doubts, but they hardly had any symptoms or complaints (Sumerford et al., 1953). Similarly, I had a case in this study of a subject handling acaricides, who had among the lowest cholinesterase activity levels on all three determinations by both methods (Spectrophometric and Tintometric), but he did not have any complaint at all regarding his health. Taking into account that headache and dizziness are well-established effects or manifestations of organophosphorus high-level of exposure or acute poisoning, and considering that these were the most prominent features among the complaints, while frequency of these complaints was relatively higher among the exposed subjects, it suggests that this association between the effects and high level of exposure could also support the assumption of the cause-effect relationship. This assumption is apparently supported by several other factors observed in this study. These factors have been outlined in a more detailed account in the pattern designed for assessment of the degree of exposure risks in Table 14. The result of the influencing factors, in the form of scores, indicate that the length of exposure and toxicity of the pesticide compounds carried the most weight, which, in other words, means that they were the most influencing factors for the effects of high level of pesticide exposure. It is, however, also essential to bear in mind that other factors connected with the work environment such as type of work as well as protective measures may have played an important role in bringing about the effects, although it is generally felt that protective clothing and devices should be the last consideration in min mizing the risk of high level of exposure (Lieben at al.,m 1953; Gamelin et al., 1964). The worker handling toxic substances, especially, involving mixing, is supposed to use protective equipments such as goggles, gloves,

Table 20 . JUDGING THE VALIDITY OF THE SCREENING TEST

	Significant inhibition (below 2.5kU/l)	Insignificant inhibition (above 2.5kU/l)	Total
High level of exposure (above 21 threshold score	29	23	52
Optimum level of exposure (below 21 threshold score)	3	12	15
Total	32	35	67

Table 21. JUDGING THE VALIDITY OF THE SCREENING TEST

	Significant inhibition (below 2.5kU/l)	Insignificant Inhibition (above 2.5kU/l)	Total
High level of exposure (above 21 threshold score)	26	26	52
Optimum level of exposure (below 21 threshold score)	3	12	15
Total	29	38	67

head-gear, overalls, impermiable aprons, gum-boots, and when indicated respiratory equipment in the form of gas or dust masks (Lieben et al., 1953; WHO Expert Committee on Pesticides, 1973). Spraymen in almost all working groups had inadequate protective clothing and devices and in some instances the clothes were torn. Most spraymen in Group B did not take off their clothes they had on while spraying, at the end of the work day, a practice which could prove a further source of contamination, not only for the workers themselves, but for their families as well. They had the most inadequate protective clothing of all groups, and only a few had at most gumboots or overalls, and but a handful had even these basic requirements.

4. 2. Proposed Screening Method for Degree of Exposure Risk to Anticholinesterases

The screening method proposed here is based on an arbitrarily adopted "threshold" score. The author termed it so because it is the borderline score above which is regarded as high level of exposure and below it is the "optimum level" of exposure. Although the exposure levels described under 2.3. were divided into three ranges: Low, moderate, and high, the author adopted a threshold score of 21 deliberately, so that index scores (the author termed the individual total scores as "index scores") above 21 were to be regarded as significant index of overexposure and those below as insignificant, in order to enable the method to undergo a statistical test. For the sake of ensuring stringency on genuinely significant inhibition of cholinesterase activity, it was considered necessary to lower the normal border-line of 3.0 kU/l as recommended (MERCK-1-TEST), to 2.5 kU/l, so that values above this figure are considered to be normal for the sake of the test, and those below it indicate significant inhibition as shown in Tables 20 and 21.

Firstly, the average cholinesterase activity levels of Groups

Table 22. MODEL FOR JUDGING THE VALIDITY OF THE SCREENING TEST
Adopted and Modified from Roberts, C.J.: Epidemiology for Clinicians pp.85-88, 1977

		Results of cholinesterase Activity Determination	
		Significant inhibition (+ve)	Insignificant inhibition (-ve)
Results of screening test	Exposure		
	high level(+ve)	agreement(a)	over-referral(b)
	high level(-ve)	under-referral(c)	agreement(d)

positive sensitivity (sensitivity) $\frac{a}{a + c}$ 100

negative sensitivity (specificity) $\frac{d}{b + d}$ 100

over-referral rate (false +ve) $\frac{b}{a + b}$ 100

under-referral rate (false -ve) $\frac{c}{c + d}$ 100

A and B combined, which were calculated from all determinations, were taken in order to test whether majority of individuals who had lower cholinesterases below 2.5 kU/l were also the victims of high level of exposure or not; conversely, did the majority of those who were subjected to high level of exposure have significantly inhibited cholinesterase? The test is based on the data in Tables 20 and 21. By using the X^2-test, the association between the high level of exposure and the inhibition of cholinesterase activity is statistically significant, since from Table 20 calculated $X^2 = 6.07$, while tabulated $X^2 = 3.841$ at 0.05 level, $p < 0.05$. Accordingly, if we take the number of those who had significant inhibition and high level of exposure = 29, over the total number of significant inhibition = 32, we get a proportion equivalent to 90 %, which indicates the positive sensitivity of the test, while taking the number of those who had insignificant inhibition, with optimum level of exposure = 12, over the total number of insignificant inhibition = 35, a proportion equivalent to 34 % is obtained which indicates negative sensitivity or specificity.

Taking another example, this time the values of cholinesterase activity for Group A and B combined, which were obtained from measurements on the second determinations the results similar to the above can be obtained by calculations from Table 21. Consequently, calculated $X^2 = 4.2$ and $p < 0.05$ with a positive sensitivity of 89.7 % and a negative sensitivity or specificity of 31.6 %.

The other relations such as the over-referal rate and under-referal rate could be also calculated. The model for judging the validity of this screening test is presented in Table 22.

As in many other screening tests, this test does not have perfect correspondence with the diagnostic procedures, but it has an appreciably high degree of validity in detecting those who are at risk of the adverse effects due to high-level of pesticide exposure of about 90 % in both above practical examples.

The method could adequately satisfy the second criterion of being reliable, because there is a model of observations which can be clearly defined, and that observer variation is very low. There is no use of instruments, so that there is no need to worry about instrumental inaccuracy. The third criterion is fully complied with, i. e. acceptability. It is such a procedure that it does not leave room for unacceptability from the side of those who undergo the testing. The test is ideal, since it is in no way painful, embarassing or causing discomfort. It would be comparatively economical and convenient to apply the method in those situations where laboratory facilities and qualified laboratory staff are unavailable. However, the best result will be obtained if it is conducted by those who are fully conversant with effects on health in respect of pesticide exposure. I believe that the test could be improved and developed as a screening test for high level exposure to organophosphorus chemical compounds in the first place, and for carbamate compounds when other factors are taken into consideration. In the long run its application may be extended to include other groups of pesticides.

4. 3. Recommendations and Conclusions

Tanzania is still economically on its infant stages of development in many respects. As many other developing countries it is faced with socio-economic problems and stresses of deprivation of basic needs in terms of better living conditions, largely aggravated by economic disadvantages such as inflation. The country has a long way to go before requirements such as better housing, education for all, adequate food and clean water supply to the rural population are satisfied in entirety. Although Tanzania is said to be one of the developing countries with an exemplary health service structure in rural areas, there are still prevailing problems in running such an infra-structure, basically economic in nature.

At present, the country does not have a unified comprehensive occupational health service programme, and what exists is only an industrial health service under the name of "Group Occupational Health Services", confined more or less to the urban industrial population in a number of towns in the country. The services rendered by the industrial health service groups, primarily curative, are operated by private or parastatal companies. The Ministry of Health merely provides advisory support and some financial assistance from time to time, as need arises. Apart from the basic medical care provided to the public as a whole, there are no specific provisions for occupational health care oriented to the needs of the agricultural population. (1)

The ambitious 3rd Five Year Development Plan launched in Tanzania since 1976, is featured by two major objectives: to revolutionise agricultural production by the application of modern farming methods and techniques; and to establish heavy industries as a basis for a sound economy, to the degree that the two objectives become complementary, the former providing nearly all the main raw materials for the latter. For some reason or another only about 3 % of the total funds has been allocated for rural health services, which is apparently inadequate for bringing about corresponding radical improvement in the rural population. Modern farming methods and techniques in this context mean an increased usage of fertilizers, pesticides, and farming implements, an increase which consequently leads to potential health hazards. (2)

Although this study has provided some indications of recognised and unrecognised health hazards to the lives and health of the people coming into contact with pesticide chemical compounds, especially the organophosphorus and carbamate compounds, there is need to extend the scope of the study to other sections of the population. The deliberations in this study provide a very valuable insight to the problem of pesticide exposure risk but can not be extrapolated to apply for the whole country (3)

without due considerations and reservations, for, the magnitude of the problem in the country has yet to be assessed! There is need, therefore, to conduct further investigations, starting with those areas where the use of pesticide is extensive. This will help to identify potential health hazards attributed to pesticide application, for the whole country. Failure to do this now, may result to an explosive situation of poisonings brought about by mass application of these dangerous chemical compounds, which would prove eventually, to be an extra burden to the health services which are already under constraint.

It should not be considered too early to start planning for an agricultural health service programme within the context of an occupational health service programme at the ministerial level, even within the framework of the existing basic health services, in terms of health education and other basic requirments in respect of agricultural health hazards, including the health risks involved in the increasing usage of pesticide chemical compounds. The programme should, in the first place, be focussed to those areas where agriculture with the use of pesticides is conducted at a large scale. Such a programme should include pre-employment and periodic medical examinations or surveillance on those who are exposed to these toxic compounds, by monitoring cholinesterase activity and application of other methods accordingly. Medical authorities concerned should involve themselves in exploring potential sources of agricultural health hazards and therefore work towards finding appropriate measures and solutions to the relevant problems.

Tanzania requires legislation to support preventive measures in respect of pesticide usage. It is necessary to define the terms and conditions under which pesticide hazards will be brought to minimum during manufacturing, transportation, storage, distribution and applications of pesticides as recommended by FAO/WHO (WHO Regional Office for Europe, 1971). In a number of well documen-

ted cases, large numbers of people have been affected disasterously after consuming consignments of food items (commonly flour) which have been contaminated during transportation or storage. Among the most important requirements from the manufacturer is the labelling of pesticide containers, the provisions of which should be laid down in legislation and strictly applied to both imported and locally produced chemicals. The labels should include both approved name (preferably a chemical name) and a trade name; the name of the manufacturer, the packager or the supplier; directions for use, preferably in the language understood by even the common man, precautions to be taken during use including details of protective equipment to be worn; symptoms and signs of poisoning; and the first aid and medical requirements for suspected poisoning. In certain circumstances it may be necessary to form a National Board for Occupational Safety and Health which will cater for the welfare of workers and their health (Second Swedish-Yugoslav Days of Occup. Med. 1972). The National Board should also be responsible to advise on matters involving importation and manufacture of pesticides of less hazardous effects to the health of the people. It will be necessary for Tanzania to set its own criteria for importing pesticide chemical compounds and to exercise her integrity in using those compounds which have been banned in certain exporting countries due to their hazardous effects on humans, but are sold to her. eg (Pakistan)

The primary phase of prevention is education, and in this case health education. Thus, any individual coming into contact with these chemical compounds, from the manufacturing process to its application in the field, should be instructed well in safe handling practices and be aware for strict personal hygiene. These features should be adhered without reservations.

Potential health hazards in respect of pesticide usage could be minimized in many cases, by more careful attention to the minimum doses required for pest control, more careful application; choice of compounds with lower mammalian toxicity, in less hazardous formulations; spraying only when there is demonstrable

need rather than by arbitrary calendar schedule; and development of integrated pest control programmes in place of exclusive reliance on chemical means of control.

I am convinced that this study has achieved some of its objectives by providing evidences of recognized pesticide effects on the health of some workers exposed to pesticide chemical compounds in the two institutes where the investigations were conducted.

The nature of the effects on health can neither be clearly defined as acute, neither can it be claimed to be "chronic". Probably the right definition lies between the two conditions of ill-health. However, repeated doses of pesticide over-exposure impose a long-term condition of ill-health to these workers who are continuously exposed to some of the pesticide chemical compounds. It is, therefore, necessary to enforce measures which will improve their health, and some of these measures should include considerations for the length of exposure and personal protective measures.

The methodology for assessing the degree of exposure risks proposed in this study leaves room for constructive criticisms, and probably improvement and development. If it stands the test, it will have accomplished one more objective, the goal of which is at least to minimize the threat to health of those who are subjected to prolonged exposures to the toxic chemical pesticide compounds. Its successful application will provide us with one more weapon to fight the enemies of our own creation!

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