AN INVESTIGATION INTO THE NEUROLOGICAL AND NEUROBEHAVIOURAL EFFECTS OF LONG-TERM AGRICHEMICAL EXPOSURE AMONG DECIDUOUS FRUIT FARM WORKERS IN THE WESTERN CAPE, SOUTH AFRICA

Leslie London
MB ChB, BSc Hons (Epidemiology), DOH

This thesis is presented in fulfillment of the requirements for the degree of Doctor of Medicine (MD) in the Department of Community Health, Faculty of Medicine, University of Cape Town, 1994. The work on which this thesis is based is original research and has not, in whole or in part, been submitted towards another degree, at this University or elsewhere. The University is empowered to reproduce either the whole or any portion of the contents for purposes of research.

October 1994

ABSTRACT

It is increasingly being recognised that agrichemical exposure may have adverse chronic health effects in humans, particularly on central nervous system function. However, much of this evidence stems from studies relating to the effects of acute intoxications (i.e. short-term high dose exposures) and little data exist on the chronic effects of long-term low-dose exposures to agrichemicals in the absence of acute poisoning. Such a finding would have substantial public health implications for prevention and control of chronic morbidity and mortality. This is particularly important in South Africa, where a sizeable portion of the rural population are employed in agricultural work, often under extremely unhealthy living and working conditions, and where occupational agrichemical exposures appear to be substantial. To address this question, this study investigated the prevalence of neurological and neurobehavioural abnormalities amongst 247 fruit farm workers in the Kouebokkeveld in the Western Cape, of whom 163 were current agrichemical applicators. Outcomes measured included neurological symptoms, peripheral vibration sense, motor tremor, as well as performance on the World Health Organisation Neurobehavioural Core Test Battery (WHO NCTB) and a set of neurobehavioural tests based on the Information Processing model of cognitive psychology. These latter tests have been developed in South Africa for subjects of low educational levels and aim to by-pass the powerful effects of culture that complicate traditional neuropsychological testing, which may mask the smaller effects due to occupational chemical exposures. Cumulative, and average lifetime intensity of exposure to organophosphates were estimated using a job-exposure matrix based on a combination of secondary industry data, interview reports and farmer records. Confounders measured included age, education, smoking and alcohol habits, non-occupational exposure to agrichemicals and other potential neurotoxins, past medical history and usage of personal protective equipment.

The study results confirmed low levels of education and high alcohol consumption amongst the sample of farm workers. Multiple logistic and linear regression were used to identify exposure-effect relationships and to control for confounding. Neurological symptoms were significantly associated with a history of previous pesticide poisoning, although this may have arisen as a result of reporting bias. Vibration sense and the neurobehavioural tests exhibited associations with established covariates, and regression modelling of the WHO NCTB tests was remarkably similar to findings in another study of solvent-exposed factory workers in South Africa. None of the vibration sense, tremor or neurobehavioural outcomes were associated with past agrichemical poisoning in the sample, and only two tests showed significant relationships with long-term occupational exposure. These included the Pursuit Aiming subtest of the WHO NCTB and one of the tests of long-term semantic memory in the Information Processing tests. However, the strength of these the associations were small (partial r^2s less than 2%) and these findings may have occurred due to chance arising from multiple comparisons. The neurobehavioural tests based on the Information Processing model appeared to offer little improvement on the WHO NCTB in terms of being less sensitive to cultural effects, although some evidence was present that tests of semantic access were able to detect occupational effects and were less sensitive to education. The absence of a demonstrable and consistent long-term agrichemical exposure-effect relationship appears to suggest that long-term agrichemical exposure is not associated with adverse chronic nervous system effects, although the lack of organophosphate specificity in construction of exposure indices in the job-exposure matrix may partly contribute to this finding. Recommendations to improve the characterisation of agrichemical exposures at farming workplace are made, as well as suggestions concerning the role of biological monitoring for agrichemicals, improving working and living conditions on South African farms, and methods of neurological and neurobehavioural assessment in occupational health.

ACKNOWLEDGEMENTS

I wish to thank the following industry personnel, scientists and researchers for their assistance in the course of data collection:

Dr Brian Barnes of the Fruit and Fruit Technology Research Institute (FFTRI)
Doctors V Scwartz and H Fourie of the Vine and Oenological Research Institute (VORI)
Messrs L Kirstein and G Collins of the National Productivity Institute (NPI)
Representatives of the agrichemicals companies and Mr P Wessels of the Agricultural and Veterinary Chemicals Association of SA (AVCASA)
Mr Matthew Addison, Malcolm Dodd and Dr Kevin Chambers of UNIFRUCO Research Division
Mr L Pienaar of KWV
Mr Frank Greef of the Rural Foundation
Ms Marina Clarke and Ms Jenny Bardin of the Rural Foundation Farm Health Worker Programme
Ms K Emanuel of the Group for Environmental Monitoring (GEM)
Dr K Pringle of the Department of Entomology, University of Stellenbosch
Dr J Cridland of the Department of Pharmacology, University of Cape Town
Talbot Plato, Dawie Bosch, Adelle Wilschut and Johan Hamman of the Centre for Rural Legal Studies

The International Research and Development Centre (IDRC), the Guy Elliot Fellowship in the Department of Medicine at UCT, the Ethel and Ernst Erikson Trust and the Medical Research Council of South Africa are all acknowledged for their financial support for the research that forms the basis for this thesis.

To Tony Davies for sensing, in 1988, that this might be the occupational health path I would follow, and for inspiring me to pursue it many years later.

To colleagues: Lilian Dudley for assisting with a pilot study, Shuaib Manjra for his initial enthusiasm and arranging the possibility for another pilot and, particularly, to Simphiwe Mbuli, for being part of the project from the outset and handling the industrial hygiene aspects.

To Archie van Biljon for being in the right place in the right time (10 years later) and for starting the chain of events that led us to the Warm- and Kouebokkevelde.

Ms Judy Katzenellenbogen for her enthusiastic assistance with questionnaire development and interviewer training, and, particularly, her inspired ability to find needles in confused chemical pathology haystacks. To the staff of the Chemical Pathology Laboratory who had their working days inevitably lengthened by the arrival of bloods for cholinesterase at all hours of the late afternoon and performed excellently nonetheless.

All the staff of the research project who laboured exceptionally hard and unflinchingly reliably to complete all our deadlines. In particular to Kelvin Groeneveldt who was a pillar of strength in supervising the interviewing team, coordinating the encoding and successfully monitoring the flow of data. And to Hanlie van Heerden who was the only person on earth who could have managed the unenviable task of liaising with a hundred busy farmers and their workers in pulling off the logistics for an extraordinarily difficult study. Also to Abi, Anton and Rashied for putting up with an enforced stay in the Ceres holiday resort in order to perform neuropsychological tests that soon lost their novelty. Also to Aneleh Midgeley, the never ending administrator prepared to put in long and hard hours to make sure everything worked out for those in the field.

To Victor Nell for providing both intellectual challenge as well as light relief on his visits. And for being responsible for grandfathering my favourite dog, Ruby Duke, who also deserves a mention for being my favourite dog.

To Tom Robins for his critical insights and to Mary Lou Thompson for assistance with data analysis.

To Jonny Myers for his invaluable guidance and encouragement to develop this research into an MD, and his carefully considered and thoughtful advice.

To all the staff of the Community Health Department for providing such a pleasant working environment, and especially to Cynthia and Desmond for the mountain of photocopying they were asked to do.

To the farmers and farm workers of the Warm- and Kouebokkeveld who gave us all an insight into a part of South Africa we would never have come to appreciate without their heartfelt contributions.

And to Phyllis, not only for dotting the i's and checking the fonts, but for enduring a winter and a summer of computer fixation with equanimity and still having the capacity to support me through this onerous experience.

TABLE OF CONTENTS - VOLUME I

Page

TABLE OF CONTENTS (Continued) Page

TABLE OF CONTENTS (Continued) Page

LIST OF TABLES

LIST OF TABLES (Continued)

LIST OF TABLES (Continued) Page

LIST OF FIGURES

Page

LIST OF APPENDICES (Volume II)

Note: All the appendices are contained in an additional (separate) volume.

PREFACE

This thesis represents one of the first major attempts to investigate aspects of the occupational health of farm workers in South Africa. In the text, reference is made to categories of population groups previously described in Apartheid legislation in South Africa, viz. "Coloured", "White" and "African". These terms are used to reflect the environmental, social and cultural experiences of individuals and groups in South Africa, which are partly attributable to the imposition of policies of racist ideology. The usage of these terms is not intended to justify their application as terms of racial segregation or supremacy, as was practiced by the previous South African government.

The thesis is set out in two volumes. Volume I contains the substance of the thesis, while all appendices are contained separately in volume II. Chapter 1 sets out the background to the study and the aims and objectives. Chapters 2 and 3 address farm labour in South Africa, and exposures to agrichemicals. Chapter 4 reviews the literature on neurological and neurobehavioural effects of agrichemicals. Chapter 5 sets out the methods used in the study. The study results are presented in two parts - univariate and limited bivariate analyses are presented in Chapter 6, and further bivariate and multivariate analyses are contained in Chapter 7. Chapter 8 concludes with policy implications arising from the study.

Spelling and date format has followed British style. Some of the appendices contain original documents (questionnaires) and are in the vernacular language practiced in the rural Western Cape, Afrikaans. Where local terms have been used in the text (volume I), their English translation has been explained.

CHAPTER 1

AN OVERVIEW OF THE RISKS OF NEUROTOXICITY POSED BY AGRICHEMICAL EXPOSURES TO FARM WORKERS.

CONTENTS Page

1.1 Introduction

Pesticides and related chemicals are widely used in farming and public health programmes worldwide. Estimates of global expenditure on agrichemicals exceeded 25 billion US dollars in 1992 (Pesticides Trust, 1993) and usage of pesticides has increased markedly over the past decades (WHO, 1990a; BMA, 1992), particularly in the less developed countries (Forget, 1991; BMA, 1992). Despite their role in improving food production (BMA, 1992), agrichemicals have considerable potential for adverse environmental and human health consequences which include both acute and chronic effects (WHO, 1990a; WHO, 1990b). Included in the latter are potential teratogenic, carcinogenic, neurological and haematological effects (WHO, 1990a; Berry, 1988; Igbedioh, 1991; Jeyaratnam, 1985; Rosival, 1985). These potential effects are explored in more detail in Chapter 4.

Most research on health effects associated with occupational exposure to agrichemicals has usually focussed on acute, severe outcomes, such as hospital admissions (Singh and West, 1985; Nhachi, 1988; Chang Yao-Tsao et al, 1990), self-reported poisoning (Jeyaratnam, 1987), case reports involving fatalities (Osorio et al, 1991), epidemic outbreaks (Baker et al, 1978) and surveys of statutory notification (Ames et al, 1989; Brown et al, 1989; Wagner, 1990; London et al, 1994; Fillimore and Lessenger, 1993). Some studies have investigated sub-acute (Richter et al, 1992) and chronic effects (Namba et al, 1971; Semchuk et al, 1992) of agrichemical exposures but these have frequently been in environmental settings (Bertazzi et al, 1989; Richter et al, 1992) or amongst groups of workers involved in agrichemical production (Berberian and Enan, 1987; Zober et al, 1990; Sathiakumar et al, 1992). Moreover, the nature of exposure in such studies has frequently been poorly defined with resultant misclassification of exposure status (Blair and Zahm, 1990; Blair and Stewart, 1992). The chronic health effects arising from long-term low dose exposures are an unexplored issue, particularly in less developed countries (Forget, 1991;

Davies, 1990), where many health care systems are struggling to cope with the burdens of morbidity and mortality due to infections and diseases of poverty (Jeyaratnam, 1993; Coye and Fenske, 1988).

Available evidence suggests that acute toxic outcomes may represent the extreme end of a wide spectrum of disease, both acute and chronic, arising from chemical exposures. Attention therefore needs to be directed toward measuring outcomes which are less obvious, more insidious in development and more difficult to measure (Davies, 1990). These sorts of investigations will make it possible to characterise fully the entire spectrum of morbidity and mortality associated with agrichemical exposure. While some authors have argued that chronic effects arising from long-term low dose exposures are not presently a priority in developing countries (Partanen et al, 1991; Jeyaratnam, 1993), there is evidence that this type of morbidity constitutes a large undetected reservoir of pathology, of which acute manifestations, such as acute intoxications, may represent only the tip of the iceberg (Davies, 1987; Davies, 1990; Myers, 1990).

1.2 Chronic Neurotoxicity from Agrichemicals in South Africa

Agrichemicals are used extensively in farming in South Africa (London, 1992), with every indication that poisoning by agrichemicals is a major occupational health problem amongst farm workers (Innes et al, 1990 ; Myers, 1990; Barlin-Brinck, 1991). Underreporting of acute morbidity has been well documented (Emanuel, 1992; London, 1992; London et al, 1994) and consultations at regional poison centres around the country regularly exceed notifications of pesticide poisoning nationally (Roberts et al, 1990; Muller et al, 1993; London et al, 1994).

However, little attention has been paid to the question of chronic health effects arising from pesticide exposures. The possibilities of environmental exposure due to pesticide contamination of water (Weaver, 1993) and food (Fourie, 1986) has been sporadically investigated, but little research into the possible long-term health outcomes of chemical exposure has been undertaken. A study of malaria control workers found evidence for mild hepatic function impairment associated with raised levels of DDT and its metabolites in the workers' blood (Bouwman, 1991), and a report of an outbreak of diarrhoea amongst agricultural college staff and students was related to prolonged low level organophosphate (OP) exposure (Perold and Bezuidenhout, 1980). However, to data, little research into chronic health effects has been directed at the large population of farm workers in South Africa.

1.2.1 Neurotoxicity from Agrichemicals

Internationally, particular interest has been aroused in the neurotoxic effects of exposure to agrichemicals (Davies, 1990). Acute exposures to agrichemicals have been shown to be capable of producing long-term neuropsychological disorders (Savage et al, 1988; Congress of the United States Office of Technology Assessment, 1990; Rosenstock et al, 1991) and the range of agrichemical neurotoxicity is fully discussed in Chapter 4. Of note, however, is that most studies of chronic neurological outcomes have been carried out amongst survivors of acute poisoning (Savage et al, 1988; Rosenstock et al, 1991) where exposures were usually high dose acute events. Distinct from chronic effects following acute poisoning, long-term low grade exposures are increasingly being suspected of having similar effects (Rosenstock et al, 1990; Davies, 1990).

In South Africa, there are little data on the presence of long-term agrichemical neurotoxicity among farm workers. A pilot study of vibration sense amongst farm workers in the apple farming industry in the Western Cape in 1993 found poorer vibration sense among farm workers exposed to pesticides than amongst a group of poorly matched packstore controls [1]. This

---

1. Diminished vibration sensation and chronic agrichemical exposure in farm workers. Manjra S, Myers JE, London L, Muller G, Lambrecht J, Barnes J. Unpublished research, Dept Community Health, UCT, July 1992.

finding was flawed by major methodological problems in the study design, but, nevertheless, suggested tentative evidence for agrichemical-related neurotoxicity amongst exposed farm workers. Moreover, the high levels of alcohol intake, malnutrition and poverty that characterise living conditions on most South African farms (Cooper, 1990; De Graaf et al, 1990) may play an important exacerbating role in promoting possible chronic chemical-related morbidity amongst farm workers, as suggested by research in other countries (Baetjer, 1983). The risks of neurotoxicity arising from agrichemical exposure amongst farm workers in South Africa may therefore be substantial and require investigation, particularly in view of the important policy implications of such a finding. Important changes in legislation pertaining to farm worker labour relations (Benjamin, 1993), occupational health and safety regulations (Department of Manpower, 1992) and environmental health policy (Department of Environmental Affairs, 1993) are in progress and the opportunity for shaping such policy appropriately is extremely topical.

1.3 An Investigation into the Potential Chronic Neurological and Neurobehavioural Outcomes of Long-term Exposure to Agrichemicals

To address the research question framed above, an investigation was undertaken in 1993 into the prevalence of selected neurological and neuropsychological disorders among farm workers with long-term exposure to agrichemicals in the rural Western Cape. The study aimed to investigate the hypothesis that the duration and intensity of agrichemical exposures amongst farm workers are associated with the development of selected neurotoxic outcomes.

The objectives of the study were:

1. To measure the levels of recent and long-term occupational and non-occupational exposure to agrichemicals amongst farm workers and to calculate indices of exposure based on work histories, current biological monitoring measurements and historical data on the industry.

2. To measure specific central nervous system and neurobehavioural indicators of toxicity and to quantify peripheral vibration sense amongst the workers.

3. To determine whether long-term exposure to agricultural chemicals in the population under scrutiny may have caused peripheral and central nervous system impairment by studying the association between occupational exposure and the above outcome measurements.

4. To determine whether impairments possibly found could be considered chronic by ruling out measurable acute and sub-acute effects.

5. To measure the presence of the following factors and to assess their role as potential confounders / effect modifiers:

   - nutritional status
   - smoking history
   - alcohol intake
   - history of head injury
   - dagga usage

6. To assess safety practices, knowledge and attitudes to hazardous chemicals amongst fruit farm workers in the Western Cape and their relationship to measures of neurological and neuropsychological morbidity.

Other objectives met within the study programme, and which do not form an integral part of this dissertation include

1) the investigation of the prevalence of other chronic morbidity outcomes (dermatological, genotoxic and respiratory),
2) the validation of presumptively relatively culture-free cognitive based neuropsychological test batteries,
3) the development of valid indices of chemical exposure for use in agricultural settings in South Africa,
4) assessment of the efficiency of personal protective equipment in preventing agrichemical exposure,
5) identifying behavioural determinants of worker exposure to agrichemicals,
6) determining whether control measures apart from personal protective equipment, reduce exposure, and
7) the assessment of the reliability and validity of a field instrument for cholinesterase estimation.

The results of the study will help to develop an understanding of the extent of chronic low-grade neurotoxic morbidity among farm workers in the Western Cape and its relationship to exposure to agrichemicals, and can make an important contribution to an understanding of how such morbidity may be prevented.

The chapters that follow provide essential background to the study by examining the conditions of farm work in South Africa in light of historical and legislative factors impinging on farm workers' health, and focus specifically on reviewing the nature of potential chemical exposures for farm workers in the major crop sectors of the Western Cape. A brief review of the health effects of agrichemicals is presented, with particular emphasis on the neurotoxic effects of chemicals used in agriculture. Details of the method used in the study are described in Chapter 5. The last three chapters outline the study results and the possible policy implications for farm workers' health.

REFERENCES

Ames RG, Brown SK, Mengle DC, et al. (1989). Protecting agricultural applicators from overexposure to cholinesterase-inhibiting pesticides: Perspectives from the California Programme. J Soc Occup Med. 39, 85-92.

Baetjer A. (1983). Water deprivation and food restriciton on toxicity of parathion and paraoxon. Arch Env Health 38 : 168-171.

Baker EL, Zack M, Miles JW, Alderman L, Warren M, Dobbin RD, Miller S, Teeters WR. (1978). Epidemic malathion poisoning in Pakistan malaria workers. Lancet 1(8054) : 31-33.

Barlin-Brinck M. (1991). Pesticides in South Africa - An Assessment of their Use and Environmental Impact. The Wildlife Society of South Africa, Durban.

Benjamin P. (1993). Changes in the law. SA Lab Bull. 17(2), 92-94.

Berberian IG, Enan EE. (1987). Neurotoxic studies in humans occupationally exposed to pesticides. J Soc Occup Med. 37 : 126-127.

Berry CL. (1988). Pesticides. Human Toxicology. 7(5) : 433-436.

Bertazzi PA, Zochetti C, Pesatori AC, Guercilena S, Sanarico M, Radice L. (1989). Ten-year mortality study of the poputlation involved in the Seveso incident in 1976. Am J Epidem. 129 : 1187-1200.

Blair A, Zahm S. (1990). Methodological Issues in Exposure Assessment for Case-control Studies of Cancer and Herbicides. Am J Ind Med, 18 : 285-293.

Blair A, Stewart PA. (1992). Do quantitative Exposure Assessments improve risk estimates in occupational studies of cancer? Am J Ind Med, 21 : 53-63.

British Medical Association (BMA) (1992). "Pesticides, chemicals and health". Edwin Arnold, Kent.

Brown SK, Ames RG, Mengle DC. (1989). Occupational Illness from Cholinesterase-inhibiting pesticides among agricultural applicators in California, 1982-1985. Arch Env Health, 44 : 34 - 39.

Bouwman H, Cooppan RM, Botha MJ, Becker PJ. (1991). Serum levels of DDT and liver function of malaria control personnel. S Afr Med J. 79, 326-329.

Chang Yao-Tsao T, Juang Y, Lan R, Shieh W, Lee C. (1990). Respiratory failure of acute organophosphate and carbamate poisoning. Chest 98, 631-636.

Congress of the United States Office of Technology Assessment. (1990). Neurotoxicity - Identifying and Controlling Poisons of the Nervous System. US Government Printing Office, Washington.

Cooper D. (1990). Agriculture: It's problems and prospects. *In*: "Critical choices for South Africa - an agenda for the 1990s." Ed: R Schrire. Oxford University Press, Cape Town.

Coye MJ, Fenske R. (1988). Agricultural Workers. In: Occupational Health. Recognising and preventing work-related disease. Ed: BS Levy. Little Brown and Co, Boston.

Davies JE. (1987) Changing profile of pesticide poisoning. Lancet 316: 807-808.

Davies JE. (1990). Neurotoxic Concerns of Human Pesticide Exposures. Am J Ind Med, 18 : 327-331.

De Graaff JF, Louw W, Van der Merwe M. (1990). "Farm Schools in the Western Cape: A Sociological Analysis." Department of Sociology Occasional Paper no 14. Research Unit for Sociology of Development, University of Stellenbosch, Stellenbosch.

Department of Manpower. (1992). Draft Bill on Occupational Safety and Health. Notice 13978. Government Printers, Pretoria.

Department of Environmental Affairs. (1993). Policy on a National Environmental Management System for South Africa. Government White Paper, Government Printers, Pretoria

Emanuel K. (1992). "Poisoned pay: Farmworkers and the South African Pesticide Industry." Group for Environmental Monitoring and The Pesticide Trust, Johannesburg.

Fillimore CM, Lssenger JE. (1993). A cholinesterase testing programme for pesticide applicators. J Occup Med. 35 : 61-70.

Forget G. (1991). Pesticides and the Third World. J Tox Envir Health. 32 : 11 - 31.

Fourie HO. (1986). Toxicological consequences of pesticidal use in the Republic of South Africa. PhD Thesis. University of Cape Town, Cape Town.

Igbedioh SO. (1991). Effects of Agricultural Pesticides on Humans, Animals and Higher Plants in Developing Countries. Arch Env Health. 46(4) : 218-224.

Innes DF, Fuller BH, Berger GMB. (1990). Low serum cholinesterase levels in rural workers exposed to organophophate pesticide levels. S Afr Med J. 78 : 581-583.

Jeyaratnam J. (1985). Health Problems of Pesticide Usage in the Third World. Br J Ind Med. 42 : 505-506.

Jeyaratnam J. (1987). Survey of acute pesticide poisoning among agricultural workers in four Asian countries. Bull WHO 65, 521-527.

Jeyaratnam J. (1993). Occupational Health Issues in Developing Countries. Environm Res. 60, 207-212.

London L. (1992). Agrichemical Hazards in the South African farming sector. S Afr Med J . 81 : 560-564.

London L, Myers J. (1993). "Agrichemical Hazards and the Work Process in Agriculture in the Western Cape." Occupational Health Research Unit Report number 1. Department of Community Health, University of Cape Town, Rondebosch, Cape Town.

London L, Ehrlich R, Rafudien S, Krige F, Vurgarellis P. (1994). Pesticide poisoning notification in the Western Cape 1987 - 1991. S Afr Med J. 84 : 269-272.

Muller GJ, Hoffman BA, Lamprecht JH. (1993). Drug and poison information - the Tygerberg experience. SA Med J. 83, 395-399.

Myers JE. (1990). Occupational Health of Farmworkers. S Afr Med J. 78 : 562-3.

Namba T, Nolte CT, Jackrel JD, Grob D. (1971). Poisoning due to organophosphate insecticides. Acute and chronic manifestations. American Journal of Medicine 50 : 475-491.

Nhachi CFB. (1988). A Study of Organophosphate poisoning at one rural and one urban hospital. C Afr J Med. 34, 180-185.

Osorio AM, Ames RG, Rosenberg J, Mengle D. (1991). Investigation of a fatality among parathion applicators in California. Am J Ind Med. 20, 533-546.

Partanen T, Kurppa K, Ngowi VF. (1991). Occupational pesticide hazards in developing countries: epidemiological considerations. African Newsletter on Occupational Health and Safety 2 : 46-51.

Perold JG, Bezuidenhout DJJ. (1980) Chronic Organophosphate exposure. SA Med J, 57 : 7-9.

Pesticides Trust. (1993). Review of the Global Pesticide Market. Pesticide News 22 : 11,13.

Richter ED, Chuwers P, Levy Y, Gordon M, Grauer F, Marzouk J, Levy S, Barron S, Gruener N. (1992). Health effects from exposure to organophosphate pesticides in workers and residents in Israel. Isr J Med Sci, 28 : 584-597.

Roberts JC, Leary PM, Mann MD, Glasstone M. (1990). The pattern of childhood poisoning in the Western Cape. S Afr Med J. 78, 22-24.

Rosenstock L, Daniell W, Barnhart S, Schwartz D, Demers PA. (1990). Chronic Neuropsychological Sequelae of Occupational Exposure to Organophosphate Insecticides. Am J Ind Med. 18 : 321-325.

Rosenstock L, Kiefer M, Daniell W, McConnell, Claypole K. (1991). Chronic central nrvous system effects of acute organophosphate pesticide exposure. Lancet 338 : 223-227.

Rosival L. (1985). Pesticides. Scand J Work Envir Health. 11 : 189-197.

Sathiakumar N, Delzell E, Austin H, Cole P. (1992). A follow up study of agricultural production workers. Am J Ind Med. 21, 321-330.

Savage EP, Keefe TJ, Mounce LM, Lewis JA, Burcar PJ. (1988). Chronic Neurological Sequaelae of Organophosphate Pesticide Poisoning. Arch Envir Health. Jan/Feb 43(1) : 38-45.

Semchuk KM, Love EJ, Lee RG. (1992). Parkinson's disease and exposure to agricultural work and pesticide chemicals. Neurology, 42 : 1328-1335.

Singh PDA, West ME. (1985). Acute pesticide poisoning in the Carribean. W Ind Med J. 34, 75-83.

Wagner SL. (1990). Pesticide Illness Surveillance: Review of the National Pesticide Hazard Assessment Programme. Am J Ind Med., 18 : 307-312.

Weaver JMC. (1993). "A Preliminary Survey of Pesticide Levels in Groundwater from a selected area on intensive agriculture in the Western Cape." Report to the Water Research Commission by the Division of Water Technology, CSIR. Water Research Commission Report 268/1/93. Pretoria.

World Health Organisation (WHO). (1990a). Public Health Impact of Pesticides used in Agriculture. WHO, Geneva.

World Health Organisation (WHO). (1990b). "Informal Consultation on Planning for the Prevention of Pesticide Poisoning." Geneva.

Zober A, Messerer P, Huber P. (1990). Thirty four year mortality follow up of BASF employees exposed to 2,3,7,8-TCDD after the 1953 accident. Int Arch Occup Environ Health 62 : 139-157.

CHAPTER 2

FARM WORKERS IN SOUTH AFRICA

CONTENTS | Page

CHAPTER 2

FARM WORKERS IN SOUTH AFRICA

2.1 Agriculture in the South African Economy

Agriculture has been one of the backbones of the South African economy since colonisation and continues to be an important contributor to Gross Domestic Product. In 1990, gross farming income in South Africa amounted to R14 849 million (CSS, 1990) and contributed 5,6% of Gross Domestic Product (FRRP, 1991). In the same year, there were 1.18 million workers employed in agriculture, which constituted 14,0% of the economically active workforce (CSS, 1992). While this represents a substantial decrease from 1980 when over 20% of economically active South Africans were employed in agriculture (Hendrie et al, 1986), agriculture is still one of the largest single employment sectors in SA today (CSS, 1992). A sizeable proportion of farm workers are employed as seasonal/casual workers (Table 2.1) (CSS, 1990; FRRP, 1991). Agriculture remains the biggest source of employment for women in South Africa (Donaldson and Roux, 1994).

Maize farming is the largest single agricultural activity contributing to farming income in South Africa, constituting 12,9% of gross value in agriculture (Table 2.2) (FRRP, 1991). Deciduous fruit farming is the sixth largest agricultural activity in South Africa following maize and various livestock sectors (FRRP, 1991).

The Western Cape is an important agricultural region for South Africa (WESGRO, 1992). Development region A (which includes statistical regions 1 to 14 and corresponds to an approximation of the W Cape plus Namaqualand, parts of the Karoo and the Southern Cape) contributed the largest proportion (22,1%) of national income derived from agricultural production in SA in 1990 (CSS, 1990). However, the nature of agricultural production in the Western Cape differs substantially from the rest of the country as reflected in Table 2.3 (CSS, 1990).

Table 2.1 Employment in the Agricultural Sector 1990 - CSS

Area *	Total Number of Farms	Total Employed Workers	Percentage of Casual/Seasonal
RSA	62 050	1 186 000	38,6%
Cape	24 390	403 000	47,1%
Development Region A	10 480	234 000	46,6%
Western Cape	6 319	84 354	N/A

(Source: CSS, 1990; FRRP, 1991)

* Area as defined by Central Statistical Services:
- RSA = Republic of South Africa, excluding "self-governing states and independent states".
- Development Region A = Magisterial districts 1 to 14 and encompasses the Western and Southern Cape, as well as Namaqualand, the West Coast and the Little Karoo.

Table 2.2 Major contributors: Agricultural revenue, SA, 1991

Agricultural activity	Income (R mill)	Percentage
Maize	2 799	12.9
Other field crops	4 632	21.3
Citrus fruit	506	2.3
Deciduous fruit	1 096	5.0
Vineyards	650	3.0
Potatoes	628	2.9
Other horticulture	556	2.6
Animal products	9 772	45.0

(Sources: FRRP, 1991; CSS, 1992)

Table 2.3 Production by sector in Agriculture in 1990.

	Percentage distribution of Gross Farming Income	
Sector	RSA Total	Development Region A *
Field Crops	33 %	11 %
Horticulture	42 %	42 %
Animals	20 %	46 %
Forestry	5 %	1 %
Other	-	-

{Source: CSS, 1990}
* Includes Western Cape

Agricultural revenue in Development Region A is derived mainly from animal husbandry and horticulture, which includes production of deciduous fruit. Field crops (cereals) are a minor component of agriculture in the Western Cape unlike the rest of South Africa. A further breakdown of production is given in Table 2.4 for each statistical region within Development Region A (CSS, 1990). Deciduous fruit production is noted as important in the regions of Grabouw/Swellendam, Worcester/Ceres and Clanwilliam/Vredendal while vineyards are an important economic activity in the latter two areas as well as the Paarl/Stellenbosch area. Vegetable production is only significant for Clanwilliam and the George area, and to a lesser extent the Worcester/Ceres area. It is also clear that forestry is insignificant in the Western Cape. Wheat farming is important in the Swartland (Malmesbury and Piketburg) and Southern Cape regions.

Table 2.4 The proportion of gross income contributed by agricultural products

Statistical Region	Fruit	Vine	Vegetable	Animal	Forestry	Total Income
01 - Greater Cape Cape Town	0,02%	0,23%	3,00%	6,2%	1,6%	R 211 697 761
02 - Stellenbosch, Paarl	9,7%	24,4%	1,6%	49,1%	<0,01%	R 593 853 579
03 - Grabouw, Swellendam	29,2%	8,6%	2,1%	26,9%	1,3%	R 403 142 029
04 - George, Mossel Bay	3,3%	0,1%	22,1%	50,0%	0,4%	R 88 923 560
05 - Uniondale	4,7%	-	1,7%	61,6%	-	R 7 314 411
06 - Oudtshoorn, Ladismith	8,6%	4,4%	1,6%	59,2%	-	R 93 287 665
07 - Ceres, Worcester	45,6%	23,4%	10,5%	9,2%	0,1%	R 360 330 643
08 - Malmesbury, Piketberg	5,3%	6,6%	2,0%	41,9%	0,5%	R 394 242 107
09 - Clanwilliam Vredendal	14,5%	23,2%	31,8%	11,8%	-	R 108 834 734
10 - Namaqualand	-	-	-	90,5%	-	R 14 006 730
12 - Beaufort West	2,4%	<0,1%	1,0%	93,9%	-	R 67 852 335
13 - Calvinia	-	-	1,8%	89,6%	-	R 39 990 316
14 - Williston	-	-	-	98,1%	-	R 10 979 833
Development Reg A	16,3%	13,6%	5,3%	35,6%	0,5%	R 2 394 455 703
Cape	12,6%	9,1%	4,8%	47,4%	0,4%	R 3 772 712 302
RSA	7,3%	3,2%	5,1%	36,9%	3,4%	R 10 829 805 615

{Source: CSS, 1990}

Table 2.5 Agricultural workforce by statistical region, 1987

Statistical Region	Farms	Total farm workers	Percent FW/Pop [a]
Greater Cape Town	200	4 733	0.6
Stellenbosch/Paarl	1230	25 417	11.0
Grabouw-Swellendam	1390	23 848	24.3
George/Mossel Bay	1360	12 821	11.9
Uniondale	160	1 602	21.5
Oudtshoorn/ Ladismith	610	7 445	13.0
Ceres/Worcester/ Montagu	1500	33 969	22.6
Malmesbury/ Piketberg	1240	17 993	14.2
Clanwilliam/ Vredendal	1200	13 378	28.1
Namaqualand	450	2 265	0.9
Walvis Bay	0	-	-
Beaufort West	1010	10 308	22.1
Calvinia	690	5 697	33.7
Williston	210	1 876	56.8
=========	=====	=======	====
Dev Reg A	11 250	161 352	9.1
RSA	65 170	1 179 590	4.0

{Sources: CSS (1987); CSS (1992)}

a - Percentage of farm workers out of total region population

2.2 The Size and Distribution of the Agricultural Workforce in the Western Cape

The Central Statistical Services (CSS) estimated that over 150 000 workers were employed in agriculture in the Western Cape in 1991 (CSS, 1991) of whom approximately 58% are permanent and 42% seasonal workers (WESGRO, 1991). An additional 265 000 (WESGRO, 1991) to 1 million (UNIFRUCO, 1989) dependants are reliant on the industry, which is made up of approximately 6 300 White-owned commercial farms (WESGRO, 1991) and a small number of Coloured farmers in Pniel and Banhoek (UNIFRUCO, 1989).

The major concentration of farms and farm workers occurs in those regions where deciduous fruit production is widespread, reflecting high labour intensiveness in this agricultural sector (Table 2.5). Statistical regions 2,3 and 7 account for 52% of workers employed in agriculture in Development Region A. These regions include most of what is known as the Boland. If the Swartland and Clanwilliam districts are included, then 71,4% of agricultural workers are covered.

Seasonal and casual workers form a large proportion of the employed workforce. There is some evidence for decreased reliance on contract labour in the Western Cape and greater recruitment from local rural African townships or rural informal settlements for seasonal workers (Groenewald, 1986; Groenewald, 1990; London, 1992). Farm work is becoming increasingly unpopular amongst Coloured residents of rural towns, presumably because of general socioeconomic "advancement" of rural Coloured communities (Groenewald, personal communication, 1992) and dissatisfaction with the working conditions. In addition, many seasonal workers are young women who take on farm work to supplement family income during school holidays (Groenewald, 1986; Groenewald, 1990). This results in poorer recruitment and higher turnover of Coloured seasonal labour. From an epidemiological point of view, this is a significant constraint to avoiding drop-out of subjects in possible cohort investigations of health problems.

Table 2.6 Farm workforce size in the Western Cape

Source (year)	Area	Type of farm	Permanent workers	Seas # workers
Groenewald (1986)	Tulbach	Wine Grape	+/- 20	+/- 20
	Koue-bokkeveld	Decid fruit/ Veg	60	92
	Franschoek	Wine/ Decid fruit	16	11
Groenewald (1990)	Berg River	Grape	15-27	80-90
London (1992)	Stellen-bosch	Wine/decid fruit	8-34	15-26
WCAU (1991) survey	Extended Western Cape	All farms in region	7	n/a*

- Seasonal workers recruited for season only
* n/a = not available

Average workforce size per farm varies widely depending on the nature of production. The Western Cape Agricultural Union (WCAU) report that there are approximately 7000 farms in the Western Cape with an average of seven permanent workers per farm (Personal communication, Mr Visser, WCAU, 1991). However, this includes many farms in the Karoo and Northern Cape which are sparsely populated sheep farms. For fruit farms, the average workforce per farm is more likely to be between 10 to 100, again depending on farm size. Estimates for workforce size from different sources are summarised in Table 2.6.

One of the implications of the differences in farm workforce size is that this may reflect differences in sophistication of production and, therefore, in approaches to workplace safety, similar to differences found between large and small-scale industries. Farm size, as a crude proxy for the level of organisation of production, may be an important confounding variable in studies of occupational health problems amongst farm workers.

Data on employment by sector are derived from sources other than the CSS and estimates for workforce size in the major farming sectors in the Western Cape are summarised in Table 2.7. The biggest employer in the region is the deciduous fruit industry. Vegetable production is another important employer but estimates for employment are scarce, presumably because of co-production with wine or fruit, with the result that the numbers of vegetable workers are generally included with the statistics for the former two farming activities (De Klerk, 1992).

Table 2.7 Estimated workforce size by major agricultural sector in the Western Cape

Agricultural Sector	Workforce Size	Estimate source
Deciduous Fruit	220 000 140 000	UNIFRUCO, 1989 FRRP, 1991
Grape (wine)	42 000	KWV, 1991
Wheat and cereals	20 000	De Klerk, 1992

2.2.1 The deciduous fruit industry

The deciduous fruit industry is centred in the Western Cape and is the most important agricultural activity in the region (Jensen, 1992). Between 1983 and 1987, the deciduous fruit industry earned R781 million which comprised 36% of agricultural income in the region for that period (WESGRO, 1992). It is labour intensive, with requirements for a relatively skilled workforce. The majority of farm workers in the region are employed in the deciduous fruit industry (Table 2.7).

Approximately 40 000 hectares (AIS, 1990; WESGRO, 1992) are cultivated for deciduous fruit in the region, though estimates range from 32 000 (Kassier, 1992) to 60 000 ha (UNIFRUCO, 1989). There are 4 400 - 5 400 deciduous fruit farmers and about 220 000 farm workers and their dependants involved in the industry (UNIFRUCO, 1989; FRRP, 1991). Apple farms tend to be larger but are less labour intensive than table grape farms (Table 2.8).

Table 2.8 Labour Intensiveness of Farming Production

	Average Size (hectare)	Size Range (hectare)	Labour Density [a] (Worker days/hectare)
Apple	30	12 - 400	1,5
Pear	25	10 - 90	1,5
Table Grape	20	8 - 25	2
Wine Grape	20	8 - 25	<1

(Sources: Unifruco, 1989; Personal communication, Mr L Kirstein, National Productivity Institute, 1992.)
a - Based on total person days worked divided by farm hectarage. Thus it includes a weighted average of seasonal, family, casual and child employment.

The bulk of production involves apples, particularly for export (Table 2.9). The distribution of farm size and production quantities is extremely skewed, with 30% of producers contributing 65% of the total production. This probably reflects the presence of large agribusiness concerns in the industry (eg: Rhodes Fruit Farm in Franschoek and large agribusiness Trusts in Grabouw/Elgin) and the dominance of exporting producers. Production in the industry is seldom monoculture with an average farm producing about 70% apples, 15% pears and 15% other fruits (Personal communication, Dave Hopkirk, agricultural consultant, Grabouw, 1992). Because patterns of agrichemical use may be fruit-specific, careful account of all farming activities is required in estimating potential worker exposures to agrichemicals.

Table 2.9 Production in the Deciduous Fruit Industry (Metric Tonnage in 1989)

	Export	Local	Total	Percent increase 1979-89	Percent of Total
Apples	225,0	185,7	409,7	+ 109	62,23%
Pears	67,2	32,6	99,8	+ 85	15,16%
Table Grape	54,0	40,7	94,6	+ 85	14,37%
Plum	10,1	5,4	15,5	+ 70	2,4%
Peaches	0,85	32,5	33,3	+ 26	5,1%
Apricot	0,68	4,7	5,3	+ 145	0,8%
Total Decid fruit	357,8	300,5	658,3	+ 94	100%

{Source: WESGRO, 1991}

Educational levels of farm workers have been explored in a few studies (Raubenheimer, 1984; Groenewald, 1986; Groenewald, 1990). The percentage of the rural Coloured population thought to have reached Standard 3 or higher was estimated to be 29,8% in 1978 (Raubenheimer, 1984). The equivalent figures found from the survey of Rural Foundation farms was 46% with the average years completed at school varying from 3,79 to 4,84 (Groenewald, 1986). This represents an educational standard of Standard 2, and suggests that the majority of farm workers are functionally illiterate, given the internationally accepted norm of four years used by UNESCO as a criterion for literacy (Weidepoel, 1984). Nonetheless, there is evidence that farm workers on fruit farms have higher levels of education than in other agricultural sectors (De Graaff et al, 1990).

2.2.2 The citrus fruit industry

The major citrus producing area in the Western Cape presently is in Citrusdal, though citrus trees are being increasingly planted in the Paarl and Stellenbosch area (Jensen, 1992; De Klerk, 1992; London and Myers, 1993). There are approximately 3 000 citrus farmers and over 60 000 workers in the industry nationally

(UNIFRUCO, 1989; FRRP, 1991) but, in the Western Cape, outside of Citrusdal, citrus farming is relatively insignificant other than as an ancillary activity.

2.2.3 The wine grape industry

Approximately 100 000 ha were planted to vines in South Africa in 1990 (AIS, 1990; KWV, 1990; FRRP, 1991) of which the bulk is in the Western Cape (WESGRO, 1991). Vineyards account for 18% of agricultural income in the Western Cape (WESGRO, 1992). Over 90% of hectarage planted to grapes in SA are for wine grapes, with the balance comprising table grapes, currants and root stock (KWV, 1990). Since patterns of agrichemical usage differ in these different forms of grape farming, it is important to note that the focus of table grape production is in Worcester and the Hex River Valley, Paarl, Porterville and Simondium as well as the Orange River Valley.

There are approximately 5 000 wine grape producers in SA (KWV, 1990; FRRP, 1991; Jensen, 1992), of whom the majority are found in the Western Cape (Table 2.10). The industry employs an estimated 42 000 farm labourers and a further 3 000 wine cellar staff, with a further 250 000 dependants linked to the industry. Mixed production with vegetables, strawberries, tobacco or fruit is common in the Paarl and Stellenbosch area (London, 1992; Jensen, 1992; personal communication, P De Bruyn, National Productivity Institute, 1992).

The economic prospects for the wine industry are equivocal. Despite the lifting of sanctions, it is unlikely that South Africa's wine producers will be able to compete effectively in an over-supplied world market (De Klerk, 1992; Jensen, 1992) and the internal market in South Africa is stagnating (Jensen, 1992). As a result, many wine estates are diversifying by producing grape juice from their grape harvest or looking to simultaneous production of other fruit and vegetables (Personal communication, P De Bruyn, National Productivity Institute, 1992).

Table 2.10 Geographic distribution of vines in SA 1990		
District	Percentage vines	Percentage hectares
Orange River	7,3	11,4
Olifants River	7,9	7,6%
Malmesbury	10,8	13,0
Klein Karoo	3,7	3,4
Paarl	19,7	20,0
Robertson	12,2	9,9
Stellenbosch	16,2	15,6
Worcester	22,2	19,1
	100	100

{Source: KWV, 1990}

Average permanent workforce size on wine grape farms is approximately 18 to 30, depending on farm size (KWV, 1990) and this figure is reported to be lower for table grape farms which tend to be smaller (Personal communication, P De Bruyn, National Productivity Institute, 1992). Wine and grape farms are characterised by intensive seasonal activities with increased labour demand. One study found that workforce requirements increased fourfold at season and that more than half of this labour supply (particularly for females) was met by sources outside of the farm (Groenewald, 1990). For an average farming activity, this implies that the workforce increases from about 20-30 to approximately 90-100 at peak season with most seasonal workers being women (Groenewald, 1990; FRRP, 1991).

However, a number of factors that may influence sampling, design and measurement strategies in epidemiologic studies of farm workers on vineyards need to be taken into account. Seasonal workers are drawn mainly from the larger rural towns, but there is higher turnover from these towns than from small rural villages (Groenewald, 1990). This implies that follow up of seasonal workers for health assessment from one season to the next at the workplace will be poor. In addition, the timing of seasonal labour requirements differ for wine and table grape farms. For the former, seasonal workers are required only for picking which occurs in peak summer (Dec - Feb) while for table grape farms, seasonal workers are required for vineyard maintenance work that begins in October as well as for harvesting (Personal communication, P De Bruyn, National Productivity Institute, 1992). All these factors need to built into strategies for sampling and exposure assessment in agricultural studies.

2.2.4 The wheat industry

The main wheat producing areas in the Western Cape are the Swartland and Caledon districts (Jensen, 1992). Wheat farms are extremely large by comparison to fruit farms. Over 400 000 hectares were planted to wheat in the W Cape in 1987 (CSS, 1987; WESGRO, 1992). However, these farms are far more sparsely populated and have far fewer workers per hectare. An estimated 20 000 workers are employed on wheat farms in the region (De Klerk, 1992).

2.2.5 The vegetable farming sector

Approximately 25% of South Africa's vegetable production comes from the Western Cape (Kassier, 1992), with Ceres being an important area for potato and onion farming. An estimated 20 000 ha are planted to vegetables in the W Cape (WESGRO, 1991). Much vegetable production, particularly in Stellenbosch and Paarl, occurs mixed with grape farming (Budlender, 1984; London, 1992). Farm and workforce size are reported as similar to that found in the deciduous fruit industry, though potato farms tend to be large (Personal communication, Dr Ferreria, Agricultural Research Council, 1992).

2.2.6 Conclusion

It has been cogently argued that the agricultural sector in the Western Cape is likely to expand in future, given expanding export prospects as well as domestic economic and market factors (De Klerk, 1992). Coupled with the likelihood of deregulation in various forms in agriculture (Jensen, 1992), this will have important implications for the numbers of workers employed in agriculture in the region and their conditions of work in the future, particularly as more sophisticated organisation of production is introduced. The following sections examine the background to, and current state of working and living conditions of farm workers in more detail.

2.3 Working and Living Conditions for Farm Workers and Rural Populations

2.3.1 A historical perspective on farm labour

Working conditions on South African farms have been noted to be notoriously poor by a wide variety of authors (Keenan and Sarakinsky, 1987; Cooper, 1990; Ball, 1990; Davies, 1990; Emanuel, 1992). Reference has been made to the low wages, poor sanitation, inadequate water supplies, the absence of housing security, high levels of physical violence, underdeveloped or absent rural health and social services and the lack of workplace health and safety measures that characterise farm labour. Data from 1985 found that farm workers' cash wages were about 20% that of incomes elsewhere in the economy, and that women, in particular, earned extremely low wages, of the order of R600 ($200) per annum (Donaldson and Roux, 1994). A study in a farming area outside Cape Town in 1986 found the average weekly wage to be less than R35 ($10) (Whittaker, 1987). Racism has also been a key factor in rural labour relations (Segal, 1991), which are extremely paternalistic (Waldman, 1993) and have often been described as feudal (Davies, 1990). Physical abuse of farm workers by farmers is common (Ball, 1990; Davies, 1990; Segal, 1991; Emanuel, 1992; Du Toit, 1992; South, 1993) and farm workers deaths due to assault by their employers is not an infrequent occurrence (Ball, 1990; Segal, 1991; Cape Times, 1994).

This neo-feudal farmer-farm worker relationship has its origins in the political economy of South Africa, and particularly, in the close links between rural, predominantly White farmers, and the political power of the Nationalist Party and its apartheid ideology for the past 40 years. Well into the 19th century, Black farmers were still able to maintain a successful productive farming sector in South Africa that was able to compete with White farmers. However, sequential legislative and coercive measures forced increasing number of Blacks into wage labour on White farms and on the mines of the Witwatersrand (Bundy, 1988). Successive South African governments in the first half of the century exhibited little enthusiasm for protecting the rights of farm workers and were more sensitive to the political pressure emanating from organisations representing White farmers (CER, 1989). Indeed, farm workers in South Africa have been subject to some of the most oppressive legislation and working conditions in international experience (Davies, 1990). These measures reached their ascendancy under the apartheid policy where political, economic and social rights of all Blacks were removed from the South African constitution and located in the apartheid-created homeland system (Bundy, 1988).

There is clearly evidence that, with the political democratisation taking place in South Africa at present, the class alliances that underpinned power relations between farmer and farm worker are now shifting. New forms of management in agriculture are being promoted that emphasise a human resources approach and more participation by workers in day-to-day decision making (Du Toit, 1992). However, these changes are confined to the more forward-thinking elements in farming (eg: wine and fruit growers) and the legacy of oppressive conditions and institutions will be difficult to change overnight. For example, research in the Western Cape showed that attempts to re-define the relationships between farmer and worker are constrained by a paternalistic culture that is extremely difficult to break down (Du Toit, 1992).

2.3.2 Living and working conditions in agriculture

The inequities that characterise the development of farming in South Africa have had profound effects on the health status of farm workers and their communities. High rates of alcoholism are endemic (Keenan and Sarakinsky, 1987), particularly in the Western Cape where the 'dop' system (payment of workers with alcohol on daily basis in lieu of wages) has remained a common practice amongst farmers employing Coloured workers (Whittaker, 1987; CER, 1989; Davies, 1990; Scully, 1992; Waldman, 1993). Malnutrition amongst farm workers' children is common (Whittaker, 1987; Edgington and Gear, 1992) and, although little published data is available on adult undernutrition, it is to be anticipated that malnutrition is widespread amongst farm workers and their families. For example, anaemia has been found to be common amongst rural antenatal clinic attenders in Gazankulu (Baynes et al, 1986). Whittaker (1987) found that 24% of mothers in a study of child malnutrition in Phillipi, Cape Town in 1986 were themselves malnourished adults (body mass index less than 20).

Education levels amongst farm workers are low (Raubenheimer, 1984; Groenewald, 1986) with many farm workers functionally illiterate. A survey in the farming area of Phillipi in 1986 found that 80% of farm workers had less than six years of schooling (Whittaker, 1987). Poor educational levels act as a major barrier to occupational mobility of the rural workforce and limits job opportunities for the rural population outside of the farming sector (Donaldson and Roux, 1994). Less than 2% of children living on farms in South Africa have access to pre-school facilities and children of farm workers tend to start school at an older age and drop out of school earlier due to the demands of child labour (UNICEF/NCCR, 1993). Almost a half of all employed adults in South Africa with less than six years of education are to be found in commercial agriculture (Donaldson and Roux, 1994).

Child labour is practiced on many farms in South Africa, particularly for seasonal labour requirements and with little regard for the child's schooling and developmental needs (Davies, 1990; Segal, 1991; UNICEF/NCCR, 1993; Waldman, 1993). The vulnerability of children to occupational pesticide poisoning has been noted by researchers in developing countries (Forget, 1991). Moreover, childhood poisoning by pesticides on farms is an important component of notified pesticide poisonings reported in South Africa (London et al, 1994). The call to abolish child labour has been one of the major demands articulated by organisations representing rural people during the current period of political transition in South Africa (Moloi, 1994).

The quality of farm workers' accommodation varies widely (CER, 1989; Ball, 1990; Davies, 1990; Waldman, 1993), ranging from single room dilapidated brick and corrugated iron structures to more developed farm workers' cottages. Electricity is rare in most farm workers' residences and wood, coal or paraffin provide for energy needs for most families. Water quality of rural farm residents has been found to be inadequate for almost a third of the rural population in South Africa and refuse removal systems to be inadequate in over a half of the rural farming population (DNHPD, 1991). Most housing for farm workers is in close proximity to nearby spraying activities (London, 1992) although no data is presently available on the extent to which this may pose a danger of agrichemical contamination.

Because farm worker housing is located on the farms on which the workers are employed, workers tend to live lives circumscribed by the orders of the farmer (Keenan and Sarakinsky, 1987; Ball, 1990; Waldman, 1993). Farm workers are frequently unable to have free access to farms, or to have non-residents visit them (Waldman, 1993). Loss of employment results in the vast majority of cases in loss of accommodation (CER, 1989; Ball, 1990; Davies, 1990; Waldman, 1993; South, 1993). The threat of eviction is frequently used by employers to ensure passivity of their workforce and is buttressed by legislation enabling a farmer-employer to evict trespassers from their property (Segal, 1991). These conditions have a major impact on curtailing the ability of farm workers to assert demands for safe working conditions.

2.3.3 Occupational health in agriculture

Health and social service facilities in rural areas are poorly provided, and many rural communities are forced to depend on private sector providers for primary medical care (London, 1993). Farm workers are dependent on their employer for access and transport to such services as do exist (Davies, 1990; Waldman, 1993). Preventive services in rural areas tend to focus on fertility control (Department of Health and Welfare, undated-a; Department of Health and Welfare, undated-b; Waldman, 1993). Occupational health services for farm workers are largely non-existent (Myers, 1990) except on a few of the larger, more sophisticated farms. Evidence from a survey in Stellenbosch, suggests that even the most minimal first aid services are not available on many farms where the primary source of medical care to the worker is the farmer or a family member of the farmer (London, 1992). Training in health and safety for pesticides and other occupational health hazards appears to be abysmally low (Emanuel, 1992; London, 1992; London and Myers, 1994). The impact of low educational levels and lack of training on pesticide safety are common to many other developing countries (Loewensen et al, 1990; Mwanthi, 1994) but are unique in South Africa given its specific combination of structural racism and economic exploitation.

As is found elsewhere in the world (Hoglund, 1990; May, 1990; Demers and Rosenstock, 1991), high rates of occupational injuries occur in agriculture in South Africa (Emanuel, 1992; Myers, 1990). The reported fatality rate from workplace accidents in agriculture in 1988 was twice that of other industrial sectors (Workmen's Compensation Commissioner, 1988). Moreover, compensation for workplace injuries on farms may be difficult to obtain due to the absence of any cooperation from employers (Segal, 1991). Availability and usage of equipment on farms for protection from pesticides is poor (Emanuel, 1992) with one study suggesting that less than 25% of farm workers exposed to pesticides made use of adequate safety gear (London, 1992).

Poisoning due to pesticides is an important public health problem in rural farming communities, frequently due to unauthorised access to farm pesticide stores (Brown and Fourie, 1987; London et al, 1994). Based on notifications to the Department of National Health and Population Development, about 80 to 170 cases are notified nationally every year with a fatality rate of 5 - 10% (Myers, 1990; Brown and Fourie, 1987). However, these cases represent the tip of an iceberg with ample evidence for under-reporting of pesticide-related morbidity of at least 80% (London and Myers, 1994). For example, incidents of pesticide poisoning accounted for between 9% and 13% of poison center consultations at the Red Cross Children's War Memorial Hospital in Cape Town in 1987 (Roberts et al, 1990), while a similar study of childhood poisoning in the Orange Free State in 1988 found that 12% of poisonings involved pesticides (Van der Merwe and Botha, 1991).

Estimates of poisoning by pesticides based on more defined outcomes confirm the problem of under-reporting. A study of fatalities seen at a Cape Town mortuary in 1979 suggested that only 5% of cases of fatal pesticide poisonings had been notified (Coetzee, 1981). More recent surveys of hospital admissions in the rural Western Cape suggested that approximately 20% of cases (fatal and non-fatal) were being notified (Emanuel, 1992; London et al, 1994). Reasons for under-reporting include the failure of health personnel to notify, misdiagnosis of milder forms of poisoning, and difficulties of access to health care in rural areas.

The only published study of biological monitoring of South African farm workers exposed to organophosphate (OP) insecticides found that 15% of workers involved in routine spraying on a fruit farm near Cape Town had biochemical evidence of OP exposure resulting in reduction of plasma cholinesterase activity (Innes et al, 1990). Further evidence for adverse occupational exposure has been reported amongst rural coffee plantation workers in the Northern Transvaal * .

2.3.3 Unionisation and health and safety

Central to the maintenance of the poor conditions for farm labour in South Africa, has been the exclusion of farm workers from trade union rights and the system of collective bargaining. Farm workers have also been excluded from other general legislation setting minimum wages and working standards (Bosch, 1991). Farmers and their organisations have been instrumental in resisting the unionisation of their workers (Lodge, 1983; Ball, 1990; Hamman, 1993). However, the approach used by farmers to labour relations is not homogeneous. For example, the deciduous fruit industry is strongly supportive of the Rural Foundation and its betterment style (Ball, 1990; FRRP, 1991) and has its own recognised code of conduct (UNIFRUCO, 1989), which represents a form of internal regulation. Similarly, large wine producers have adopted a programme of rights for Black and Coloured workers, largely as a result of the industry's sensitivity to foreign pressures (Davies, 1990).

Recent developments in the past 24 months, however, have seen collective bargaining rights extended to farm workers, albeit in amended form. Laws enabling unionisation and the setting of minimum working conditions have been promulgated (Benjamin, 1993b). However, given the paternalism and coercive history of labour relations in South Africa (Ball, 1990; Segal, 1991) and farm workers' rural isolation, it is unlikely that unionisation of farm workers will grow rapidly in the near future (Hamman, 1993). Moreover, those organisations organising farm workers, will be unlikely to address health and safety conditions as an immediate priority, given the vast number of basic demands competing for union resources, as has been the experience of COSATU (Baskin, 1991).

*** Jaga K, Rama DBK, Rees D. (1992). Poster presented to 11th ESSA Conference, Johannesburg: Cholinesterase Activity in workers exposed to organophosphate pesticides at a coffee plantation.**

Nonetheless, there is evidence of growing interest in the health of farm workers by both trade unions and rural advice groups (Ball, 1990). New legislation on workplace safety and health (Department of Manpower, 1993a) will promote the training and monitoring of workers involved in handling hazardous chemicals such as pesticides (Benjamin, 1993a). However, given the lack of enforceability of previous occupational safety measures due to an inadequately staffed labour inspectorate (Keenan and Sarakinsky, 1987), it is doubtful that these regulations will have immediate impact on workplace health and safety on farms in South Africa (London and Myers, 1994).

2.3.4 The legislative framework for agrichemical safety in South Africa

In addition to the general contextual legislation impacting on health conditions of farm workers outlined above, there are a number of statutes dealing specifically with pesticide safety in South Africa. However, these legislative measures are characterised by extensive duplication, overlap and poor administrative coordination amongst a range of State Departments (London and Myers, 1994). To a large extent, this reflects the situation with the regulation of non-agricultural hazardous chemicals in general, where the environmental, occupational and scheduling responsibilities for health are divided across different State Departments. Table 2.11 summarises the diverse pieces of legislation that pertain to agrichemical safety in South Africa at present, and the State Department to which they refer.

Table 2.11 Legislation pertaining to agrichemical safety in South Africa.

State department	Legislation and scope
Agriculture	Fertiliser, Farm Feeds, Agricultural Remedies and Stock Remedies Act (34/67): Controls the registration, labelling, distribution and classification of toxicity.
National Health and Population Development	Health Act 63/77: Notification of pesticide poisoning. Hazardous Substances Act 15/73: Toxicity classification, licensing. Foodstuffs, Cosmetics and Disinfectant Act 54/72: Regulates maximum permissible pesticide residues in food.
Manpower	Occupational Safety and Health Act 85/93: Occupational safety, training, medical monitoring, surveillance and inspections. Compensation for Occupational Injuries and Diseases Act 130/93: Compensation for occupational illness and injury.
Water Affairs	Environmental Conservation Act
Environmental Affairs	Environmental Conservation Act

Arising from the presence of multiple administrative bureaucracies, there are many gaps in the legislative framework, and the respective inspectorates are largely understaffed and undertrained to enforce such legislative measures as do exist (Keenan and Sarakinsky, 1987). As a result, legislative measures exist to control the importation, distribution, retailing and labelling of agrichemicals (Fertiliser, Farm Feeds and Agricultural Remedies and Stock Remedies Act of 1947; Hazardous Substances Act of 1973) but, until recently, failed to address the prevention of hazards in the application of pesticides in agriculture, safety training or medical monitoring of potentially affected workers. This contrasts sharply with requirements in the UK (Ministry of Agriculture, Fisheries and Food, 1990) and USA (Ames et al, 1989), where substantial statutory provisions have been in existence to ensure agrichemical safety and health. Only with the recent changes in health and safety legislation (Benjamin, 1993a) have legal requirements been introduced that address the need for improved pesticide safety practices. Historical exposures of farm workers to pesticides are thus likely to be both considerable in extent and poorly documented as a result.

Notwithstanding the duplication and shortcomings in current legislation, government moves indicate an awareness of the need for a rational national environmental policy (Department of Environmental Affairs, 1993). Key political players in the current political transition in South Africa have already committed themselves to policies that are sensitive to issues of environmental health * though differences in strategy are evident (Lumby, 1994). How research findings on the impact of agrichemical exposures on farm workers' health may be implemented in this context is explored in more detail in the last chapter of this thesis.

* For example, the ANC Environmental Policy Desk has called for the establishment of a Commission for the Environment - Cape Times, 16 June 1994.

REFERENCES

Agricultural Information Services (AIS). (1990). Pesticide Survey 1989. Agricultural Information Services, R Parker, London.

Ames RG, Brown SK, Mengle DC, et al. (1989). Protecting agricultural applicators from overexposure to cholinesterase-inhibiting pesticides: Perspectives from the California Programme. J Soc Occup Med. 39, 85-92.

Ball A. (1990). Organisating farmworkers. SA Lab Bull 14(8) : 52-61.

Baskin J. (1991). Striking back - the history of COSATU. Raven Press, Johannesburg.

Baynes RD, Menwether WD, Bothwell TH, Fernandes Costa FJ, Bezwoda WE, MacPheil AP. (1986). Iron and folate status of pregnant black women in Gazankulu. S Afr Med J. 70 : 148-150.

Benjamin P. (1993a). Occupational Health and Safety Act. SA Lab Bull 17(3) 85-87.

Benjamin P. (1993b). Farm Labour Law: recent devlopments. SA Lab Bull 17(5) 88-90.

Bosch D. (1991). The NMC and labour legislation for farm workers: the problems and possibilities of negotiated labour law. SA Lab Bull 16(2) : 51-60.

Brown AC, Fourie HO. (1987). Pesticidal poisoning in the Republic of South Africa. Journal of Comrehensive Health 3(1) : 8-10.

Budlender D. (1984). Agriculture and Technology: Four case studies. Carnegie Conference Paper number 23. SALDRU, UCT.

Bundy C. (1988). The Rise and fall of the South African peasantry. 2nd Edition. David Phillip, Cape Town.

Cape Times. (1994). Farm worker killed: AWB couple fined. Wednesday, January 5th.

Central Statistical Services (CSS). (1987). Statistical News Release P1101 - Agricultural Survey. CSS, Pretoria.

Central Statistical Services (CSS). (1990). Statistical News Release P1101 - Agricultural Survey. CSS, Pretoria.

Central Statistical Services (CSS). (1991). Statistical News Release P1101 - Agricultural Survey. CSS, Pretoria.

Central Statistical Services (CSS). (1992). South African Statistics 1992. CSS, Pretoria.

Community Education Resources (CER). (1989). It's a struggle on the farms. SRC Press. University of Cape Town, Cape Town.

Coetzee GJ. (1981). "The Epidemiology of Pesticide Mortality in the Western Cape." Thesis. Department of Community Health, University of Cape Town, 1981.

Cooper D. (1990). Agriculture: It's problems and prospects. *In*: "Critical Choices for South Africa - An Agenda for the 1990s." Ed: R Schrire. Oxford University Press, Cape Town.

Davies W. (1990). We cry for our land: farm workers in South Africa. Oxfam, Oxford.

De Graaff JF, Louw W, Van der Merwe M. (1990). Farm schools in the Western Cape: A sociological analysis. Research Unit for Sociology of Development. Department of Sociology Occasional Paper 14. University of Stellenbosch. Stellenbosch.

De Klerk M. (1992). Prospects for Commercial Agriculture. Working paper 3, Growing the Cape. WESGRO, Cape Town.

Demers P, Rosenstock L. (1991). Occupational Injuries and Illnesses among Washington State Agricultural Workers. Am J Public Health 81 : 1656-1658.

Department of Environmental Affairs. (1993). Policy on a National Environmental Management System for South Africa. Government White Paper, Government Printers, Pretoria

Department of Health and Welfare. (Undated-a). Hoe die boer se vrou gesinsbeplanning kan bevorder. (How the farmer's wife can promote family planning). Pamphlet G.P.-S.004-2299. Pretoria.

Department of Health and Welfare. (Undated-b). Health care for the farm worker. Brochure. ISBN 0 621 04206 4. Pretoria.

Department of Manpower. (1993a). Occupational Safety and Health Act 85/93. Government Printers, Pretoria.

Department of Manpower. (1993b). Compensation for Occupational Injuries and Diseases Act 130/93. Government Printers, Pretoria.

Department of National Health and Population Development. (1947). Fertiliser, Farm Feeds, Agricultural Remedies and Stock Remedies Act. (36/1947, as amended). Government Printers, Pretoria.

Department of National Health and Population Development. (1991). Basic Subsistence Indicators. Report 91/2. Pretoria.

Department of National Health and Population Development. (1973). Hazardous Substances Act (15/1973). Government Printers, Pretoria.

Donaldson A, Roux A. (1994) Education, employment and income of black South Africans in 1985. Development Southern Africa 11(1) ; 131-143.

Du Toit A. (1992). The farm as family. Paternalism, management and modernisation on Western Cape wine and fruit farms. Centre for Rural Legal Studies, Stellenbosch.

Edgington ME, Gear JSS. (1992). Child health in farm workers' communities. S Afr Med J. 81 : 213-215.

Emanuel K. (1992). "Poisoned pay: Farmworkers and the South African Pesticide Industry." Group for Environmental Monitoring and The Pesticide Trust, Johannesburg.

Farmworkers Research and Resource Project (FRRP). (1991). Sectors of South African agriculture. FRRP, Witwatersrand University, Johanesburg.

Forget G. (1991). Pesticides and the Third World. J Tox Envir Health. 32 : 11 - 31.

Groenewald CJ. (1986). Gemeenskapsontwikkeling op plase in die Weskaap. Geleentheidspublikasie 9, Department Sociology, University of Stellenbosch, Stellenbosch, 1986.

Groenewald CJ. (1990). Seisoenwerkers in die tafeldruifbestuur van die Bergrivier. Bergrivier Tafeldruif Produsente Vereneging, Paarl, 1990.

Hamman J. (1993). Labour law in agriculture. SA Labour Bulletin 17(5) : 55-59.

Hendrie D, Adams A, Ariefdien Y. (1986). Handbook of Labour and Social Statistics, SALDRU, Univeristy of Cape Town, Cape Town.

Hoglund S. (1990). Farmer's Occupational Health Care - Worldwide. Am J Ind Med 18 : 365-370.

Innes DF, Fuller BH, Berger GMB. (1990). Low serum cholinesterase levels in rural workers exposed to organophophate pesticide levels. S Afr Med J. 78, 581-583.

Jensen R. (1992). An outline of the Western Cape agricultural sector. Working paper 2, Growing the Cape, WESGRO, Cape Town.

Kassier E. (1992). The Agricultural Sector. Working paper 1, Growing the Cape, WESGRO, Cape Town.

Keenan J, Sarakinsky M. (1987). Reaping the Benefits: Working conditions in agriculture and the bantustans. In: "South African Review 4." Ed: Moss G, Obery I. Raven Press, Johannesburg.

KWV. (1990). KWV annual report, Stellenbosch.

Lodge T. (1983). Black Politics in South Africa since 1945. Raven Press, Johanessburg.

Loewensen R, Nhachi C, Gona P, Murambiwa W. (1990). Current findings of field research on practices of use and user knowledge of pesticides in Zimbabwe. Paper presented to Research Workshop into Pesticide Safety, Zimbabwe Congress of Trade Unions, Harare.

London L. (1992). Pesticide safety practices on farms in the Stellenbosch Region. Report to the Stellenbosch Regional Services

Council Health Department. Department of Community Health. University of Cape Town, Cape Town.

London L, Myers J. (1993). "Agrichemical Hazards and the Work Process in Agriculture in the Western Cape." Occupational Health Research Unit Report number 1. Department of Community Health, University of Cape Town, Rondebosch, Cape Town.

London L (1993). The Ray Alexander Workers Clinic - A Model for worker-based health services for South Africa? Social Science and Medicine 37 : 1521-1527.

London L, Myers JE. (1994). Critical issues for agrichemical safety in South Africa. Am J Ind Med (in press).

London L, Ehrlich R, Rafudien S, Krige F, Vurgarellis P. (1994). Pesticide poisoning notification in the Western Cape 1987 - 1991. S Afr Med J ; 84 : 269-272.

Lumby AB. (1994). The 'Earth summit' and environmental economics: the case of the missing link. Development Southern Africa 11(1) : 81-90.

May JJ. (1990). Issues in agricultural health and safety. Am J Ind Med 18 : 121-131.

Ministry of Agriculture, Fisheries and Food (MAFF) Health and Safety Commission. (1990). Pesticides: Code of Practice for the safe use of pesticides on farms and holdings. HMSO, London.

Moloi D. (1994). Rural people speak. New Gound 15 : 16 - 17.

Mwanthi M. (1994). Agrochemicals: Potential Hazards to heatlh. Africa Health 16 : 18-19.

Myers JE. (1990). Occupational Health of Farmworkers. S Afr Med J. 78 : 562-563.

Raubenheimer LP. (1984). Demographie en Bevolkingsbeskrywing: 'n Werkboek. UUB, University of Stellenbosch, Stellenbsoch.

Roberts JC, Leary PM, Mann MD, Glasstone M. (1990). The pattern of childhood poisoning in the Western Cape. S Afr Med J. 78, 22-24.

Scully P. (1992). Liquor and labour in in the Western Cape, 1870-1900. In: (Eds: J Crush, C Ambler) Liquor and Labour in Southern Africa". Ohio University Press, Athens.

Segal L. (1991). A Brutal Harvest. The roots and legitimation of violence on farms in South Africa. Black Sash and the Project for the Study of Violence, Johannesburg.

South. (1992). Stellenbosch - behind the gabled facade. South Feature. Dec 5 to Dec 9 1992, Cape Town.

South. (1993). Flogging - A normal part of farm life. South Feature. June 5 to June 9 1993, Cape Town.

UNICEF/National Children's Rights Committee. (1993). Children and women in South Africa: A situation analysis. UNICEF / NCCR, Johannesburg.

UNIFRUCO. (1989). The Deciduous Fruit Industry in Perspective, UNIFRUCO, Bellville.

Van der Merwe PJ, Botha JJD. (1991). Epidemiologiese studie van vergiftigings in kinders onder 18 jaar in Bloemfontein en omgeweing. S Afr Med J. 79 : 253 - 255.

Waldman PL. (1993). Here you will remain: Adolescent experience on farms in the Western Cape. MA Thesis, Department of Anthropology, University of Cape Town, Cape Town, South Africa.

Weidepoel L. (1984). Learning from a literacy project. A survey of adult literacy in South Africa. Centre for Extra-Mural Studies, University of Cape Town, Cape Town.

WESGRO. (1991). Growing the Cape. Documentation for preparation of working papers on Prospects for Commercial Agriculture. WESGRO, Cape Town.

WESGRO. (1992). South Africa's leading edge? A guide to the Western Cape economy. Editors Bridgeman D, Thomas W, Palmer D. Wesgro, Cape Town.

Whittaker S. (1987). A nutritional and socio-economic study of Phillipi farm children and their mothers during November 1986. Dissertation in fulfilment of requirements for the degree M Med (Community Health), Department of Community Health, University of Cape Town.

Workmen's Compensation Commissioner (1988). Report of the Workmen's Compensation Commissioner, Department of Manpower, Pretoria.

CHAPTER 3

POTENTIAL AGRICHEMICAL EXPOSURES IN SOUTH AFRICA

CONTENTS PAGE

CONTENTS **PAGE**

CHAPTER 3

POTENTIAL AGRICHEMICAL EXPOSURES IN SOUTH AFRICA

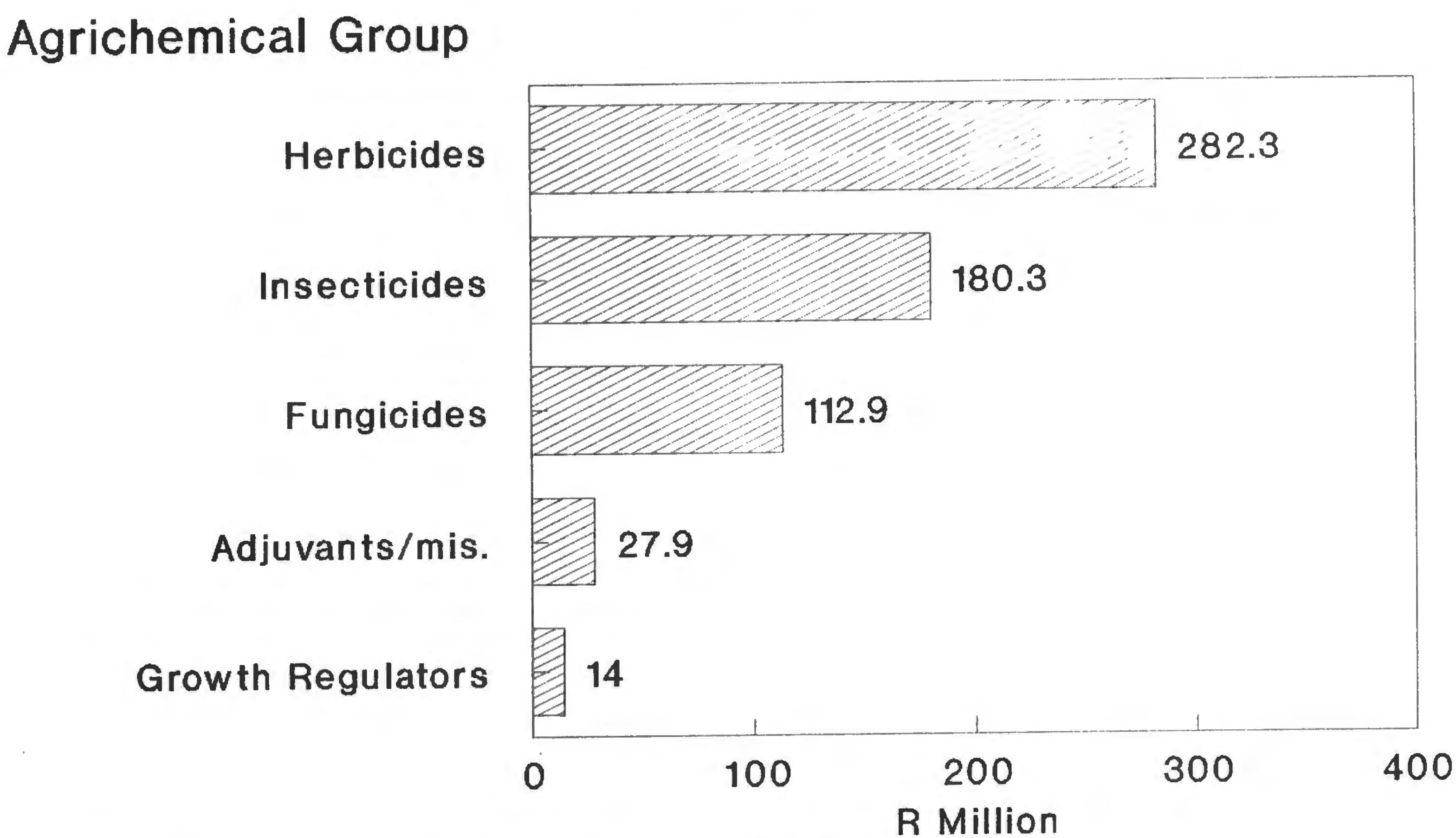
3.1 Introduction

The increase in use of pesticides in South Africa in recent years has paralleled that of developing countries worldwide (WHO, 1990; Forget, 1991; BMA, 1992; Mwanthi, 1994). Figures for South Africa released by the Agricultural and Veterinary Chemicals Association of South Africa (AVCASA) report that R670 million was spent on agrichemicals in 1990, a 90% increase from the equivalent figures in 1985 (London, 1992a). Herbicides constitute the biggest proportion of the market, particularly in the large scale maize farming regions (Figure 3.1).

While the bulk of the agrichemical market is centred around crop protection in agriculture, transport and uses of agrichemicals in other industries and services result in other categories of occupational hazards for pesticide exposure (Moses, 1983; Coye and Fenske, 1988). These are summarised in Table 3.1.

Data on these non-agricultural exposures in South Africa is scant (London and Myers, 1994). A study of workers involved in the malaria control programme in Natal in 1989 found raised serum levels of DDT and its metabolites and evidence for impaired liver function (Bouwman et al, 1991). While most industrial processing of pesticides in South Africa involves the formulation and packaging of agrichemicals, rather than their manufacture, no published data are available on results of workplace surveillance for organophosphate (OP) toxicity. However, an occupational fatality due to organophosphate intoxication was reported at a plant in the Transvaal in 1988 (Department of Justice, 1988), suggesting that industrial production and formulation may be an important site of potentially hazardous exposure to agrichemicals. The extent of non-farming exposures, and their potential health effects, have yet to be adequately quantified in South Africa.

Figure 3.1 Agrichemical Sales in SA 1990
Expenditure in R million



Source: Correspondence with Mr P Wessels
Agricultural and Veterinary Chemicals
Association (AVCASA), 1991.

Table 3.1 Occupations with potential agrichemical exposure

* Agriculture

  Direct: Application, mixing, storage
  Indirect: Field work, spray drift, contact with foliar residues

* Public Health personnel: vector control
* Forestry workers
* Aerial spray and maintenance staff
* Commercial pest control operators
* Manufacture, formulation and packaging agrichemicals
* Transport of chemicals
* Municipality or parks employees
* Railway workers applying wood preservatives
* Dock workers

{Source: Moses, 1983; Coye and Fenske, 1988}

By far the biggest occupational group exposed to agrichemicals in South Africa are farm workers and the characterisation of their exposure to agrichemicals is the subject of the rest of this chapter. Qualitative information concerning work processes in the industry originate from repeated interviews with biologists, safety personnel, management and staff at State, University and Agricultural Institutions. Quantitative data on volumes and amounts of agrichemicals used are derived from crop protection market surveys performed by the agrichemical industry and from figures supplied by the Agrichemical and Veterinary Chemical Association of South Africa. This chapter will first give an overview of the nature of agrichemical usage and general consideration relevant to toxicity before going on to detail agrichemical exposures for farm workers.

3.2 A Background to Agrichemical Usage in Agriculture - General Considerations for Exposure

In general terms, agrichemicals may be used in order to:

a) Protect crops from unwanted pests:
- fungicides used against mildew, rot, molds;
- insecticides against insect predators;
- herbicides against unwanted weed growth;
- acaricides (miticides) against mites;
- nematicides (including fumigants) against eelworms in soil.

b) Promote healthy crop growth:
- plant growth regulators;
- metabolic sprays;
- adjuvants and miscellaneous agrichemicals.

Before distribution and use in South Africa, agrichemicals must be registered with the Department of Agriculture in terms of the Fertiliser, Farm Feeds and Stock Remedies Act (Act 36 of 1947 as amended) (Vermeulen et al, 1990). Currently, approximately 1 800 agrichemicals are registered with the Department of Agriculture for use (Vermeulen et al, 1990; Vermeulen et al, 1991; Vermeulen and Greyling, 1990b) and about 10 to 15 new agents are registered on average per year (London and Myers, 1993). By comparison, Zimbabwe has about 500 registered agrichemical formulations (Loewensen, 1989), Senegal about 200, and Malaysia 320 (Pesticides Trust, 1989).

The process of registration of a chemical in South Africa involves grading by its acute toxicity in experimental rats (based on oral and dermal LD50s), and the basis for the grading is illustrated in Table 3.2. (IPCS, 1991). Appendix 3.1 explains the nomenclature used in this thesis for classifying agrichemicals. The classification is based on that used by the International Programme for Chemical Safety (IPCS) of the World Health Organisation/International Labour Organisation (IPCS, 1991).

Table 3.2 Classification of Pesticide Toxicity (mg/Kg)

	ORAL		DERMAL	
	Solid	Liquid	Solid	Liquid
IA (Extremely hazardous)	< 5	< 20	< 10	< 40
IB (Highly hazardous)	5-50	20-200	10-100	40-400
II (Moderately hazardous)	50-500	200-2000	100-1000	400-4000
III (Slightly hazardous)	> 500	> 2000	> 1000	>4000
O - Unlikely to cause hazard in normal use				

{Source: (IPCS, 1991) }

However, many aspects of pesticide toxicity are not fully addressed by this classification (London, 1992a). These include the presence of impurities, interaction with climatic conditions, time elapsed since exposure, repeated and chronic exposures, synergism and many other variables. It has been argued that insufficient information on which to base assessment of their health effects is currently available for over two-thirds of the thousands of pesticides in use today (Loewensen, 1989).

Methods of application of agrichemicals (Table 3.3) vary depending on the type of crop and the agrichemical. Aerial application is largely confined to wheat and potato farming in the region, and is not commonly practiced in the fruit industry, where tractor-based application methods are standard. Herbicide tractor application methods in general appear to have lower chances of human exposure than the equivalent methods for insecticides and fungicides. In the latter case, the spray is generally directed upward into the target tree or plant, while in the case of herbicides, the spray is directed down onto the soil away from the plant and is usually administered from a fixed boom. Herbicides also tend to require smaller volumes and fewer (less than three times a year) applications. Because of the high cost of most herbicides and the danger of damage to the crop from misdirected application, there is a greater likelihood of careful application and supervision with herbicide application (London and Myers, 1993).

<u>Table 3.3 Agricultural application methods</u>

Aerial (aeroplane or helicopter)

Tractor-based: Mist blower
Platform with workers holding handgun
Workers holding handgun behind tractor
Workers carrying hoses behind tractor
Fixed boom attached to tractor

Knapsack spray
Ultra low volume hand spray devices

Water cannon

Chemirrigation

Nematicides for soil treatment require special forms of application, including specific safety precautions because of their high toxicity and because they may be in the form of liquid, granules or gas.

Mixing of agrichemicals in applications may play an important role in human toxicity, because of synergism and chemical interactions. Some spray materials are already formulated as mixtures of different agrichemicals and the practice of mixing agrichemicals in applications is fairly common. Common examples in practice include mixing of different herbicides or the mixing of insecticides with fungicides or metabolic sprays.

The frequency and agrichemical application will be determined by a number of factors, chiefly the seasonal variations in the density of the pest population and the stages of development of the crop, as well as the mode of action of the agrichemical. Routine application of agrichemicals according to a set schedule clearly results in greater potential for exposure than if spraying is based on in-field pest surveillance, where chemicals will only be used if indicated. Increasingly, fruit farmers are making use of selected workers as monitors, whose job (sometimes their only job) is to check the fields and orchards for the levels of pests and diseases (London and Myers, 1993). This approach is motivated both by the high costs of agrichemicals as well as a concern to reduce potential environmental contamination. However, few farming sectors are using this approach and the bulk of applications in agriculture continue to be applied as routine spray programmes which result in considerable amounts of unneeded application and potential for exposure (London and Myers, 1993).

Important technological developments in the agrichemical industry include the development of insect growth regulators (IGRs) and methods of biological control, such as biopesticides (viruses, bacilli and fungi), pheromone disruptors and mechanical methods. These methods appear to pose less human health risks (Leslie and Cuperus, 1993; London and Myers, 1993) but evidence for their quantification is still awaited. In South Africa, IGRs are used substantially in citrus farming, largely as a result of the development of resistance by the major pests in the sector to conventional (and highly toxic) organophosphates (Bedford et al, 1985). These developments, while constituting only a small segment of the crop protection market at present, are likely to become more important in agriculture (London and Myers, 1993), particularly as a consequence of growing insect resistance to standard insecticides and global concern for the preservation of a healthy environment (Davies, 1991; Charles, 1991).

3.3 Assessing Agrichemical Exposure Among Farm Workers in South Africa

Estimates from Central Statistical Services for total agrichemical expenditure in South Africa amounted to R210 million in 1991 (CSS, 1991). These underestimate the figures released by the agrichemical industry (Figure 3.1) by approximately 66%. Based on information from AVCASA, herbicides, insecticides and fungicides were the biggest three contributors to agrichemical expenditure in

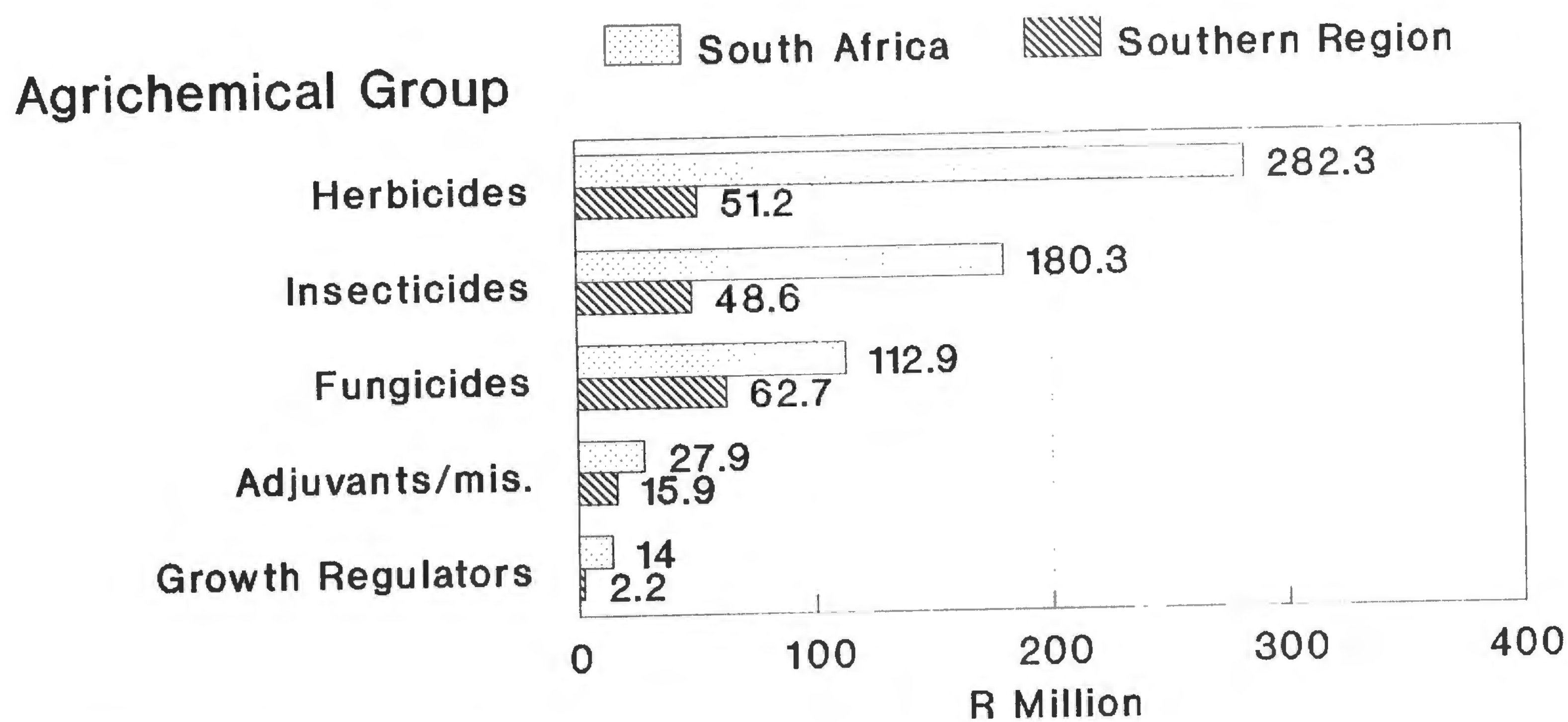
SA (London, 1992a). Forty six percent of total expenditure in 1990 on agrichemicals was on herbicides alone, reflecting the predominance of maize farming, where requirements for weed control are very high (De Klerk, 1983).

In the Western Cape, where the grain production predominantly involves wheat and barley (Kassier, 1992), the dominance of herbicide usage is not in evidence. Data from the agrichemical industry for the Southern Region of South Africa is presented in Figure 3.3 which compares expenditure on agrichemicals in the Southern region to that of South Africa as a whole (London and Myers, 1993). The Southern Region (Figure 3.2) comprises the Western, Southern and Eastern Cape as far as East London. For the Southern region, fungicides are extensively used and, while the cost of herbicide use also exceeds that of insecticides, quantitative use of herbicides is still far less than for the rest of the country.

Most expenditure on agrichemicals in the Western Cape occurs in the deciduous fruit, grape, and to a lesser extent, in wheat farming sectors (London and Myers, 1993). Central Statistical Services release data for expenditure on agricultural remedies by statistical region and these are listed in Table 3.4 for 1991 for Development Region A (CSS, 1991). Remedies include plant and animal feeds, veterinary medicines as well as agrichemicals and this accounts for the high expenditures in regions 1 and 2 where intensive animal husbandry requires high feeding inputs. Aside from these areas, regions 3 (Grabouw, Caledon, Hermanus, Bredasdorp, Swellendam, Heidelberg), 4, (Mossel Bay, George), 7 (Worcester, Ceres, Tulbach, Robertson, Montagu) and 8 (Malmesbury, Hopefield, Piketburg, Hopefield) have the highest expenditure on remedies per hectare, and region 3 has the highest expenditure per agricultural worker (Table 3.4). These are regions noted to have a high income from deciduous fruit, grape, animal, vegetable and, for regions 3 and 8, wheat production (CSS, 1991).

Figure 3.2 The Southern Region of South Africa - crop market protection source data.

Figure 3.3 Agrichemical Sales in 1990 South Africa (SA): Total SA and Southern Region, R million.



Source: London and Myers, 1993; Agricultural and Veterinary Chemicals Association (AVCASA), 1991.

Table 3.4 Expenditure per hecare and per worker on remedies in 1991 in Development Region A by statistical region [1].

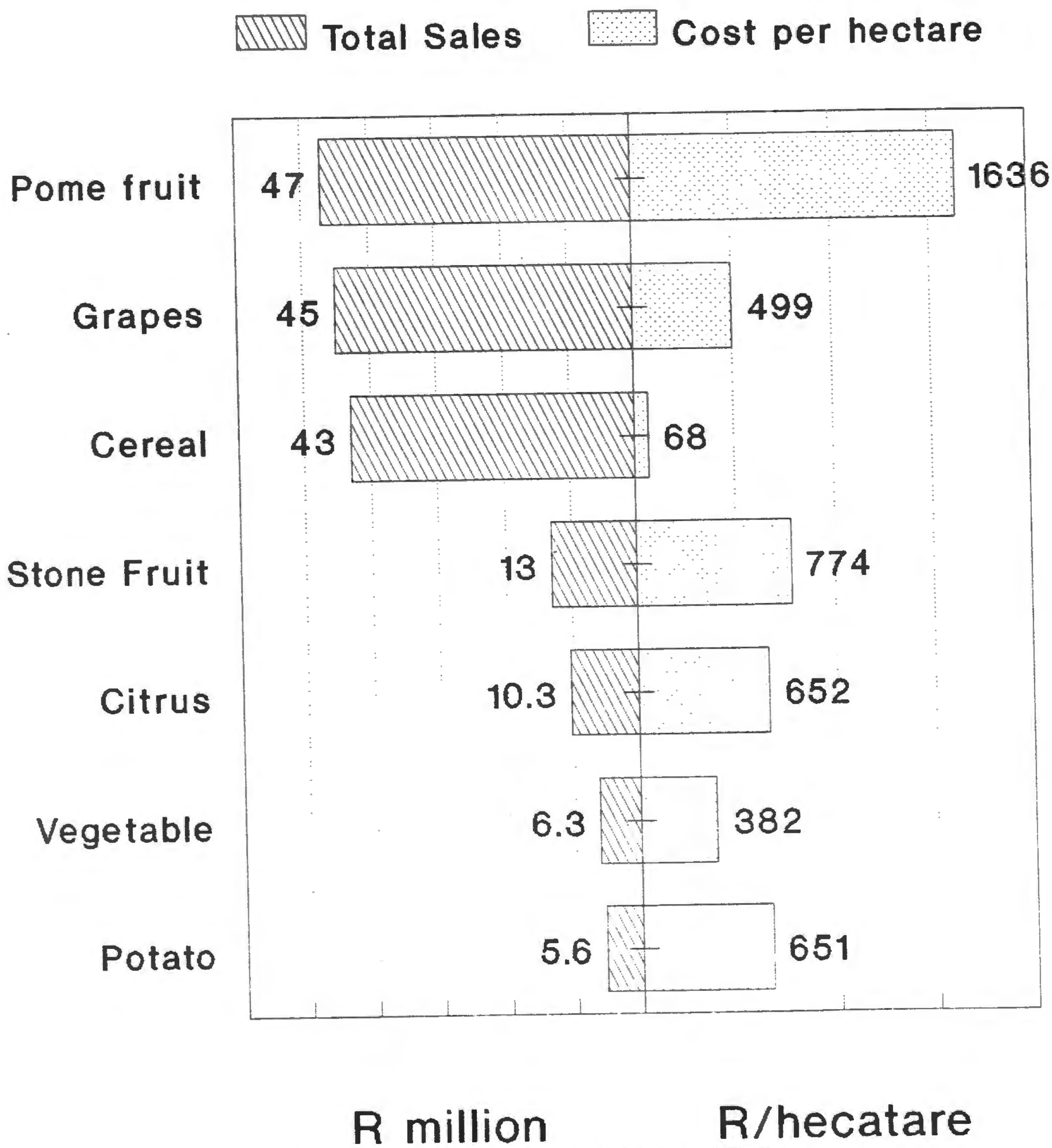
Statistical Region	Expenditure on Remedies (R 1000s)	Rands per hectare	Rands per worker
01	R 1 187	36.5	213.7
02	R 2 799	18.0	85.7
03	R 7 833	7.0	539.3
04	R 3 536	4.5	245.2
05	R 885	0.6	157.2
06	R 1 129	2.0	128.7
07	R 4 265	3.5	96.5
08	R 2 856	3.3	223.4
09	R 1 010	0.6	94.0
10	R 476	0.1	288.3
12	R 2 134	0.4	269.6
13	R 1 210	0.3	349.6
14	R 194	0.1	162.1
Dev Reg A	R 28 758	1.4	181.2
RSA	R 210 549	2.5	980.4

{Source: CSS, 1991}

[1] Remedies include plant and animal feeds, veterinary medicines and agrichemicals

Market research data from the agrichemical industry confirm that the deciduous fruit, grape and wheat sectors are the major users of pesticides in the region. The relative estimates of hectarage and expenditure on agrichemicals by different crop sector are listed in Figure 3.4. Deciduous fruit, and pome fruit in particular (apples and pears) is the highest agrichemical user. Total estimated expenditure in the Southern Region on

Figure 3.4 Crop Protection Market
Agrichemical sales and turnover, 1989/90



Sources: 1. AVCASA, 1991
2. WESGRO, 1992

agrichemicals in 1989 amounted to between R150 and R200 million (London and Myers, 1993).

3.4 Drawbacks of Data on Agrichemical Expenditure

Data on agrichemical expenditure are not useful for assessment of potential human exposure, other than for the detection of trends over time, as might be used in ecological studies (Sitas and Thompson, 1993). This arises because chemical cost may not reflect quantities used nor individual chemical toxicity. For example, herbicides tend to be expensive, yet most herbicides fall into the less toxic hazard groups (Vermeulen et al, 1991).

On the other hand, official data on the quantities of different types of agrichemicals used in agriculture are not presently available in South Africa (London, 1992a), unlike the situation in other countries where there are statutory requirements for the reporting and monitoring of hazardous chemical exposures (Heikkila and Kauppinen, 1992). Previously, the Department of Agriculture collected statutory information from agrichemical companies on quantities and types of chemicals produced. However, this practice was discontinued in 1976, because of reported inaccuracies and unreliability of data (Barlin-Brinck, 1991; Emanuel, 1992). As a result, no ongoing agrichemical exposure surveillance database exists in South Africa. The last published figures for annual agrichemical use by Kg in South Africa are reflected in Table 3.5 for 1978-1979 (Fourie, 1986).

Notwithstanding the lack of exposure surveillance data, accurate quantitative estimation of exposure is essential to the investigation of any health risks (Blair and Zahm, 1990; Hawkins et al, 1992; Blair and Stewart, 1992). This aspect has proven most deficient in the literature on pesticide-related morbidity to date (Maroni and Fait, 1993) and has resulted in inadequate exposure information or in exposure misclassification (Blair et al, 1992). The principal consequence of non-directional misclassification is an underestimation of possible risks involved in exposure to agrichemicals (Copeland et al, 1977; Rothman, 1986; Blair and

Table 3.5 Annual Agrichemical Use in SA, 1978-1979

		Active ingredient (metric tons)
Insecticides		9 689
Organochlorines	666	
Carbamates	1 224	
Organophosphates	1 220	
Pyrethroids	14	
Mineral Oil	4 758	
Carbaryl	1 017	
Sulphur	375	
Parathion	230	
Mercaptothion	185	
Herbicides		6 083
Triazines	1 958	
Phenoxyacetic acids	1 316	
Urea and ureacils	1 094	
Aliphatics	711	
Carbamates / thiocarbamates	444	
Amides	431	
Bipyridyliums	129	
Fungicides		4 741
Sulphur	2 432	
Dithiocarbamates	1 717	
Copper salts	519	
Systemic fungicides	26	
Carboximides	47	
Fumigants		3 300
Plant growth regulators		291
Seed dressings		94
Acaricides		90
Verminicides		2
Slug and snail killers		8
=====		======
TOTAL		24 598

(Source : Fourie, 1984)

Stewart, 1992), thereby reducing the study power, particularly where the true relative risk is less than 2. This situation is frequently the case with agrichemical health risks, particularly for cancer outcomes, where the strengths of associations have typically been shown to be relatively weak (Lilienfield and Gallo, 1989; Council for Scientific Affairs, 1988; Blair et al, 1992).

For this reason, data drawn from industry market surveys will be used in the absence of statutory information on agrichemical use in the country. While this database may have limitations in its generalisability (it is not based on random sampling), it is regarded within the industry as fairly authoritative and is consistent with interviews held with key informants in the field (London and Myers, 1993). Because of its importance from the epidemiological point of view, subsequent discussion will concentrate on the accurate characterisation of potential chemical exposures in agriculture with a focus on the deciduous fruit farming industry of the Western Cape. Data presented in the following sections will be used to generate job-exposure matrices (Hoar et al, 1990; Pannet et al, 1985) on which to base estimates of exposure for workers involved in agricultural production.

3.5 Standardisation of Agrichemicals to Overcome Non-equivalence : Biological Equivalents (BEs)

Two agrichemicals of equal quantity in Kg may not necessarily be equivalent in a biological sense because of their different toxicities. For example, 1 mg of paraquat may be lethal, while 1 mg of a dithiocarbamate will have no acute effect on exposed subjects. To address this, it is important to be able to identify a method of standardising quantities of agrichemicals in a meaningful manner. Weighting the amount of agrichemical by the inverse of its oral LD50 generates a biological equivalent (BE). Such a measure is useful for studies of acute effects, since it takes acute toxicity (as measured by the LD50) into account and may also have utility in studies of chronic sequelae of agrichemical exposure. Appendix 3.2 outlines some examples to illustrate the use of standardisation by the LD50 to address the problem of non-equivalence of chemicals.

It must be remembered that biological equivalent units have important drawbacks. They rely on the same assumptions on which the LD50's rely (London, 1992a). They are measurements of acute toxicity only and do not take into account factors such as the synergism of multiple chemicals, the presence of toxic contaminants, the effects of repeated applications or time elapsed from application to exposure. For this reasons the subsequent tables present both biological equivalents and Kg for consideration. For purposes of estimation of risks for chronic effects, mass (Kg) may also be a useful measure of risk.

3.6 Agrichemical Usage in the Southern Region of South Africa

Table 3.6 summarises usage of agrichemicals in the Southern Region of SA by Kg of active ingredient and by BEs. Fungicides are the largest group of chemicals by Kg (57% of total in the region) but contribute only 1.55% of BEs because of their low acute toxicity. The converse relationship is apparent for nematicides, which constitute 70% of BEs but only 2% of active ingredient by Kg. In comparison to Figure 3.1, it is clear that the high cost of herbicides are not reflected in either Kg or BEs, underlining the importance of using alternative methods of quantification other than expenditure.

Insecticides as a whole comprised 25% of agrichemical usage by Kg in the region in 1989 and herbicides comprised 10% of agrichemical usage by Kg and 2,38% of biological equivalents in the region in 1989 (Table 3.6). More detailed information on agrichemical usage patterns in the Southern Region as a whole is available elsewhere (London and Myers, 1993).

Table 3.6 - Agrichemical usage in the Southern region, 1989.

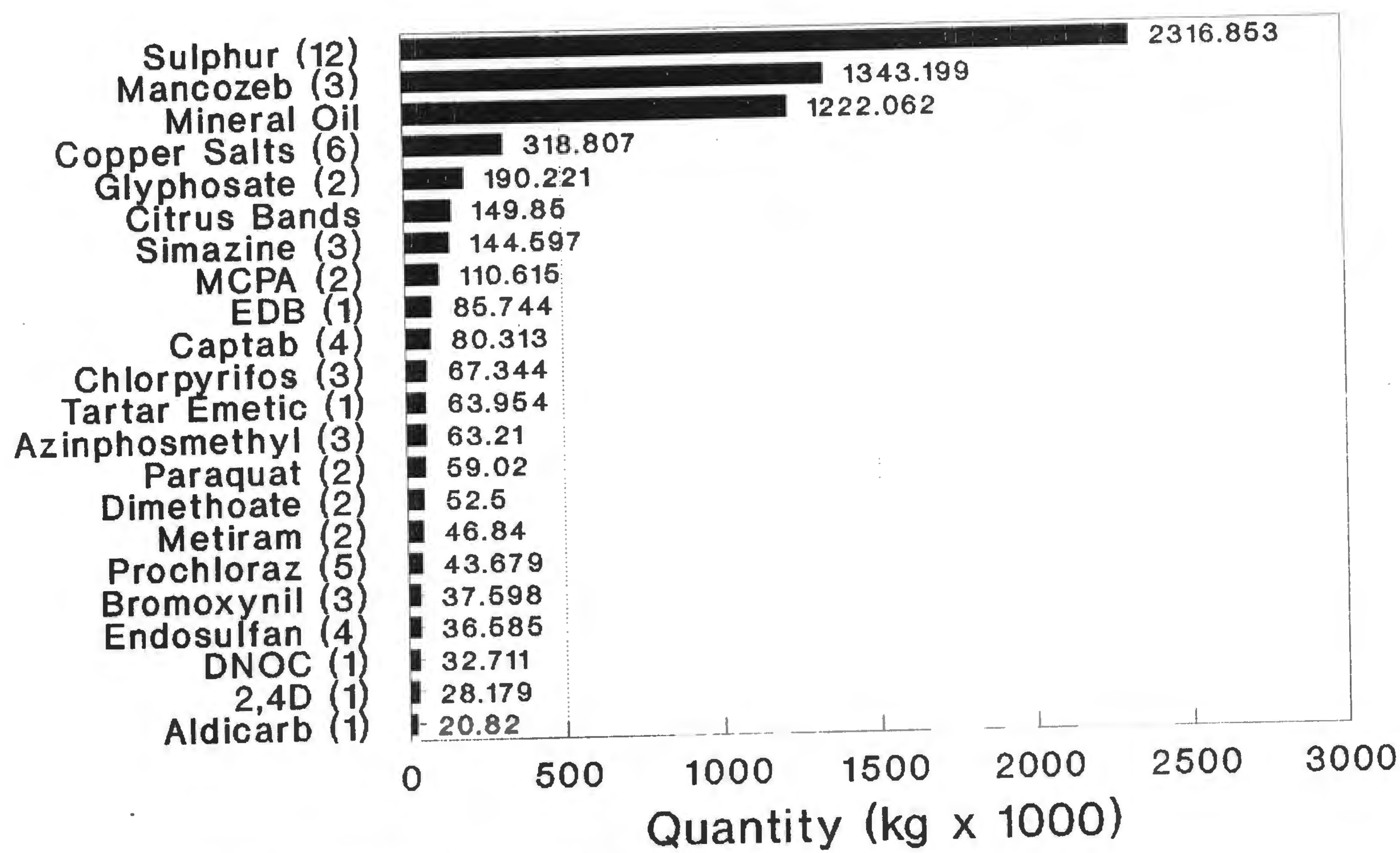
Agrichemical Group	Kg active ingredient	Percent	BEs	Percent
Insecticides	567 122	7.9	10 984	25.8
Fungicides	4 067 396	56.9	660	1.6
Herbicides	714 553	10.0	1 012	2.4
Fumigants	130 713	1.8	29 697	69.7
Acaricides	48 502	0.7	117	0.3
Growth regulants	14 796	0.2	87	0.2
Seed Treatment	17 240	0.2	18	<0.1
Mineral oil	1 222 062	17.1	-	-
Miscellaneous	361 234	5.1	5	<0.1
TOTAL	7 143 618	100.0	42 580	100.0

{Source: London and Myers, 1993}

3.6.1 Specific agrichemicals

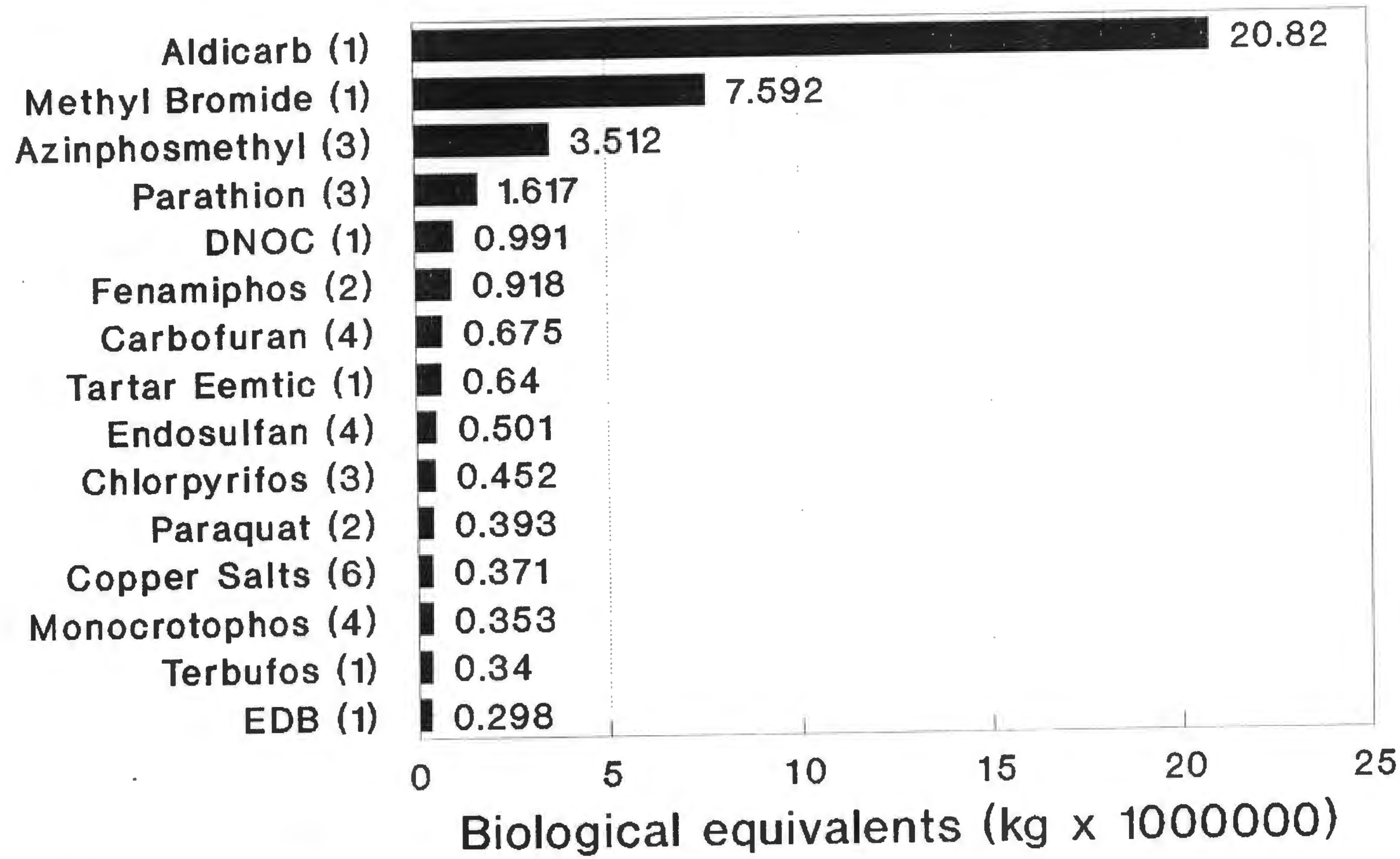
Specific agrichemicals that are either very toxic or are used widely, may contribute large proportions of the overall sum of biological hazard units and kilograms in the above tables. From an epidemiological perspective, these agents will be of more importance in studies wishing to assess human health risks associated with agrichemical exposure. Figures 3.5 and 3.6 examine the biggest individual agrichemicals (generic names) responsible for potential exposures, both by Kg and by biological equivalents.

Figure 3.5 Leading Agrichemicals Used Southern Cape Region 1989



Frequency of different brand types in parentheses

Figure 3.6 Leading Agrichemicals Used
Southern Cape Region - 1989



Frequency of different brand types
in parentheses

Aldicarb is a highly toxic carbamate nematicide with an oral LD50 of 1 g/Kg. Its extensive use constitutes 49,3% of total biological hazard units making it the single biggest agrichemical contributor to biological equivalents in the region. It is also amongst the top 20 agrichemicals by Kg for the region as a whole.

However, nematicide use is infrequent as it occurs only with replanting of the crop. For grape or fruit farming, this may only be once every 10 or 20 years, while for potato and onion farming, and some of the more intense nursery and vegetable lines (particularly strawberries), replanting is a yearly event (London and Myers, 1993).

In contrast, the dithiocarbamates are extensively used, but contribute little biological hazard units. Mancozeb, of which more than a million Kg of active ingredient is used in the region, contributes only 0,4% of overall hazard units and about 25% of biological hazard units attributed to fungicides. A number of OPs may be noted amongst the leading agrichemicals in the region.

3.6.2 Historical trends

For estimating long-term exposure, data on previous chemical usage is essential. However, farm records are generally not kept for more than one or two seasons (London, 1992b), making them unsuited for reliance for exposure data for epidemiological investigation of long-term health effects. In the absence of accurate registry-based information on usage patterns (for reasons outlined above), interviews with industry and farming experts have proved useful to identify historical trends. Agrichemicals which appear to have been widely used in the past include parathion (an OP insecticides), amitrole (herbicide used in vine and pome fruit farming) as well as DDT, dieldrin and endosulphan (organochlorines) (London and Myers, 1993). DDT and dieldrin are no longer registered for use in South Africa, and parathion usage presently is largely confined to citrus farming. In general, it appears that quantities used in agrichemical applications have decreased in past years, particularly for herbicides in wheat and for fungicides because newer agrichemicals have become more active per mass unit of active ingredient (London and Myers, 1993).

3.6.3 Overview

Implicit in the discussion of costs and quantities of agrichemicals is a paradox that may adversely affect agrichemical safety. Table 3.7 illustrates this by listing the major agrichemical groups used in the Southern Region in 1989 in decreasing order of magnitude for both kilograms of active ingredient and for BE units. Substantial differences in patterns of use emerge depending on what measure of usage is utilised, as illustrated in Tables 3.7 and Figure 3.3. Agrichemical expenditure parallels neither usage by mass nor by BE and this suggests that the application of financial cost savings may perhaps encourage greater control efforts directed at the more costly, but less widely applied or less acutely toxic agrichemicals.

Table 3.7 Major agrichemical groups used in the Southern Region of SA in 1989 in decreasing order of magnitude for Kg of active ingredient and for BEs.

Quantity by Kg	Biological Equivalents (BEs)
Fungicides	Nematicides
Insecticides	Insecticides
Herbicides	Herbicides
Miscellaneous	Fungicides
Nematicides	Acaricides

{Source: London and Myers, 1993}

In addition, the data confirm the very wide range of agrichemicals in use in farming, which serves to complicate attempts to characterise farm worker exposure. The figures presented above on general patterns of agrichemical exposure are useful for generating hypotheses concerning major occupational and environmental health hazards or for use in ecological studies (Sitas and Thompson, 1993). However, for accurate estimation of exposure-effect relationships in studies of possible human health risk from agrichemicals, exposure information needs to be more specific to particular agricultural sectors and workplace practices. These data are presented in the following sections.

3.7 Sector Specific Agrichemical Use in the Region

Tables 3.8 and 3.9 outline agrichemical usage for major categories of agrichemicals in the main agricultural sectors in the region.

For the region, pome fruit farming is the biggest user of insecticides by Kg and by BE. Large quantities of sulphur (in vineyards) and mineral oil (in deciduous and citrus fruit farming), which have no BEs contribute to high Kg usage of agrichemical in the region.

Tables on sector-specific agrichemical usage for the main agrichemical groups are contained in Appendix 3.3 for brevity. These tables list the number of chemical types in each category of agrichemical subgroup, the Kg of active ingredient and the BEs (and percentage that each subgroup forms of the total) as well as the Kg and BEs per hectare for each major crop sector in the region. (Data on the denominator for estimations of hectarage are presented in Table A.3.1.4) What follows is a discussion on the nature of the work process in different crop sectors that draws on the data in the appendix to characterise farm worker exposure to chemicals. The focus will be on the deciduous fruit industry in order to provide a meaningful basis on which to base exposure estimations in this study.

Table 3.8 QUANTITY OF ACTIVE.AGRICHEMICAL (Kg) USED
BY MAJOR FARMING SECTOR IN THE SOUTHERN REGION OF SA, 1989

	Pomme	Stone	Vine	Citrus	Wheat	Potato	Other	TOTAL
Insecticides	175 512	48 057	54 790	112 370	55 860	260	120 524	567 122
Fungicides	530 780	193 690	2 149 780	25 780	95 580	35 020	1 035 956	4 067 396
Herbicides	103 510	35 730	211 190	35 030	206 830	8 000	114 269	714 559
Fumigants	0	0	14 760	4 710	0	27 580	83 663	130 713
Growth Reg.	2 960	260	3 480	1 300	0	0	6 796	14 796
Acaracides	31 480	7 980	5 000	1 150	0	0	2 892	48 502
Seed Treatm.	0	0	0	0	16 990	0	250	17 240
Oil	844 908	49 583	0	327 320	0	0	0	1 222 062
Miscellan.	7 510	197 470	50	155 610	0	0	594	361 234
TOTAL	1 696 670	532 770	2 439 050	663 270	375 260	71 660	1 364 944	7 143 624

Table 3.9 BIOLOGICAL EQUIVALENTS OF ACTIVE.AGRICHEMICAL (BE) USED BY MAJOR FARMING SECTOR IN THE SOUTHERN REGION OF SA, 1989

	Pomme	Stone	Vine	Citrus	Wheat	Potato	Other	TOTAL
Insecticides	4 765	787	204	2 034	651	5	2 538	10 984
Fungicides	53	84	141	15	73	5	289	660
Herbicides	101	66	206	61	525	14	39	1 012
Fumigants	0	0	7 618	3 986	0	4 561	13 532	29 697
Growth Reg	18	2	28	20	0	0	19	87
Acaracides	88	17	1	0,2	0	0	11	117
Seed Treatm.	0	0	0	0	17	0	1	18
Miscellaneous	3	1	0,1	0,1	0	0	0.1	4,3
TOTAL	5 028	957	8 198	6 166	1 266	4 585	16 429	42 579

3.7.1 Agrichemical hazards and the work process in the deciduous fruit industry

The deciduous fruit sector includes a wide range of fruit lines, such as pome fruit (apples and pears), stone fruit (peaches, apricots, plums and nectarines) and grapes, but is dominated by the production of apples and pears (Chapter 2). Work patterns in pome and stone fruit farming are broadly similar but different agrichemicals may be used. Where relevant, distinction will be made between pome and stone fruit, and data in Appendix 3.3 is listed separately for the two deciduous fruit types.

In general, agrichemical spraying is far more intense in the deciduous fruit sector than in other farming sectors (Figure 3.4). Over 60% of insecticide use by Kg in the region occurs in pome and stone fruit farming. Average expenditure per hectare on agrichemicals ranged from R784 for apricots to over R2 000 for apples in 1990 (Emanuel, 1992; London and Myers, 1993).

Most spraying in the sector occurs from September onwards with the bulk of spraying taking place from November to January. Apple farms may require up to 10 to 15 sprays of insecticide and 10 to 12 fungicide sprays per season. Herbicide applications are less frequent, not exceeding two to three times per year. Minimal spraying may occur in winter months to combat scale disease.

The bulk of spraying in the deciduous fruit sector is done by tractor. Insecticides, fungicides, growth regulants and metabolic sprays are usually applied by mist blowers, which release a vapourised mist spray into the orchard at pressure sufficient to penetrate orchard foliage. Semi-manual methods involving workers holding sprayguns at the back of a tractor may also be used, usually for technical reasons where use of mist blowers are not practical. Herbicides are generally applied by low boom sprays or through handheld sprayguns or rubber hoses behind the tractor. Maintenance and calibration of spray apparatus, in particular the mist blower, to ensure the correct droplet size and deposition of agrichemical is important both for efficient agrichemical application and for safety reasons. Backpack spraying in which the worker carries a knapsack and applies the agrichemical with a hand-held nozzle, may be used for small patches or for small winter applications, but is not substantially practiced. Aerial spraying is not used in the deciduous fruit industry in South Africa.

The workforce directly exposed to agrichemicals comprises tractor drivers, who usually both mix and apply the chemicals, as well as supervisors, foreman, managers, farmers themselves, and, on larger farms, storemen who have sole responsibility for the poison store. Dependent on the size of the farm, the average permanent workforce size will vary between 10 and 60 and most farms will have between one or two to 20 tractor drivers (on large farms) involved in spraying (London, 1992b). Seasonal job activities on farms, such as thinning of the fruit trees and orchard maintenance may also result in indirect exposure through spray drift or contact with chemical residues on crops and trees (Wicker and Guthrie, 1980; Davies et al, 1982; Griffith and Duncan, 1985), particularly as these activities on fruit farms may coincide with periods of intense spraying. Approximately 10 to 15% of seasonal workers may be involved in these activities (London, 1992b). Picking of fruit is not thought to be as exposed an activity because, in general, most spraying on deciduous fruit farms has ceased by the time fruit is picked. However, if different cultivars of fruit are planted alongside each other in the orchards, workers involved in fruit picking may be exposed though drift of spray from a neighbouring orchard.

3.7.2 Specific agrichemical exposures in the deciduous fruit industry

The agrichemicals used in the pome and stone fruit sectors in 1989 are summarised in Appendix 3.3. Tables A3.2 to A3.11 list the insecticide, fungicide, herbicide, acaricide and miscellaneous agrichemical groups used in pome and stone fruit farming.

Insecticides are the most relevant hazardous agrichemical exposure in the industry. They comprise only 10% by Kg but over 80% (95% for pome fruit) of BEs from all agrichemicals in the sector. Indeed, over a third of all insecticides by Kg in the Southern Region are used for pome and stone fruit (London and Myers, 1993). Most insecticide use is for combating the codling moth, the control of which may require up to 10 or more applications of organophosphates during the spraying season. To a lesser extent, pyrethroids are also used (especially pome fruit) and insect growth regulators are likely to become more important in the future. Carbaryl, a carbamate insecticide, was previously the main treatment for bollworm infestations, but is now used only for chemical thinning. The only organochlorine still used substantially is endosulfan, now that DDT has been phased out for agricultural use. It is applied as a single spray, has a short residual period and is regarded as less dangerous, even though it is a Grade I toxin with a low oral LD50. In previous years, endosulfan had much wider use than at present (London and Myers, 1993).

Growing interest in Integrated Pest Management (IPM) (Wooldridge, 1991), as a result of export market preferences, has become an important modulating factor over the past years. Under IPM, attempts to lessen dependence on chemical control and to integrate methods of biological and mechanical control of pests and weeds have been evaluated and introduced. However, in practice, IPM has not necessarily resulted in the removal of agrichemical hazards. For instance, pyrethroids, which are used in low concentrations and are relatively less toxic to humans, are poorly suited for IPM because of their broad spectrum of invertebrate toxicity. In the example of codling moth control (the major pest in the deciduous fruit industry), this has led over the past five years to a shift away from broad-spectrum pyrethroids to more selective, but more hazardous organophosphates, even if in smaller quantities. The impact of IPM has been to change the types of chemical used rather than simply to reduce quantities (London and Myers, 1993).

Dinitro-ortho-cresol (DNOC) is an agrichemical used substantially in pome and, to a slight extent, stone fruit farming, to combat delayed foliation, a developmental problem of fruit trees in the Western Cape where winters are too mild to produce the temperature change needed to precipitate synchronous blossoming. DNOC is usually applied in August and its application usually coincides with the first winter OP application. Workforce exposure to DNOC is limited since labour activity at that time is low, and only those handling or applying DNOC are exposed. Farms in the Kouebokkeveld, where winters are more severe, do not experience delayed foliation, and do not need to apply DNOC.

Fungicides also form a substantial portion of agrichemical usage in the pome and stone fruit sectors, comprising roughly a third of overall usage by Kg in both sectors. Because of their lower spectrum of toxicity, their contribution to biological equivalents is much less.

Like organophosphates, fungicide applications are frequent. From approximately the end of September, fungicides are usually applied as a weekly preventive programme of a dithiocarbamate, for about 4 weeks, followed by less frequent curative applications that rely on triazoles. Most fungicide application takes place in the first half of the season, the total number of sprays varying from 6-12 in a season.

The types of fungicides most frequently used include the dithiocarbamates and pthalic acid derivatives, while copper and sulphur are extensively used in both pome and stone fruit. Captab, a pthalic acid fungicide, is being increasingly used in pome fruit relative to the dithiocarbamates because of its lesser propensity to lead to a "rusty" discolouration on apples (London and Myers, 1993). Sulphur is a Grade IV toxin (relatively non-toxic) and copper salts also tend to have lower acute toxicities.

Herbicides are a small segment of the agrichemical usage in the deciduous fruit sector, comprising between 6% and 7% of total agrichemical use in the deciduous fruit sector by Kg. Herbicide applications are less frequent than insecticides or fungicides, and will not exceed two or four applications per season. Glyphosate is an important herbicide used in both stone and pome fruit, and triazines are important in pome fruit. While Paraquat is not used in large quantities, it still constitutes over 70% of biological equivalents for herbicides in the sector as a result of its low oral LD50, and therefore is an important herbicide hazard in both pome and stone fruit.

Nematicides are not significantly used in the deciduous fruit sector. Fumigation and worm treatment is performed only with replanting. For pome orchards, this amounts to once every 20-25 years for apple or longer in the case of pear orchards. When treatment is used, it is usually with methyl bromide.

Acaricides are a small but significant segment of the agrichemical usage in the deciduous fruit sector. While they comprise less than 2% of Kg of agrichemicals used in the sector, the deciduous fruit industry accounts for over 80% of the usage by Kg of acaricides in the Southern Region as a whole. Acaricide use is almost exclusively to treat red spider mite. Acaricides include chemicals such as organotins, pyrethroids and others. They tend to be expensive, especially the organotins, and are used only once or twice per season.

Other chemicals used in pome fruit farming include mineral oil, either for its insecticidal properties, or as a carrier for other chemicals, particularly DNOC, and fumigation sulphur (196 000 Kg) for drying fruit on the farms. Neither has any recorded LD50s based on animal toxicity and therefore contribute 0 BEs to the total for the region.

Figure 3.7 Leading agrichemicals used
Southern Cape Region 1989
Pome Fruit - Quantity in kg x 100

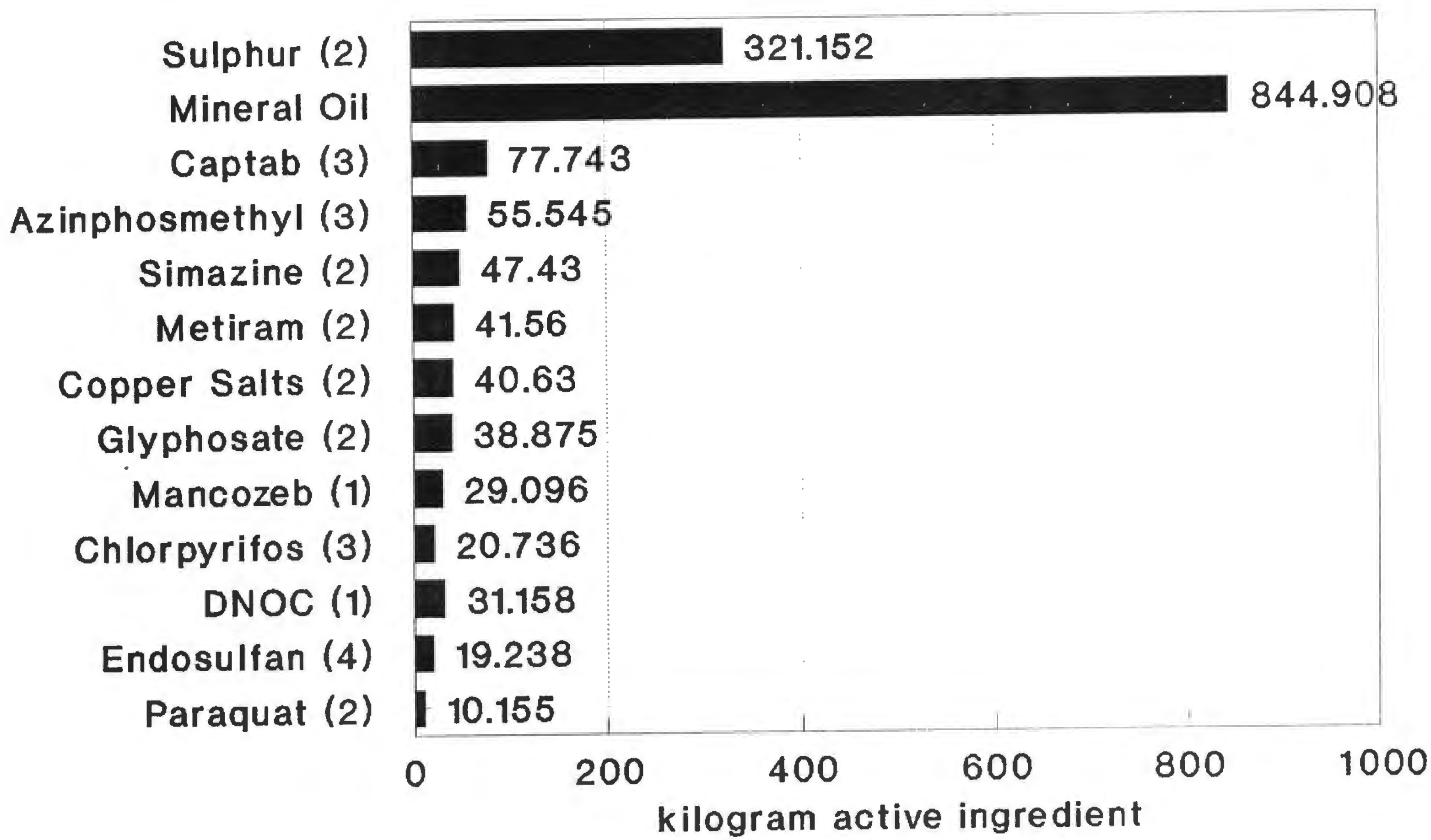
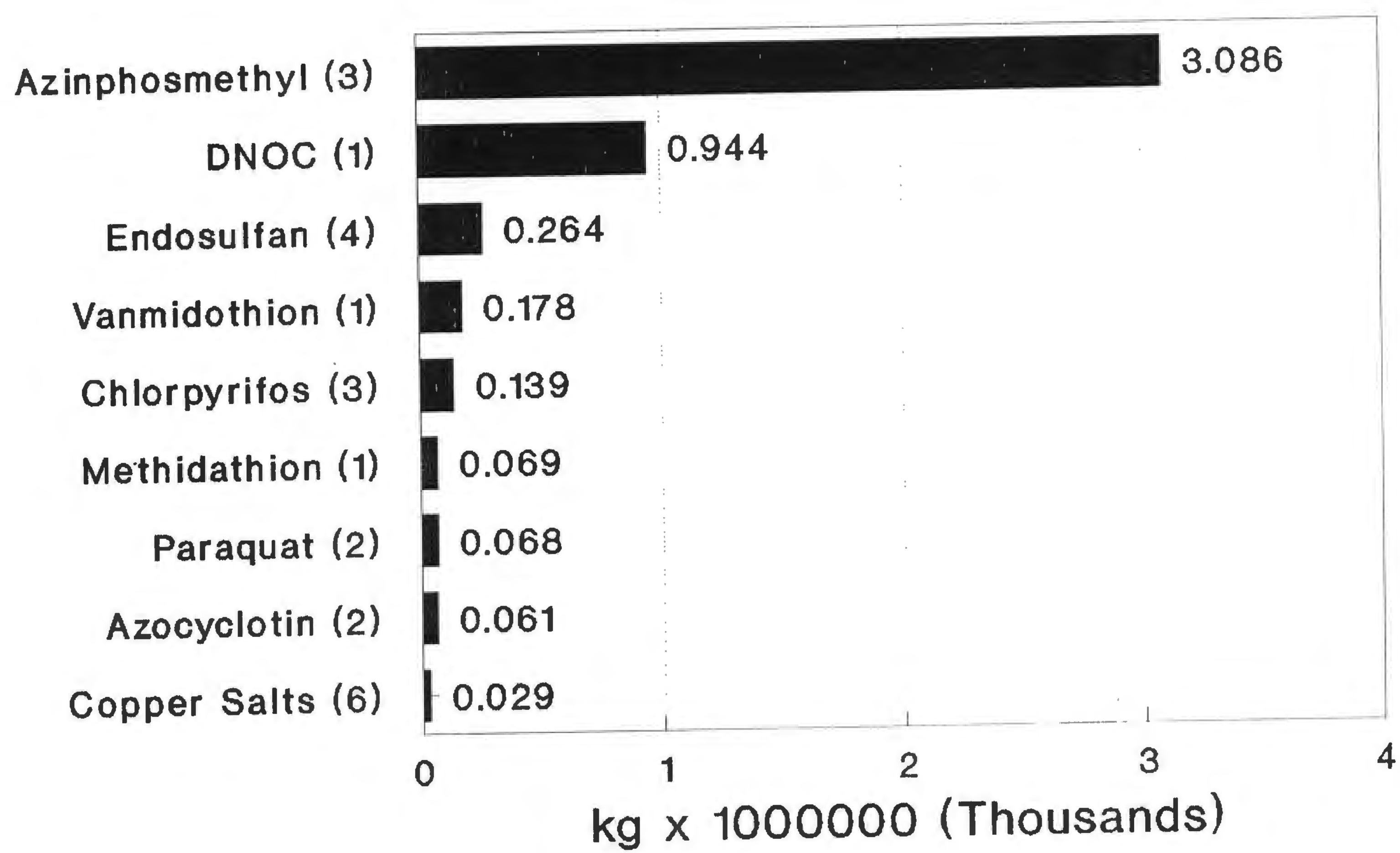


Figure 3.8 Leading agrichemicals used
Southern Cape Region 1989
Pome Fruit - Biological Equivalents



The most commonly used individual agrichemicals in the pome fruit sector are listed in the Figure 3.7 (by Kg) and Figure 3.8 (by biological equivalents). These potential exposures include various organophosphates (azinphos methyl, chlorpyrifos, vanmidothion and methidathion); pthalic acid (captab) and dithiocarbamate (mancozeb) fungicides; copper salts and sulphur; endosulfan, an organochlorine insecticide and herbicides such as triazines (simazine), glyphosate and dipyridyls (paraquat). These patterns of use are peculiar to the deciduous farming sector and differ substantially from exposures in other agricultural activities.

The deciduous fruit farming sector is therefore characterised by extensive use of fungicides and, to a greater extent, insecticides which also constitute the biggest contributor to BEs in the sector. In terms of a structural classification (IPCS, 1991), organophosphates are the major insecticide exposure hazard for both pome and stone fruit, with, to a lesser extent, DNOC (in the Grabouw region) and the organochlorine endosulphan being important in pome and stone fruit respectively. The diversity of chemicals in use is again noted, with 17 different types of organophosphates in use in the industry (Table A.3.2).

3.8 Agrichemical Exposures in Other Agricultural Sectors

Many farms, particularly fruit farms, in the Western Cape engage in the simultaneous cultivation of different types of products (Budlender, 1984; London, 1992b), with the result that workers may experience multiple agricultural hazards related to different work processes. In addition, workers' cumulative exposures are of critical importance in studies of chronic effects, and exposures experienced in previous jobs on farms other than deciduous fruit farms will need to be taken into account. For this reason, it is important to review briefly the nature of agrichemical hazards and work processes in other farming activities in the region.
Detailed data on Kg of active ingredient, BEs, percentage that each subgroup forms of the total and the Kg and BEs per hectare

for different agrichemical groups by major crop sector in the region is contained in Appendix 3.3 (Tables A.3.2 to A.3.35).

3.8.1 Agrichemical hazards in grape farming

Thirty four percent of total agrichemical use by Kg in the Southern region (Tables 3.8 and 3.9) occurs in grape farming. In general, spraying patterns are less frequent than for deciduous fruit, though, in the case of table grape farming, costs per hectare on agrichemicals tend to approach those of deciduous fruit farms. Estimates of average expenditure on agrichemicals range from R500 (wine grapes) to R1 400 (table grapes) per hectare (London and Myers, 1993).

Application methods in vineyards are similar to those on fruit farms but there is greater use of backpack sprays, particularly on smaller farms (Budlender, 1984). Mixed agriculture is an important aspect of wine and grape farming in the Paarl and Stellenbosch area, with a number of producers farming other crop lines such as tobacco, strawberries and vegetables (London, 1992b). Even on farms with monoculture of grapes, farmers may allow their workers to take on piece-work on neighbouring farms during the off-season (Budlender, 1984), with the result that some workers may be involved in diverse production with mixed exposures to agrichemicals.

Seasonal workers on table grape farms may also experience significant exposures to chemicals, more so than that experienced on fruit farms. For table grape farms, a large seasonal workforce is taken on to perform maintenance work during October to December, during which period the vineyards are extensively sprayed. The waiting period before workers re-enter a sprayed area is usually not more than one day. This implies that seasonal workers on vineyards are likely to have a large degree of potential exposure to agrichemicals.

Organophosphates are widely used in grape farming. Fungicide usage in vineyards is even more pronounced than that on deciduous fruit farms, and more than half of the fungicides used in the Southern region are used on vines. The bulk of fungicides are applied as preventive measures and include the dusting sulphurs, copper and dithiocarbamates. Nematicide use for soil treatment is an important feature of vineyard agrichemical use and includes Ethylene dibromide and aldicarb. Cyanamide is another agrichemical of high toxicity used as a growth regulant for table grapes (approximately 3484 Kg was used in 1989). While the absolute amount of cyanamide use is small (1 280kg; 20 BEs), it is the most toxic chemical amongst the growth regulants, and contributes about one-third of biological equivalents due to growth regulants in the Southern Region.

3.8.2 Agrichemical hazards in wheat farming

As a result of the huge size of most wheat farms (De Klerk, 1983; De Klerk, 1992) and wet soil conditions (London and Myers, 1993), usage of tractors for agrichemical application is impractical except on small holdings. Aerial spraying is thus the main form of application for wheat farms. Workers who stand as human markers for the aeroplanes are at considerable risk for exposure and the possibility of environmental contamination is greatly enhanced.

Substantial herbicide use is characteristic of all grain farming and organophosphates are only sparsely used. However, the total quantity of agrichemicals used in wheat farming is far less than for other agricultural sectors. The wheat sector constituted only 5,25% of the overall crop protection market by Kg in 1989. Most of this was herbicides of low acute toxicity (Table A.3.23), and the percentage of biological equivalents used in the wheat sector was as low as 3,25% (Table 3.9).

The frequency of spray application in wheat farming may be as little as a single spray per year in low yield areas to a maximum of four sprays per season. This would include, on average, an application of two herbicides, one fungicide and one insecticide. This is still perhaps 10 times less than on fruit farms. The Chlorphenoxy acids (MCPA and 2,4D), the dipyridyls (paraquat and diquat) and other miscellaneous herbicides (such as bridged diphenyls, sulphonylureas, etc.) are the most commonly used herbicides and are frequently applied in cocktails.

3.8.3 Agrichemical hazards in the citrus sector

The citrus industry has a low consumption of agrichemicals compared to other crops (Figure 3.4), though there is evidence that agrichemical costs have increased rapidly as a proportion of production expenses over the past few years (Citrus Fruit Board, 1990). Less than 10% of the overall crop protection market by Kg is attributable to citrus and estimates of expenditure on agrichemicals range from R650 (London and Myers, 1993) to R700 per hectare (Citrus Fruit Board, 1990). Tables A.3.25 to A.3.30 in appendix 3.3 list the different agrichemicals within chemical groups used on citrus in the Southern region in 1989.

Citrus is one of the few sectors still to make substantial use of parathion, an OP classed as a Grade I toxic chemical. However, growing resistance to parathion by scale disease has led to the development of biological controls and insect growth regulators in pest control in citrus (Bedford et al, 1985; Citrus Fruit Board, 1990) and is likely to lead to a decrease in the usage of parathion in future. Another important potential chemical hazard is tartox (tartar emetic containing antimony), used mainly in the Eastern Cape for thrip control (Vermeulen et al, 1990). It contains an antimony salt and is an important contributor to biological toxicity as a result of its low oral LD50. Fungicide and herbicide use in citrus is limited.

Nematicides are an important agrichemical in the citrus sector because of the extensive use of aldicarb, an extremely toxic carbamate nematicide. Aldicarb is applied as a granule to the soil, and is then irrigated to wash in the nematicide (London and Myers, 1993) and the suppliers will frequently supply a dispensing applicator along with the chemical. Nematicides are applied not more than once a season. In 1989, usage of aldicarb amounted to nearly 4 000 Kg of active ingredient (4 000 BEs).

The only other significant agrichemical in use is Calcium Arsenate, a growth regulator in the citrus sector to adjust the sugar acid ratio in Valencia oranges. The citrus sector is the only farming sector for which arsenicals are registered (Vermeulen et al, 1990), and in 1989 over 1 200 Kg active ingredient were used in the region.

3.8.4 Agrichemical hazards in the vegetable sector

Potatoes and onions are the biggest vegetable crops in the region (De Klerk, 1992) and are produced in close association with fruit farms in the Kouebokkeveld. Application of agrichemicals in vegetable farming is usually by means of hand-held sprayguns, rubber hoses or fixed booms at the back of a tractor, though more hazardous forms of application involving cannon sprays or aerial spray that rely on spray drift may occasionally be used. Potatoes and onions are frequently grown together, and their agrichemical spray profile is similar.

Total usage of agrichemicals by Kg in this sector amounted to roughly 1% of overall usage in the Southern region (Table 3.8), and the significant components are fungicide, herbicide and nematicide application. Insecticides are applied approximately 6 to 8 times per season, and usually consist of relatively non-toxic pyrethroids which require small volumes for application. Fungicides are usually applied about 6 or 7 times a season and make use of a different range of chemicals to that used in fruit farming (see Tables A.3.4, A.3.5 and A.3.32 in Appendix 3.3).

Acid amides, triazines and paraquat are the major herbicides used. Paraquat is reportedly applied before harvesting, to kill off the foliage of potato plant so as to render harvesting easier. While the harvesting of the crop is largely mechanical, there still is a manual element to the subsequent processes and this may be of importance in regard to indirect farm worker exposure to paraquat, though further research would be needed to confirm this hypothesis.

Soil treatment with nematicides is a major part of crop protection in the potato sector. It is the single sector with the largest nematicide consumption by Kg in the Southern region, and 38,5% of agrichemical usage in the sector by Kg is on nematicides. Because nematicides are extremely toxic agrichemicals, they contribute over 99% of biological equivalents in the sector.

Other types of vegetable farming may also pose significant risks of exposure to agrichemicals out of proportion to the amounts used for reasons particular to the farming process:

1. Production of vegetables may require picking of one line of vegetable at around the same time as another line is sprayed. This means that workers involved in picking may be fairly intensely exposed to agrichemical.

2. For some vegetables, particularly strawberries, few agrichemicals are registered for use (Vermeulen et al, 1990; Vermeulen et al, 1991; Vermeulen and Greyling, 1990b) because of the high costs for agrichemical companies in developing and registering new chemical agents. This may lead to a situation where farmers may be forced to use agrichemicals they have acquired for use on other crops (London and Myers, 1993).

3. Tunnel or greenhouse production involves working in a confined space which increases the risk of exposure to hazardous agrichemicals. Repair of tunnels or frames in semi-outdoor vegetables may also necessitate workers having to enter an area recently sprayed.

As for potatoes, soil fumigation is a very important practice for most ground vegetables such as tomatoes. Methyl bromide is frequently used for soil treatment for strawberries.

3.8.5 Conclusion

In summary, data presented here confirm the extensive usage of a wide range of different agrichemicals in the main farming sectors in the Southern Region of South Africa. Farm workers, even if only ever employed on one farm, are likely to experience substantially heterogeneous exposures within the course of a normal working life, and this complexity is exaggerated in the presence of a working life involving many different types of farms. The problem of non-equivalence of different chemicals is therefore best addressed by using the standardisation methods outlined earlier in this chapter involving Kg of active ingredient and BEs.

As far as quantifying exposure is concerned, important differences are apparent depending on whether Kgs or BEs are used. Fungicides are by far the most widely used chemicals by Kg in the region, followed by insecticides and herbicides. In contrast, in analysing BEs, nematicides represent the major exposure followed by insecticides, herbicides and fungicides. Moreover, within agrichemical groups differences emerge for individual chemicals. For example, glycine derivatives (glyphosate) are the most commonly used herbicide by mass active ingredient, while the dipyridyls (paraquat and diquat) were the most important contributors to BEs for herbicides in the region in 1989.

Knowledge of the above chemical exposures will be used in the last section of this chapter to characterise exposure amongst farm workers. For this study investigating chronic health effects arising from long-term health exposures, kilograms of active ingredient will be primarily used, since BEs appear more suited to studies of acute exposures. However, exposure indices based on BEs will still be examined to take full account of possible long-term effects of the full spectrum of agrichemical exposure.

3.9 Other Factors Influencing Workplace Exposure

Many factors other than chemical quantities will determine actual workplace exposures. These are summarised in Table 3.10.

<u>Table 3.10 Factors influencing workplace exposure to agrichemicals</u>

* Work practices and work organisation
* Training and behavioural factors
* Use of Personal Protective Equipment
* Environmental routes of exposure

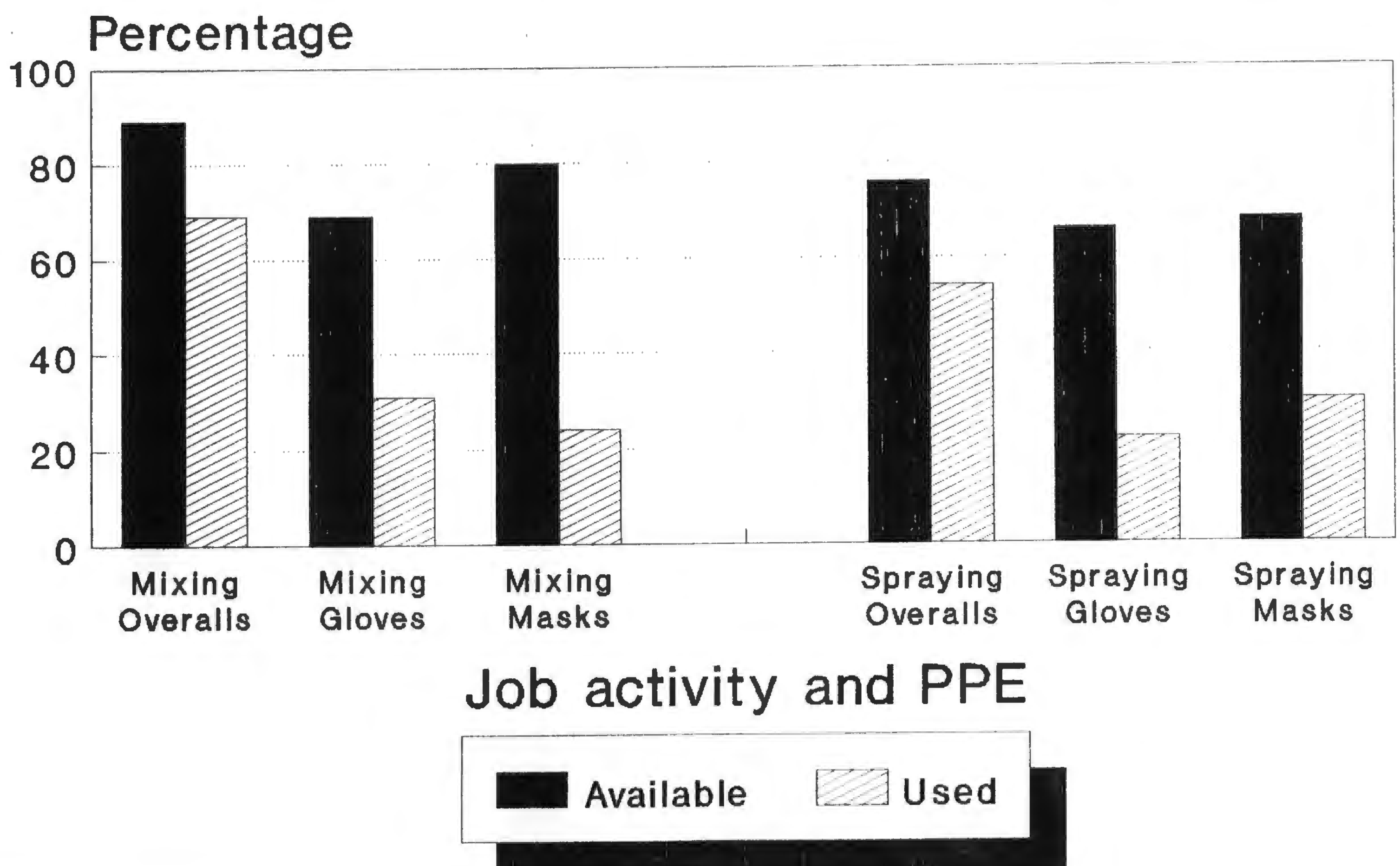
Workplace safety practices are a key element determining hazardous exposures (Loewensen et al, 1990; Mwanthi, 1994; Brouwer et al, 1994). For example, use of contaminated personal protective equipment, eating or smoking in the fields between or while applying chemicals, inappropriate handling or mixing of chemicals, use of unsafe techniques for repair or maintenance of equipment are all important contributing factors for exposures (Moses, 1993; Coye and Fenske, 1988). These are variables that are difficult to quantify, particularly in studies investigating the effects of long-term exposures. Knowledge of, and attitude towards chemical safety may be determinants of safety behaviour (Loewensen et al, 1990) and these may be measured more simply. However, studies of Knowledge, Attitude and Practices (KAPs) have many limitations, particularly with regard to the lack of reliability and validity of their data, and their failure to characterise adequately the intensity of opinions or attitudes reported (Hauser, 1993).

Use of protective equipment is frequently regarded as the first line of industrial hygiene for agrichemical safety. Even though this is not necessarily appropriate (Loewensen et al, 1990), particularly in the farm setting, where high temperatures make use of PPE difficult, the provision and use of PPE may be relatively easily gauged by questionnaire or observation. Little published data on this in South Africa are available, though a random sample of 45 farms in a rural area of the Western Cape found that usage of protective equipment in the storage, mixing and application of agrichemicals to be low (London, 1992b) (Figure 3.9). The low usage of PPE is common in many developing (Gupta et al, 1984; Matos et al, 1987; Mwanthi, 1994) and developed countries (Moses, 1988; Brouwer et al, 1994) worldwide.

A number of different environmental routes of contamination may be important in the rural setting. Poor control of chemical storage in farm stores in South Africa is common (Brown and Fourie, 1987; Emanuel, 1992) and may be an important additional route for worker contamination with agrichemicals. This is supported by findings of a review of pesticide poisoning notification in the Western Cape from 1987 to 1991, where unauthorised access to farm pesticide stores was the most common source for the poisoning (London et al, 1994). In the same audit referred to earlier (London, 1992b), more than half of the farms surveyed were found to have farm stores unlocked at the time of inspection, and a number of farms had no secure locking facility. These findings are replicated in research from other areas in the Cape (A Reid, 1991, personal communication, Child Health Unit, Red Cross Children's Hospital, Cape Town).

Because farm workers' residences in South Africa are frequently located within or adjacent to orchards, vineyards or fields (London, 1992b), domestic environmental exposure may be a possible result of contamination of drinking or washing water, or of direct drift of spray into households. Reports in the literature suggest that environmental routes of contamination may be responsible for pesticide related neurotoxicity (Barbeau et al, 1986; Kaplan et al, 1993).

Figure 3.9 Personal Protective Equipment Availability / Use on Western Cape farms



Random sample of 45 farms
Source: London, 1992b

For farm workers, water contamination may result from the re-use of agrichemical containers for domestic purposes such as for drinking water or washing (Emanuel, 1992). This has been shown to be responsible for a number of episodes of acute poisoning reported to the Department of National Health and Population Development (London et al, 1994). Where water is obtained by borehole, as is the case on many farms in South Africa (London, 1992b), contamination of the water table has not been well researched to date, unlike the situation in the United States (Hogmire et al, 1990). Two studies conducted in the Western and Northern Cape for the Department of Water Affairs, found little evidence of ground water contamination by currently used pesticides (Weaver, 1993). However, in the one study, surface water entering an irrigation scheme was found to have high levels of atrazine which was thought to have occurred as a result of run-off from surrounding maize growing areas (Weaver, 1993). Similar concerns for the lack of national effective groundwater surveillance have been expressed by researchers in other countries (Richter et al, 1992).

Spray drift onto residents adjacent to kibbutzim in Israel where agrichemicals were applied has been shown to be associated with increased symptoms and lowered cholinesterase levels (Richter et al, 1986). Evidence for the possible role of domestic contamination in South Africa is suggested by two reported studies. Elevated levels of DDT and its metabolites were found in breast milk of lactating mothers in a rural area of Natal where DDT is widely used for malaria vector control (Bouwman et al, 1990). These findings arose in the setting of deliberate indoor application of an environmentally persistent insecticide, which would be expected to result in high exposure. Another study (unpublished) amongst plantation workers in the Northern Transvaal exposed to organophosphates, found that rural control subjects had lower cholinesterase levels than the occupationally exposed group and the authors' hypothesis was that widespread environmental contamination was responsible [1] . However, poor comparability between index and control group was a major limitation of this study.

Nonetheless, these hypotheses concerning mechanisms of domestic exposure require further investigation, since such routes may add considerably to the lifetime burden of chemical exposure of individuals in rural areas. To take these factors into account, data on agrichemical knowledge and attitudes, availability of washing facilities, usage of PPE, re-use of chemical containers, unauthorised (domestic) use of chemicals and proximity of dwelling to drift sources should also be recorded in the investigation of adverse health effects of chronic low-dose agrichemical exposures. In this study, these will be translated into cumulative years of residential exposure, weighted for type of farm, type of spray activity and proximity to nearest spraying site (Chapter 5).

3.10 Exposure Estimates for Farm Work - Job-Exposure Matrices.

3.10.1 The rationale for the use of job-exposure matrices

In the absence of detailed industrial hygiene measurements of workplace chemicals in the working environment, or biological monitoring data, the use of job-exposure matrices (JEMs) has been proposed as a method of estimating workplace exposure (Hoar et al, 1980; Pannet et al, 1985). A JEM makes use of a matrix with job history variables on one axis, chemical agents on the other and the relationship between the two listed within the matrix. It has particular value when the subject's recall for job activity exceeds their ability to recall information relevant to particular chemical exposures, as might be expected in agricultural settings (Nanni et al, 1993; Migli et al, 1993), particularly where education levels are low.

---

1 Jaga K, Rama D. (1993). Cholinesterase activity in workers exposed to organophosphate pesticides at a coffee plantation. Poster presented to 8th Conference of the Epidemiological Society of Southern Africa. Johannesburg, July 1993.

Job activity is usually defined by a combination of industry and job title, and chemical agents frequently selected according to their known toxicity profiles. Traditionally, the relationship between job history and exposure has been expressed as a dichotomous (exposed or unexposed) or ordinal variable (high, medium or low). However, more recent work suggests the value of using probabilities of exposure within the matrix to produce greater accuracy of risk estimation (Bouyer and Hemon, 1993). Various methods to refine JEMs have been developed, particularly in relation to their applicability to populations different to those in whom the JEM was initially developed (Kromhout et al, 1992; Kauppinen et al, 1992). More recently, the applicability of JEMs to agricultural work has also been reported (Nanni et al, 1993; Migli et al, 1993; Daures et al, 1993; Brouwer et al, 1994).

French researchers have developed a JEM for agrichemical exposure in vine growing that utilises information on calendar year of spray activity, farm location and agrichemical-specific data on application method, duration of application, hectarage and quantity applied to estimate cumulative exposure to a specific agrichemical amongst farmers in a vine-growing area of France (Daures et al, 1993). A similar JEM that also takes into account type of crop production has been developed for use in two Italian case-control studies on cancer currently in progress (Migli et al, 1993). Both groups of researchers report validating these JEMs against an assessment by agricultural experts with good results. However, no comparison of these JEMs against farmer records or biological monitoring data was possible, and further research was indicated as necessary by both researchers.

A further reported refinement to agricultural JEMs is the inclusion of method of application and the use of personal protective equipment to estimate cumulative exposure (Brouwer et al, 1994). This study drew on previously published research into method-specific exposure rates and weighted the key components of the JEM to take into account the primary role of dermal absorption for agrichemicals. Another set of researchers reported the iterative use of a priori matrices utilising information on crop cultivation, hectarage and pest infestation to improve exposure characterisation for agricultural studies (Nanni et al, 1993).

3.10.2 A job-exposure matrix for workers in the fruit farming industry in the Western Cape

Drawing of the above models of JEMs for agriculture, the JEM used in this study will take into account the type of farming activity (crop/product) and the specific job activity that the worker carries out on that farm to characterise the subject's work exposure history. Based on an a priori knowledge of agrichemical use within each sector of crop production, an estimate of the probability of different agrichemical exposures for the subject may be obtained. This allows for a JEM to be adapted to local agricultural conditions.

The key elements to the agricultural JEM are therefore:

A - An identification of all relevant agricultural activities in different agricultural sectors with possible exposure to agrichemicals and a relative rating of the exposures experienced in these activities.

B - The characterisation of typical agrichemical usage patterns for different types of farming.

Based on a cross-tabulation matrix, the product of A and B will give the estimated probability of exposure for each activity. The probabilities will be expressed as a relative percentage on a scale based on a typically high exposure activity, such as driving a tractor with a mist blower having a relative exposure of 100, and is illustrated in Table 3.11.

Since workers may be involved in different activities in different, and even the same, farm jobs, exposures may be summed over time. This may then be used to derive cumulative and average lifetime intensity exposure estimates (Checkoway et al, 1989).

Where additional information exists on the specifics of a chemical exposure, or the absence of an exposure for a particular activity, this may be included in the matrix. This is illustrated further in the examples below and in Appendix 3.4.

Cumulative exposure is generally appropriate for the investigation of dose-response relationships in chronic diseases, though there may be instances where peak exposures may be more relevant (Checkoway and Rice, 1992), or where non-linear relationships are more suitable (Seixas et al, 1993). However, for most agrichemicals with neurotoxic potential, there is little empirical data available on the nature of the dose-response relationship and the assumption of a linear dose-response relationship implicit in the use of cumulative exposure may be considered a reasonable strategy (Brouwer et al, 1994).

Information to derive the first component (A) of the JEM in this study, is based on extensive interviews in the industry (London and Myers, 1993) and is summarised in Table 3.11. This job rating was revised on a number of occasions based on repeated interviews with key informants in the industry, using the Delphi technique. While such iteration may represent a form of "validation", more formal validation of JEMs is essential (Kauppinen et al, 1992) and this requires one or more field industrial hygiene studies of workers involved in the job activities identified in the scale to confirm or adjust the a priori estimates. This approach has been used successfully in other settings of research into pesticide hazards (Nanni et al, 1993) and is to be performed for the deciduous fruit setting at a future point in time.

Table 3.11. Relative rating of exposure in agricultural job activities

Tractor spraying with mist blower	
also mixes indoors	100
also mixes but outdoors	80
no mixing	70
Tractor driver of handsprayer configuration	50
Mixing of pesticides (separate from spraying)	
mixes indoors	100
mixes outdoors	80
Handspray from the back of a tractor	
also mixes indoors	100
also mixes but outdoors	80
no mixing	70
Backpack spray	
also mixes indoors	100
also mixes but outdoors	80
no mixing	70
Maintenance of equipment (separate from spraying)	20
Thinning work in orchards	10
Shaping work in vineyards	5
Monitors in orchards	5
Occupational gardening (of farmer's garden)	5
Animal dipping	50

Data for the second component of the JEM (B), originates in the preceding discussion in this chapter and are contained in the last two columns of Tables A.3.2 to A.3.35 (Appendix 3.3) where amount of agrichemical per hectare is listed for each major crop sector. The basis on which hectarage for each crop sector is estimated is presented in Table A.3.1.4. The usage of a rate per hectare as an appropriate proxy for estimating exposure is grounded in the practice whereby the application of agrichemicals is calculated on dosages per hectare. This will most closely approximate a dosage measure for subjects in epidemiological terms. However, it should be remembered that individual subject tissue dose may not be a linear function of exposure dose, and estimates of exposure-effect relationships may either be under- or overestimated depending on the pharmacokinetics of the chemical agent concerned (Smith, 1992). An example of this method is illustrated in the box below.

> A JEM for agricultural work - A simple example:
>
> Worker Mr M has worked as a tractor sprayer on a fruit farm for 7 years spraying, on average, 8 months per year, 5 days per week (695 spraying days). He also worked in the fruit orchards doing thinning for six seasons, on average 2 days per week for two weeks per year (24 thinning days) and occasional gardening for the farmer (28 gardening days). In his previous job, he worked on a vineyard as a seasonal worker for two years for a month every time doing general vine maintenance (48 days).
>
> To derive A for Mr M's first job:
>
> A tractor driver, who also does his own indoor mixing, scores 100% for exposure (Table 3.11). Multiplying by the number of days of tractor driving spraying, he accumulates 695 day-equivalents for tractor driving.
> For thinning, he accumulates an additional 5% of 24 days = 1.2 days-equivalents, and for gardening an additional 5% of 28 days = 1.4 days. This totals 697.6 day-equivalents in deciduous fruit farming.
>
> To derive B for Mr M's first job:
>
> Yearly exposure to OPs in pome fruit industry amounts to 4.98 Kg of active ingredient of OP per hectare (Table A.3.2).
>
> Multiplying A and B, one derives 697.6 X 4.98/365 for Kg active OP exposed in a lifetime = 9.518 lifetime Kg OP.
>
> To derive A for Mr M's first job in grape farming, his exposure day-equivalents are 10% of 48 days = 4.8 day-equivalents. From Table A.3.1.14, yearly exposure to Kg active ingredient OP is 0.24 Kg per hectare in grape farming.
> The product of A and B is 4.8 X 0.24/365 = 0.003 lifetime Kg OP.
> Summing the two jobs produces a cumulative exposure of 9.521 lifetime Kg OP.
>
> Similar calculations may be made for specific types of OP where such data are available.

Where farm specific data on the number of hectares allocated to a sprayman is available, more accurate estimates of sprayer/hectare may be used. For farms on which the worker is currently employed, and where data on actual chemical use in the past season are available, the need for secondary data extrapolation to derive the (B) component of the JEM will be obviated. However, for retrospective ascertainment of historical exposure, where farm records are not available, as appears to be the case for farming in the Western Cape (London, 1992b), extrapolation will be needed and the JEM will be utilised to estimate cumulative exposure.

3.10.3 Critical issues for the use of job-exposure matrices

There are a number of critical issues, applicable to JEMs in general and to the above model:

1. The accuracy of the denominators is important, since errors in the size of relative hectarage on different crop sectors may produce large differences in intensity of agrichemical usage (B). Since the process weights exposure by this factor, it will have a large impact on the estimate. However, the sources of data identified in Table A.3.1.4 have been seen to be fairly consistent and suggest that errors in estimates of hectarage are not large.

2. The use of an average applied to the sector assumes a homogeneity of usage patterns, which is clearly not always the case (Brouwer et al, 1994). For example, DNOC is a chemical used extensively in apple farming in Grabouw but hardly at all in apple farming in the Kouebokkeveld. To assume an average of exposure for all the apple industry will misclassify individuals with regard to DNOC exposure, with workers from the former area being underestimated and those from the Kouebokkeveld being overestimated. One way to obviate this is to further stratify the estimation of sector-based use patterns by geographical area (Migli et al, 1993) or other measurable variables known to influence usage patterns. However, for OP insecticides in the fruit industry, differences in geographical

usage patterns are minimal (London and Myers, 1993). Inclusion of further strata to the JEM may introduce unworkable levels of complexity to the matrix and may only be worth attempting where such heterogeneity of use patterns is known.

3. Different job activities may have chemical specificity (Brouwer et al, 1994). For example, backpack sprayers on fruit farms may only apply herbicides. This would mean that the general pattern of exposure for the sector is not homogeneous within the different activities in the sector. To address this, job activities associated with specific exposures should be identified in data collection. In the case of backpack spraying identified on interview, it will be necessary to ask as follow up, whether the spraying was for herbicide or insecticide. This strategy has been included in the study questionnaire (Appendix 5.1). This data can then be included in interpretation of the matrix.

4. Large variations in exposure levels are present within methods-specific types of agrichemical application and the JEM is not easily calibrated against other techniques of exposure assessment, such as biological monitoring (Brouwer et al, 1994). Therefore the JEM does not necessarily reflect absolute exposure, but may usefully provide a ranking within a population under study, or an exposure score to compare across groups.

5. The reliability of the JEM is critically dependent on the accuracy of information provided by respondents. Where reliability of data on job activity is shown to be good (Brouwer et al, 1994), the estimates generated from the JEM may be used with relative confidence. There is evidence that self-reported work histories have adequate validity for distant recall (Migli and Masala, 1991) and for farmers reporting pesticide exposure (Blair and Zahm, 1990). However, even when misclassification of component data for the JEM exists, the effect on estimates of risk in dose-response studies may not necessarily be substantial (Kauppinen et al, 1992) if it can be

shown empirically that the JEM is relatively insensitive to changes in the relevant variables making up the JEM (Brouwer et al, 1994).

6. Changes in patterns of agrichemical usage over time should ideally be incorporated into JEMs (Daures et al, 1993; Migli et al, 1993; Brouwer, 1994) as failure to do so may lead to substantial misclassification and bias. However, evidence from a study of bulb farmers in the Netherlands suggests that within a particular functional group of agrichemicals, there may be consistency of use of one of a number of members of the same class of agrichemical (Brouwer et al, 1994). This means that, for example, in fruit farming, the use of one OP (parathion) has been replaced by another member of the organophosphate group (azinphos methyl) over a period of 10 to 20 years (London and Myers, 1994) and that a JEM for OP exposure may be less sensitive to these changes in usage pattern. Nonetheless, further research would be indicated to include period specific patterns of use in a JEM for agriculture in South Africa.

However, despite the limitations of job-exposure matrices, these methods of exposure ascertainment offer a substantial advance over conventional dichotomous exposed-nonexposed categories. Careful attention has been paid in the preceding sections to make explicit the assumptions underlying the particular JEM to be used in this investigation and to make maximal use of available data. More complex examples of the use of this JEM are illustrated in Appendix 3.4 and are based on the real-life histories of subjects interviewed in the course of the study.

REFERENCES

Barbeau R, Roy Cloutier L, Plasse L, Paris S. (1986). Environmental and genetic factors in the aetiology of Parkinson's disease. In: Yahr MD, Bergmann KJ (eds), Parkinson's disease. Adv Neur 45 : 299-306. Raven Press, New York.

Barlin-Brinck M. (1991). "Pesticides in South Africa - An Assessment of their Use and Environmental Impact." The Wildlife Society of South Africa, Durban.

Bedford ECG, Vercuil SW, Deacon V. (1985). General Guide to the Integrated Control of Citrus Pests with Red Scale under Biological Control. H47/1985. Citrus and Subtropical Fruit Research Institute, Nelspruit.

Blair A, Zahm S. (1990). Methodological Issues in Exposure Assessment for Case-control Studies of Cancer and Herbicides. Am J Ind Med 18 : 285-293.

Blair A, Stewart PA. (1992). Do quantitative Exposure Assessments improve risk estimates in occupational studies of cancer? Am J Ind Med 21 : 53-63.

Blair A, Zahm S, Pearce NE, Heineman EF, Fraumeni JF. (1992). Clues to cancer aetiology from studies of farmers. Scand J Work Envir Health 18 : 209-215.

Bouwman H, Coppan RM, Reinecke AJ, Becker PJ. (1990). Levels of DDT and metabolites in breast milk from KwaZulu mothers after DDT application for malaria control. Bull WHO 68, 761-768.

Bouwman H, Cooppan RM, Botha MJ, Becker PJ. (1991). Serum levels of DDT and liver function of malaria control personnel. S Afr Med J. 79, 326-329.

Bouyer J, Hemon D. (1993). Comparison of three methods of estimating odds ratios from a job-exposure matrix in occuapational case-control studies. Am J Epid 137 : 472-481.

Brouwer DH, Brouwer EJ, Van Hemmen JJ. (1994). Estimation of long-term exposure to pesticides. Am J Ind Med. 25 : 573-588.

Brown AC, Fourie HO. (1994). Pesticidal poisoning in the Republic of South Africa. Community Health in South Africa. (?vol) : 8-10.

British Medical Association (BMA) (1992). "Pesticides, chemicals and health". Edwin Arnold, Kent.

Budlender D. (1984). Agriculture and Technology: Four case studies. Carnegie Conference Paper number 23. SALDRU, UCT.

Central Statistical Services (CSS). 1991. Statistical News Release P1101 - Agricultural Survey, Central Statistical Services, Pretoria.

REFERENCES

Barbeau R, Roy Cloutier L, Plasse L, Paris S. (1986). Environmental and genetic factors in the aetiology of Parkinson's disease. In: Yahr MD, Bergmann KJ (eds), Parkinson's disease. Adv Neur 45 : 299-306. Raven Press, New York.

Barlin-Brinck M. (1991). "Pesticides in South Africa - An Assessment of their Use and Environmental Impact." The Wildlife Society of South Africa, Durban.

Bedford ECG, Vercuil SW, Deacon V. (1985). General Guide to the Integrated Control of Citrus Pests with Red Scale under Biological Control. H47/1985. Citrus and Subtropical Fruit Research Institute, Nelspruit.

Blair A, Zahm S. (1990). Methodological Issues in Exposure Assessment for Case-control Studies of Cancer and Herbicides. Am J Ind Med 18 : 285-293.

Blair A, Stewart PA. (1992). Do quantitative Exposure Assessments improve risk estimates in occupational studies of cancer? Am J Ind Med 21 : 53-63.

Blair A, Zahm S, Pearce NE, Heineman EF, Fraumeni JF. (1992). Clues to cancer aetiology from studies of farmers. Scand J Work Envir Health 18 : 209-215.

Bouwman H, Coppan RM, Reinecke AJ, Becker PJ. (1990). Levels of DDT and metabolites in breast milk from KwaZulu mothers after DDT application for malaria control. Bull WHO 68, 761-768.

Bouwman H, Cooppan RM, Botha MJ, Becker PJ. (1991). Serum levels of DDT and liver function of malaria control personnel. S Afr Med J. 79, 326-329.

Bouyer J, Hemon D. (1993). Comparison of three methods of estimating odds ratios from a job-exposure matrix in occuapational case-control studies. Am J Epid 137 : 472-481.

Brouwer DH, Brouwer EJ, Van Hemmen JJ. (1994). Estimation of long-term exposure to pesticides. Am J Ind Med. 25 : 573-588.

Brown AC, Fourie HO. (1987). Pesticidal poisoning in the Republic of South Africa. Journal of Comprehensive Health. 3(1) : 8-10.

British Medical Association (BMA) (1992). "Pesticides, chemicals and health". Edwin Arnold, Kent.

Budlender D. (1984). Agriculture and Technology: Four case studies. Carnegie Conference Paper number 23. SALDRU, UCT.

Central Statistical Services (CSS). 1991. Statistical News Release P1101 - Agricultural Survey, Central Statistical Services, Pretoria.

Charles D. (1991). California's war on pesticides. New Scientist. 129 : 43-47.

Checkoway H, Pearce N, Crawford-Brown DJ. (1989). Research methods in occupational epidemiology. Oxford University Press, Oxford.

Checkoway H, Rice CH. (1992). Time-weighted averages, peaks and other indices of exposure in occupational epidemiology. Am J Ind Med 21 : 25-33.

Citrus Fruit Board (1990). Citrus Cost Project, Citrusdal.

Copeland KT, Checkoway H, McMichael J, Holbrook RH. (1977). Bias due to misclassification in the estimation of relative risk. Am J Epi 105 : 488-495.

Council for Scientific Affairs. (1988). Cancer Risk of pesticides in agricultural workers. J Amer Med Ass 260 : 959-966

Coye MJ, Fenske R. (1988). Agricultural workers. In: "Occupational Health. Recognising and preventing work-related disease." Editor: BS Levy. Little Brown and Co, Boston.

Daures JP, Momas I, Bernon J, Gremy F. (1993). A vine-growing exposure matrix in the Herault Area of France. Int J Epidem. 22(6) Suppl 2 : S36-41.

Davies JE, Stevens ER, Staiff DC, Butler LC. (1982). Potential exposure of Apple thinners to Phosalone. Bull Environm Contam Toxicol. 29 : 592-598.

Davies WP. (1991). Seminar PM 2000: Pest Management and the Environment in the year 2000. Pesticide Outlook 2 : 42.

De Klerk M. (1983). Maize Farm Technology and Employment. South African Labour Bulletin 9(2) : 19-46.

De Klerk M. (1992). Prospects for commercial agriculture. Working Paper number 3. Growing the Cape. WESGRO, Cape Town.

Department of Agriculture. (1983). Fertiliser, Farm Feed and Stock Remedies Act. Notice R1449. Government Gazette 1 July 1983, Government Printer, Pretoria.

Department of Justice. (1988). Inquest proceedings into the death of Mr Eric Nhlapo. Inquest 5/88. Springs Magistrates Court, Springs, 1988.

Emanuel K. (1992). "Poisoned pay: Farmworkers and the South African Pesticide Industry." Group for Environmental Monitoring and The Pesticide Trust, Johannesburg.

Forget G. (1991). Pesticides and the Third World. J Tox Envir Health. 32 : 11 - 31.

Fourie HO. (1986). Toxicological consequences of pesticidal use in the Republic of South Africa. PhD Thesis. University of Cape Town, Cape Town.

Griffith JG, Duncan RC. (1985). Alkyl phosphate residue values in the urine of Florida citrus field workers compared to the National Health and Nutrition Examination Survey (HANES) sample. Bull Environm Contam Toxicol. 34, 210-215.

Gupta SK, Jani JP, Saiyed HN, Kashyap SK. (1984). Health hazards in pesticide formulators exposed to a combination of pesticides. Ind J Med Res. 79 : 666-672.

Hauser PM. (1993). The limitations of KAP studies. In: M Bulmer, DP Warwick (Eds), Social research in developing countries. pp 65-69. UCL Press, London.

Hawkins NC, Jaycock MA, Lynch J. (1992). A Rationale and Framework for establishing the quality of human exposure assessments. Am Ind Hyg Assoc J 531 : 34-41.

Heikkila P, Kauppinen T. (1992). Occupational Exposure to Carcinogens in Finland. Am J Ind Med. 21 : 467-480.

Hoar SK, Morrison AS, Cole P, Silverman DT. (1980). An Occupational and exposure linkage system for the study of occupational carcinogenesis. J Occup Med 22 : 722-725.

Hogmire HW, Weaver JE, Brooks JL. (1990). Survey for pesticides in wells associated with apple and pear orchards in West Virginia. Bull Envir Contam Toxicol. 44, 81-86.

International Programme on Chemical Safety (IPCS). (1991). The WHO Recommended Classification of Pesticide by hazard and Guidelines to Classification 1990-91. WHO, Geneva, 1991.

Kaplan JG, Kessler J, Rosenberg N, Pack D, Schaumberg HH. (1993). Sensory neuropathy associated with Dursban (chlorpyrifos) exposure. Neurology 43 : 2193-2196.

Kassier E. (1992). "Working Papers on the Economy of the Western Cape: The Agricultural Sector." Growing the Cape, Wesgro, Cape Town.

Kauppinen TP, Mutanen PO, Seitsamo JT. (1992). Magnitude of misclassification bias when using a job-exposure matrix. Scand J Work Environ Health 18 : 105-112.

Kromhout H, Heederik D, Dalderup LM, Kromhout D. (1992). Performance of two general job-exposure matrices in a study of lung cancer morbidity in the Zutphen cohort. Am J Epid 136 : 698-711.

Leslie A, Cuperus GW. (1993). "Successful Implementation of Integrated Pest Management for Agricultural Crops." Lewis/CRC Press, Florida.

Lilienfield DE, Gallo MA. (1989). 2,4-D, 2,4,5-T and 2,3,7,8-TCDD: An Overview. Epidemiologic Reviews 11 : 28-58.

Loewensen R. (1989). Epidemiological studies of the effects of agrichemicals. Paper presented to Zimbabwe Occupational Safety Council, Safety and Health at Work Conference. Zimbabwe Congress of Trade Unions, Harare.

Loewensen R, Nhachi C, Gona P, Murambiwa W. (1990). Current findings of field research on practices of use and user knowledge of pesticides in Zimbabwe. Paper presented to Research Workshop into Pesticide Safety, Zimbabwe Congress of Trade Unions, Harare.

London L. (1992a). Agrichemical Hazards in the South African farming sector. S Afr Med J. 81 : 560-564.

London L. (1992b). "Pesticide safety on farms in the Stellenbosch area." Report to the Health Department, Stellenbosch Division of the Western Cape Regional Services Council. Department of Community Health, University of Cape Town, Cape Town.

London L, Myers JE. (1993). "Agrichemical Hazards and the Work Process in Agriculture in the Western Cape." Occupational Health Research Unit Report number 1. Department of Community Health, University of Cape Town, Rondebosch, Cape Town.

London L, Ehrlich R, Rafudien S, Krige F, Vurgarellis P. (1994). Pesticide poisoning notification in the Western Cape 1987 - 1991. S Afr Med J. 84 : 269-272.

London L, Myers JE. (1994). Critical Issues in agrichemical safety in South Africa. Am J Ind Med (in press).

Maroni M, Fait A. (1993). Health Effects in man from long-term exposure to pesticides. A review of the 1975-1991 literature. Toxicology. 78 : 1-174.

Matos EL, Loria DI, Albiano N, Sobel N, de Bujan EC. (1987). Pesticides and intensive cultivation : effects on working conditions and workers' health. PAHO Bulletin 21(4) : 405-421.

Migli L, Masala G. (1991). Methods of expposure assessment for community-based studies: aspects inherent to validation of questionnaires. Appl Occup Environ Hyg 6 : 502-507.

Migli L, Settimi L, Masala G, Maiozzi P, Alberghinin Maltoni S, Seniori Costantini A, Vineis P. (1993). Pesticide Exposure Assessment: A crop exposure matrix. Int J Epidem. 22(6) Suppl 2 : S42-45.

Moses M. (1983). Pesticides. In: "Environmental and Occupational Medicine." Editor Rom WR. Little, Brown and Company, Boston.

Moses M. (1988). Field survey of pesticide-related working conditions in the US and Canada. Monograph. PAN International, San Fransisco.

Mwanthi M. (1994). Agrochemicals: Potential hazards to health. Africa Health 16 : 18-19.

Nanni O, Ricci M, Lugaresi C, Amadori D, Falcini F, Buiatti E. (1993). Iterative use of a priori exposure matrices to improve the characterisation of chemical exposures in agriculture work studies. Scan J Work Environm Health. 19 : 191-199.

Pannet B, Coggon D, Acheson ED. (1985). A job-exposure matrix for use in population based studies in England and Wales. Br J Ind Med 42 : 777-783.

Pesticides Trust. (1989). The FAO Code: Missing Ingredients. Prior Informed Consent in the International Code of Conduct on the Distribution and Use of Pesticides. Final Report October 1989. PAN International and Pesticides Trust, London.

Richter ED, Rosenvald Z, Kaspi L, Gruener N. (1986). Sequential cholinesterase tests and symptoms for monitoring organophosphate absorption in field workers and persons exposed to pesticide spray drift. Toxicology Letters 33 : 25-35.

Richter ED, Chuwers P, Levy Y, Gordon M, Grauer F, Marzouk J, Lvey S, Barron S, Gruener N. (1992). Health effects from exposure to organophosphate pesticides in workers and residents in Israel. Isr J Med Sci 28 : 584-597.

Rothman KJ. (1986). Modern Epidemiology. Little Brown and Company, Boston.

Seixas NS, Robins TG, Becker M. (1993). A novel approach to the characterisation of cumulative exposure for the study of chronic occupational disease. Am J Epi. 137 : 463-471.

Sitas A, Thompson ML. (1993). A role for ecological studies in the developing world. S Afr Med J 83 : 753-756.

Smith TJ. (1992). Occupational exposure and dose over time: Limitations of cumulative expsoure. Am J Ind Med 21 : 35-51.

Vermeulen JB, Sweet S, Krause M, et al. (1990). A Guide to the Use of Pesticides and Fungicides in the Republic of South Africa. Plant Protection Institute, Department of Agriculture, Pretoria, 1990.

Vermeulen JB, Greyling J. (1990b). A guide to the use of plant growth regulants, defoliants and dessicants in South Africa. Plant Protection Research Institute, Department of Agricultural Development, Pretoria, 1990.

Vermeulen JB, Greyling J, Grobler H. (1991). A guide to the use of herbicides in South Africa. Plant Protection Research Institute, Department of Agricultural Development, Pretoria, 1991.

Weaver JMC. (1993). "A Preliminary Survey of Pesticide Levels in Groundwater from a selected area on intensive agriculture in the Western Cape." Report to the Water Research Commission by the Division of Water Technology, CSIR. Water Research Commission Report 268/1/93. Pretoria.

Wicker GW, Guthrie FE. (1980). Worker-crop contact analysis as a means of evaluating re-rentry hazards. Bull Environm Contam Toxicol. 24 : 161-167.

Wooldridge J, Botha JH. (1991). Observations on orchard floor management practices: Implications for integrated pest management. Deciduous Fruit Grower 41, 296-298.

World Health Organisation (WHO). (1990). Public Health Impact of Pesticides used in Agriculture. WHO, Geneva.

CHAPTER 4

A REVIEW OF THE HEALTH EFFECTS OF AGRICHEMICALS

CONTENTS **Page**

CHAPTER 4
A REVIEW OF THE HEALTH EFFECTS OF AGRICHEMICALS

4.1 Introduction

Most chemicals developed to control pests in agriculture have unwanted effects on humans (Berry, 1988; Minton and Murray, 1988; Igbedioh, 1991; Wall, 1993). Indeed, the history of the development of the organophosphorus insecticides is closely interwoven with the development of highly toxic agents for chemical warfare during the Second World War (Minton and Murray, 1988). While the mode of chemical action of differing pesticides may help to explain the health hazard posed to humans (Igbedioh, 1991), it is known that there are no generic effects specific to different classes of pesticides (Wall, 1993) and that chemicals with differing methods of action may yet pose similar health problems (Berry, 1988). As a result, the spectrum of illness attributable to agrichemicals varies widely depending on the responsible agent and may include acute, sub-acute and chronic effects. Table 4.1 summarises these categories of health effects and lists specific syndromes attributable to particular pesticides.

Acute cholinesterase inhibition by organophosphates and carbamates has been well documented as a clinical entity, causing dizziness, blurring of vision, increased secretions and ultimately muscle paralysis and respiratory failure (Minton and Murray, 1988; Lotti, 1991). Other known acute outcomes include central nervous system intoxication by organochlorines (WHO, 1979; WHO, 1982) and methyl bromide (Bishop, 1992; Hustinx et al, 1993) and changes in nerve excitability following pyrethroid exposure (He et al, 1991). These acute neurotoxic outcomes are discussed in more detail below. Less common acute outcomes associated with pesticide exposure include reports of acute pancreatitis after organophosphate (OP) exposure (Marsh et al, 1988) and acute psychosis following exposure to an organophosphate (Conyers and Goldsmith, 1971).

Table 4.1 - Health effects due to agrichemicals

Local Effects (skin, respiratory tract and conjunctiva)

- local irritation : contact dermatitis
  conjunctivitis
  cough

Systemic Effects

a) Acute effects :

- Cholinesterase inhibition (Organophosphate, carbamates)
- Pulmonary oedema (MeBr)
- Metabolic effects (chlorophenols)

b) Subacute effects :

- Central Nervous System stimulation (organochlorines)
- Chloracne (TCDD)
- Porphyria (HCB)
- Contact allergic dermatitis

c) Chronic effects :

- Reproductive effects (DBCP)
- Carcinogenesis (Arsenicals)
- Immunotoxicity
- Neurotoxicity
- Respiratory
- Hepatotoxicity

{Source: London, 1992}

Amongst sub-acute outcomes, dermatitis may be caused by a wide range of pesticides including paraquat (Bernadini, 1986b; Hoffer and Taitelman, 1989; World Health Organisation, 1984), organophosphates (Sharma and Kaur, 1990; Hogan and Lane, 1986), carbamates (Sharma and Kaur, 1990), arsenicals (Bernadini, 1986a), chlorphenoxy herbicides (Sharma and Kaur, 1990), dithiocarbamates (Hogan and Lane, 1986; Sharma and Kaur, 1990; Lisi et al, 1986) and methyl bromide (Hogan and Lane, 1986). Dioxin and the chlorphenoxy herbicides are also associated with the development of chloracne and porphyria cutanea tarda amongst exposed humans (Lilienfied and Gallo, 1989). The systemic toxicity of paraquat has been well described (WHO, 1984; Bernadini, 1986b).

Of possible long-term effects, the teratogenic and carcinogenic potential of pesticides has aroused the most controversy (Newsday, 1981; O' Brien, 1985). Dichlorobromopropane (DCBP) has been shown to have reproductive effects in humans (Whorton et al, 1977) and, in an extensive review of the recent literature on human health effects of pesticides, DBCP and Ethylene Dibromide (EDB) have been identified as causing sperm abnormalities amongst exposed male workers (Maroni and Fait, 1993). TCDD, a contaminant of phenoxyaliphatic herbicides and present in the defoliant "Agent Orange" used extensively in the Vietnam conflict, has been shown to cross the human placenta and to be teratogenic in laboratory animals (Sterling and Arundel 1986; Burg, 1988; Peterson et al, 1993). However, epidemiological studies in humans accidentally contaminated with TCDD have shown inconclusive results (Lilienfield and Gallo, 1989). Of many pesticides suspected of having teratogenic effects based on laboratory animal experiments, further epidemiological evidence is needed to clarify the teratogenic and reproductive potential of these agents (Maroni and Fait, 1993).

A range of pesticides including some organophosphates, dioxins, ethylene dibromide, hexazachlorobenzene and ethylene thiourea have been shown to demonstrate carcinogenic or mutagenic potential in laboratory experiments (Moses, 1983; Sterling and Arundel, 1986; WHO, 1982; Xu, 1987; Council on Scientific Affairs, 1988) but evidence for carcinogenesis amongst humans is less clear-cut. Table 4.2 summarises some of the findings of major studies investigating the question of pesticide carcinogenesis over the past 20 years (Council on Scientific Affairs, 1988). Currently the Environmental Protection Agency (EPA) classifies arsenical pesticides and vinyl chloride as definite carcinogens and a further 13 agents as probable or possible carcinogens, including amitrole, chlorophenols, ethylene dibromide (EDB), phenoxy acids and TCDD (Council on Scientific Affairs, 1988).

Amongst other chronic health outcomes, a wide range of adverse hepatic effects have been reported following different organochlorine pesticide exposures (Moses, 1983). Kepone, an organochlorine, is recognised as a known hepatotoxin in animals and causes reversible adaptive liver changes in humans (Tolman 1983; Maroni and Fait, 1993). Chlorphenoxyacetic acid herbicides have also been implicated in hepatic injury but the epidemiologic evidence is less clearcut (Lilienfield and Gallo, 1989). Hepatic effects of arsenic and copper sulphate have also been recorded (Maroni and Fait, 1993).

Substantial laboratory evidence exists for TCDD causing suppresion of cellular and humoral immunity as well as toxicity to marrow maturation of lymphocytes and to cell lines involved in innate immune mechanisms (Holsapple et al, 1991). However, the evidence for immunological impairment among humans exposed to TCDD after environmental spillage remains inconsistent (Lilienfield and Gallo, 1989). Impaired granulocyte function has been demonstrated amongst workers manufacturing zineb (Tsvetkova et al, 1992) and functional immunosuppression and autoimmunity amongst residents of wooden homes treated with pentachlorophenol (McConnachie and Zahalsky, 1991).

Neurotoxicty of agrichemicals, both acute and chronic is becoming an increasingly important subject of research (WHO, 1986a). While toxin-induced neuropathies used to be dominated by reports of drug-induced disease, developments over the past 20 years have firmly defined occupational exposures to metals, solvents and agrichemicals, particularly OP insecticides, as potential neurotoxicants (O' Donoghue, 1983; WHO 1986a). These are discussed in detail in the following sections.

Table 4.2. Studies of Pesticides and Carcinogenicity

Author	Study Population	Association demonstrated	No association demonstrated
Sharp, et al	Agricultural workers	Brain tumours	
Wiklund et al	Pesticide applicators	Testicular cancer	
El Zayadi et al	Farmers exp to orgphos, orgchlor and arsenic	Hepatic angiosarcoma	
Saftlas et al	Herbicide, fertiliser users	Cancer rectum, eye, stomach. leukaemia	Brain tumours CNS tumours
Weissen-burger	Nebraska farmers	Leukaemia Lymphoma	
Blair	US farmers	Acute and chronic leukaemias	
Coggon et al	Herbicides workers	Soft tissue sarcomas	
Hardell et al	Exposure to herbicides	Soft tissue sarcoma Hodgkins disease Non-Hodg lymphoma	
Wiklund et al	Swedish agr, forestry workers		Soft tissue sarcoma
Pearce et al	New Zealand workers exp to herbicides		Non-Hodgkins lymphoma
Hoar et al	Kansas farmers exp to herbicides	Non-Hodgkins lymphoma	Hodgkins lymphoma Soft tissue sarcoma Colon cancer
McLaughlin et al	Swedish farmers		Renal cancer
Musicco et al	Hospital cases/controls	Brain Tumours	
Littorin et al	Swedish gardeners	Lung	Brain Melanoma

(Sources: Council for Scientific Affairs, 1990; London, 1992)

4.2 General Considerations for Neurotoxicity due to Occupational Exposures

With the rapidly growing number of xenobiotic chemicals being introduced in the workplace environment, there has been growing public concern for the hazards posed by chemicals to human health (WHO, 1986a). Tissues of the human nervous system are uniquely susceptible to toxic effects since they differ from other body organs in two important respects. Firstly, nerve cells are unable to replicate and the nervous system as a whole has a limited capacity for cellular repair (O' Donoghue, 1983; Lolin, 1989; Kyrklund, 1992), especially following damage to axons in the central nervous system (O' Donoghue, 1983). Moreover, nerve cells form a complex system responsible for the control of several vital body functions and neurotoxic damage can result in death or in severe lifelong reduction in the quality of life (Kyrklund, 1992). The nervous system is also sensitive to malfunctioning of other organ systems arising from chemical intoxication (Saxena, 1990). The potential for neurotoxicity arising from occupational exposure has therefore become a major focus for ongoing research (Iregren and Gamberale, 1990), particularly directed at the prevention of neurotoxic illness (US Congress, Office of Technology Assessment, 1990; Becking et al, 1993; Landrigan et al, 1993).

Because of anatomical, physiological, pharmacological and biochemical specialisation of neurons, neurotoxins may affect selective groups of neurons disproportionately, with the result that neurotoxins can appear to have highly specific effects. For example, dimethylaminoproprionitrile acts on small myelinated and unmyelinated fibres resulting in autonomic dysfunction in affected humans. However, in most cases, such neurotoxins have toxic effects on other neural cells but to a lesser degree (O' Donoghue, 1983). Transport across the blood-brain barrier is also responsible for determining selective toxicity of chemicals (WHO, 1986a). Certain anatomical areas, such as the dorsal root ganglia and the area postrema, are not protected by the blood-brain barrier and are thus reached by chemical toxins that would usually be unable to cross the blood-brain barrier (eg: doxorubicin) (O' Donoghue, 1983).

Neuronal injury due to toxins is usually associated with axonal damage (Kyrklund, 1992; O' Donoghue, 1983) in both the central and peripheral nervous system. Axons are particularly vulnerable because of their length and their dependence on the cell body for nutrition. The primary pathology is thought to be located in the nerve cell body and results in interference with transport of metabolic nutrients along the length of the axon. The most distal regions of the largest and longest axons become poorly nourished and degenerate, with the result that the nerve fibres deteriorate proximally toward the cell of origin. This process is frequently referred to as a "dying-back" neuropathy and has been demonstrated in post mortem studies on patients dying of paraquat poisoning (Grcevic et al, 1977) and in animal studies with OPs (Lotti, 1992). Secondary degeneration of myelin surrounding the large nerve fibres usually accompanies the axonal damage and primary toxic effects on the myelin sheath are extremely uncommon (O' Donoghue, 1983).

Clinical manifestations of peripheral nerve damage usually present as a gradual onset of a symmetrical sensorimotor polyneuropathy. Autonomic manifestations are generally uncommon except in the case of aminoproprionitrile neurotoxicity. This general description applies well to organophosphates responsible for delayed onset peripheral neuropathy (Professor Marcello Lotti, personal communication, 1993; Maroni and Fait, 1993).

Evidence from studies amongst workers exposed to hexacarbons and to acrylamide have shown that axonal damage affects both peripheral nerves and the central nervous system simultaneously (O' Donoghue, 1983; Schaumberg and Spencer, 1976). These effects may manifest as overt clinical signs (eg: ataxia, spasticity) but more frequently take the form of changes in CNS function, detectable rather through neuropsychological and behavioural assessment. While neurotoxic studies have traditionally identified histological or pathological (tissue damage) end-points, it is increasingly being realised that disorders of function of the nervous system are a more sensitive end-point for the assessment of chemical neurotoxicity (WHO, 1986a; Iregren and Gamberale, 1990), since they integrate the effect of toxins on multiple sites and on multiple organs systems whose functional disturbances impact on the nervous system. Neurotoxicity has therefore a continuum of symptoms and effects, which may depend on the type of chemical, the dose and duration of exposure.

Measurement of behavoural neurotoxicity is therefore playing an increasingly important role in risk assessment and standard setting (Weiss, 1990; Spencer, 1990; Iregren and Gamberale, 1990; Landrigan et al, 1993, Becking et al, 1993). In particular, the development of quantitative test measures capable of detecting early subclinical signs of chemical-induced neurotoxicity following low dose exposures has become an important component of modern occupational toxicology (Spencer, 1990; Iregren and Gamberale, 1990; Buffler, 1990; Landrigan et al, 1993, Becking et al, 1993). Chapter 5 deals further with the literature concerning availability and appropriateness of various methods for neurobehavioural assessment.

That acute and chronic exposures may result in substantially different pathophysiological outcomes (Kyrklund, 1992), is well illustrated in the case of organophosphate insecticides. Neurotoxicty in acute intoxication is due to inhibition of acetylcholinesterase in the nervous system, while chronic neuropathy due to organophosphates is associated with inhibition of an entirely different esterase (Neuropathy Target Esterase - NTE), and the pathogenetic mechanisms in the two presentations are entirely different. These considerations have led to a growing emphasis on the need for accurate characterisation of human chemical exposures in studies of occupational (Iregren and Gamberale, 1990; Blair and Zahm, 1990) and environmental toxicity (Landrigan et al, 1993) and to take into account the impact of multiple potential toxins (Spencer, 1990; Iregren and Gamberale, 1990).

A recent advance in approaching the assessment of neurotoxic risk of specific chemicals has been the devlopment of a set of criteria for evaluating the strength of evidence from published reports (Simonsen et al, 1994), akin to the system used by the International Agency for Research against Cancer (IARC) for evaulating chemical cancer risks (Council on Scientific Affairs, 1988). In this approach, effects reported as being due to chemical exposure are rated according to the strength of the type of effect under review. Reversible, subjective symptoms are listed as the weakest, while neurological or morphological changes are regarded as the strongest on a continuum of effects. In conjunction with an assessment of the quality of the study methods, these criteria are applied in a step-wise fashion: 1) to data from single studies individually; then, 2) to data from all animal and all human studies pertaining to that chemical; 3), then to evaluating all studies together; 4), lastly to the evaluation of the potency of neurotoxic effects.

The first three steps enable the classification of the chemical into categories of neurotoxicity comparable to that used by IARC for carcinogenicity. While this approach is targeted at the quantification of risk associated with specific chemicals, the tools it uses appear to be a useful framework for assessing the literature on OP neurotoxicity to date, and will be incorporated in the discussion that follows.

4.3 Neurotoxic Effects of Agrichemical Exposures

Many widely used agrichemicals exert their insecticidal effects on the invertebrate nervous system (Igbedioh, 1991; Berry, 1988). Some of these mechanisms are operative in higher mammals, and are the basis for some, but not all, of the findings demonstrating neurotoxicity in humans (Vijverberg and van den Bercken, 1990). Neurotoxic outcomes include acute, sub-acute and chronic effects and are elaborated upon further below.

Most studies of neurotoxic outcomes associated with agrichemicals have been carried out in the setting of acute exposures to agrichemicals such as occurs following para-suicide attempts or workplace accidents (Table 4.3). These studies may represent only the tip of an iceberg of widespread chronic morbidity amongst workers exposed to agrichemicals. Moreover, the possibility of chronic morbidity arising from low-dose exposures (i.e. in the absence of identifiable acute intoxication) has received scant attention until the past few years (Rosenstock et al, 1990). For this reason, the discussion on the literature on agrichemical neurotoxicity pays close attention to distinguishing peripheral from central nervous system effects, and to identifying the nature of the exposure examined.

Evidence for the possible neurotoxicity of agrichemicals that follows is therefore presented in terms of the nature of exposure (acute or chronic) and the nature of outcome (acute, sub-acute or chronic) and studies dealing with non-acute effects are summarised in Table 4.3. In the table, use is made of a rating of the strength of evidence for neurotoxicity as outlined earlier (Simonsen et al, 1994). The rest of this chapter goes on to review acute agrichemical neurotoxicity followed by relevant experimental and autopsy data before epidemiological evidence for chronic neurotoxicity in humans is considered.

Table 4.3 - Non-acute neurotoxic effects in humans from organophosphate exposures: A summary of the literature.

Sample, type of exposure and quality rating #	Effect recorded	Reference
I. ACUTE EXPOSURES		
1 farm worker occupationally poisoned (I)	Acute psychosis	Conyers, 1971
1 crop duster handling OPs 5 years prior to diagnosis (I)	Parkinson's disease	Davies, 1978
1 case parasuicidal ingestion (S)	Clinical and electrophysiological evidence of peripheral neuropathy	Hierons, 1978
77 plant workers with history of poisoning more than 1 year previously 38 unexposed controls (L)	EEG changes	Duffy, 1979
13 parasuicidal ingestion 1 occupational poisoning 30 healthy controls (S)	Clinical, EMG and nerve conduction changes	Vasilescu, 1980
4 cases accidental ingestion (S)	Clinical, electrophysiological and biopsy findings of a "dying-back" neuropathy	Vasilescu, 1984
1 parasuicide with an OP (S)	Clinical, electrophysiological and biopsy findings of a "dying-back" neuropathy	Lotti, 1986
100 cases from statutory poisoning reports 100 matched controls (L)	Increased risk of poor intellectual and cognitive functioning. Personality effects.	Savage, 1988
36 cases discharged from hospital for OP poisoning (L) 36 matched controls	Decreased performance on WHO and other neuropsych tests	Rosenstock, 1991
(S)	Elevated vibrotactile thresholds	McConnell, 1994
128 cases notified for OP poisoning in California (L) 90 unmatched controls	Decreased performance on 2 WHO NCTB tests Trend effects Elevated vibrotactile thresholds	Steenland, 1994
8 people contaminated after domestic chlorpyrifos application (L)	Sensory neuropathy, memory loss and cognitive slowing	Kaplan, 1993

Table 4.3 - (Continued) Non-acute neurotoxic effects in humans from organophosphate exposures: A summary of the literature.

Sample, type of exposure and quality rating #	Effect recorded	Reference
I. ACUTE EXPOSURES (Continued)		
1 person contaminated after workplace spray application of phosphothorothiate (I)	Decreased cerebral blood flow, parasthesia, hemiballismus	Callender, 1994
II. SHORT-TERM BUT LOW-LEVEL EXPOSURES		
13 applicators and 11 farmers exposed in past 2 weeks (I)	Increased anxiety	Levin, 1976
9 workers involved in aerial application (L)	No detectable changes in electrophys tests despite drop in NTE	Lotti, 1983
46 pest-control workers (N) 53 non-exposed supervisors	No changes in neuro-psychological performance	Maizlish, 1987
146 kibbutz and city applicators (I)	Psychiatric disturbances associated with exposure in past month	Ilianis, 1988
39 kibbutz workers 51 kibbutz residents (L)	Reversible neuropsych changes across spraying season	Richter,1992
III. LONG-TERM LOW-LEVEL EXPOSURES		
Unspecified number of insecticide factory workers (I)	Increased serum neurotransmittors Raised BP, Bl sugar	Berberian, 1987
24 sprayers of an OP 19 controls (I)	Nerve conduction abnormalities	Misra, 1988
229 workers at pesticide plant 180 fertiliser plant workers, 167 textile workers as controls at routine medicals (I)	Decreased NTE levels Increased tremor No neuropsych effects	Otto, 1990
49 pesticide applicators 49 matched controls (L)	No neuropsych effects	Daniell, 1992

Rating using "strength-of-the-evidence" criteria (Simonsen et al, 1994):

S - Sufficient Evidence: Well performed, high quality studies describing morphological, pathological, physiological, behavioural or specific biochemical (NTE) changes.

L - Limited evidence: Well performed, high quality studies describing effects embracing symptoms or biochemical effects (excl NTE), or less well performed studies describing morphological, pathological, physiological, behavioural or specific biochemical (NTE) changes.

I - Inadequate evidence: Poor quality studies, or studies with little relevance.

N - Negative evidence: Well-performed studies showing no effects (at any level).

4.3.1 Acute neurotoxic effects

4.3.1.1 Organophosphate and carbamate poisoning.

The syndrome of acute organophosphate (OP) intoxication is perhaps the most familiar to clinicians and has been well described (WHO, 1986b; Minton and Murray, 1988; Lotti 1991; Lotti, 1992). Organophosphates exert their toxicity by phosphorylating the enzyme acetylcholinesterase, which is found in the central nervous system and at nicotinic and muscarinic nerve junctions in the peripheral nervous system (WHO, 1986b; Lotti, 1992). The enzyme is responsible for breaking down the neurotransmitter chemical acetylcholine at the synaptic end-plate and maintaining a physiological balance in neurotransmitters at the nerve junction. Once the OP is bound, the enzyme is inactivated, with the result that a pathological accumulation of acetylcholine occurs at susceptible receptors. Depending on the type of nerve junction, this over-accumulation of neurotransmitter results in toxic muscarinic, nicotinic and central nervous system effects and may differ at different sites in the nervous system depending on access of the inhibiting OP (Lotti, 1992).

Clinical manifestations of poisoning generally present within hours of exposure (Minton and Murray, 1988), though this may be delayed up to 5 days (Lotti, 1992). In circumstances where poisoning occurs through dermal absorption following contamination of overalls, there may be a considerable time delay between initial exposure and absorption, resulting in an apparent delay in symptoms (Clifford and Nies, 1989). Phosphorothioates (such as chlorpyrifos) require activation by liver metabolism before manifesting toxicity, and therefore tend to have a slower onset of toxicity than other types of organophosphates. Furthermore, because they are fat-soluble, it is possible for a secondary episode of clinical symptoms to appear days or weeks later if the OP is mobilised from body adipose stores (Davies et al, 1975; Minton and Murray, 1988). Chronic exposure to organophophates leads to an asymptomatic sub-clinical lowering of cholinesterase functioning (tolerance) (Lotti, 1992) and may render the subject particularly sensitive to further small exposures (Coye et al, 1987).

Cholinesterase poisoning due to certain organphosphates may be reversible in the early stages of intoxication (Minton and Murray, 1988; Lotti, 1992). After phosphorylation by the pesticide, the enzyme complex can undergo spontaneous reactivation at a rate that varies according to the species, tissue and nature of the chemical group involved in the reaction (Minton and Murray, 1988; Lotti, 1992). The administration of exogenous oximes which are able to promote reactivation of the enzyme forms the basis for aspects of early treatment of acute poisoning (Minton and Murray, 1988; Lotti, 1991). However, once the enzyme complex undergoes de-alkylation, a change in configuration of the enzyme occurs (referred to as "ageing") and the complex is not amenable to reactivation. Recovery from clinical symptoms depends on regeneration of fresh acetylcholinesterase at the nerve end-plate. The propensity for ageing varies widely between different types of OPs (Lotti, 1992).

Carbamate pesticides exert a similar effect on acetylcholinesterase with the important difference that the bond between the pesticide and the enzyme does not "age" and remains reversible (WHO, 1986c; Lotti, 1992). For this reason, clinical symptoms of carbamate poisoning, which are similar to the acute effects of organophosphates, tend to recover rapidly.

4.3.1.2 Neurotoxicity of pyrethroid insecticides

Pyrethroids are naturally occurring insecticides that are derived from pyrethrum flowers and have long been used in traditional agriculture for their pesticidal properties. Today synthetic pyrethroids of much greater insecticidal efficacy and higher potency are widely in use, particularly in China. Pyrethroids are known to be neurotoxic to mammals and their mode of action is thought to be due to interference with sodium permeability in the nerve cell membrane, resulting in repetitive nerve activity. Clinically, these effects manifest as tremor, hypersalivation, choreo-athetoid movements and seizures (Aldridge, 1980; Vijverberg and van der Bercken, 1982).

The significance of animal toxicity data for human hazard assessment is not clear. Generally, the pyrethroids were thought to be relatively safe for human health (Aldridge, 1990) but a growing number of reports have identified synthetic pyrethroids as responsible for neurotoxicity amongst exposed workers. Acute poisoning by pyrethroids has been manifested by transient cutaneous facial parasthesias, headache, weakness and muscle fasciculation in mild cases to seizures and loss of consciousness in severe cases (Aldridge, 1990; He et al, 1989). A study of 24 adult males involved in deltamethrin application found short-term changes in nerve excitability occuring two days after stopping a 72-hour period of deltamethrin application (He et al, 1991). However, nerve conduction changes that persist into chronic morbidty have not been reported with pyrethroids to date and current consensus suggests that, at doses commonly encountered in usual working practice, these functional neurophysiological changes are unlikely to progress to irreversible neurotoxic lesions (Aldridge, 1990; Maroni and Fait, 1993).

4.3.1.3 Neurotoxicity associated with other pesticides

Organochlorines include a wide range of chemicals and are all generally thought to have neurotoxic potential (Johnson et al, 1987). Acute exposures to DDT cause paraesthesias, irritability, vertigo, ataxia, tremor, seizures and coma, depending on the dose of exposure (Moses, 1983). Seizures are also noted to be a manifestation of acute exposure to high doses of dieldrin (Weiss, 1990) and endrin (CDC, 1984). The mechanism for this is thought to arise from disruption of sodium and potassium transport across axonal membranes, affecting nerve transmission (Johnson et al, 1987).

Other pesticides with acute neurotoxic effects following acute exposures include methyl bromide (Hustinx et al, 1993) and organic tin compounds (WHO, 1980; Johnson et al, 1987).

4.3.2. Chronic neurotoxic effects arising from acute exposures to organophosphates.

4.3.2.1 Peripheral neurotoxicity following acute exposures

The presence of a syndrome of post acute OP induced delayed neuropathy (OPIDN) has been well documented in a series of reports (Hierons and Johnson, 1978; Senanyake and Johnson, 1982; Vasilescu et al, 1984). OPIDN is a symmetrical distal sensorimotor polyneuropathy developing after exposure to certain categories of organophosphates (Lotti, 1992). It usually occurs in the setting of massive exposure, frequently that of self-inflicted ingestion, and is almost always preceded by an acute phase in which clinical or biochemical evidence of cholinergic poisoning are present (Lotti, 1992). OPIDN usually presents within 2 to 5 weeks after recovery from the acute phase of cholinergic poisoning as a sudden onset of cramping muscle pain and progressive weakness (Maroni and Fait, 1993) affecting predominantly the lower limbs and, in more severe cases, the upper limbs (Lotti, 1992). The pathology involved is distal axonopathy with progressive proximal nerve degeneration, a feature typical of most toxic neuropathies (Kyrklund, 1992; O' Donoghue, 1983). Recovery from OPIDN may be incomplete and may take up to a year or longer (Maroni and Fait, 1993; Lotti 1992). Table 4.4 lists organophosphates currently identified as having potential to cause OPIDN in animals and in humans (Lotti, 1992; WHO, 1986a).

Table 4.4 - Organophosphates identified as having potential to cause OPIDN.

OPIDN in Hens	OPIDN in humans
Mipafox	Mipafox
Haloxon	Leptophos
EPN	Methamidophos
Trichlormnat	Trichlorphon
Leptophos	Trichlonat
Desbromoleptophos	EPN
DEF	Chlorpyrifos
Cyanofenphos	Dichlorvos
Ethyl 2,4,5-trichlorophenyl phenylphosphonate	Omethoate
Ethyl 2,4-dichlorophenyl phenylphosphonate	Parathion
Isofenphos	TOCP
Dichlorvos	
Amiprophos	
Coumaphos	
Chlorpyrifos	
Salithion	
O-n-propyl phenylphosphonate	
Methamidophos	
Primiphos-methyl	
Sarin	

(Source: WHO, 1986b; Lotti, 1992)

In OPIDN, a different enzyme to that targeted in acute intoxication has been identified as the site of action for the development of chronic effects - the enzyme, previously known as Neurotoxic Esterase is now referred to as Neuropathy Target Esterase (NTE) (Lotti, 1992). NTE is present in the human central nervous system, as well as in peripheral lymphocytes and platelets (Bertoncin et al, 1985; Lotti, 1992). Inhibition of NTE has been shown to be associated with the development of OPIDN in experimental chickens (Gordon et al, 1983; Lotti and Johnson, 1978) and has been identified as a predictor of OPIDN in humans acutely exposed to high doses of certain organophosphates (Lotti and Johnson, 1978; Lotti et al, 1986; Lotti et al, 1983). Testing of various organophosphates for their ability to induce OPIDN in hens has formed the basis of the protocol for assessing the neurotoxic potential of existing and new OP insecticides (Lotti and Johnson, 1978; WHO, 1986a).

The exact mechanism by which NTE is related to OPIDN is still unclear (Lotti et al, 1993). Phosphorylation of the esterase at its active site, resulting in enzyme inhibition, may be followed by spontaneous restoration of the catalytic site, the speed of which differentiates between substrates and inhibitors (Lotti, 1992). However, an alternative reaction may occur involving an intramolecular rearrangement of the enzyme, resulting in irreversible inhibition called "ageing". The propensity of inihibited NTE to undergo aging has been thought to be related to the likelihood of developing OPIDN (Lotti 1992).

A number of phosphinates, carbamates and other agents may cause either promotion of, or protection from, OPIDN in experimental animals, depending on the dose of the promoting/protecting agent and on the sequence in which the promoting/protecting agent is presented (Lotti, 1992). This suggests that competition for binding sites is important in the biochemical mechanisms for OPIDN. In general, OPs with low cholinesterase inhibiting potentials have been shown to have greater propensity to induce OPIDN than those OPs with high cholinesterase inhibiting potential. The latter cholinesterases are able to inhibit both cholinesterase and NTE, while, at the same time, do not induce ageing of the NTE enzyme complex, thereby protecting from OPIDN (Lotti, 1992).

It has also been suggested that treatment with atropine or pralidoxime in the acute hospitalised phase may also play a role in potentiating the neuropathic potential of OPIDN-inducing OPs (Davies, 1987), perhaps by increasing permeability of the blood brain barrier to neuropathic chemicals (Lotti, 1992). However, more recent work suggests that all OP compounds have the ability to produce OPIDN, independent of their ability to induce aging of the complex (Lotti et al, 1993), and the authors suggest an analogy to pharmacological concepts of agonism, partial agonism and antagonism.

Considerable research is still required to elaborate the exact mechanism of this disorder. The diagnosis of OPIDN remains essentially a clinical one, and, while NTE may be a useful predictor in the acute or sub-acute stage of the probability of chronic neuropathy (Lotti, 1986), no markers for chronic morbidity due to OPs are presently available. Moreover, the importance of chemical interactions in the pathogenesis of OPIDN makes it critically relevant to characterise exposures as accurately as possible in epidemiological investigations of potential chronic health effects due to OP exposures in humans.

In addition to OPIDN, an intermediate neurotoxic syndrome was described in Sri Lanka in a case series of 10 adults of whom 9 presented following para-suicide attempts using organophosphates (Senanyake and Johnson, 1982). In this series, proximal muscle weakness developed within 24 to 96 hours of acute poisoning, was uninfluenced by atropine administration and recovered by 3 weeks. The organophosphates implicated differed from those previously reported in OPIDN, electromyographic findings were dissimilar to those in OPIDN and the syndrome developed in the absence of cholinesterase inhibition. The researchers postulated a combination of central, peripheral and neuromuscular sites of action as the mechanism for the syndrome. However, this remains an isolated finding that has not been reported elsewhere in the literature.

A more recent study of long-term peripheral nervous system effects found increased vibrotactile thresholds among 36 workers previously poisoned by organophosphates compared to an age- and gender-matched control group and the authors suggested that OPIDP represents the extreme end of a continuum of neurotoxic impairment, both central and peripheral, following acute OP exposure (McConnell et al, 1994). Similar findings of decreased vibrotactile sensation in the absence of nerve conduction abnormalities were made in a California study of 128 workers previously poisoned by organophosphates (Steenland et al, 1994). These findings have considerable public health importance, and appear to be consistent across a number of studies for both central and peripheral nervous system effects.

4.3.2.2 Central nervous system toxicity following acute exposures

Some evidence for the potential of agrichemical exposures to cause chronic central nervous system toxicity may be found in animal experiments. Gralewicz et al (1990) found that rabbits exposed to the organophosphate chlorphenvos experienced EEG changes in the absence of depression in plasma and red blood cell cholinesterase. On sectioning a similar group of exposed animals after their serum and red blood cell cholinesterase had returned to within 90% of their baseline levels, cholinesterase levels in the central nervous system were found to be significantly lower than those of a control group, and the authors argued that functional changes in the brain following acute poisoning may outlast blood cholinesterase depression. This hypothesis is supported by the report of prolonged electro-encephalogram (EEG) changes in monkeys exposed to the OP sarin (Burchfiel et al, 1976) and findings of long-term EEG abnormalities amongst 77 workers tested at least 1 year after an acute poisoning with organophosphates when compared to controls (Duffy et al, 1979). A more recent case report noted the presence of decreased cerebral blood flow on SPECT brain imaging in a patient with tremor, hemiballismus, and parasthaesias following acute OP poisoning (Callender et al, 1994).

More rigourous case-control studies amongst survivors of acute poisoning with pesticides have demonstrated an association between the presence of chronic neuropsychological effects and acute intoxication. A matched case control study of 100 subjects with documented past OP poisoning (average of 7 to 11 years previously) were found to have poorer performance on tests of intellectual functioning, academic skills, abstraction, flexibility of thinking and simple motor skills (Savage et al, 1988). A similar comparison of 36 Nicaraguan men who were previously poisoned with OPs to matched controls found significantly impaired performance on 5 out of 6 subtests of the World Health Organisation Neurobehavioural Core Test Battery and 2 out of a further 6 additional neurobehavioural tests

(Rosenstock et al, 1991). More recently, a case control study of 128 men notified for acute OP poisoning in California compared to 90 controls, showed similar adverse long-term central nervous system effects (Steenland et al, 1994). All three studies strongly suggest that chronic neurological sequaelae may arise from acute OP poisoning and confirm the value of neurobehavioural tests as an approprate method to detect subclinical neurotoxicity in this setting. In terms of an assessment of the "strength-of-the-evidence" approach (Simonsen et al, 1994), there appears sufficient evidence for the presence of long-term neurobehavioural effects following acute exposures.

4.3.3 Neurotoxic effects arising in the abscence of acute intoxication

While the above studies have focussed on chronic outcomes arising from acute poisoning, less attention has been paid to the possibility of adverse outcomes arising from low-dose exposure (i.e. in the abscence of clinical or biochemical intoxication). The paucity of such studies have partly arisen from the methodological and logistic difficulties inherent in addressing this hypothesis. The results of the few studies that have been performed in this area are discussed below.

Four studies of low-dose exposures have investigated the impact of short-term exposures on central nervous system outcomes. Psychiatric manifestations arising from low-dose OP exposures using personality tests and structured interviews were evaluated in 13 commercial applicators and 11 farmers with exposure to an OP in the 2 weeks prior to examination (Levin et al, 1976). The researchers found elevated anxiety levels amongst the commercial applicators associated with a moderate decrease in plasma cholinesterase levels that still fell within "normal limits". Similar results in the absence of plasma cholinesterase depression were reported amongst 146 nurse-selected kibbutz and city pesticide applicators in Israel for psychiatric inventory scores (Ilianis et al, 1988). A study of kibbutz workers and residents (n=90) exposed to spray drift found significant changes across a season for a range of neurobehavioural tests drawn from the WHO battery (Richter et al, 1992). These changes, however, disappeared at the end of the season, and were not measured twice in the control group, limiting the validity of the findings. A comparable study of pest control operators in California, using a standard neurobehavioural battery, found no evidence of dose-related behavioural effects when evaluating exposed subjects across a shift compared to non-exposed supervisory workers (Maizlish et al, 1987). The authors identified industrial hygiene measures such as personal protective equipment and direct worker supervision as contributing to low levels of exposure.

However, while psychiatric and neurobehavioural changes following short-term exposures may be useful in investigating the possible mechanisms for the development of chronic outcomes, only a few studies are available addressing the relationship of these outcomes to long-term low-dose exposure, particularly in relation to the role of specific chemical agents.

A study at an OP manufacturing plant in Egypt found decreased tactile sensistivity amongst 229 chronically exposed workers compared to controls in a fertiliser and a textile factory (Otto et al, 1990). This increase in tactile threshold was found to be related to percent inhibition of lymphocytic NTE and suggested a relationship between chronic exposure and long-term neurological effects. A second study found evidence of nerve conduction velocity abnormalities amongst 24 men involved in regular application of the OP fenthion who did not show any clinical signs of neuropathy (Misra et al, 1988). However, in neither study was any information provided on previous acute morbidity, and chronic exposure in the absence of acute intoxication appears to have been assumed from the job activities of the subjects. Moreover, method of subject selection in both studies was not specified and neither study attempted to quantify exposure beyond a dichotomous exposed versus unexposed variable using external control subjects.

Central nervous system outcomes of chronic OP exposures were also evaluated in the study of pesticide factory workers (Otto et al, 1990). These failed to show significant differences on Santa Anna dexterity test and on the Block Design subtest of the Wechsler Adult Intelligence Scale (WAIS) when adjusted for age and education but inadequate study design makes interpretation of these results difficult.

A more recent study of 49 pesticide applicators with low, intermittent and well-controlled exposure to pesticides in Washington State found no clear evidence of clinically significant decrements in standard neuropsychological test performances compared to a control group of abbatoir workers when adjusted for age, education, language preference and cross-seasonal changes (Daniell et al, 1992). This study was important in that it sought to adjust for possible acute effects of seasonal spray application by measuring workers across season. It also flagged workers with a past history of acute pesticide intoxication in order to separate effects due to long-term low-dose exposures from those arising from past acute poisoning. Despite the presence of these methodological strengths, the study failed to demonstrate any adverse effects from long-term low-dose exposures, partly because of the small numbers of subjects involved.

An overall assessment of the literature (Table 4.3), shows that evidence for chronic effects arising from low-dose long-term OP exposure is presently inadequate, or at best, limited. This contrasts with the situation for chronic effects following acute exposures, where the evidence is stronger. The studies on the potential for OPs to cause long-lasting neurological and neurobehavioural effects therefore remain inconclusive and further investigations with accurate exposure estimates and standardised outcome assessments have been recommended (Maroni et al, 1986; Maroni and Fait, 1993).

Other chronic neurotoxic outcomes arising from long-term pesticide exposure have also been investigated. Neuroendocrine abnormalities were assessed amongst workers at a plant manufacturing organochlorine, organophosphate and carbamate pesticides in Egypt (Berberian and Enan, 1987) and lowered plasma cholinesterase was found amongst chronically exposed workers in association with a raised serum adrenaline level, lowered monoamine oxidase activity, raised blood pressure and raised blood sugar. The authors suggested that these changes may result in neurobehavioural effects seen with agrichemical exposures, but no other studies of similar investigations have been reported to date and the outcomes of this study remain an isolated finding.

The relationship between Parkinson's disease (PD) and agrichemical exposure, particularly paraquat, has been investigated in a number of studies. These include a case report of a crop duster who developed PD after repeated episodic exposures to organophosphates (Davis et al, 1978), ecological studies showing correlations between herbicide usage and rates of PD in geographical areas of Canada (Rajput et al, 1986; Barbeau et al, 1986), a cross-sectional analytical study in Hong Kong which found an association between PD and rural residence, farming activities and pesticide and herbicide use (Ho et al, 1989) and a population-based case-control study that found that previous herbicide use was associated with PD amongst cases and residents in rural Canada, when adjusted for age and sex. While a number of studies have suggested a link between paraquat and the development of PD, the toxicological mechanism for such a possible relationship has not been demonstrated to date.

Other agrichemicals for which associations between industrial exposure and neurobehavioural effects have been demonstrated include methyl bromide (Anger et al, 1986; Bishop, 1992) and pentachlorophenol (Triebig et al, 1981).

4.4 Biological Monitoring for Adverse Effects of Pesticides

Biological Monitoring of subjects exposed to pesticides has been widely used for the prevention of pesticide poisoning (Coye et al, 1986a; Ames et al, 1989a; Ames et al, 1989b) and for purposes of epidemiological research (Hulka and Margolin, 1992).

The validity of methods for biological monitoring has recently been critically reviewed (Woolen, 1993). However, biological monitoring has typically been applied in the setting of acute effects of agrichemical exposure usually for exposure to cholinesterase-inhibiting compounds, the organophosphates and carbamates (Peedicayil et al, 1991; Lander and Lings, 1991; Yeary et al, 1993). For the latter two groups of agrichemicals, plasma and, particularly, erythrocyte cholinesterase measurement present eminently suitable methods for biological effect monitoring of recent exposure (Coye et al, 1986a).

In contrast, chronic exposures are far more difficult to characterise (Krieger and Ross, 1993) due to the complexity of interactions between work practices, external dose and environmental factors outlined in Chapter 3. While some researchers have made use of cholinesterase measurement as an index of chronic low-dose exposures to organophosphates (Levin and Rodnitzky, 1976; Spigiel et al, 1981), these studies have not quantified chronicity or duration of exposure, nor have they investigated outcomes that could be said to be chronic sub-clinical biological effects. For this reason, doubts have been expressed as to the value of cholinesterase measurements in predicting health effects of chronic exposure to organophosphates (Coye et al, 1986a).

From a toxokinetic point of view, once aging of the enzyme-organophosphate complex has occured, re-establishment of enzyme activity is dependent on regeneration of the enzyme at its source (liver for plasma and bone marrow production for erythrocyte) (Coye et al, 1986a; Lotti, 1992). Plasma cholinesterase is said to return to normal levels within a few weeks of withdrawl from exposure, and erythrocyte cholinesterase takes approximately 60 to 120 days to recover, which is the average turnover of erythrocyte production in the marrow (Coye et al, 1986a). Accordingly, a lowered plasma cholinesterase is said to reflect recent exposure to organophosphates while a lowered erythrocyte level is said to reflect more accurately, the state of cholinesterase activity in the nervous system (Minton and Murray, 1988). Given the enzyme kinetics of these assays, it is not plausible to regard these tests as markers for chronic outcomes arising from long-term low-dose exposure.

Urine analyses for residues and metabolites of a range of agrichemicals are available (Coye et al, 1986b; Kutz and Cook, 1992). Again, however, there is little to suggest that these assays are anything more than acute or, at most, sub-acute markers of pesticide exposure. Most studies report on urine residues being present in the urine of workers for a period ranging from hours (Hayes et al, 1980; Griffiths and Duncan, 1985; Drevencar et al, 1991) to days (Kolmodin-Hedman et al, 1983; Moody et al, 1992) after exposure. Although the persistence of urinary organophosphates metabolites in symptomatic subjects 4.5 months after household application of diazinon has been reported (Richter et al, 1992), most studies where metabolites or intact pesticides were found in human tissues or urine long after exposure involve chemicals known to have high biological persistence, such as dioxin (Skene et al, 1989; Schecter and Ryan, 1992). The relevance of these types of esoteric exposures for monitoring of farm workers whose most important exposures are to organophosphates, is limited.

NTE has been recommended as a method for biological monitoring of workers exposed to organophosphates with neuropathic potential (Lotti, 1986). However, studies amongst healthy workers exposed to DEF (Lotti et al, 1983) as well as subjects developing OPIDN (Lotti et al, 1986) found that, while NTE levels declined immediately after exposure, they returned to normal within 6 weeks. This suggests that NTE may be useful as an acute or sub-acute marker of a chronic outcome (OPIDN post-acute intoxication), but is not useful as a marker of a chronic biological (neurotoxic) effect in workers with ongoing low-dose exposures examined for subclinical neurologic or neurobehavioural deficits.

4.5 Conclusion

Non-cancer morbidity due to low-levels of agrichemical exposures is suggested by a range of studies to date. However, the literature, particularly with regard to accurate exposure assessment, is still too scanty to be conclusive on the issue. Research is hampered by the absence of reliable and valid biological markers of chronic exposure to organophosphates in study subjects.

The lack of studies on non-cancer morbiidty may be due to many factors, including difficulties in obtaining morbidity data as compared to mortality data (particularly the case when compared to cancer studies), less appeal to researchers and the need for exacting study designs (Richter et al, 1992; Maroni and Fait, 1993). In particular, the question of chronic subclinical neurotoxic effects arising from long-term exposures, in the absence of acute poisoning, requires further investigation and is the subject of ongoing international collaborative research (Maroni et al, 1986).

Moreover, there is growing concern at the impact of widespread exposures to neurotoxic chemicals in Less Developed Countries (LDCs) whose indigenous capacities to identify and control such exposures, and to treat neurological and neuropsychological disease, is limited (Davies, 1988; Saxena, 1990; El Batawi, 1990; Forget, 1991). This has important policy implications for occupational health services and resource distribution in LDCs, and makes the investigation of potential health effects of such exposure amongst workers in these countries particularly important.

REFERENCES

Aldridge W. (1990). An assessment of the toxicological properties of pyrethroids and their neurotoxicity. Toxicology 21 : 89-104.

Ames RG, Brown SK, Mengle DC, Kahn E, Stratton JW, Jackson RJ. (1989a). Protecting agricultural applicators from overexposure to cholinesterase-inhibiting pesticides: Perspectives from the California Programme. J Soc Occup Med 39 : 85-92.

Ames RG, Brown SK, Mengle DC, Kahn E. (1989b). Cholinesterase activity depression among California agricutlural pesticide applicators. Am J Ind Med 15 : 143-150.

Anger WK, Moody L, Burg J, Brightwell WS, Taylor BJ, Russo JM, Dickerson N, Stezer JV, Johnson BL, Hicks K. (1986). Neurobehavioral evaluation of soil and sturctural fumigators using methyl bromide and sulfuryl fluoride. Neurotoxicology 7 : 137-156.

Barbeau R, Roy Cloutier L, Plasse L, Paris S. (1986). Environmental and genetic factors in the aetiology of Parkinson's disease. In: Yahr MD, Bergmann KJ (eds), Parkinson's disease. Adv Neur 45 : 299-306. Raven Press, New York.

Becking GC, Boyes WK, Damstra T, MacPhail RC. (1993). Assessing the neurotoxic potential of chemicals - a multidisciplinary approach. Envir Res 61 : 164-175.

Berberian IG, Enan EE (1987). Neurotoxic studies in humans occupationally exposed to pesticides. J Soc Occup Med. 37 : 126-127.

Bernadini P. (1986a). Paraquat and diquat: toxicological and occupational hazards. Arch Sci Lav. 2 : 117-124.

Bernadini P (1986b). Pathologies caused by arsenic pesticides. Arch Sci Lav. 2 : 102-110.

Berry CL. (1988). Pesticides. Human Toxicology 7 : 433-436.

Bertoncin D, Russolo A, Caroldi S, Lotti M. (1985). Neuropathy target esterase in human lymphocytes. Arch Env Health 40 : 139-144.

Bishop CM. (1992). A case of methyl bromide poisoning. Occupational Health 42 : 107-109.

Blair A, Zahm S. (1990). Methodological Issues in Exposure Assessment for Case-control Studies of Cancer and Herbicides. Am J Ind Med 18 : 285-293.

Buffler PA. (1990) Epidemiological approach in the assessment of health effects associated with chemical waste sites. In : Advances in neurobehavioural toxicology: Applications in Environmental and Occupational Health. Ed: Johnson BL, Anger WK, Durao A, Xintaras C. pp 123-132. Lewis Publishers, Michigan.

Burchfiel JL, Duffy FH, Sim VM. (1976) Persistent effects of sarin and dieldrin on the primate electroencephalogram. Toxicol Appl Pharmacol. 35 : 365-379.

Burg RV. (1988). Toxicology Update - TCDD. J Appl Tox 8(2) : 145-148.

Callender TJ, Morrow L, Subramanian K. (1994). Evaluation of chronic neurological sequaelae after acute pesticide exposure using spect brain scans. J Toxicol Envir Health 41 : 275-284.

Centre for Diseases Control (CDC) (1984). Leads from the MMWR: Acute convulsions associated with Endrin poisoning - Pakistan. JAMA 253 : 334-335.

Clifford NJ, Nies AS. (1989). Organophosphate poisoning from wearing a laundered uniform previoulsy contaminated with parathion. JAMA 262 : 3035-3036.

Conyers RAJ, Goldsmith LE. (1971). A case of organophosphorus-induced psychosis. Med J Austr, vol : 27-29.

Council on Scientific Affairs. (1988). Cancer Risk of Pesticides in Agricultural Workers. JAMA 260(7) : 959-966.

Coye MJ, Lowe JA, Maddy KT. (1986a). Biological Monitoring of agricultural workers exposed to pesticides: I. Cholinesterase Activity Determinations. J Occup Med 28(8) : 619-627.

Coye MJ, Lowe JA, Maddy KT. (1986b). Biological Monitoring of agricultural workers exposed to pesticides: II. Monitoring of Intact Pesticides and their metabolites. J Occup Med 28(8) : 628-636.

Coye MJ, Barnett PG, Midtling JE, Velasco AR, Romero P, Clements CL, Rose TG. (1987). Clinical confirmation of organophosphate poisoning by serial cholinesterase analyses. Arch Int Med 147 : 438-442.

Daniell W, Barnhart S, Demers P, Costa LG, Eaton DL, Miller M, Rosenstock L. (1992). Neuropsychological performance among agricultural pesticide applicators. Envir Res 59 : 217-228.

Davies JE, Barquet A, Freed VH, Haque R, Morgade C, Sonneborn RE, Vaclavek C. (1975). Human pesticide poisonings by a fat-soluble organophosphate insecticide. Arch Envir Health 1975 30 : 608-613.

Davies JE. (1987). Changing profile of pesticide poisoning. N Eng J Med "March 26" : 807-808.

Davies JE. (1988). A global need: Farm worker safety. Am J Ind Med 13 : 725-729.

Davies JE. (1990). Neurotoxic Concerns of Human Pesticide Exposure. Am J Ind Med. 18 : 327-331.

Davis KL, Yesavage JA, Berger PA. (1978). Possible organophsophate-induced Parkinsonism. J Nerv Ment Dis. 166 : 222-225.

Drevencar V, Radic Z, Vasilic Z, Reiner E. (1991). Dialkylphosphorus metabolites in the urine and activities of esterases in the serum as biochemical indices for human absorption of organophosphorus pesticides. Arch Environ. Contam. Toxicol. 20 : 417-422.

Duffy FH, Burchfiel JL, Bartels PH, Gaon M, Sim VM. (1979). Toxicol and Appl Pharmacol 47 : 161-176.

El Batawi. (1990). Investigative Strategies for developing countries. In : Advances in neurobehavioural toxicology: Applications in Environmental and Occupational Health. Ed: Johnson BL, Anger WK, Durao A, Xintaras C. pp 467-468. Lewis Publishers, Michigan.

Forget G. (1991). Pesticides and the Third World. J Tox Envir Health. 32 : 11-31.

Gordon JJ, Inns RH, Johnson MK, Leadbeater L, Maidment MP, Upshall DG, Cooper GH, Rickard RL. (1983). The delayed neuropathic effects of nerve agents and some other organophosphorus compounds. Arch Toxicol. 52 : 71-82.

Gralewicz S, Kowalczyk W, Gorny R, Socko R. (1990). Brain electrical activity (EEG) after repetitive exposure to chlorphenvinphos, an organophosphate anticholinesterase: I. Rabbit. Pol J Occ Med. 3 : 51-68.

Grcevic N, Jadro-Santel D, Julic S. (1977). Cerebral changes in paraquat poisoning. In: Neurotoxicology. Eds: Roizin L, Shiraki H. Raven Press, New York.

Griffiths JG, Duncan RC. (1985). Alkyl phosphate residue values in the urine of Florida citrus fieldworkers compared to the National Health and Nutrition Examination (NHANES) sample. Bull Envir Contam Toxicol. 34 : 210-215.

Hayes AL, Wise RA, Weir FW. (1980). Assessment of occupational exposure to organophosphates in pest control operators. Am Ind Hyg J. 41 : 568-575.

He F, Wang S, Liu L, Chen S, Zhang Z, Sun J. (1989). Clinical manifestations and diagnosis of acute pyrethroid poisoning. Arch Toxicol 63 : 54-58.

He F, Deng H, Ji X, Zhang Z, Sun J, Yao P. (1991). Changes of nerve excitability and urinary deltamethrin in sprayers. Int Arch Occup Envir Health 62 : 587-590.

Hierons R, Johnson NK. (1978). Clinical and toxicological investigations of a case of delayed neuropathy in man after acute poisoning by organophosphorus pesticide. Arch. Toxicol. 40 : 279-284.

Ho SC, Woo J, Lee CM. (1989). Epidemiological study of Parkinson's disease in Hong Kong. Neurology 39 : 1314-1318.

Hoffer E, Taitelman U. (1989) Exposure to paraquat through skin absorption: Clinical and laboratory observations of accidental splashing on healthy skin of agricultural workers. Human Toxicol, vol : 483-485.

Hogan DJ, Lane P. (1986). Dermatological disorders in agriculture. Occupational Medicine - State of the art reviews. 1: 285 - 300.

Holsapple MP, Snyder NK, Wood SC, Morris DL. (1991). A review of 2,3,7,8-tetrachlorodibenzo-p-dioxin-induced changes in immunocompetence: 1991 update. Toxicology 69 : 219-255.

Hulka BS, Margolin BH. (1992). Methodological Issues in Epidemiological Studies using biologic markers. Int J Epidem 135 : 200-209.

Hustinx WNM, van de Laar RTH, van Huffelen AC, Verwey JC, Meulenbelt J, Savelkoul TJF. (1993). Systemic effects of inhalational methyl bromide poisoning; a study of nine cases occupationally exposed due to inadvertent spread during funigation. Br J Ind Med 50 : 155-159.

Igbedioh SO. (1991). Effects of Agricultural Pesticides on Humans, Animals and Higher Plants in Developing Countries. Arch Env Health 46 : 218-224.

Ilianis S, Goldsmith JR, Israeli R. (1988). Neurotoxicity of organophosphate insecticides among a Negev population with long-term exposures. In: Progress in Occupational Epidemiology pp 253-262. Eds Hogstedt C, Reurewell C. Elsevier, Amsterdam.

Iregren I, Gamberale F. (1990). Human behavioural toxicology. Scan J Work Envir Health 16 (suppl) : 17-25.

Johnson BL, Baker EL, Batawi ME, Gilioli R, Hanninen H, Seppalainen AM, Xintaras C, editors (1987): Prevention of neurotoxic illness in working populations. John Wiley and Sons, New York.

Kaplan JG, Kessler J, Rosenberg N, Pack D, Schaumberg HH. (1993). Sensory neuropathy associated with Dursban (chlorpyrifos) exposure. Neurology 43 : 2193-2196.

Kolmodin-Hedman B, Hoglund S, Akerblom M. (1983). Studies on phenoxy acid herbicides. I. Field Study. Occupational Exposure to phenoxy acetic acid herbicides (MCPA, Dichlorprop and 2,4-D) in agriculture. Arch Toxicol 54 : 257-265.

Krieger RI, Ross JH. (1993). Risk assessments in the pesticide regulatory process. Ann Occup Hyg. 37 : 565-578.

Kutz FW, Cook BT. (1992). Selected pesticide residues and metabolites in urine from a survey of the US general population. J Toxicol Envir Health 37 : 277-291.

Kyrklund T. (1992). The Use of Experimental Studies to reveal suspected neurotoxic chemicals as occupational hazards: Acute and chronic exposures to organic solvents. Am J Ind Med. 21 : 15-24.

Lander F, Lings S. (1991). Variation in plasma cholinesterase activity among greenhouse workers, fruitgrowers and slaughtermen. Br J Ind Med 48 : 164-166.

Landrigan PJ, Graham DG, Thomas RD. (1993). Strategies for the Prevention of Environmental Neurotoxic Illness. Envir Res 61 : 157-163.

Levin HS, Rodnitzky RL, Mick DL. (1976). Anxiety associated with exposure to organophosphorus compounds. Arch Gen Psych 33 : 225-228.

Levin HS, Rodnitzky RL. (1976). Behavioural effects of organophosphate pesticides in man. Clin Toxicol 9(3) : 391-405.

Lilienfield DE, Gallo MA. (1989). 2,4-D, 2,4,5-T and 2,3,7,8-TCDD: An overview. Epidemiologic Reviews 11 : 28-58.

Lisi P, Caraffini S, Assalve D. (1986). A test series for pesticide dermatitis. Contact Dermatitis 15 : 266-269.

Littorin M, Attewell R, Skerfving S, Horstmann V, Moller T. (1993). Mortality and tumour morbidity amongst Swedish market gardeners and orchardists. Int Arch Occup Environ Health 65 : 163-169.

Lolin Y. (1989). Chronic neurological toxicity associated with exposure to volatile substances. Human Toxicol. 8 : 293-300.

London L. (1992). Agrichemical hazards in the South African farming sector. S Afr Med J. 81 : 560-564.

Lotti M, Johnson MK. (1978). Neurotoxicity of organophosphorus pesticides: predictions can be based on In Vitro studies with hen and human enzymes. Arch Toxicol. 41 : 215-221.

Lotti M, Becker CE, Aminoff MJ, Woodrow JE, Seiber JN, Talcott RE, Richardson RJ. (1983). Occupational exposure to the cotton defoliants DEF and merphos. J Occup Med. 25 : 517-522.

Lotti M, Moretto A, Zoppellari R, Dainese R, Rizzuto N, Barusco G. (1986). Inhibition of lymphocytic Neuropathy Target Esterase predicts the development of organophosphate induced delayed peripheral neuropathy. Arch Toxicol 59 : 176-179.

Lotti M. (1986). Biological monitoring for organophosphate induced peripheral neuropathy. Tox Lett 33 : 167-172.

Lotti M. (1991). Treatment of acute organophosphate poisoning. Med J Austr 154 : 51-55.

Lotti M. (1992). Central neurotoxicity and behavioural effects of anticholinesterases. In: Clinical and experimental toxicology of organophosphates and carbamates. Eds Ballantyne B, Marrs TM, Aldridge WN. Butterworth, Stoneham, MA.

Lotti M, Moretto A, Capdicasa E, Bertolazzi M, Periaca M, Scapellato ML. (1993). Interactions between Neuropathy Target Esterase and its inhibitors and the development of polyneuropathy. Toxicol Appl Pharm. 122 : (in press).

Maizlish N, Schenker M, Weisskopf C, Selber J, Samuels S. (1987). A behavioural evaluation of pest control workers with short-term, low-level exposure to the organophosphate diazinon. Am J Ind Med. 12 : 153-172.

Marsh WH, Vukov GA, Conradi EC. (1988). Acute pancreatitis after cutaneous exposure to an organophosphate insecticide. Am J Gastroenterology 83 : 1158-1160.

Maroni M, Jarvisalo J, La Ferla F (1986). The WHO-UNDP epidemiological study on health effects of exposure to organophosphorus pesticides. Toxicol Lett 33 : 115-123.

Maroni M, Fait A. (1993). Health Effects in man from long-term exposure to pesticides. A review of the 1975-1991 literature. Toxicology 78 ; 1-174.

Mastroiacovo P, Spagnolo A, Marni E, et al. (1988). Birth Defects in the Sevesco Area after TCDD Contamination. JAMA 259(11) : 1668-1672.

McConnachie PR, Zahalsky AC. (1991). Immunological consequences of exposure to pentachlorophenol. Arch Envir Health 46 : 249-253.

McConnell R, Keifer M, Rosenstock L. (1994). Elevated quantitative vibrotactile threshold among workers previously poisoned with methamidophos and other organophosphate pesticides. Am J Ind Med. 25 : 325-334.

Minton NA, Murray VSG. (1988). A review of organophosphate poisoning. Medical Toxicology 3 : 350-375.

Misra UK, Nag D, Khan WA, Ray PK. (1988). A study of nerve conduction velocity, late responses and neuromuscular synapse function in organophosphate workers in India. Arch Toxicol 61 : 496-500.

Moody R, Webster R, Melendres, Maibach HI. (1992). Dermal absorption of the phenocy herbicide 2,4-D Demethylamine in humans: effect of DEET and anatomic site. J Tox Envir Health 36 : 241-250.

Moses M. (1983). Pesticides. In Environmental and Occupational Medicine. Pages 547-571. Ed: Rom MD, Little, Brown and Company, 1983.

Newsday (1981). "US-Made Poisons Hurt More Than Just Pests". Newsday. 14 Dec 1981 : 9-13.

O' Brien M. (1985). Surveying Occupational Damage after the facts. In Northwest Coalition Against Pesticides (NCAP) News 5(1) : 16-18.

O'Donoghue JL. (1983). Neurotoxicology. In: A guide to general toxicology. Eds: Homburger F, Hayes JA, Pelikan EW, Karger, Elsevier, Basel.

Otto D, Soliman S, Svensgaard D, Soffar A, Ahmed N. (1990). Neurobehavioural assessment of workers exposed to pesticides. In : Advances in neurobehavioural toxicology: Applications in Environmental and Occupational Health. Ed: Johnson BL, Anger WK, Durao A, Xintaras C. pp 305-322. Lewis Publishers, Michigan.

Peedicayil J, Ernest K, Thomas M, Kanagasabapathy AS, Stephen PM. (1991). The effect of organophosphorus compounds on serum pseudocholinesterase in a group of industrial workers. Human and Experimental Toxicology 10 : 275-278.

Peterson RE, Theobald HM, Kimmel GL. (1993). Developmental and reproductive toxicity of dioxins and related compounds: cross-species comparisons. Critical Reviews in Toxicology. 23 : 283-335.

Rajput, AH, Uitti RJ, Stern W, Lavery W. (1986). Early onset Parkinson's disease and childhood environment. In: Yahr MD, Bergmann KJ (eds), Parkinson's disease. Adv Neur 45 : 295-297. Raven Press, New York.

Richter ED, Chuwers P, Levy Y, Gordon M, Grauer F, Marzouk J, Lvey S, Barron S, Gruener N. (1992). Health effects from exposure to organophosphate pesticides in workers and residents in Israel. Isr J Med Sci 28 : 584-597.

Rosenstock L, Daniell W, Barnhart S, Schwartz, Demers PA. (1990). Chronic neurological sequalae of occupational exposure to organophosphate insecticides. Am J Ind Med 18 : 321-325.

Rosenstock L, Kiefer M, Daniell W, McConnell, Claypole K. (1991). Chronic central nervous system effects of acute organophosphate pesticide exposure. Lancet 338 : 223-227.

Savage EP, Keefe TJ, Mounce LM, Lewis JA, Burcar PJ. (1988). Chronic Neurological Sequaelae of Organophosphate Pesticide Poisoning. Arch Envir Health. Jan/Feb 43(1) : 38-45.

Saxena VB. (1990). Problems of Third World countries in the development of neurobehavioural approaches to occupational and environmental health. In : Advances in neurobehavioural toxicology: Applications in Environmental and Occupational Health. Ed: Johnson BL, Anger WK, Durao A, Xintaras C. pp 87-98. Lewis Publishers, Michigan.

Schaumberg HH, Spencer PS. (1976). The neurology and neuropathology of the occupational neuropathies. J Occ Med 18 : 739-742.

Schecter A, Ryan JJ. (1992). Persistent brominated and chlorinated dioxin levels in a chemist. J Occup Med 34: 702-707.

Semchuck K,M, Love EJ, Lee RG. (1992). Parkinson's disease and exposure to agricultural work and pesticide chemicals. Neurology 42 : 1328-1335.

Senanyake N, Johnson MK. (1982). Acute polyneuropathy after poisoning by a new organophosphate insecticide. Lancet 306 :155-157.

Senanyake N, Karalliedde L. (1987). Neurotoxic effects of organophosphorus insecticides. An intermediate syndrome. N Eng J Med 316 : 761-763.

Sharma VK; Kaur S. (1990). Contact sensitisation by pesticides in farmers. Contact Dermatitis 23 : 77-80.

Simonsen L, Johnsen H, Lund SP, Matikainen E, Midtgard U, Wennberg A. (1994). Methodological approach to the evaluation of neurotoxicity data and the classification of neurotoxic chemicals. Scand J Work Environ Health 20 : 1-12.

Skene SA, Dewhurst IC, Greenberg M. (1989). Polychlorinated dibenzo-p-dioxins and polychlorinated dibenzofurans: The risks to human health. A review. Human Toxicol. 8 : 173-203.

Spencer PS. (1990). Neurotoxicological Vaticinations (The Hanninen Lecture). In : Advances in neurobehavioural toxicology: Applications in Environmental and Occupational Health. Ed: Johnson BL, Anger WK, Durao A, Xintaras C. pp 13-25. Lewis Publishers, Michigan, 1990.

Spigiel RW, Gourley DR, Holcsaw TL. (1981). Organophosphate pesticide exposure in farmers and commercial pesticide applicators. Clin Toxicol Consult 3 : 45-50.

Steenland K, Jenkins B, Ames RG, O'Malley M, Chrislip D, Russo J. (1994). Chronic neurological sequelae to organophosphate pesticide poisoning. Am J Public Health 84 : 731-736.

Sterling TD, Arundel AV. (1986). Health Effects of Phenoxy Herbicides : A Review. Scand J Work Envir Health 12(3) 161 - 173.

Tolman KG. (1983). Gastrointestinal system. In: Environmental and Occupational Medicine. Pages 397-401. Ed: Rom WN. Little, Brown and Company, Boston.

Triebig G, Krekeler H, Gobler K, Valentin H. (1981). Investigations on neurotoxicity of chemicals at the workplace. II Determination of motor and sensory conduction velocity in persons occupationally exposed to pestachlorophenol. Int Arch Occup Envir Health 48 : 357-367.

Tsvetkovà T, Andonova S, Zvetkova E, Blagoeva S. (1992). Aspects of granulocyte function in workers professionally exposed to pesticides. Int Arch Occup Environ Health 64 : 275-279.

US Congress, Office of Technology Assessment. (1990). Neurotoxicity: Identifying and Controlling Poisons of the Nervous System. Washington, 1990.

Vasilescu C, Alexianu M, Dan A. (1984) Delayed neuropathy after organophosphorus insecticide (Dipterex) poisoning: a clinical, electrophysiological and nerve biopsy study. J Neurology Neurosurgery and Psychiatry 47 : 543-548.

Vijverberg HPM, van den Bercken J. (1990). Neurotoxicological effects and the mode of action of pyrthroid insecticides. Toxicology 21 : 105-126.

Wall L. (1993). Protecting against pesticides. Occupational Health. vol, 84-86.

Weiss B. (1990). Neurotoxic risks in the workplace. Appl Occup Envir Hyg. 5 : 587-594.

Whorton MD, Krauss RM, Marshall S, Milby TH. (1977). Infertility amongst male pesticide workers. Lancet ii: 1259-1261.

Woolen BH. (1993). Biological monitoring for pesticide exposure. Ann Occup Hyg. 17 : 525-540.

World Health Organisation (1979). DDT and its derivatives. Environmental Health Criteria 9. WHO, Geneva.

World Health Organisation (1979). Endrin. Environmental Health Criteria 130. WHO, Geneva.

World Health Organisation (1980). Tin and organotin compounds: A preliminary review. Environmental Health Criteria 15. World Health Organisation, Geneva.

World Health Organisation (1982). Technical Report No 677. Recommended Health-based Limits in Occupational Exposure to Pesticides. Geneva.

World Health Organisation (1984). Paraquat and Diquat. Environmental Health Criteria 39. World Health Organisation, Geneva.

World Health Organisation (1986a). Principles and methods for the assessment of neurotoxicity associated with exposure to chemicals. Environmental Health Criteria 60. World Health Organisation, Geneva.

World Health Organisation (1986b). Organophosphorus insecticides : A general introduction. Environmental Health Criteria 63. World Health Organisation, Geneva.

World Health Organisation (1986c). Carbamate pesticides: A general introduction. Environmental Health Criteria 64. World Health Organisation, Geneva.

Xue S. (1987). Health Effects of Pesticides : A Review of Epidemiological Research from the Perspective of Developing Nations. Am J Ind Med 12(3) : 269-279.

Yeary RA, Eaton J, Gilmore E, North B, Singell J. (1993). A multiyear study of blood cholinesterase activity in urban pesticide applicators. J Tox Envir Health 39 : 11-25.

CHAPTER 5

STUDY METHODS FOR THE INVESTIGATION OF THE NEUROTOXIC IMPACT OF AGRICHEMICALS AMONG DECIDUOUS FRUIT FARM WORKERS IN THE WESTERN CAPE

CONTENTS Page

CHAPTER 5

STUDY METHODS FOR THE INVESTIGATION OF THE NEUROTOXIC IMPACT OF AGRICHEMICALS AMONG DECIDUOUS FRUIT FARM WORKERS IN THE WESTERN CAPE

The study aims and objectives are set out in Chapter 1. This chapter outlines the methods used in the study and draws on discussion in Chapter 3 as the basis of methods used for long-term agrichemical exposure ascertainment. A preliminary discussion is presented below to clarify some issues that are critical for an understanding of neurobehavioural research, particularly in the rural farming setting in South Africa.

5.1 A Background to the Choice of Study Methods - Some Critical Issues for Neurotoxicity Research in the Farming Setting

5.1.1 Sampling in rural farm settings

The difficulties of operationalising field research in rural areas in developing countries has been well described (Zarkovich, 1993; Hershfield et al, 1993). In particular, sampling in farming communities is complicated by the irregular social and geographical structures that characterises rural farming activities and access to rural subjects is often fraught with situational obstacles such as vested power interests (Peil, 1993).

Similar problems exist in South Africa where data on the numbers of farm employees and residents on specific holdings is often inaccurate, because of seasonal and other fluctuations in the numbers of workers on farms. This may often occur with movement of workers between farms, and illicit accommodation of both working and non-working residents by fellow farm workers (Budlender, 1984; Waldman, 1993). Databases on farm holdings are surprisingly poorly suited to research needs. Official registries, particularly local authority records (London, 1992), document farms poorly as geographical entities in official registers and tend to rely primarily on owner name. In practice, the farming unit may bear no relationship to that registered in the deeds office (personal communication, Mr G van der Spuy, District Health Inspector, Stellenbosch Regional Services Council Health Department, 1992).

As a result, the construction of a general sampling frame of workers or farms for the purposes of random sampling is often not feasible. Under these circumstances, the best access for sampling is through the farmer co-operatives that operate in various farming sectors. This method of sampling will tend to miss extremes of farm production including the small holding, and the large scale producer who is able to market and process their produce independently. Both categories of farms are likely to differ systematically in their safety and health monitoring practices.

However, the logistics of access to rural farm worker populations must take account of the socio-political context of rural social relations (Ball, 1990; Bundy, 1992). Given the tight control that farmers have over their workforces, the reality is that access for workplace studies in agriculture is overwhelmingly dependent on the employers. This raises additional ethical questions as to the likelihood of appropriate employer action following on study results, and the influence on selection in the study. Unionisation of farm workers is minimal at present and, while legislation has been amended to allow for freedom of association for farm workers, there is little likelihood that unionisation will grow rapidly (Hamman, 1993), or that, in the near future, access for health interventions and research may be made possible by the organisation of farm workers.

However, the key obstacle from an epidemiological perspective is the selection of appropriate control subjects for any study investigating farm workers' health. For optimal validity, the control group should be chosen to be as comparable as possible to the source population for the exposed group in as many respects as possible other than the exposure of interest. However, the life and work experiences of farm workers are unique, especially so in

South Africa, and there are exceedingly few groups who share any of these experiences. The result is that selection of external controls is fraught by the possibiity of non-comparability and confounding by unknown factors, and is, additionally, often not feasible.

Some experiences of other research in South Africa amongst farm workers serve to illustrate this point:

- Innes et al, (1990) examined the serum cholinesterase of a group of fruit farm sprayers during a season of agrichemical application. The study made use of laboratory personnel as a control group from which a "normal" range for serum cholinesterase was derived. The role of dietary, environmental, race, gender and class differences as possible confounders in this comparison was not explored and may have invalidated some of their conclusions about the effects of agrichemical exposure in their subjects.

- Barnes et al, (1992) [1] undertook a similar but larger-scale study in which serum and erythrocyte cholinesterase was compared between fruit farm sprayers and fruit packing store workers. No difference was found in mean cholinesterase levels between the two groups. However, the two groups were substantially different in their age and education profiles, and were suspected of being different in the type of work they performed and in their relative urbanisation and familiarity with the test situation (Dr S Manjra, personal communication, 1993). These issues are of critical importance when the investigation involves neurobehavioural assessments known to be sensitive to class, educational and cultural factors.

---

1. Barnes JM, Muller GJ, Lamprecht JH. (1992). Health survey of deciduous fruit farm workers occupationally exposed to organophosphate sprays. Poster presentation to Annual Pharmacology Conference, Bloemfontein.

- A study by the National Centre for Occupational Health (NCOH) [1] in Venda of cholinesterase levels among coffee plantation workers compared exposed workers to a sample of rural women attending a local hospital as controls. The study found that the rural women had lower mean serum and erythrocyte cholinesterase levels, and the authors postulated widespread environmental contamination by organophosphates (OPs) as a possible explanation. Usages of mixes of insecticides containing OPs for indoor spray as part of vector control appears to be a possible source of exposure in this instance (personal communication, Dr D Kielkowski, National Centre for Occupational Health, Johannesburg). If this hypothesis were true, it implies that rural populations experience relatively homogenous agrichemical exposures and sampling of rural controls will not achieve adequate exposure contrast. However, the study was limited by methodological flaws related to non-comparability of control subjects (who were hospital staff and patients), and to the use of different laboratories for cholinesterase ascertainment.

Serious difficulties, therefore, exist in selecting appropriate control populations for epidemiological studies involving farm workers' health. Few of these issues have been explored in any depth in South Africa to date.

5.1.2 Measurenent of subclinical effects of exposure to neurotoxic agents in occupational settings

Much early research into neurotoxicity due to chemical agents relied on the presence of abnormal clinical (Hanninen, 1985) or pathological findings (Weiss, 1990; Iregren and Gamberale, 1990), or on electrophysiological derangements, such as abnormal EEGs or nerve conduction studies as outcome measures. However, with increasing knowledge of the epidemiology and toxicology of chemical neurotoxicity it became clear that these measures

---

1. Jaga K, Rama DBK, Rees D. (1992). Poster presented to 11th ESSA Conference, Johannesburg: Cholinesterase Activity in workers exposed to organophosphate pesticides at a coffee plantation.

reflected gross pathology and were not suited to early detection of subclinical changes associated with exposure to neurotoxins (Iregren and Gamberale, 1990).

One area in which new tests methods for early detection of neurotoxicity has focused is that of the functioning of various modalities of peripheral and central sensation. These methods have included measurement of temperature sensitivity (Arezzo et al, 1986; Bove et al, 1989), olfactory function (Sandmark et al, 1989; Fortier et al, 1991), vibration sense (Bove et al, 1989; Gerr and Letz, 1988; Gerr et al, 1990a), colour vision (Mergler et al, 1988; Mergler et al, 1990) and postural sway (Savolainen et al, 1980; Antti-Poika et al, 1989).

Non-invasive measurement of peripheral vibration sense is one of the recommended methods for determining early neurotoxic effects of chemicals on the peripheral nervous system (Johnson et al, 1987), particularly where electrophysiological studies are not possible (Gerr et al, 1990b). Quantitative measurement of vibration sense is included in the WHO protocol for investigation of adverse chronic health effects of pesticide exposure in Europe (Maroni et al, 1986). The use of the Vibratron II (Sensortek, Inc., Clifton, N.J.) to measure vibrotactile threshold has been successfully validated against electrophysiological methods (Gerr et al, 1990b), and its reliability has also been demonstrated amongst diabetic (Gerr et al, 1990a) and volunteer subjects (Gerr and Letz, 1988).

While the use of vibration sense measurement has been most frequently applied to studies of solvent neurotoxicity (Husman and Karli, 1980; Gregersen et al, 1984; Bove et al, 1989), fewer studies have reported on the value of measurement of peripheral vibration sense in relation to pesticide exposure (Otto et al, 1990; McConnell et al, 1994). More recently, the use of postural sway testing has also been applied to pesticide-exposed workers (Sack et al, 1993). Experience in South Africa to date (Bachmann and Myers, 1992; Bachmann et al, 1993) has largely relied on measurement of peripheral vibration sense amongst industrial workers using the Vibratron II and tuning fork extinction time, and preliminary evidence from a pilot study amongst farm workers exposed to pesticides suggest the Vibratron II is a reasonably robust and practicable instrument for use in this rural worker population [1].

5.1.3 Cross-cultural issues in neurobehavioural research

The second area of research in which massive growth has occurred with regard to new methods for use in the evaluation of potential chemical neurotoxicity, is in the field of neurobehavioural [2] assessment (Hanninen, 1985; Weiss, 1990; Anger and Cassito, 1993; Letz, 1993). Increasingly sophisticated methods have been developed to measure subtle behavioural impairments, rather than relying on traditional neurological and psychometric tests which detect gross brain damage (WHO, 1986; United States Congress Office of Technology Assessment, 1990; Iregren and Gamberale, 1990; Landrigan et al, 1993). This has led to the development of a range of tests which aim to identify early neurobehavioural signs of toxic damage to the central nervous system (Valciukas and Lilis, 1980; Johnson et al, 1987; Otto, 1989; Anger and Cassito, 1993) of which two of the most widely used and researched

---

1. Diminished vibration sensation and chronic agrichemical exposure in farm workers. Manjra S, Myers JE, London L, Muller G, Lambrecht J, Barnes J. Unpublished research, Dept Community Health, UCT, July 1992.

2. Terminology: This thesis uses the term "Neurobehavioural" as a generic term to describe all aspects of central nervous system functioning measured by a variety of psychological tests. Within the rubric "neurobehavioural", the author includes: 1) those tests originating in the paradigm of neuropathology (or neuropsychology) described here as "Neuropsychological" tests (such as the WHO NCTB), and 2) those tests originating in the Information Processing Model of cognitive psychology, which in this study include Performance Probes and tests involving the Hick Box. Neurobehavioural is therefore used as an embracing term to include a wide range of tests currently used to evaluated central nervous system function. The term "Psychometric" is used to describe conventional testing procedures rooted in the clinical neurological examination that are of less importance in occupational epidemiology today.

batteries are those developed by the World Health Organisation (the WHO Neurobehavioural Core Test Battery (NCTB) - WHO, 1986) and by Baker and Letz (the Neurobehavioural Evaluation System (NES) - Baker et al, 1985a).

The NES test battery is computer-administered and has been shown to be similar to conventional tests in terms of reliability and relationships to known covariates (Letz, 1993). Factors found to influence performance on neurobehavioural batteries include age, gender, education (Valciukas and Lilis, 1980; Baker et al, 1983; Johnson et al, 1987; Agnew et al, 1991; Letz, 1993), chronic alcohol intake, fatigue, acute alcohol or drug consumption (Johnson et al, 1987; Letz, 1993), experience with video games and a history of head injury (Letz, 1993).

Neurobehavioural tests are increasingly being used in working populations in developing countries (He et al, 1990; Ramirez et al, 1990; Anger and Cassito, 1993). Despite research to evaluate the usefulness of these tests in different countries (Cassito et al, 1990; Anger and Cassito, 1993), concerns have been raised that almost no attempt has been made to address cross-cultural factors impinging on test outcomes (Nell et al, 1993). Indeed, published peer-reviewed papers recommending criteria for selection of neurobehavioural test batteries may not even include cross-cultural considerations as one of the criteria (White and Proctor, 1992). It has been shown that differences in test performance may result from cultural and other group differences between (Cassito et al, 1990) and within countries (Valciukas et al, 1986). Myers, et al (1994) showed that South African paint factory workers exposed to organic solvents had outcome results comparable to those of a group of Dutch volunteers (Hooisma et al, 1990) for the more physiological tests of motor speed (simple reaction time), but performed much more poorly on tests of higher function (pursuit aiming, digit symbol substitution). The authors argued that education and other socio-cultural variables were the most powerful predictors of outcomes on the latter tests and might mask the substantially weaker effects of solvent exposure. They suggested that these tests might be too sensitive to these confounders to be appropriate for use in developing countries for the detection of milder subclinical neurobehavioural (Myers et al, 1994). This problem is aggravated by imprecise outcome definitions which reduce the sensitivity of culturally-dependent tests of neurotoxic effects even further.

In addition, the validity of certain subtests of the WHO NCTB (Subjective Symptoms Questionnaire and the Profile of Mood States, POMS) have been found to be of questionable validity in studies in China (Liang et al, 1990) and in South Africa (Brown et al, 1991; Nell et al, 1993) because of poor intelligibility to the subjects and unexpected direction of association. Because of their questionable validity, these tests have not been used in this study and those neurobehavioural tests from the WHO NCTB included in this study, are only those shown to have performed adequately in previous studies amongst working populations in South Africa (Nell et al, 1993).

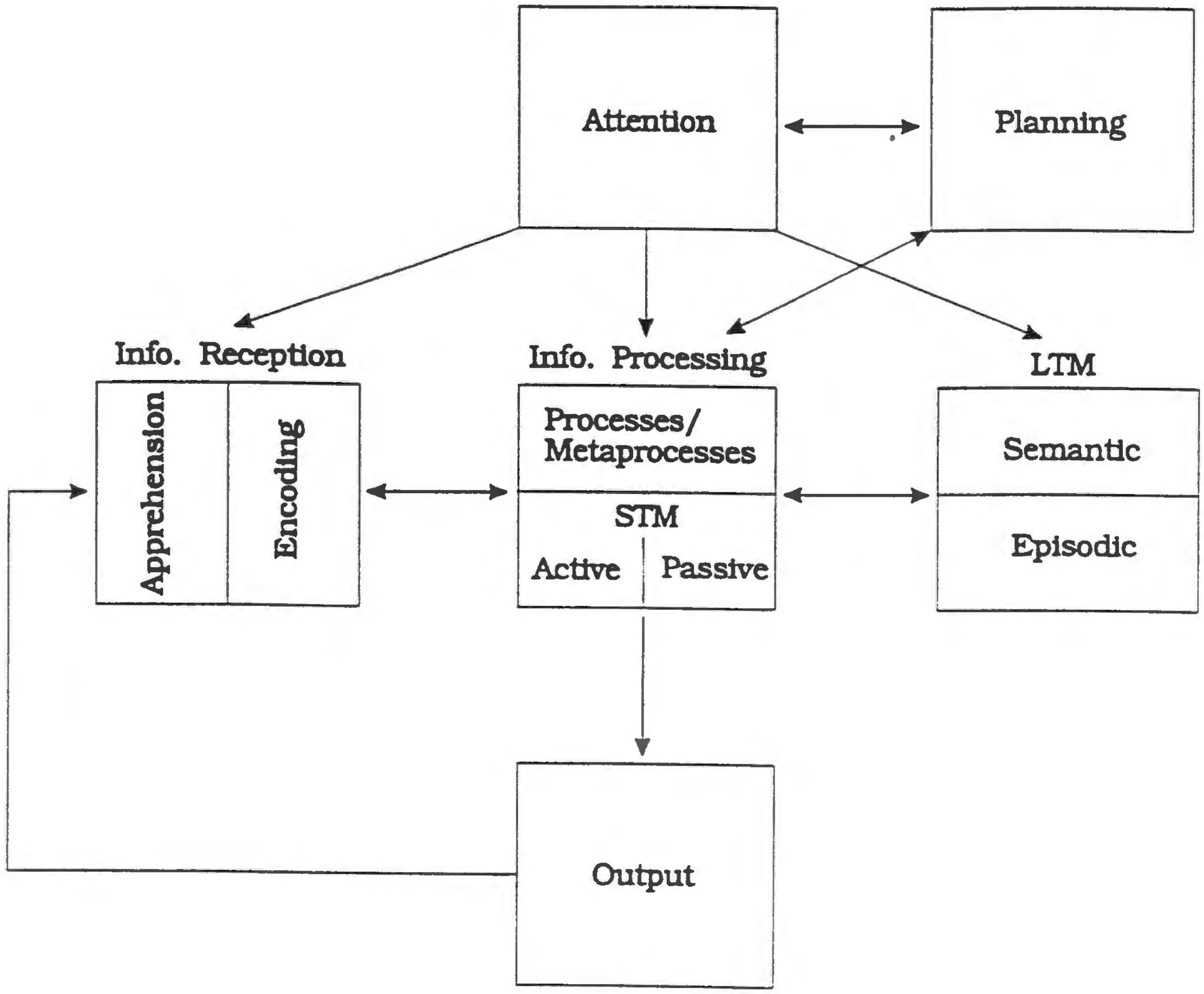
Why is it that supposedly standard neuropsychological tests apparently fail to exhibit reproducibility of results in different settings? Most psychometric tests in use currently have little grounding in psychological theory and have often relied on post-hoc empirical research to derive theory to support the tests (Taylor and Nell, 1993). This is also the case in much of neuropsychological assessment, particularly where the tests are purportedly used to identify and measure universals in human brain functioning. Most tests rely on measuring broad and theoretically ill-defined constructs, such as intelligence, spatial ability and nonverbal reasoning (Taylor and Nell, 1993), which place demands on higher cognitive processes that are culturally determined and sensitive to teaching. Cross-cultural research has demonstrated that many of these assumptions about cognitive universals are not supportable (Van der Vijver and Poortinga, 1982).

An alternative theory-driven approach, drawing on the body of theory in cognitive psychology (Luria, 1971; Vygotsky, 1988), has been advanced by researchers in South Africa (Taylor and Nell, 1993) and in Australia (Williamson, 1990; Williamson and Winder, 1993). This approach makes use of an information-processing model of cognition in which the different sub-processes involved in receiving, handling and integrating information are the object of testing, in contrast to traditional neuropsychological tests which tend to measure performance on a summative task, which usually reflects the outcome of several sub-processes integrated into one outcome.

Figure 5.1 illustrates the model graphically by identifying the main components of cognitive functioning: Information Reception, Processing and Retrieval, and their interactions with each other and with other functional units (Attention and Planning). Subcomponents for each main component are also identified. The tests developed on this model therefore measure behavioural outputs specific to these cognitive functions. Although a certain amount of contamination will occur, for some of the cognitive paradigms, this can be controlled by implementing a subtractive methodology (Taylor and Nell, 1993). The tests, and the functional cognitive units they reflect, are summarised later in the chapter in Table 5.3.

The use of the information-processing model, therefore, focusses on processes that are analogous to the basic building blocks of intelligence in contrast to metaprocesses (Taylor and Nell, 1993) which are more substantially culturally determined. In this manner, tests based on the information processing model may succeed in measuring neurobehavioural function below the level of culture. Such tests should be expected to be less sensitive to cultural and other social confounders (Taylor and Nell, 1993), particularly to the effects of education, which have been noted to be strong predictors of test performance in the WHO and NES test batteries (Letz, 1993; Anger and Cassito, 1993).

Figure 5.1 Information processing model of neuropsychological assessment



(Source: Taylor and Nell, 1993.)

Subjects experiencing neurobehavioural testing undergo a learning curve as they progress through the test, and will improve their performance simply as a result of practice. The degree of improvement with practice may be substantial in subjects who have no previous experience of the testing situation (Nell et al, 1993). This applies to most farm workers, particularly with tests that make use of computers. An integral part of the administration of the tests is therefore to provide sufficient training to the subject to ensure that the peak of his/her learning curve is reached before the subject's performance is measured. The theoretical rationale for this approach ("educating the executive") has been elaborated in the neuropsychological literature (Vygotsky, 1988) and the practical application to the test administration method outlined elsewhere (Nell et al, 1993). Additional measures taken to avoid subject-test incompatibility in this study included the use of Coloured personnel as testers (all the subjects were Coloured workers) and adherence to a careful protocol intended to address the uneven power relations inherent in the testing situation (Nell and Taylor, 1992).

5.1.4 Latent vs manifest effects in neurobehavioural research

As neurobehavioural assessment methods become more subtle, the clinical significance for individuals of abnormalities detected as differences in performance between groups remains uncertain (Baker et al, 1985b). In the absence of a better mechanistic understanding for the neurotoxic processes suggested by research outcomes, many tests used in epidemiological studies are inappropriate for clinical use (White and Proctor, 1992). There is no clarity as to whether differences on neurobehavioural battery performance amongst otherwise clinically healthy individuals signify a milder central nervous system effect (than overt encephalopathy) or are forerunners of more severe damage (Hanninen, 1985). The implications of the latter are that intervention at a point in the progression where neurobehavioural changes are detectable can prevent the development of overt neurotoxicity. This is the basis for regulatory, surveillance and other preventive strategies for the control of neurotoxic illness due to chemicals (Haninen, 1985; Johnson et al, 1987; United States Congress Office of Technology Assessment, 1990; Iregren and Gamberale, 1990).

Nonetheless, even if subclinical changes are not prognostic of overt disease, insufficient data exist as to the impact of these "subtle" behavioural effects on workers' ability to cope with both their working and social environments (Hanninen, 1985). These impacts may be anything from limited to substantial and it is therefore appropriate, particularly in light of the WHO definition of health as being more than the absence of disease (Johnson et al, 1987; Iregren and Gamberale, 1990), to regard the prevention of neurobehavioural effects of chemical exposure as of critical importance.

Hanninen (1985) also suggests a third possible explanation for the discrepancies between latent and manifest effects of neurotoxin exposures. She argues that compensation may occur in response to the changes in mental and sensorimotor functioning, and that this may be the site at which individual sensitivity may play a key role in determining whether the subject develops behavioural manifestations or more severe overt signs of neurotoxicity. The lack of research data on the contribution of interindividual variation to behavioural outcomes has been noted (Iregren and Gamberale, 1990).

Similar parallels exist between the presence of early neurobehavioural signs as an early marker and the presence of subclinical sensory signs. A study involving 36 Nicaraguan workers who survived acute poisoning with organophosphates found impaired quantitative vibration sense amongst survivors of acute poisoning who did not manifest overt OPIDP poisoning compared to age- and gender-matched controls (McConnell et al, 1994). The authors argued that these subclinical changes were part of a spectrum of severity of neurotoxic damage, of which only the worst cases manifest as overt disease.

Given an understanding of these critical issues, the following sections elaborate on the methods used for the investigation of neurological and neurobehavioural effects of long-term agrichemical exposure amongst farm workers.

5.2 Methods

5.2.1 Study design

The study was performed as a cross-sectional analytical survey from January to March 1993 during peak spraying season. The prevalence of neurobehavioural and neurological test abnormalities was determined and related to various indices of long-term worker exposure to organophosphates, as elaborated in Chapter 3. Acute exposure (defined as any exposure to organophosphates in the current pesticide application season) was treated as one of a number of potential confounders, as was a history of previous pesticide poisoning. The study was therefore designed explicitly to address the relationship between long-term low-dose exposure (in the absence of obvious poisoning) and possible neurotoxic effects, adjusting for the impact of short-term pesticide exposure and for previous pesticide related clinical morbidity. Acute exposure was therefore used to denote a longer time period than conventionally used in clinical medicine (i.e. in the past 6 to 9 months).

Even though the purpose of asessing recent exposure was primarily to meet the study objective of separating the effects of acute exposure from those of chronic exposure, it was nonetheless possible to use the data to examine the impact of recent exposure on cholinesterase levels in the subjects.

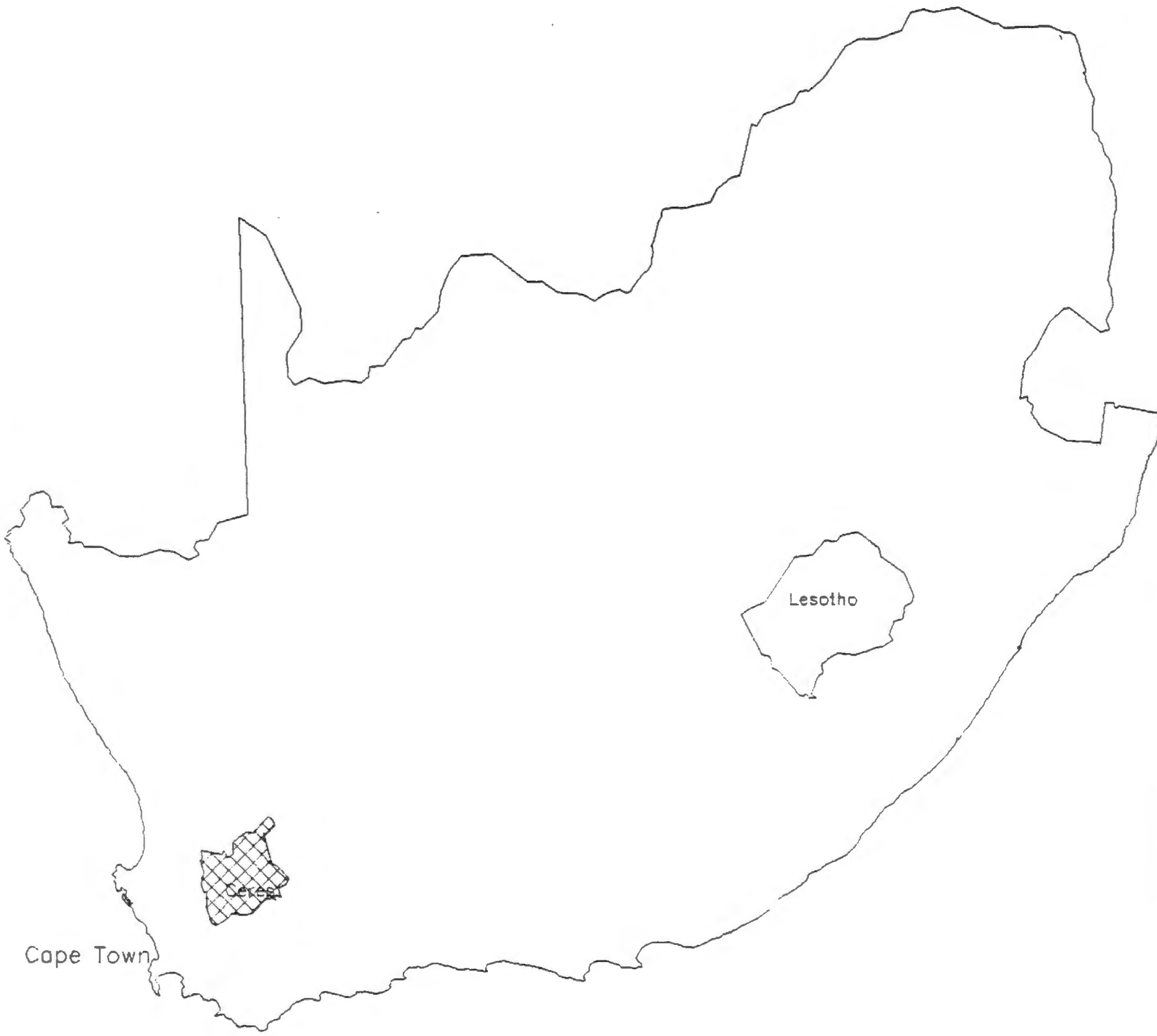
5.2.2 Study population and sampling

Because of its high agrichemical use and its central importance as an employer in the region (see Chapters 2 and 3), the deciduous fruit industry was selected as the farming sector for study. The Kouebokkeveld region (Figure 5.2) was chosen as the specific study site, as one of the two major fruit producing areas in the region. Access to the farms was arranged through two large cooperatives in the area (Ceres Fruit Growers (CFG) and Du Toit Cooperative), and through the marketing company for the industry, UNIFRUCO. Farms were all sampled during a period of active application of agrichemicals when maximal exposure to pesticides would be anticipated (January 1993 to March 1993).

All farms belonging to either cooperative, and who farmed deciduous fruit within the Koue- or Warm-bokkeveld regions were included in the farm sample (a total of 113 farms). The study sample therefore comprised all the spraymen from these farms (n=231). This group constituted the index group. There were 5 farms (20 sprayers) who were not members of either cooperative and did not form part of the study population.

Study subjects were restricted to male coloured farm workers. Female farm workers' exposures are too erratic for accurate epidemiological estimation (London and Myers, 1993), and high exposure jobs on fruit farms are almost exclusively done by men (London, 1992). In addition, neuropsychological tests are notoriously sensitive to sociocultural factors (Nell et al, 1993), and the study population was therefore confined to coloured workers, who form the bulk of the workforce on farms in the Western Cape.

Figure 5.2 Study Area: Ceres and the Kouebokkeveld



The population included all those in current high exposure categories (see Table 3.11). These jobs included the driving of a tractor/mist blower for agrichemical application or work as a mixer of agrichemicals. Backpack spraying was also a criteria for inclusion in the index group but was not found to be practiced as an exclusive job activity in the farms surveyed.

An internal exposure control group was selected of workers from the same farms in low current exposure categories matched on age and education. A 2:1 frequency matching strategy was used with one internal control for every 2 index subjects per farm. Random selection was used to identify the index subject on which to match the control, and to select controls in the case of uneven numbers of index cases on a farm. Both groups of subjects were selected on the basis of a pre-survey interview with farm management.

An external control group was sought from amongst rural dairy, chicken and forestry workers. However, a combination of difficulties, as outlined in section 5.1 above made it unfeasible to include an external control. Farmers tend to employ African workers in animal husbandry, and the majority of forestry workers at a nearby forestry station had previous employment as farm workers. The size of these workforces were also too small to make their inclusion worthwhile. As a result the study remained with only an internal control group. This did not influence the power of the study.

The exclusion criteria for cases and controls that were used included:

1. Clinical evidence of vitamin deficiency or encephalopathy of known origin.
2. Long-term administration of psychotropic medication.
3. Previous injury resulting in deformity and/or other abnormality of the lower limbs interfering with peripheral sensation.

Non-responding farms were exhaustively followed up and the reason for their non-response documented. Thirteen farms declined to participate because they were "too busy" and could not spare their staff. Four of the larger farms (over 100 hectares in size) gave no reason for non-participation. The remaining 23 farms were small holdings that were located over an hour's drive from Ceres,as a result of which the logistics for their participation was impractical. Five farms that missed their initial date were included in the timetable at the end of the study. This period still coincided with spraying activities on the farms concerned and the timing of their examination was within the study limits. Amongst farms that participated, no workers declined to participate in the study. Where illness or other difficulties prevented participation on the set day, special arrangements were made to include the subject in the timetable for the subsequent visit to the area. This applied to seven subjects in the course of the study.

5.2.3 Study size

Sample size determination was based on the ability of neuropsychological tests to detect a specified difference, given a known prevalence, and a set level of type I and type II error. Given the absence of local normative data and experience with occupational neuropsychological evaluation, criteria for sample size were based on data reported from the WHO neurotoxicology programme (Johnson et al, 1987; Cassito et al, 1990; He et al, 1990; Hooisma et al, 1990). The least departure of interest from reference values was assumed to be 10%, with power of 90% and an alpha of 0.05. Results for eleven of the WHO neuropsychological tests gave sample sizes of between 100 and 244. The approach used was rather conservative in that a 90% level of power as opposed to the more usual 80% was used. A sample size of 250 was therefore chosen as more than adequate to ensure the ability to detect small departures from the reference means of the WHO NCTB and other tests. For the tests based on the information processing model, normative data are as yet unavailable and sample size estimations could not be performed for these tests.

5.3 Measurement - Data Collection

Table 5.1 summarises the exposure variables, confounders and effect modifiers and outcome variables measured in the study and lists the methods by which these variables were measured in the study. Questionnaires and data sheets were designed with coding columns in the right hand margin for ease of computer data entry. Examples of these forms are contained in Appendix 5.1.

<u>Table 5.1 Measured variables</u>

Variable	Instrument
I. Exposure variables	
Non-occupational exposure	
- domestic use	Interview
- lifetime environmental exposure	Interview
- Exposure through family member	Interview
Occupational exposure	
- cumulative exposure - average exposure intensity - peak lifetime exposure	Interview and modelling
- acute exposure	Interview, blood for plasma and erythrocyte cholinesterase estimation Farmer questionnaire Farm records
II. Outcome variables	
Neurological symptoms	Interview
Impaired vibration sense	Vibratron II Tuning fork extinction time
Motor tremor	La Fayette testing device
Neurobehavioural	WHO NCTB battery UNISA probes ACT

Table 5.1 Measured variables (continued)

III. Confounders / Effect modifiers

Smoking	Interview
Alcohol intake	Interview Serum GGT
Nutritional status	Serum albumen
Dagga (cannabis) use	Interview
Previous Brain Injury / loss of consciousness	Interview
Previous pesticide poisoning	Interview
Education	Interview
Parental occupation	Interview
Previous experience of video games	Interview
Numeracy	Examination
Age	Interview
Height	Examination
Visual acuity	Examination
Occupational exposure to non-pesticide neurotoxins	Interview
Knowledge, attitude and practice with regard to PPE	Interview
Non-occupational exposure to non-pesticide neurotoxins	Interview
Medical history of neurological or related disorders	Interview
Use of medications	Interview

A study team of 10 researchers were responsible for the interviews, examinations and administration of special neurological tests. These were carried out once a week at sequential sites central to groups of farms over a period of 3 months early in 1993 following a set timetable. Interviewers were selected from the local population of Ceres and Prince Alfred Hamlet, and were of similar age, sex and language preference (Afrikaans) to the subjects and were familiar with farm life. Training of interviewers to standardise interview technique was carried out in-situ two weeks prior to implementation of the study proper.

Three psychology graduates were employed full-time for the duration of the study to administer the neurobehavioural test batteries and were resident in Ceres for this purpose. A detailed protocol for administration of the test batteries was developed for the study (Nell and Taylor, 1992) and supervision provided by the Health Psychology Unit from UNISA in Johannesburg. A strict order was maintained for administration of the different components of full battery, with the WHO NCTB being administered first, the ACT second and the UNISA probes last (Appendix 5.2 describes the test sequencing procedure in the field). Given the possible effects of fatigue on neuropsychological performance (Johnson et al, 1987), this ordering ensured maximum comparability of study results based on the WHO NCTB outcomes.

Different observers were involved in exposure and outcome ascertainment. This made it possible to conduct all interviews blind to outcome status, and conversely, all ascertainment of outcome status blind to exposure status.

5.3.1 Assessment of exposure/absorption

Recent occupational exposure to organophosphates was assessed by a number of different means. On history, information was collected on the date of last exposure (first and last dates) and the frequency of usage af agrichemicals in the last season month-by-month. Measurement of plasma and erythrocyte cholinesterase was used as a biological marker of recent exposure, and was done on the same day as medical examination and interview, and within a 10-day radius of neurobehavioural assessment. In addition, records were obtained from the farmers of chemicals applied in the past season, and particularly in the 10 days prior to examination. This included data on specific OP use on each farm. A further source of data on recent exposure was drawn from modelling based on information provided by field extension advisors from both co-operatives on recommended spray programmes for their farms.

Long-term exposure was primarily determined using occupational histories utilising the job-exposure matrix outlined in Chapter 3. In the JEM developed for this study, secondary data from industry are used to weight job days of exposure. In order to enable the use of the JEM, the occupational history explored job activities in great detail. Examples of the questionnaires are included in Appendix 5.1 and Table 5.2 summarises the detail to which job exposures were recorded. Attention was paid to every past job performed by the subjects in their lifetime (up to 10 jobs were coded), and every job had a minimum of 5 variables recorded.

Table 5.2 Occupational history variables

For every job performed in a lifetime:

- age at start of job
- duration of job
- industry
- job description
- geographical location

For every farm job in a lifetime:

- duration of job
- seasonality of work
- exposure to the tot system
- type of farm (produce)
- performance of 13 specific job tasks with 9 additional subtasks
- intensity of specific job activities by month and year
- use of, types of, and reasons for use of personal protective equipment
- previous poisoning events

Additional questionnaires were applied if the subject had ever previously worked in any occupation known to have any agrichemical exposure (Table 3.1 in Chapter 3). Jobs in farming, forestry and local municipality employ received additional questionnaires in order to elicit information required for the JEM. Each farming questionnaire included up to 70 variables relevant to the JEM. Factory work elicited a specific questionnaire for exposure to agrichemicals and other potential neurotoxins. In total, a maximum of 755 variables were available per subject to derive summary measures to characterise long-term agrichemical exposure adequately (Appendix 5.1).

The method used to derive long-term exposure measures was as follows:

1. Job activities were weighted according to probability of exposure in a job-exposure matrix (Table 3.11 in Chapter 3).

2. A weighted duration of each exposure was derived by multiplying duration of the activity by the probability of exposure for that activity.

3. Crop sector-specific yearly agrichemical usage patterns (Kg/hectare) were applied to each activity to derive the product of the quantity of agrichemical for that crop sector and the weighted probability of exposure in that activity (2 above). Based on data in Appendix 3.3, the average Kg OP used for each sector per year is as follows: Pome: 4.98 Kg/ha; Vines 0.24 Kg/ha; Stone fruit 2.46 Kg/ha; Wheat: 0.03 Kg/ha; Citrus 1.03 Kg/ha; Potato 0.01 Kg/ha; Other sectors 0.001 Kg/ha.

   A similar calculation of BEs OP / hectare per year is: Pome: 156.93 BEs/ha; Vines 1.65 BEs/ha; Stone fruit 41.89 BEs/ha; Wheat: 0.36 BEs/ha; Citrus 30.00 BEs/ha; Potato 0.071 BEs/ha; Other sectors 0.10 BEs/ha.

4. Cumulative exposure was derived by summing all the exposures derived above (3) for every lifetime job.

5. Average lifetime exposure was derived by dividing (4) by working life years for each subject. A log transformation {log [(cumulative days / working life) + 1]} was used to derive average lifetime intensity according to the method suggested by Berberian and Enan (1987).

The method is fully outlined in Chapter 3 and Appendix 3.4.

Additional occupational variables included total years worked in agriculture and, for spraymen, the number of spraying jobs held in a lifetime. Cumulative and average lifetime intensity of exposure was also calculated for past lifetime chronic exposure experienced on deciduous fruit farms.

5.3.2 Outcome variables - health effects

The outcomes that were assessed and the methods by which they were measured are summarised in Table 5.1. These include the presence of neurological symptoms and signs and neurobehavioural deficits based on selected test batteries. In addition, as part of the testing, a directed neurological clinical examination was performed to identify subjects meeting possible exclusion criteria, or subjects with frank neurological disease requiring further investigation. Clinical neuropathy was not regarded as the primary endpoint of interest, as the study was focussing rather on subclinical effects of long-term agrichemical exposure. Nonetheless, clinical status based on a standard clinical neurological examination was also included in the assessment.

1. Symptoms

A symptom checklist used in previous studies of solvent-related neuropathy (Bachmann et al, 1993) was modified for use in this study and included symptoms associated with peripheral and central neurotoxicity (12 symptoms - Table 6.18 in Chapter 6). All symptoms reported were qualified by an additional question on chronicity (whether the symptom had been present for the past 3 months). Included in the series of symptom questionnaires were two questions on ear pain and chest pain which served as blank questions for the assessment of the specificity of symptom reporting. A score was derived for symptom reporting for the 12 symptoms that were possibly "neurologically related" (out of 12) and for the "dummy" symptoms (out of 2).

2. Vibration sense

Impaired vibration sense was measured in the study population with the Vibratron II in the large toe of the non-dominant leg, using the method of limits (Gerr and Letz, 1988). This method involves the determination of a threshold of Vibratron voltage units at which the subject's vibration sense is extincted. Nine readings are performed and the final used variable is the natural logarithm of the average of the last 8 readings (Operating Manual, Vibratron II, Sensortek Inc, Physitemp Instruments, New Jersey, 1989). The lower limb was chosen for examination because of the propensity of toxic peripheral nerve damage to manifest first in the legs, and because the clinical pattern of OPIDP tends to affect predominantly the lower limbs (Lotti, 1992). Callosities on the digits are also likely to be less important as possible confounders (McConnell et al, 1994) when vibration sense is measured in the foot rather than the hand.

The application of the tests was performed by a single observer throughout the study, and a single apparatus was used to enable standardisation of the amplitude of vibration delivered by the device. This was achieved by calibration of the device against an external accelerometer at the start and end of each testing session. In addition, a wooden box was used to support the subject's foot during the test procedure such that the toe was resting lightly on the vibrating post of the Vibratron, slightly above flush with the box. This posture had been demonstrated, in an earlier pilot study by two medical students, to yield the most repeatable results on testing, presumably on the basis of producing the least strain in the subject's foot muscles during testing. Similarly, on examination days where the ambient temperature was low, skin temperature was kept within a 5^0 C range by allowing the subjects' feet to warm up prior to examination by use of a dry air heater in front of which the subjects were seated barefoot. Callus formation has previously been reported as covariate of vibration sense (McConnell et al, 1994). However, with testing confined to the big toe amongst a relatively homogenous manual working population, it was not thought that this would contribute to significant confounding in the study.

A previous study amongst a South African worker population found that the tuning fork extinction time was a better predictor of solvent related neuropathy than quantitative vibration threshold measurement (Bachmann et al, 1993). For this reason, vibration sense was also measured by use of a 256 Hz frequency tuning fork according to a modification of previously reported methods for standardisation of measurement of perception thresholds (Goldberg and Lindblom, 1979). A polyvynyl cylinder with a slot for the ends of the tuning fork was developed by the Biomedical Engineering Department at UCT for use in the study to standardise the amplitude of vibration delivered by the tuning fork.

The test was performed as follows: The arms of the fork were compressed and inserted to the full depth of the slot within the cylinder. The tuning fork was then sharply removed from the cylinder, thereby releasing the arms of the tuning fork. The base of the fork was then immediately applied perpendicular to the medial malleolus of the subject's non-dominant leg, with the subject sitting upright in a comfortable position with his foot resting on a carpet on the floor. Care was taken that no clothing or other contact damped the delivered vibration. The subject was immediately asked to confirm the sensation of vibration, and if he could, was asked to inform the examiner when he could no longer feel the vibration.

The extinction time (ET) was measured in seconds from release of the tuning fork till the subject reported that he could no longer feel the vibration. The average of the last two out of three readings was used as the final tuning fork extinction time variable. For all subjects, a preliminary examination was performed where the vibrating tuning fork was applied to a bony prominence on the hand, and the subject was asked to comment on the presence of absence of vibration, while the examiner damped the vibration. This was performed to ensure they were able to distinguish vibration from other contact sensations (eg: pressure, cold, etc).

3. Motor tremor

Measurement of fine motor tremor was done by means of a La Fayette apparatus routinely used at the Neuropsychology Laboratory at the University Hospital and Medical School in Madison, Wisconsin (personal communication, Prof V Nell, UNISA, 1992). The testing procedure included two subtests. The first involved a metal plate with holes of diminishing diameter into which the subject is asked to hold a stylus pen for 15 seconds. If the stylus touched the side of the hole, a counter recorded the contact as a count, and if 12 or more counts were recorded, the test was terminated. If the subject maintained the stylus in the hole with less than 12 counts, the subject progressed to the next hole.

Two scores for motor tremor were derived:

a) the number of holes the subject achieved
b) a weighted average of counts per hole given by the formula:

$$\text{Tremor intensity} = x1/1 + x2/4 + \ldots xn/v,$$

where x1 = the number of counts registered on hole #1
x2 = the number of counts on the second hole, ...
xn = the number of counts on the last hole but one
(The last hole's counts are discarded since they are all 12 or more.)
V = the square of the number of holes achieved.
The score was log transformed as (natural) log (score+0.1).

The test is repeated for dominant and non-dominant hands in sequence.

The second tremor subtest involves a maze mounted on a board at an angle of 45^0 facing the subject. The subject was asked to move a stylus pen from the starting to the end point, and each contact with the side of the maze resulted in a count. The test was performed twice for both dominant and non-dominant hands and the final variables were the average time and the average count for dominant and non-dominant hands.

Dedicated observers were involved in application of the Vibratron, the Tuning fork and the La Fayette device to obviate inter-observer variation.

4. Neurobehavioural tests

The test batteries used in this study were selected on the basis of:

- expected sensitivity to neurotoxic effects;
- being appropriate to a non-Western study population with low educational levels;
- having international comparability;
- past experience with neurobehavioural test batteries in occupational populations in South Africa.

Based on these criteria, table 5.3 summarises tests chosen for use in this study.

The WHO Neurobehavioural Core Test Battery (NCTB) screening subtests (Johnson et al, 1987) were all included except for the Profile-of-Mood-States (POMS) and the Subjective Symptoms questionnaire. These tests were excluded because of poor performance in previous studies amongst South African workers with low education (Brown et al, 1991; Nell et al, 1993), suggesting that further validation and/or modification was needed before these tests could be used to determine neuropsychological performance of exposed workers. Careful attention was paid to standardisation of test administration following WHO guidelines (WHO, 1986).

The remaining tests are based on the information processing model of cognitive psychology and measure behavioural outputs of the different components of cognitive function illustrated in figure 5.1 (Taylor and Nell, 1993).

The tests consist of two components: 1) Performance Probes and 2) tests for measurement of simple and choice reaction times and inspection time, based on the use of the Hick Box (Smith, 1986). Because all tests make use of at least one chronometric score (time), computer administration of these tests is essential. The tests have been specifically developed for use in this study in a low-education level population and were piloted with farm workers for appropriate modification before use in the main study.

Whereas the WHO NCTB tests have been extensively described in the literature, these information processing tests are not as familiar to neurobehavioural researchers and will be briefly summarised in the paragraphs below with reference to the information processing model presented in Figure 5.1.

Apprehension is measured by the time taken for the subject to respond to the illumination of one of two lights at the centre of the face panel of the Hick Box. One of the light sources is illuminated and, after 300ms, a backlight of 7 other lights comes on. The subject must respond by pressing the correct identifying button, which then extinguishes the light source. This test is called "Inspection time" and generates variables for Reaction Time (time from illumination to the subject lifting their finger off the base point), Movement Time (time from lifting their finger to extinguishing the light source) and Power Score (number of correct responses). The duration for which the light source is left on before the backlighting appears is gradually reduced in steps of 20ms to generate a window at a latency where the subject starts to make significant errors. The test is then run at three levels of backlighting delay at, and slightly below, the threshold at which the subject begins to make errors. This test is called "Inspection Window" and generates similar variables for Reaction Time, Movement Time and Power Score, using a weighting of performance results.

Encoding is measured by recording the time taken to respond to the illumination of a single light in a similar fashion to that described above but with the other lights on the panel blocked out by a mask. This test measures "Simple Reaction Time" (as in the WHO NCTB) and generates variables for Reaction Time and Movement Time. Choice Reaction Time is measured by applying the same test but with increasing numbers of lights as response options (2, 4 and 8 lights - i.e. more lights are uncovered and more options are presented), representing increasing complexity of cognitive information processing. Each Choice Reaction Time trial generates Reaction Times and Movement Times.

Attention is measured from the sustained accuracy and speed of performance on a simple monotonous task - 2 sets of digits of differing size appear on a screen in sequence. The subject must identify whether the strings are of the same number or not. This test, called "Continuous Number Checking", generates a Reaction Time, a Speed Index (items completed per millisecond (ms)), an Efficiency Index (items correct per ms), a Variabilty Index (a weighting of differences in correct items per 3 minute segment), a Transformed Accuracy Index (inverse transformation of the natural log of the proportion of incorrect responses) and a Work Gradient Index (difference in correct responses in first and second halves of the test). The glossary at the end of the Chapter gives a full explanation of the computation of these variables.

Passive Short-term Memory is measured by presenting a string of digits on a screen after which the subject is asked to identify whether that single digit was present in the original string ("Short-term Memory Scanning"). This test generates a Reation Time in ms. Active Short-term Memory ("Working Memory") is measured by presenting the subject with a task that requires the holding of three digits in short-term memory and the sequential addition of the number one to the set of numbers. This test is called "Manipulating Numbers I". As the depth of addition is increased to two levels ("Manipulating Numbers II") and three levels ("Manipulating Numbers III"), the complexity of the test increases. For each condition, a Reaction Time in ms is generated, as well as a count for correct responses. For Manipulating Numbers II and III, an Efficiency Score (average time per correct response) is also estimated.

Long-term Semantic Memory is measured using a variety of tests of Semantic Access. Traditional tests of Semantic Access rely on the comparison of two letters for physical or conceptual identity. Because of the low levels of literacy in the farm worker population, tests in this study make use of seated and standing animals (dogs, cows, sheep). In Animal Postures I, the subject is asked to compare two figures for physical identity (eg: Are they both standing dogs?) which is not itself a test of Semantic Access, while in Animal Postures II they are asked to compare for conceptual identity (eg: Are they both dogs?), which is a task requiring Semantic Access. These tests generate Reaction Times in ms, and the difference in Reaction Times between the two represents the additional cognitive processing time required by the demand for semantic access in Animal Postures II.

A second test of Semantic Access is the performance of the subject in interpreting a pointing arrow and comparing the meaning of the arrow to a presented diagram ("Speaking Arrows"). Variables are generated for Reaction Time (ms) and Count Incorrect.

A further sub-category of Semantic Access is Stimulus Resistance. The subject is presented with an arrow on the screen. In the first sub-test the subject must identify the side on which the arrow is located, while in the second test the subject must identify the direction to which the arrow is pointing ("Pointing Arrows I and II"). This second phase requires interrogation of the residual conflicting command for "side" rather than "direction". Variables are generated for Reaction Times and for the difference in

Reaction Times between the two test phases. Stimulus Resistance is further examined by the application of the tapping test of Echopraxis after completion of the computer probes. In this test, the subject is instructed to tap in response to the examiner's taps, but the correct response is to tap twice if the examiner taps once, and to tap once if the examiner taps twice. The performance is scored on a scale by examiner.

Planning is difficult to measure as a cognitive function. The Anomalous Concept Test (National Institute for Personnel Research, 1988), a test of abstract reasoning used for industry work placement (an indirect measure of the planning and monitoring functioning in the information processing model) was included in the test battery to assist in the process of concurrent validation of the cognitive theory-based testlets. The test generates a score for the ability to identify an atypical figure from a series of 6 figures of which 5 share a characteristic geometric feature. As a test of analogical reasoning, it is effectively a test of global intellectual ability, and is not intended to measure any of the discreet components identified in the information processing model of Figure 5.1.

The details of all the neurobehavioural tests and the cognitive domains tested by the subtests are outlined in Table 5.3. Tests were administered in an ordered sequence as outlined in Appendix 5.2 with the WHO NCTB tests preceding the other components of the assessment. The different variables used in the neurobehavioural outcome analyses are included in the abbreviated list in the glossary at the end of this chapter. A complete list of all variables used in preliminary and final analyses is contained in Appendix 5.3.

Table 5.3 Composite test batteries used

Source	Domain	Test
WHO:	Dexterity	Santa Ana pegboard Pursuit aiming
	Clerical speed	Digit symbol substitution
	Visuospatial function	Benton visual retention
	Attention	Digit span
	Motor speed	Simple reaction time
HPU:	Apprehension	Inspection time
	Encoding	Reaction time Choice reaction time
	Attention	Continuous number checking
	Passive short-term memory	Short-term memory scanning
	Active short-term memory (Working memory)	Manipulating numbers (I, II and III)
	Semantic access	Animal postures I and II Speaking arrows Stimulus resistance: Pointing arrows Echopraxis
HSRC	Global intellectual ability	Anomalous Concept Test (ACT)

(Sources: WHO, 1986; Nell and Taylor, 1992; National Institute for Personnel Research, 1988)

5.3.3 Effect modifiers / confounders

Many other variables were recorded in the study in order to control for confounders or to assess the impact of effect modifiers on a possible exposure effect. These are listed in Table 5.1.

Serum albumen was measured as a marker for nutritional status. Personal variables such as age, height (rounded to the nearest centimetre (cm)) and education (years of schooling and highest standard passed), which in previous studies have been shown to be related to peripheral nerve sensation and neuropsychological performance (Gerr et al, 1990a), were also recorded. Numeracy was determined from the ability of subjects to identify randomly ordered digits on a self-held card before testing. This was controlled for visual acuity by a test which involved the identification of a 1 millimetre (mm) gap in a circle of ever decreasing size (30 point, 18 point and 12 point) to check that failure to identify numbers was not due to poor eyesight (Appendix 5.4). Subjects with decreased visual acuity not improved by the use of spectacles were excluded from those Performance Probes and WHO NCTB tests requiring adequate eyesight.

Alcohol in known to be an important cause of acute and chronic neurotoxic effects (Juntunen, 1984) and may play an important confounding or effect modifying role in the investigation of occupational neurotoxic illness (Johnson et al, 1987). Given the high levels of alcohol intake amongst farm workers (Scully, 1992), particular attention was given to the characterisation of this variable in the interview. Subjects were asked for their usual drinking pattern by day of the week as well as their most recent pattern, and for what they thought was normal and abnormal drinking. In a previous study, usual drinking pattern (gram (gm) per day) was shown to be a confounder for solvent-related liver damage (Rees et al, 1993) and felt by the authors to be an accurate reflection of true alcohol intake (Rees D, personal communication, National Centre for Occupational Health, Johannesburg, 1992). These were quantified in grams of alcohol based on detailed recording of the size of the beverage container consumed (examples of empty containers were on hand during the interview).

In addition, subjects were asked a series of questions derived from two widely used inventories of alcohol intake, the CAGE questionnaire (Mayfield et al, 1974; Bernhadt et al, 1982) and the

MAST interview (Selzer, 1971). The latter instrument was shortened based on experiences in pilot studies conducted with fruit farm workers in the Stellenbosch region in the course of 1992. These were scored with a scale of 0 to 4 for the CAGE questions (all 4 cage questions were used) and 0 to 27 for the MAST questions (12 of 25 questions). (Scoring of the CAGE and MAST questions is explained in Appendices 6.3 and 6.4.) Serum gamma glutamyl transferase (GGT) was measured as a biological effect marker for short-term alcohol consumption (Juntunen 1984).

Smoking history was summarised as pack years and dagga (cannabis) usage was recorded for current and previous use. Other possible neurotoxic workplace exposures (lead, solvents, wood preservatives and other neurotoxic chemicals) were specifically sought for, as was family contact with other sprayers at home, both currently and historically. Hobbies with potential contact with neurotoxic chemicals was also recorded, such as woodwork, use of glue for model-building and painting. Use of medication may also be a confounder in occupational epidemiology studies (Vanhoorne et al, 1992) and was sought on history.

Non-occupational exposure was measured on history based on the use of pesticides at home, the use of pesticide containers for domestic purposes, gardening activities and lifetime residential exposure to possible spray drift.

Recent occupational exposure was identified on history and treated as a potential confounder in the analysis. Additonal information was obtained by questionnaire from farmers and by perusal of farm records to assess recent exposure.

5.3.4 Laboratory procedures

Measurement of plasma and red blood cell cholinesterase was performed by the Department of Chemical Pathology at Groote Schuur Hospital. The former was measured using butyrylthiocholine as substrate (Knedel and Boetger, 1967) and the latter using acetylthiocholine as substrate (Ellman, 1961). Reagents were supplied as kits (Boehringer-Mannheim Gmbh) and analyses were performed at 30^{0}C using an automated analyser (Hitachi 704). Commercial quality control sera, two each for PCE and ECE (Precipath and Precinorm, Boehringer-Mannheim Gmbh), were run within the batches of assays for PCE and ECE and good agreement was found with the stated mean values provided by the suppliers. Subject samples were taken in the field as 10 ml of heparinised venous blood and were transported to the laboratory on ice within 8 hours of venepuncture. A 10% random subsample of subjects had an additional 10 ml taken and sent to the laboratory under a false name for blinded estimations in order to assess the reliability of the laboratory measurements.

5.4 Reliability of the Data Collected

All project staff underwent intensive training in the specific tasks to which they were allocated. Interviewers, in particular, were given a week-long workshop in December 1992 during which the questionnaire was piloted and interviewers were thoroughly trained. A 10% random subsample of subjects had repeat interviews performed by the chief interviewer for the study to assess reliability of data. Questions on demographic factors were also repeated in the neurobehavioural and main study questionnaires from which reliability of data could be guaged. In addition, laboratory methods were checked for reliability as described above. All questionnaires and instructions were administered in the vernacular language, Afrikaans.

5.5 Ethical Considerations

All workers who participated in the study gave written consent after full explanation of the purpose and methods of the investigation. This was done in accordance with the Declaration of Helsinki of the 25th World Medical Assembly (WHO, 1982), and was transacted in Afrikaans, the first language for the subjects. Workers undergoing repeat questionnaires were also asked specifically for consent to participate in that particular part of the study.

Full confidentiality was observed for the subjects, and only when appropriate (for example, if blood chemistry was found to be low) were the usual medical attendants of the workers informed of the need for retesting, or for withdrawl from any further pesticide exposure. Follow up of affected workers was provided through Groote Schuur Hospital tertiary facilities.

5.6 Data Analysis

5.6.1 Data management and quality assurance

In the field all questionnaires and data sheets were checked for completeness and consistency by a single field supervisor before the subject left the examination site. Where indicated, the missing or relevant data was obtained from the subject before he left the venue. Colour coding of questionnaires was used, and a checklist was placed on the outside of an envelope containing each individual subject's data to facilitate completeness of data collection.

Questionnaire data was encoded by a single researcher within ten days of the field visit, in the process of which he was able to check for consistency and logicality of the responses entered for each subject. Field workers were available in the study region to follow up subjects who had missing or inconsistent questionnaire data, particularly for exposure characterisation. This was necessary in less than 10 cases but ensured that exposure data was complete and internally consistent for all subjects.

The bulk of the data was entered onto a Vax mainframe computer by the Data Capture Service at the University of Cape Town. WHO NCTB test battery and ACT results were scored by a single psychologist blinded to exposure status at the Health Psychology Unit in Johannesburg and the results entered into Epi Info Version 5 (USD Inc, 1990) at the Department of Community Health at UCT, and then exported into SAS (SAS Institute Inc, 1989). Results from the

Performance Probes and Hick Box tests were generated from the raw data at the Health Psychology Unit.

Each data set was cleaned by examining it for outlying or ineligible data points evident on frequency distributions and univariate printouts, and then drawing the relevant subject's data envelope to check the correctness or otherwise of the variable. This was done in turn for each of the three data sets described above.

Because of the vastness of the data sets (excluding the neurobehavioural outcomes, each subject had over 1 500 variables in their data set), reduction of the data was performed to derive pertinent variables for further analysis. This was done by summarising exposure and confounding / effect modifying variables using programmes written in SAS (SAS Institute Inc, 1989). Different ways of summarising the data were explored initially to identify the optimal method for deriving these variables. The full glossary of variables used in the univariate, bivariate and multivariate analyses in Chapters 6 and 7 are explained in Appendix 5.3.

5.6.2 Statistical methods of analysis

All analyses were conducted using SAS software (SAS Institute Inc, 1989).

a) Univariate analyses

The results were initially explored in univariate analyses with particular attention to normality of distributions and ranges. These univariate data (frequencies, or means, standard deviations and ranges) are presented in Chapter 6. Where indicated transformation of outcome data to normality was performed for subsequent analysis. Log transformation was applied to mean vibratron threshold results and to tremor intensity scores for both dominant and non-dominant hands, as well as to most of the Performance Probe results involving reaction times. Square root transformations were used for 4 of the Performance Probe outcomes. All the variables as well as the transformations used in the subsequent analyses are explained in the glossary in Appendix 5.3.

Where scores have been derived for use in data analyses, the basis for these scores is explained in the text, and in the glossary at the end of this chapter. The methods used to score alcohol consumption, and pesticide knowledge, attitude and practice are explained in Appendix 6.1 and 6.2.

b) Repeatability

After univariate analyses, assessment of repeatability was made by comparing data from repeat questionnaires of the 29 subjects who underwent repeat interview by means of kappa statistics for categorical data (Fleiss, 1981), and Pearson's and Spearman's correlation coefficients for continuous data with normal and non-normal distributions, respectively (Rosner, 1990). These results are presented at the end of Chapter 6.

c) Bivariate analyses

The next step in analysis was bivariate comparison of a range of outcomes with all exposures, confounders and effect modifiers (Table 5.1) as an initial exploration of the data. These comparisons are summarised in Appendix 7.1 which lists only those variables which were significantly associated with the various neurological and neurobehavioural outcomes. These findings are discussed in brief at the start of Chapter 7. The bivariate analyses included the following:

1. Individual symptom outcomes were categorical variables. To identify variables related to these symptom outcomes, Chi^2 tests for differences in proportions were used for variables that were categorical data, while students t-tests and Wilcoxon tests were used to compare means and medians for continuous data with normal, and non-normal distributions respectively.

2. Most outcomes other than individual symptoms were continuous data. Where these outcome variables lacked normality in their distributions, transformation of these variables to normality was performed as described above and explained in the glossary. These outcomes were analysed for their relationship to independent variables (continuous data) using linear regression techniques. For independent variables that were categorical, students t-tests and Wilcoxon tests were used where outcome data had normal, and non-normal distributions respectively. As above, all these exploratory tests were conducted for each dependent variable-independent variable pair respectively.

   Where the assumptions for linear regression could not be met, in spite of transformation of the outcome data, the continuous outcome data were reduced to categorical (dichotomous) variables and similar analyses performed as described above for symptom outcomes. In particular, this applied to score and time data on the tests of tremor, and to symptom score data for both neurological and "dummy" symptoms.

These analyses were therefore able to identify all the associations present on bivariate comparisons, which formed the basis for later multivariate modelling.

d) Identifying variables for multivariate analysis

In order to control for confounders and effect modifiers, multiple logistic and linear regression modelling were used. The choice of variables for inclusion in the models is outlined below and summarised in Figure 5.3 and was a combination of a priori decisions and selection based on the exploratory findings of the bivariate analyses. This procedure for identifying variables for inclusion in the modelling was decided upon before any bivariate anayses were performed and was rigorously followed for each outcome variable in turn.

1. A priori variables:

Based on review of the literature and consideration of the study hypothesis, the following factors were identified for a priori inclusion in the modelling: age, education, past history of pesticide poisoning, alcohol consumption, recent agrichemical exposure, non-occupational residential exposure and long-term occupational agrichemical exposure. The last factor was measured as cumulative, *or* average lifetime intensity of *occupational* agrichemical exposure. This last variable represented the primary exposure of interest.

The specific variables representing each of these factors are listed below in Table 5.4.

Table 5.4 A priori variables included in multivariate modelling

FACTOR	MEASURED BY:
AGE:	Age (years)
EDUCATION:	Schooling (years)
PAST HISTORY OF PESTICIDE POISONING	Present=1 ; Absent=0
ALCOHOL CONSUMPTION	Lifetime alcohol consumed (Gms)
RECENT AGRICHEMICAL EXPOSURE	Plasma cholinesterase (U/l)
RESIDENTIAL NON-OCCUPATIONAL EXPOSURE	Years lived in proximity (<10m) to spray activity
LONG-TERM OCCUPATIONAL EXPOSURE	
(i) CUMULATIVE EXP	Cumulative lifetime Kg OP per hectare
(ii) INTENSITY EXP	Average lifetime intensity exposure (log OP/hectare-year)
HEIGHT *	Height (cm)

* Height only included as a priori variable for mean log vibratron threshold and tuning fork extinction time.

2. Variables included from bivariate analyses

Variables other than those included a priori were selected as illustrated in Figure 5.3. Each individual variable found to be associated with each outcome variable on bivariate analysis was included individually with the 7 a priori variables listed above in a multiple regression model for that outcome. Only those variables for which the parameter estimate (linear regression) was significantly different from 0 ($p<0.05$) or for which the odds ratio (logistic regression) was significantly different from 1 ($p<0.05$) were then included in the final model.

For example, if 4 variables - innumeracy, previous head injury, use of pesticide containers and lifetime experience of the tot system - were found to be related on bivariate analyses to vibration tremor intensity in the dominant hand, each variable was included in turn in 4 separate linear regressions predicting tremor intensity along with the 7 a priori variables listed above. If innumeracy and previous head injury were found to be significant predictors of tremor intensity in the separate regression models, then they were included in a single final model consisting of the 7 a priori variables plus innumeracy and previous head injury.

The form of the general model is therefore given in the box below.

$$
\begin{aligned}
\text{OUTCOME} = a &+ B_1(\text{AGE}) \\
&+ B_2(\text{EDUCATION}) \\
&+ B_3(\text{PREVIOUS POISONING}) \\
&+ B_4(\text{ALCOHOL INTAKE}) \\
&+ B_5(\text{ACUTE EXPOSURE}) \\
&+ B_6(\text{LONG-TERM OCCUPATIONAL EXPOSURE}) \\
&\quad [\text{CUMULATIVE or AVERAGE LIFETIME INTENSITY}] \\
&+ B_7(\text{CUMULATIVE NON-OCCUPATIONAL EXPOSURE}) \\
&+ B_8(\text{HEIGHT})^{*} \\
&+ B_{9...N}{}^{\#}(\text{VARIABLES FROM BIVARIATE EXPLORATIONS})
\end{aligned}
$$

* Height only included routinely for mean log vibratron threshold and tuning fork extinction time.
# Where N is 8 plus the number of bivariate associations included in the final model.

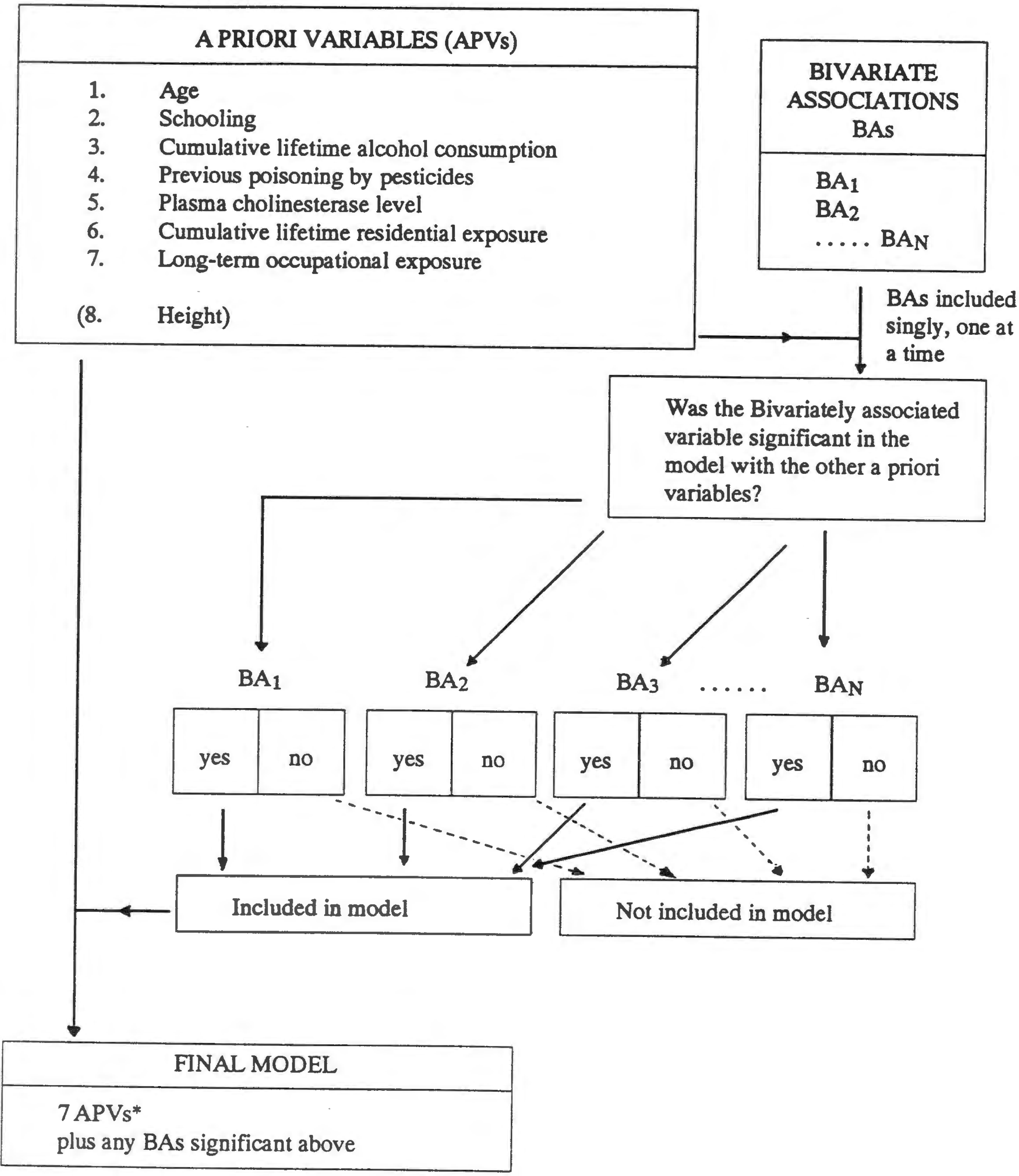


FIGURE 5.3 Strategy for selection of predictor variables for multivarite modelling or neurological and neuropsychological outcomes - Ceres 1993.

* For Log vibration threshold and tuning fork extinction time, height was added to the group of a priori variables.

For analyses of the tuning fork extinction time and vibratron thresholds, height was added to the group of a priori variables for inclusion, making a total of 8 a priori variables. This process enabled selection of relevant variables for multivariate modelling.

e) Regression modelling

After confirming that there was no evidence of non-linear relationships on plots of each outcome variable against the individual independent continuous variables to be used in the model, linear regression was chosen for analysis of all the continuous outcome data.

For linear regression, outcomes were transformed to normal distributions where appropriate by means of square root or log transformations as described above. These transformed variables are explained in the glossary in Appendix 5.3. Where the assumptions for linear regression were not met, the dependent variables consisting of continuous data were reduced to dichotomous categorical variables (using the median of the distribution as the cut-off) and multiple logistic regression applied. This was the case for outcome data pertaining to the tremor counts, tremor scores, maze counts and maze time outcomes. Logistic regression was also used for symptom outcomes (categories) with the same procedure for identifying variables for inclusion as outlined above.

Multiple linear and logistic regression were performed using full modelling, with all identified variables forced into the model. Assumptions required for linear regression (normality of the residuals and homoscedasticity) were checked in each individual case.

f) Collinearity

All multivariate models were checked to avoid the presence of collinearity amongst explanatory variables.

Because of collinearity (correlation coefficients in excess of 0.7) between cumulative lifetime OP exposure, and average lifetime intensity of OP exposure ($r>0.9$; Table 6.12 in Chapter 6), these variables could not be included in the models simultaneously. Separate regressions were therefore run, one using cumulative exposure, and one using intensity of exposure. Only where the results were substantively different were both models reported in the text in Chapter 7, although the analyses are presented in full in Appendix 7.2.

No collinearity was found between any of the other variables identified a priori. Where collinearity was identified involving one of the a priori group of variables (APVs in Figure 5.3) and one of the bivariate association variables for inclusion (BAs in Figure 5.3), the a priori variable took precedence. For example, the ability to sign consent was highly correlated with schooling years (Spearman's $r = 0.85$). Schooling years was chosen for inclusion in the model rather than the ability to sign consent.

g) Different measures of long-term occupational exposure

All the analyses involved occupational exposure with Kg as unit (whether cumulative (Kg OP per hectare) or average lifetime intensity (Kg OP per hectare-year), but a limited number of analyses were repeated using BEs OP (as outlined in Chapters 4 and 5) to assess whether these offered any advantage over the former unit of measurement. The results of these analyses are summarised in the text in section 7.4 of Chapter 7. Again, the full analyses are detailed in Appendix 7.4.

h) Biochemistry analyses

In the case of biochemical outcomes, a different approach to analysis was used. This involved multiple forward stepwise regression from a range of variables (total of 8 variables) that included:

1) Three measures of recent exposure as independent variables:
   1) Current status as a pesticide applicator (Yes/No),
   2) Days reported by subject since last contact with organophosphates (Number of days),
   3) Total days of contact with OPs in the past 3 months reported by the subject.
   The three variables were not collinear (low correlation).

2) In addition, age, serum albumen (as a marker of nutrition), cumulative lifetime alcohol consumption, cumulative occupational exposure and PPE usage score were also included as independent variables based on their known or suspected association with cholinesterase levels.

The criterion for forward stepping inclusion was improvement in explained variance at a significance level of $p<0.15$.

i) Presentation of analyses

Univariate data are presented in tables giving frequencies for categorical data, and means and standard deviations (and medians and ranges where appropriate) for continuous data. Results of multiple linear regression modelling are presented in tables that list the overall model variance explained, the variables that were significant predictors of each outcome, the direction of association, and the partial r2 for the predictor variable as a measure of the strength of association. Variables that were used in the modelling but which were not significant predictors were not listed in the tables, although the full models are presented in Appendix 7.2.

Results for multiple logistic regression are presented in tables listing the odds ratios for the association between each predictor and outcome concerned, with an associated 95% confidence interval. Again, only those variables for which a significant association was demonstrated are presented, although the full models are listed in Appendix 7.2. In the case of analyses of symptoms scores, the full models for logistic regression are presented to assist discussion of the results.

The results of these analyses are presented in the following two chapters. Chapter 6 presents the univariate analyses with a few simple bivariate comparisons included. Chapter 7 briefly summarises the findings of bivariate analyses before presenting the results of the multivariate modelling.

REFERENCES

Agnew J, Schwartz BS, Bolla KI, Ford DP, Bleecker ML. (1991). Comparison of computerised and examiner-administered neurobehavioural testing techniques. J Occ Med 33 : 1156-1162.

Anger WK, Cassito MG. (1993). Individual-admininstered human behavioural test batteries to identify neurotoxic chemicals. Environ Research 61 : 93-106.

Antti-Poika M, Ojala M, Vaheri E, Juntunen J. (1989). Occupational exposure to solvents and cerebellar, brainstem and vestibular functions. Int Arch Occup Envir Health 61 : 397-401.

Arezzo JC, Schaumberg HH, Laudadio C. (1986). Thermal sensitivity tester. Device for quantitative assessment of thermal sense in diabetic neuropathy. Diabetes 35 : 590-592.

Bachmann O, Myers JE. (1992). Acrylamide monomer and peripheral neuropathy in chemical workers. Am J Ind Med. 21 : 217-222.

Bachmann O, De Beer Z, Myers JE. (1993). n-Hexane neurotoxicity in metal can manufacturing workers. Occup Med. 43 : 149-154.

Baker EL, Feldman RG, White RF, Harley P, Dinse GE, Berkey CS. (1983). Monitoring neurotoxins in industry: development of a neurobehavioural test battery. J Occ Med 25 : 125 - 130.

Baker EL, Letz RE, Fidler AT, Shalat S, Plantamura DL, Lyndon M. (1985a). A computer-based neurobehavioural evaluation system for occupational and environmental epidemiology: Methodolgy and validation studies. Neurobehav Toxicol Teratol. 7 : 369-377.

Baker EL, White RF, Murawski BJ. (1985b). Clinical evaluation of neurobehavioural effects of occupational exposure to organic solvnets and lead. Int J Mental Health 14 : 135-158.

Ball A. (1990). Organisating farmworkers. SA Lab Bull 14(8) : 52-61.

Berberian IG, Enan EE (1987). Neurotoxic studies in humans occupationally exposed to pesticides. J Soc Occup Med. 37 : 126-127.

Bernhadt MW, Mumford J, Taylor C, Smith B. (1982). Comparison of questionnaire and laboratory tests in the detection of excessive drinking and alcoholism. Lancet 1(8267) : 325-328.

Bove FJ, Letz R, Baker EL. (1989). Sensory thresholds among construction trade painters: A cross-sectional study using new methods for measuring temperature and vibration sensitivity. J Occ Med. 31 : 320-325.

Brown DSO, Wills CE, Yousefi V, Nell V. (1991). Neurotoxic effects of chronic exposure to manganese dust. Neuropsychiatry, Neuropsychology and Behavioural Neurology 4 : 238-250.

Budlender D. (1984). Agriculture and Technology: Four case studies. Carnegie Conference Paper number 23. SALDRU, UCT.

Bundy C. (1992). Land, Law and Power in Rural South Africa. New Ground 8 : 6-8.

Cassito MG, Camerino D, Hanninen H, Anger WK. (1990). International collaboration to evaluate the WHO neurobehvioural core test battery. In: BL Johnson (Ed), Advances in neurobehavioural toxicology: Applications in environmental and occupational health. Chelsea, MI: Lewis.

Ellman GL, Courtney KD, Andres V, Featherstone RM. (1961). A new and rapid colourimetric determination of acetylcholinesterase activity. Biochem Pharmacol. 7 : 88-95.

Fleiss JL. (1981). Statistical methods for rates and proportions. 2nd ed. New York: John Wiley. pp212-236.

Fortier I, Ferraris, Mergler D. (1991). Measurement precision of an olfactory perception threshold for use in field studies. Am J Ind Med. 20 : 495-504.

Gerr FE, Letz R. (1988). Reliability of a widely used test of peripheral cutaneous vibration sensitivity and a comparison of two testing protocols. Br J Ind Med. 45 : 635-639.

Gerr FE, Hershman D, Letz R. (1990a). Vibrotactile threshold measurement for detecting neurotoxicity: Reliability and determination of age- and height-standardised normative values. Arch Envir Health 45(3) : 148-154.

Gerr FE, Hershman D, Letz R. (1990b). Comparison of vibrotactile thresholds with physical examination and electrophysiological assessment. Occasional Paper, Division of Environmental and Occupational Medicine, Mount Sinai School of Medicine, New York.

Goldberg JM, Lindblom U. (1979). Standardised methods of detemining methods of vibration perception thresholds for diagnosis and screening in neurological investigation. J Neurol Neurosurg Psychiatry 42 : 793-803.

Gregersen P, Angelso B, Nielsen TE, Norgaard B, Uldal C. (1984). Neurotoxic effects of organic solvents in exposed workers: An occupational, neuropsychological and neurological investigation. Am J Ind Med. 5 : 201-225.

Hamman J. (1993). Labour law in agriculture. SA Labour Bulletin 17(5) : 55-59.

Hanninen H. (1985). Twenty-five years of behavioural toxicology within occupational medicine: A personal account. Am J Ind Med 7 : 19-30.

He F, Zhang S, Li G, Zhang Z, Dong X, Wang H, Li F, Hu F. (1990). Assessment of the adverse effects of acrylamide on occupationally-exposed workers - neurological and electroneuromyographical studies. In: BL Johnson (Ed), Advances in neurobehavioural toxicology: Applications in environmental and occupational health. pp 377-387. Chelsea, MI: Lewis.

Hennekens CH, Buring JE. (1987). Epidemiology in Medicine. Little Brown and Company. Boston.

Hershfield AF, Rohling NG, Kerr GB, Hursh-Cesar G. (1993). Fieldwork in rural areas. In: M Bulmer, DP Warwick (Eds), Social research in developing countries. pp 241-252. UCL Press, London.

Hooisma J, Emmen HH, Kulig BM, Muijser H, Poortvliet D. (1990). Factor analysis of tests from the neurobehavioural evaluation system and the WHO neurobehavioural core test battery. In: BL Johnson (Ed), Advances in neurobehavioural toxicology: Applications in environmental and occupational health. pp 245-255. Chelsea, MI: Lewis.

Husman K, Karli P. (1980). Clinical neurological findings among car painters exposed to a mixture of organic solvents. Scand J Work Environ Health 6 : 33-39.

Innes DF, Fuller BH, Berger GMB. (1990). Low serum cholinesterase levels in rural workers exposed to organophophate pesticide levels. S Afr Med J 78 : 581-583.

Iregren I, Gamberale F. (1990). Human behavioural toxicology. Scan J Work Envir Health 16 (suppl) : 17-25.

Johnson BL, Baker EL, Batawi ME, Gilioli R, Hanninen H, Seppalainen AM, Xintaras C, editors (1987). Prevention of neurotoxic illness in working populations. John Wiley and Sons, New York.

Juntunen J. (1984). Alcohol, work and the nervous system. Scand J Work Envir Health 10 : 461-465.

Knedel M, Bottger R. (1967). Eine kinetische methode zur bestemming der aktiwitat der psuedocholinesterase. (A kinetic method for determining pseudocholinesterase). Klinische Wochenschrift 45 : 325.

Landrigan PJ, Graham DG, Thomas RD. (1993). Strategies for the prevention of environmental neurotoxic illness. Environ Research 61 : 157-163.

Letz R. (1993). Covariates of computerised neurobehavioural test performance in epidemiologic investigations. Environ Research 61 : 124-132.

Liang Y, Chen Z, Sun R, Fang Y, Yu J. (1990). Application of the WHO Neurobehavioural Core Test Battery and other neurobehavoural screening methods. In Advances in Neurobehavioural Toxicology: Applications in Environmental and Occupational Health. Ed: BL Johnson. Lewis, Chelsea, MI.

London L. (1992). Pesticide safety practices on farms in the Stellenbosch area. Report to the Western Cape Regional Services Council Health Department. Stellenbosch.

London L, Myers J. (1993). "Agrichemical Hazards and the Work Process in Agriculture in the Western Cape." Occupational Health Research Unit Report number 1. Department of Community Health, University of Cape Town, Rondebosch, Cape Town.

Lotti M. (1992). Central neurotoxicity and behavioural effects of anticholinesterases. In: Clinical and experimental toxicology of organophosphates and carbamates. Eds Ballantyne B, Marrs TM, Aldridge WN. Butterworth, Stoneham, MA.

Luria AK. (1971). Towards the problem of the historical nature of psychological processes. Intnl J Psychol. 6 : 260-272.

Maroni M, Jarislavo J, La Ferla F. (1986). The WHO-UNDP epidemiological study on the health effects of exposure to organophosphorus pesticides. Toxicol Letters 33 : 115-123.

Mayfield DG, Mcleod G, Hall P. (1974). The CAGE questionnaire: validation of new alcoholism screening instrument. Am J Psych 131 : 1121-1123.

McConnell R, Keifer M, Rosenstock L. (1994). Elevated quantitative vibrotactile threshold among workers previously poisoned with methamidophos and other organophosphate pesticides. Am J Ind Med. 25 : 325-334.

Mergler, D, Belanger S, de Grosbois S, Vachon N. (1988). Chromal Focus of Acquired Chromatic Discrimination Loss and Solvent Exposure among Printshop Workers. Toxicology 49 : 341-348.

Mergler D, Bowler R, Cone J. (1990). Colour vision loss among disabled workers with neuropsychological impairment. Neurotox Teratol. 12 : 669-672.

Myers JE, Nell V, Colvin M, Rees D, Cronje R, Thompson ML. (1994) Neuropsychological and neurological function in paint manufacturing workers with long-term exposure to organic solvents in two South African factories. Manuscript in progress.

National Institute for Personnel Research. (1988). Test administrator's manual for the industrial test battery. Human Sciences Research Council, Pretoria.

Nell V, Taylor TR. (1992). Bypassing Culture. Administration manual. Technical Report 2.92. Health Psychology Unit, UNISA, Johannesburg.

Nell V, Myers JE, Colvin M, Rees D. (1993). Neuropsychological assessment of organic solvent effects in South Africa: Test selection, adaptation, scoring and validation issues. Environ Res. 63 : 301-318.

Otto DA. (1989). Neurotoxicity testing of agricultural workers exposed to pesticides. In: Principles of Health and Safety in Agriculture. pp 402-406. Ed: JA Dosman, DW Cockcroft. CRC Press, Boca Raton, Florida.

Otto D, Soliman S, Svensgaard D, Soffar A, Ahmed N. (1990). Neurobehavioural assessment of workers exposed to pesticides. In : Advances in neurobehavioural toxicology: Applications in Environmental and Occupational Health. Ed: Johnson BL, Anger WK, Durao A, Xintaras C. pp 305-322. Lewis Publishers, Michigan.

Peil M. (1993). Situational variables. In: M Bulmer, DP Warwick (Eds), Social research in developing countries. pp 71-88. UCL Press, London.

Ramirez JA, Arsimendi G, Cedillo L, Revvelta AM, Topete LM, Silva A. (1990). Advances in a psychodiagnostic test battery for Mexican workers exposed to toxic substances in the petrochemical and other industries. In: BL Johnson (Ed), Advances in neurobehavioural toxicology: Applications in environmental and occupational health. pp97-105. Chelsea, MI: Lewis.

Rees D, Soderlund N, Cronje R, Song E, Kielkowski D, JE. (1993). Solvent exposure, alcohol consumption and liver injury in workers manufacturing paint. Scan J Work Envir Health 19 : 236-244.

Rosner B. (1990). Fundamentals of Biostatistics. 3rd edition. PWS Kent, Boston, Massachusetts.

Sack D, Linz D, Shukla R, Rice C, Bhattacharya A, Suskind R. (1993). Health Status of pesticide applicators: Postural stability assessments. J Occ Med. 35(12) : 1196-1202.

Sandmark B, Broms I, Lofgren L, Ohlson C. (1989). Olfactory function in painters exposed to organic solvents. Scand J Work Environ Health 15 : 60-63.

SAS Insitute Inc. (1989). SAS/STAT User's Guide, Version 6.08. Fourth edition. Cary.

Savolainen K, Riihmaki V, Vaheri E, Linnoila M. (1980). Effects of xylene and alcohol an vestibular and visual functions in man. Scand J Work Envir Health 6 : 94-103.

Scully P. (1992). Liquor and labour in in the Western Cape, 1870-1900. In: (Eds: J Crush, C Ambler) Liquor and Labour in Southern Africa". Ohio University Press, Athens.

Selzer ML. (1971). The Michigan alcoholism screening test: the quest for a new diagnostic instrument. Am J Psych 127 : 1653-1658.

Smith GA. (1986). Inspection time and response strategies in a choice response task. Personality and Individual Differences 7 : 701-707.

Taylor TR, Nell V. (1993). Bypassing culture: An approach to neuropsychological assessment informed by cognitive theory. Manuscript submitted for publication. Human Sciences Resource Council and Health Psychology Unit, University of South Africa, Johannesburg.

United States Congress Office of Technology Assessment. (1990). Neurotoxicty. Identifying and controlling poisons of the nervous systems. OTA-BA-436. Washington DC: US Government Printing Office.

USD Incorporated. (1990). Epi Info, Version 5. Stone Mountain, Georgia.

Valciukas JA, Lilis R. (1980). Psychometric techniques in environmental research. Envir Research 21 : 275-297.

Valciukas JA, Levin SM, Nicholson WJ, Selikoff IJ. (1986). Neurobehavioural assessment of Mohawk Indians for subclinical indications of methyl mercury neurotoxicity. Arch Env Health 41 : 269-272.

Van der Vijver FJR, Pooringa Y. (1982). Cross-cultural generalisation and universality. Journal of Cross-cultural psycholgy 13 : 387-408.

Vanhoorne M, Blancke V, De Bacquer D, Depoorter AM, Bogaert M. (1992). Use of pharmaceuticals in industrial workers - possible implications for epidemiological studies. Int Arch Occup Envir Health 64 : 25-30.

Vygotsky L. (1988) Thought and Language. MIT, Cambridge, Mass.

Waldman PL. (1993). Here you will remain: Adolescent experience on farms in the Western Cape. MA Thesis, Department of Anthropology, University of Cape Town, Cape Town, South Africa.

Weiss B. (1990). Neurotoxic risks in the workplace. Appl Occup Envir Hyg. 5 : 587-594.

White RF, Proctor SP. (1992). Research and Clinical Criteria for Development of Neurobehavioural test batteries. Journal of Occupational Medicine 34 : 140-148.

WHO. (1982). Declaration of Helsinki - Proposed International Guidelines for Biomedical Research involving Human Subjects. Council for International Organization of Medical Sciences, revised 1975 by 29th World Medical Assembly, Tokyo. WHO, Geneva.

WHO. (1986). Operational Guide for the WHO neurobehavioural core test battery. World Health Organisation. Office of Occupational Health, Geneva.

Williamson AM. (1990). The development of a neurobehvioural test battery for use in health evaluations in occupational settings. Neurotoxicol Teratol. 12 : 509-514.

Williamson AM, Winder C. (1993). A prospective cohort study of the chronic effects of solvent exposure. Environmental Reseach 62 : 256-271.

Zarkovich SS. (1993). Some problems of sampling in underdeveloped countries. In: M Bulmer, DP Warwick (Eds), Social research in developing countries. pp 101-108. UCL Press, London.

CHAPTER 6

NEUROLOGICAL AND NEUROBEHAVIOURAL EFFECTS OF AGRICHEMICAL USE AMONG DECIDUOUS FRUIT FARM WORKERS IN THE WESTERN CAPE, SOUTH AFRICA

CONTENTS — Page

CHAPTER 6

NEUROTOXIC EFFECTS OF AGRICHEMICALS AMONG DECIDUOUS FRUIT FARM WORKERS IN THE WESTERN CAPE, SOUTH AFRICA

I. UNIVARIATE ANALYSES AND LIMITED BIVARIATE ANALYSES

6.1 Sample Participation and Demographic Characteristics

Two hundred and forty seven subjects from 73 farms participated in the study. This represented 68% of eligible subjects and 65% of eligible farms. Seventy-seven percent of the participant farms were greater than 25 hectares in size. By contrast, of the farms that did not participate (39), most (64%) were smaller than 25 hectares in size (X^2=18.07 ; p< 0.0001). These farms were geographically more remote and logistics for their participation were more difficult. The smaller farms were also less willing to spare their only spray operator to participate in the study. A review of pesticide poisoning notifications reported to the regional department of health for the period 1987 - 1991 (London et al, 1994) did not demonstrate the presence of any previous reported pesticide poisoning on these particular farms. Nonetheless, the possibility still exists that the smaller farms may have poorer safety measures which may result in this study being a best-case scenario.

The mean age of the subjects was 36.9 years (SD 10.0) and mean educational level achieved was 5.1 years (SD 2.9). This is slightly higher than the levels found in a study of fruit and grape farms in the Western Cape between 1983 and 1985 where the average years of schooling was found to be 4.3 (Groenewald, 1986). Education was measured in two ways - years of schooling (including years repeated at school) and highest standard reached. The two variables were highly correlated with each other (r=0.89) and with equivalent questions asked by examiners in the course of the neurobehavioural assessment (r=0.86 and r=0.96 repectively). Because higher agreement was found for highest standard achieved, this variable (as measured in the general study questionnaire - Appendix 5.1) was chosen as the variable to represent educational status in all analyses.

Another aspect of education was the ability of the subjects to write their own names. Twenty-one percent of subjects were unable to sign their names in giving consent for the study, suggesting substantial illiteracy. Using a modification of UNESCO criteria (less than 6 years of completed schooling - Weidepoel, 1984), approximately 44% of subjects would be considered illiterate. Non-numeracy was another indicator of low education, and 9 subjects (3.7%) were found to be innumerate.

One hundred and sixty-four of the subjects were workers in currently exposed job activities (the exposed group, E) and the remaining 83 were controls (the non-exposed group, NE). Table 6.1 summarises the demographic variables of the sample by current exposure status. Differences between the two groups in age and education were small and were not statistically significant, indicating that the matching strategy was successful. The rationale for this strategy has been outlined in Chapter 3.

Table 6.1 Demographic characteristics of study sample

Demographic variable	Exposed (E) Mean (SD) (n=164)	Non-exposed (NE) Mean (SD) (n=83)	Total Mean (SD)
Age in years (n=247)	36.9 (9.8)	36.9 (10.6)[1]	36.9 (10.0)
Schooling in completed years (n=247)	4.8 (2.8)	5.5 (3.1)[2]	5.1(2.9)
Illiteracy * (n=247)	20.7% (34/164)	21.7% [3] (18/83)	21.1 (52/247)

* - Illiteracy defined as proportion of subjects unable to sign names.
1 - Wilcoxon 2-sample test for difference in medians: P=0.84
2 - Wilcoxon 2-sample test for difference in medians: P=0.09
3 - Chi^2 for difference in proportions = 0.15 ; P = 0.69

In most of the subsequent data presentation, reference will no longer be made to current exposure status, unless it is a confounding variable, or is considered to be an independent variable of interest. The major exposure outcome relationships will be examined in terms of the long-term exposure variables outlined earlier in Chapters 3 and 5.

Parental occupation of the subjects is listed in Table 6.2. The most common parental employment was as farm worker and very few of either of the subjects' parents had ever held skilled or supervisory jobs. This confirms the closed nature of farm life (Ball, 1990; Waldman, 1993a) and suggests that the influence of work outside of the agricultural setting is minimal.

Table 6.2 Parental occupation of deciduous fruit farm workers (n=241)

	Father	Mother
Farm worker	191 (79.5%)	94 (39.0%)
Supervisory/ semi-skilled work on a farm	10 (4.1%)	1 (0.4%)
Labourer in another industry	36 (14.9%)	11 (4.6%)
Domestic service	-	35 (14.5%)
Housewife	-	93 (38.6%)
Other	4 (1.7%)	7 (2.9%)
TOTAL	241	241

6.2 Life History - Years Spent Living in a Farming Environment

The majority of subjects had spent most of their lives resident on a farm. Three variables describing lifetime experience of farm residence are summarised in Table 6.3: 1) the number of years lived on a farm (TOTYEARS), 2) the number of years lived on a farm that was sprayed by aeroplane or tractor (TOTEXP) and, 3) the number of years lived both on a farm that was sprayed by aeroplane or tractor, and within 5m proximity of the nearest field, orchard or vineyard (TOTNEAR). Equivalent variables are also summarised for lifetime experience of residence on a deciduous fruit farm (FDYEARS, FDEXP and FDNEAR) in the table. Variables TOTEXP and TOTNEAR, and FDEXP and FDNEAR are thus weighted for more stringent criteria of residential exposure to pesticides.

Table 6.3 Lifetime residence on a farm among deciduous fruit farm workers *

	Mean	SD	Range
I. Any farms:			
* Total years resident	32.3	11.1	0.25 - 63
* Total years resident on a farm sprayed by air or tractor	27.8	11.7	0.25 - 61
* Total years resident in proximity to spray by air or tractor	9.4	11.9	0 - 47
II. Only deciduous fruit farms:			
* Total years resident	27.4	11.9	0.25 - 61
* Total years resident on a farm sprayed by air or tractor	26.0	11.6	0.08 - 61
* Total years resident in proximity to spray by air or tractor	9.2	12.0	0 - 47

* N = 247

Most subjects had spent the majority of their lives resident on a farm, and particularly, on deciduous fruit farms. These findings are consistent with anthropological studies of farm workers' life histories and experiences in the Western Cape (Waldman, 1993b). Exposure to pesticides in the environment in one's childhood may play an important role in any possible adverse neurobehavioural effects. Figure 6.1 presents a frequency distribution of childhood (up to the age of 16) years spent resident on a farm, and on a deciduous fruit farm. Most subjects spent all their childhood years growing up on a farm, and over three-quarters of subjects spent more than half their childhood years growing up on a deciduous fruit farm.

6.3 Lifestyle Factors: Alcohol and Smoking

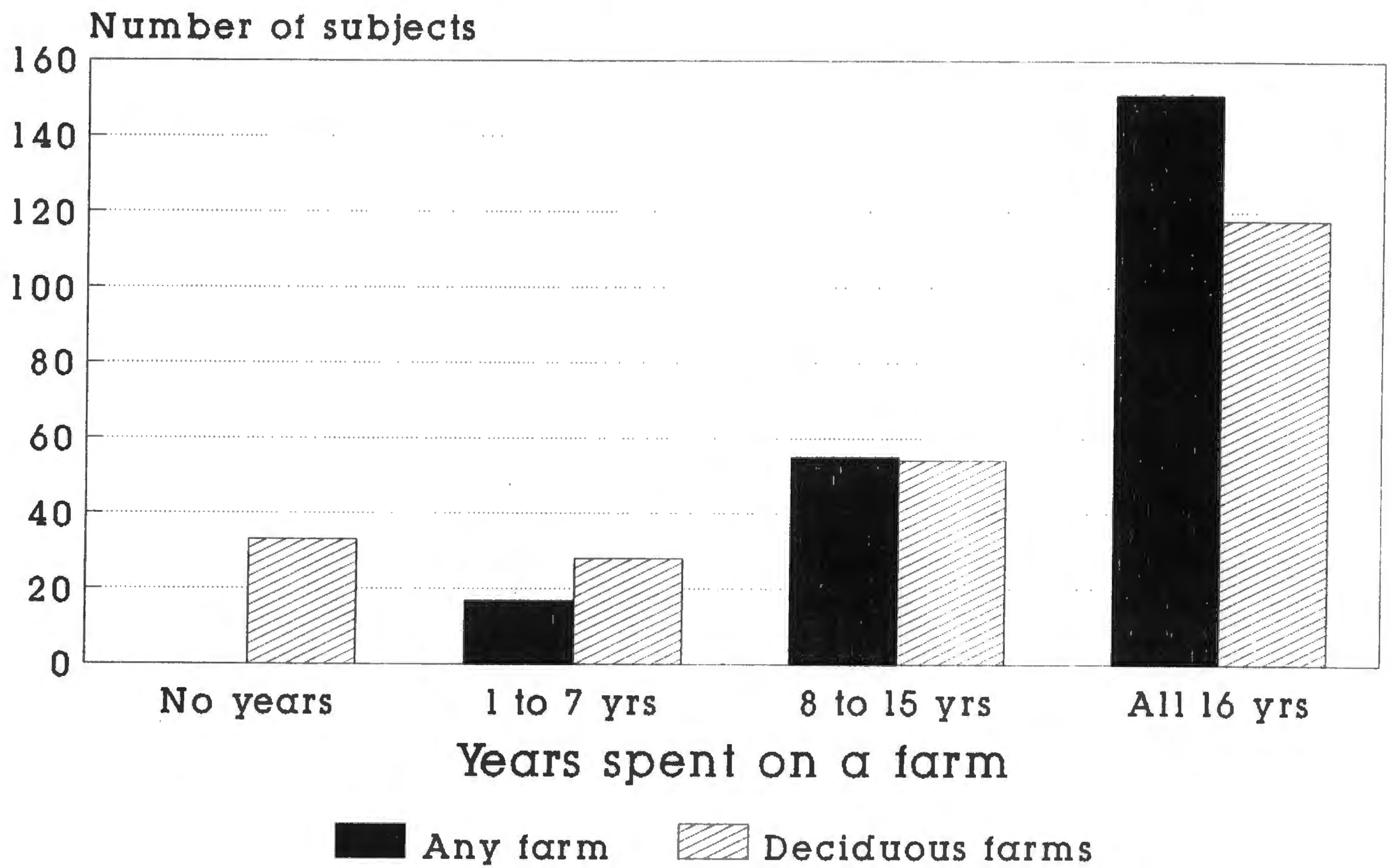
High prevalences of smoking and alcohol use are reflected in Table 6.4. Eighty-one percent of subjects reported being current smokers and average cumulative lifetime consumption (including all forms of tobacco) was 12.0 (SD 12.9) pack year equivalents. Less than 5% reported having never used alcohol. These figures are likely to be underestimates, particularly with regard to volunteering alcohol and dagga usage, and alcohol data is complemented by other measures in tables that follow.

Table 6.4 Prevalence of lifestyle habits amongst deciduous fruit farm workers

	Percentage
Alcohol use (n=247)	
Current	67.6
Past	27.9
Never	4.5
Smoking habits (n=247)	
Current	81.0
Past	10.9
Never	8.1
Dagga use (n=245)	
Current	3.7
Past	24.1
Never	72.2

Lifetime experience of the tot system (see Chapter 2) is likely to influence drinking patterns amongst workers. Almost one-fifth

Figure 6.1 Childhood years on a farm Deciduous fruit and All farms



Maximum years 16

(19.4%) of workers interviewed reported current use of the tot system, and 47.8 % of workers had experience of 1 or more farms in the past where the tot system had been used.

Various quantitative measures of alcohol use are summarised in Table 6.5.

<u>Table 6.5 Measures of alcohol usage amongst fruit farm workers</u>

Alcohol measure	n	Mean	SD	Range
* Cumulative lifetime kilograms of alcohol	247	216.8	204.0	0 - 1000.5
* Grams alcohol consumed on a usual weekend	236	260.0	190.2	1 - 940
* Grams alcohol consumed in preceding week	236	241.5	192.4	0 - 952
* Grams alcohol consumed at a sitting	236	135.6	146.6	2 - 810
* Grams alcohol regarded as excessive by subject	216	165.6	119.3	10 - 564
* CAGE score (max 4)	247	2.8	1.3	0 - 4
* MAST score (max 27)	247	7.5	5.9	0 - 27
* Serum GGT (U/l)	247	22.8	19.0	5 - 124

These results are interesting from a number of perspectives. Firstly, they confirm the high alcohol drinking patterns reported amongst farm workers (Whittaker, 1987). Using the clinical range quoted by Groote Schuur Hospital Chemical Pathology laboratory (0-40 U/l), 10.5% of the sample exhibited elevated levels of Gamma Glutamyl Transferase (GGT), which may be regarded as a non-specific marker of liver injury due to alcohol insult.

Secondly, the sample exhibits very high scores on both inventories developed in the United States for detection of alcholism (CAGE and MAST). Scoring used on both inventories is explained in Appendix 6.1. Using criteria of 2 or more positive answers to the CAGE questionnaire (Mayfield et al, 1974; Bernhadt et al, 1982), 87% of the sample would be defined as alcoholic. Similarly, using a criteria of a score of 5 or more based on the MAST questionnaire (Selzer, 1971), 65% of the sample would be considered to have a drinking problem. This is in spite of the abbreviation of the MAST questionnaire in this study to a maximum score of 27 (the original MAST scores go up to 50). However, the application of screening tests developed in a hospital setting in a developed country for the detection of alcoholism in other settings should be critically evaluated, particularly given the difficulties in establishing the cross-cultural validity of such instruments.

Nonetheless, the quantitative measures of alcohol consumption recorded in Table 6.5 suggest that drinking patterns are high in relation to other South African (Wolmarans et al, 1988; Rees et al, 1993; Bourne et al, 1993) and Southern African studies (Chinyadza et al, 1993), and comparable to a previous study of farm workers in the Western Cape (Whittaker, 1987). For example, the amount of alcohol reported as consumed in the past week was more than double that of rural White residents (Wolmarans et al, 1988) and urban Africans of similar age range (Bourne et al, 1993) in the Western Cape. Expressed in distributional terms, over 80% of farm workers in this study reported consuming more alcohol than the highest average intake (110 grams/week) reported for any of the age strata in either of the two studies above.

Correlation between different measures of alcohol consumption are presented in Table 6.6 (as Pearson correlation coefficients). Reported cumulative lifetime, usual weekend and past week consumption of alcohol tended to be better correlated with each other, but not with either the CAGE or MAST scores, and gave very low correlation with an "objective" measure of alcohol consumption, GGT. Similarly, categorisation of CAGE scores into high (4) and low (3 or less) and reduction of GGT to high (greater than the median 18) versus low (18 or less) failed to show any significant relationship between the two variables (Kappa=0.02).

Table 6.6 Correlation between different measures of Alcohol intake

	Ethanol	Alcwknd	Recalc	Sitquant	Abnquan	CAGE	MAST	GGT1
Ethanol	1.00	0.64	0.57	0.10	0.14	0.30	0.39	0.07
n	247	236	232	236	216	247	247	247
Alcwknd		1.00	0.84	0.18	0.16	0.32	0.42	0.01
n		236	232	236	216	236	236	236
Recalc			1.00	0.12	0.16	0.30	0.43	0.01
n			232	228	212	232	232	232
Sitquant				1.00	0.17	0.10	0.12	-0.06
n				236	216	236	236	236
Abnquan					1.00	-0.02	-0.07	-0.04
n					216	216	216	216
CAGE						1.00	0.56	0.10
n						247	247	247
MAST							1.00	-0.04
n							247	247
GGT1								1.00
n								247

* Ethanol = Cumulative lifetime kilograms of alcohol
* Alcwknd = Grams alcohol consumed on a usual weekend
* Recalc = Grams alcohol consumed in preceding week
* Sitquant = Grams alcohol consumed at a sitting
* Abnquan = Grams alcohol regarded as excessive by subject
* CAGE = CAGE score
* MAST = MAST score
* GGT1 = Serum GGT

6.4 Medical and Psychiatric History

A past history of relevant medical disorders was found in a minority of subjects. However, previous brain injuries were common in the sample, and there was a history of 303 brain injuries causing loss of consciousness among 169 subjects (69.8%). Eighty-two subjects (33.9%) experienced two or more episodes of loss of consciousness as a result of a brain injury, and in 79 subjects (32.6%) the loss of consciousness was reported as lasting an hour or longer. A small proportion of subjects (3.3%) were flagged for visual difficulties and were excluded in analyses of neurobehavioural tests reliant on adequate vision. These findings are summarised in Table 6.7.

Table 6.7 Medial, psychiatric and neurological findings on interview and examination

	Percentage	Total N
Past history of:		
Epilepsy	2.1	240
Diabetes	0.8	240
Psychiatric disorder	0.4	240
Past history of brain injury (BI):		
Any BI	70.1	242
BI causing loss of consciousness	69.8	242
BI causing loss of consciousness > 1 hr	32.6	242
Currently on medication	11.2	242
Unable to recognise numbers	3.7	242
Visual acuity difficulty	4.9	242
Past experience of:		
Watching video games	75.6	221
Playing video games	18.6	221

The commonest types of brain injury were either from a blunt object (39% of all subjects) or from a penetrating wound (16% of all subjects). These were about twice to three times as common as motor vehicle accidents or sport injuries, and this probably reflects high levels of interpersonal violence experienced by farm workers. Other types of brain injury included near-drownings, asphyxiation by fire smoke and sports injuries.

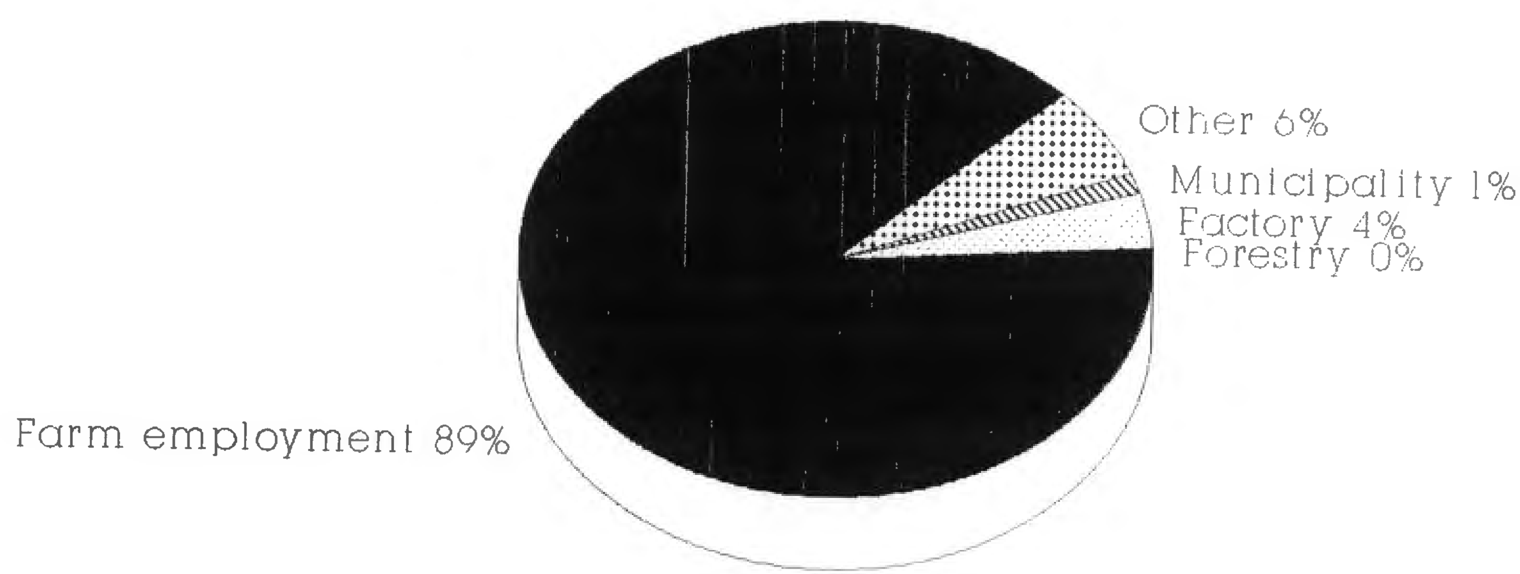
Past occupational poisoning with pesticides was reported by 22 subjects (8.9%) of whom 15 (6.1%) reported time off work or consulting a doctor. All cases were reported as occuring during farm jobs, and no cases of pesticide poisoning were reported during previous factory, forestry or municipality work. In none of these cases was the chemical responsible identified. Past exposure to chemical fumes or vapours resulting in dizziness or collapse was reported by 28 subjects (11.7%; n=240). Agreement between these two reported sources of poisoning was poor (Spearman's r=0.076) and these cases of fume poisoning (including solvents, pesticides, toxic gases, etc.) may have included cases of mild or non-occupational pesticide poisoning not reported in the occupational history.

6.5 Occupational Exposure History

6.5.1 Lifetime exposures

The total number of previous jobs reported was 814, an average of 3.3 jobs per subject. Sevnty-six percent of the sample reported at least one other previous job. Figure 6.2 presents the frequency distribution of lifetime employment in the sample. The most common previous job was overwhelmingly in agriculture (88.2%). Of the rest, 3.6% were in municipality work, 1.3% in a factory and the rest in jobs with no obvious potential for occupational pesticide exposure (eg: clerical, shop assistant). Only one worker reported previous employment in forestry. Long-term exposures amongst this group therefore appear to be relatively homogenous, with little presence of non-agricultural neurotoxic exposures occuring in other industries.

Figure 6.2 Current and past jobs amongst deciduous fruit farm workers



N ▪ 812 jobs among 247 workers

Various measures of long-term occupational exposure are summarised in Table 6.8. These exposure indices progress in complexity from simple measures of total years worked on a farm (JYR10) and the number of jobs held as sprayman (SPRYJOBS) to more elaborate indices of long-term exposure based on arguments outlined in Chapter 3 and 5. The variables are explained in more detail at the foot of the table.

The difference between measures CUMULTR and CUMULTOT in the table reflects the contribution of routes of occupational exposure other than mist blower activities, as modelled in Table 3.11 of Chapter 3, as well as the contributions of exposures in other jobs. However, the latter was found to be minimal in this study with only 2 workers experiencing pesticide exposure in non-farming jobs, both of which were municipality jobs. No pesticide exposures were recorded in previous factory or forestry work. This suggests that past non-farming exposures in farm worker populations in this setting are likely to be minimal.

Occupational exposures to pesticides other than through mist blower operation appear to contribute a large proportion (45%) to overall lifetime exposure (Table 6.8 and Figure 6.3). These activities included handspray with pesticides (20.5% of total cumulated weighted exposure days), backpack spraying (7.5%), general orchard work (12.3%) and gardening (1.8%). In terms of actual days spent in specific activities, thinning was reported as an activity by more subjects (224 thinned; 172 mist blower) and average real lifetime days spent thinning was almost as common as mist blower operation (496 thinning; 516 mist blower). However, because of their relative weighting (Chapter 3 - Table 3.11), mist blower operation accumulated more than 4 times the total weighted days cumulated by thinning activities in the sample as a whole.

Table 6.8 Measures of long-term occupational exposures among fruit farm workers

	N	Mean	(SD)	Range
1. JYR10 (years)	247	19.6	(10.8)	0.3 - 53
2. SPRYJOBS (jobs)	172[a]	1.6	(0.96)	1 - 7
3. CUMULTR (days)	247	249.9	(495.1)	0-1651.2
4. CUMULTOT (days)	247	456.18	(636.80)	0-4669.8
5. POMDYS (days)	245	444.9	(625.4)	0-4669.8
6. EXWGHT (Kg OP per hectare)	247	5.65	(8.17)	0-63.71
7. EXWGHTB (BE OP per hectare)	247	177.2	(257.6)	0-2007.8

* JYR10: Total years as farm worker

* SPRYJOBS: Total number of jobs held as sprayman

* CUMULTR: Cumulated lifetime days of driving a tractor while operating a mist blower applying agrichemicals.

* CUMULTOT: Cumulated lifetime days of any relevant job with agrichemical exposure weighted for the probability of exposure in each job activity (Table 3.11).

* POMDYS: Cumulated lifetime days of any relevant job with agrichemical exposure in pome fruit farming weighted for the probability of exposure in each job activity.

* EXWGHT: Cumulated lifetime days of any relevant job with agrichemical exposure weighted for the probability of exposure in each job activity and for Kg OP usage per hectare per year per specific crop sector.

* EXWGHTB: Cumulated lifetime days of any relevant job with agrichemical exposure weighted for the probability of exposure in each job activity and for BE OP usage per hectare per specific crop sector.

a - N includes 163 subjects in current jobs as mist blower operators as well as 9 workers currently not exposed who had previous employment as a mist blower operator.

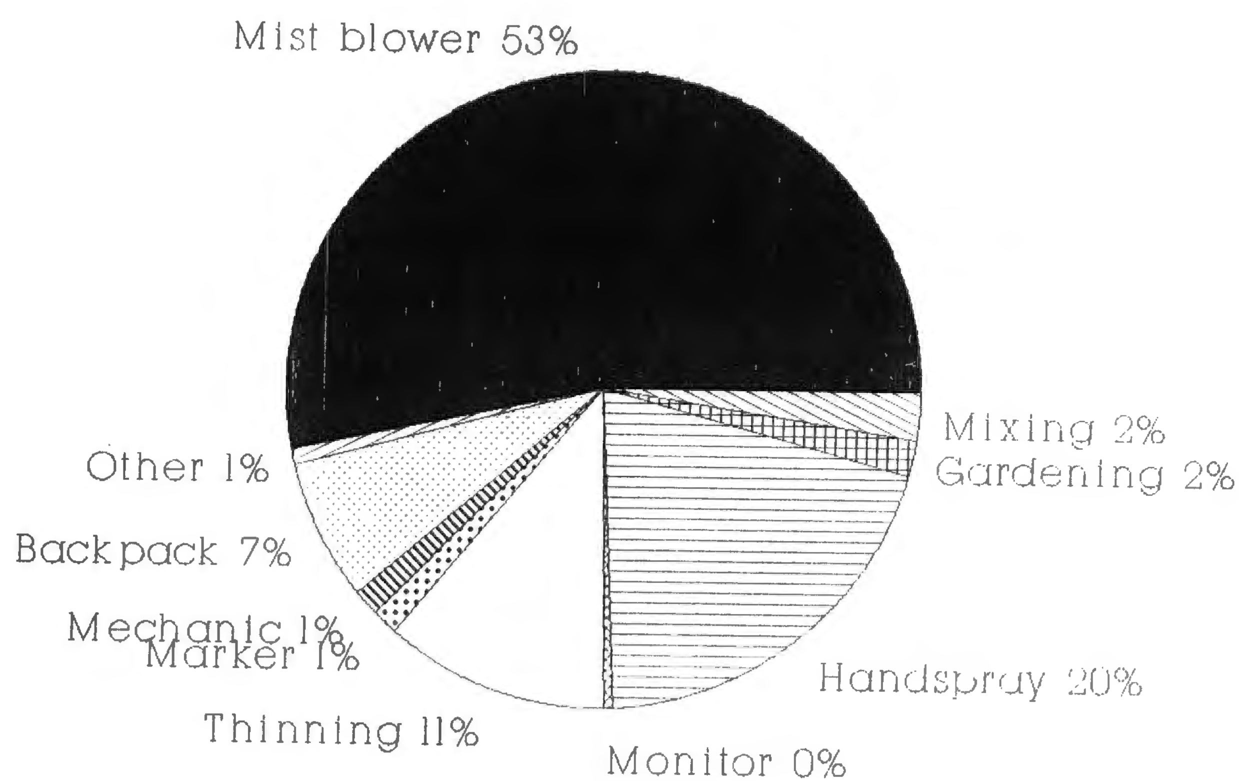
Forty-eight subjects (19%) reported exposure as human markers for aerial spraying in their lifetimes, with 24 subjects (9.7%) reporting exposures as a human marker in their current job. While these exposures may be considered to be episodic, they are likely to involve high levels of exposure and will be flagged as a specific variable in subsequent exposure effect analyses.

Table 6.9 Agrichemical exposures by job activities

	Subjects [1]	Total cumul weighted days [2]	Actual lifetime days[3] Median	Range
Mist blower operator	172	61 715.9	516	13 - 5805
Handspray	112	23 066.3	101	1 - 2580
Backpack spray	68	8 389.1	59.5	1 - 1032
Mixing	9	2 870.8	310	17 - 1204
Marker	48	1 500.0	7	1 - 149
Orchard work				
Thinning	224	13 309.0	496	5 - 2258
Monitor	19	495.9	243	52 - 3096
Dipping	97	724.6	5.75	1 - 122
Mechanic	6	775.4	268	16 - 1805
Gardening	60	2089.2	245	5 - 6966
Other	11	925.0	15	1 - 452

1 - Subjects reporting listed exposure activity. Exposure activities are not mutually exclusive.
2 - Sum of all subjects' weighted exposure days (CUMULTOT) for that specific job activity category (see Table 3.11 in Chapter 3 for weighting).
Total for all categories for the total sample = 115 861.2 weighted days.
3 - Median and range of total days of unweighted lifetime exposure (actual lifetime days spent doing that activity) reported by subjects in each job activity.

Figure 6.3 Work exposure among deciduous fruit farm workers by activity



Days weighted by agricultural activity

The bulk of mist blower and non-mist blower exposures occured on the deciduous fruit farms as shown by the small difference in mean values for CUMULTOT and POMDYS in Table 6.8. Table 6.10 confirms this by presenting the contributions of different farming sectors to overall weighted exposure days of subjects (CUMULTOT).

Table 6.10 Sector specific cumulative exposure days amongst deciduous fruit workers.

Sector	Cumulated lifetime days	Percentage
Pome fruit	109 000	91.8
Stone fruit	1 847	1.6
Citrus fruit	100	0.1
Potatos	4 309	3.6
Vines	1 344	1.1
Wheat	1 600	1.3
Other (animal, dairy)	600	0.5

Because the measures of cumulative exposure days presented above are partially a function of age, average intensity of chronic exposure may be derived by adjusting for duration of working life. Two measures are presented in Table 6.11: a) long-term exposure divided by the duration of the subject's working life, and b) long-term exposure as given by the formula log [(cumulative days / working life) + 1] (Berberian and Enan, 1987). These are presented for all the source variables (see Table 6.8) for cumulative exposure. Average lifetime intensity of organophosphate (OP) in Kg/hectare year (EXWGHTI) is the occupational exposure intensity variable of interest in the bulk of subsequent bivariate and multivariate analyses.

Table 6.11 Average lifetime intensity of different measures of long-term occupational exposures.

Source variable*		Derived variables	Mean (SD)	Range
JYR10 [1]	a)	JT2	0.88 (0.17)	0-1.00
	b)	JT4	0.63 (0.11)	0-0.72
SPRYJOBS [2]	c)	SPR1	0.45 (0.38)	0-1.00
	a)	SPR2	0.06 (0.09)	0-1.00
CUMULTR [3]	a)	CTR2	12.06 (19.92)	0-116
	b)	CTR4	1.44 (1.56)	0-4.76
CUMULTOT [3]	a)	CMLTOT2	21.33 (26.17)	0-144
	b)	CMLTOT4	2.43 (1.24)	0-4.97
POMDYS [3]	a)	POM2	21.24 (25.93)	0-144
	b)	POM4	2.41 (1.26)	0-4.97
EXWGHT [4]	a)	EXWGHTA	0.27 (0.35)	0-1.96
	b)	EXWGHTI	0.21 (0.23)	0-1.09
EXWGHTB [5]	a)	EXWGHTBA	8.47 (10.89)	0-61.8
	b)	EXWGHTBI	1.69 (1.06)	0-4.14

a) - "Source Variable" / working life years
b) - Log [("Source Variable"/working life years)+1]
c) - Sprayjobs/Total lifetime jobs = proportion jobs held as sprayman

* See Table 6.8 for source variables

Units: 1 a) Unitless (Years/years) or b) log(years/years)
2 c) Unitless (jobs/jobs) or b) log(jobs/jobs)
3 a) Days/year or b) log(days/year)
4 a) Kg/hectare-year or b) log(Kg/hectare-year)
5 a) BE/hectare-year or b) log(BE OP/hectare-year)

Figures 6.4 and 6.5 present the distribution of the main long-term occupational exposure variables of interest: cumulated Kg OP per hectare [EXPWGHT], and average lifetime intensity of exposure - Kg OP exposure per hectare-year [EXPWGHTI]. A bimodal distribution of cumulative Kg OP per hectare exposure is noted with some subjects having high cumulative lifetime exposures. The data are stratified by current applicator status, and indicate that there is considerable lifetime exposure amongst workers who are not currently applying pesticides. This included 9 subjects who were currently included as non-sprayers but who had previously performed as pesticide applicators as well as subjects with other job activities giving rise to exposure. Only 6 subjects (2.4%) had no exposures recordable during their lifetime. Given the wide range of exposure evident in Tables 6.8 and 6.11, and Figures 6.4 and 6.5, there appears to be sufficient exposure contrast to facilitate the detection of exposure-effect relationships.

It is comforting to observe that the bulk of these lifetime exposures took place in deciduous fruit farming, and thus the application of job-exposure matrices reliant on sector-wide agrichemical market data should be reasonably accurate. Table 6.12 summarises correlations between different measures of long-term exposure.

Table 6.12 Correlations between different measures of long-term agrichemical exposure

	SPRYJOBS	CMLTOT	PMDYS	EXWGHT	EXWGHTI	EXWGHTB	EXWGHTBI
SPRYJOBS	1.00	0.26	0.17	0.33	0.30	0.17	0.23
	247	247	245	247	246	247	246
CUMULTOT		1.00	0.91	0.95	0.78	0.94	0.68
		247	245	247	246	247	246
POMDYS			1.00	0.97	0.82	0.97	0.75
			245	245	244	245	244
EXWGHT				1.00	0.93	1.00	0.93
					246	247	246
EXWGHTI					1.00	0.93	1.00
						246	246
EXWGHTB						1.00	0.93
							246
EXWGHTBI							1.00

Strong correlations are evident between measures of cumulative exposure and average intensity of exposure. For this reason, multivariate regression modelling in Chapter 7 will not make use of the two variables in the same model, to avoid problems of collinearity.

Figure 6.4 Cumulative exposure years Weighted on job and crop sector by current applicator status

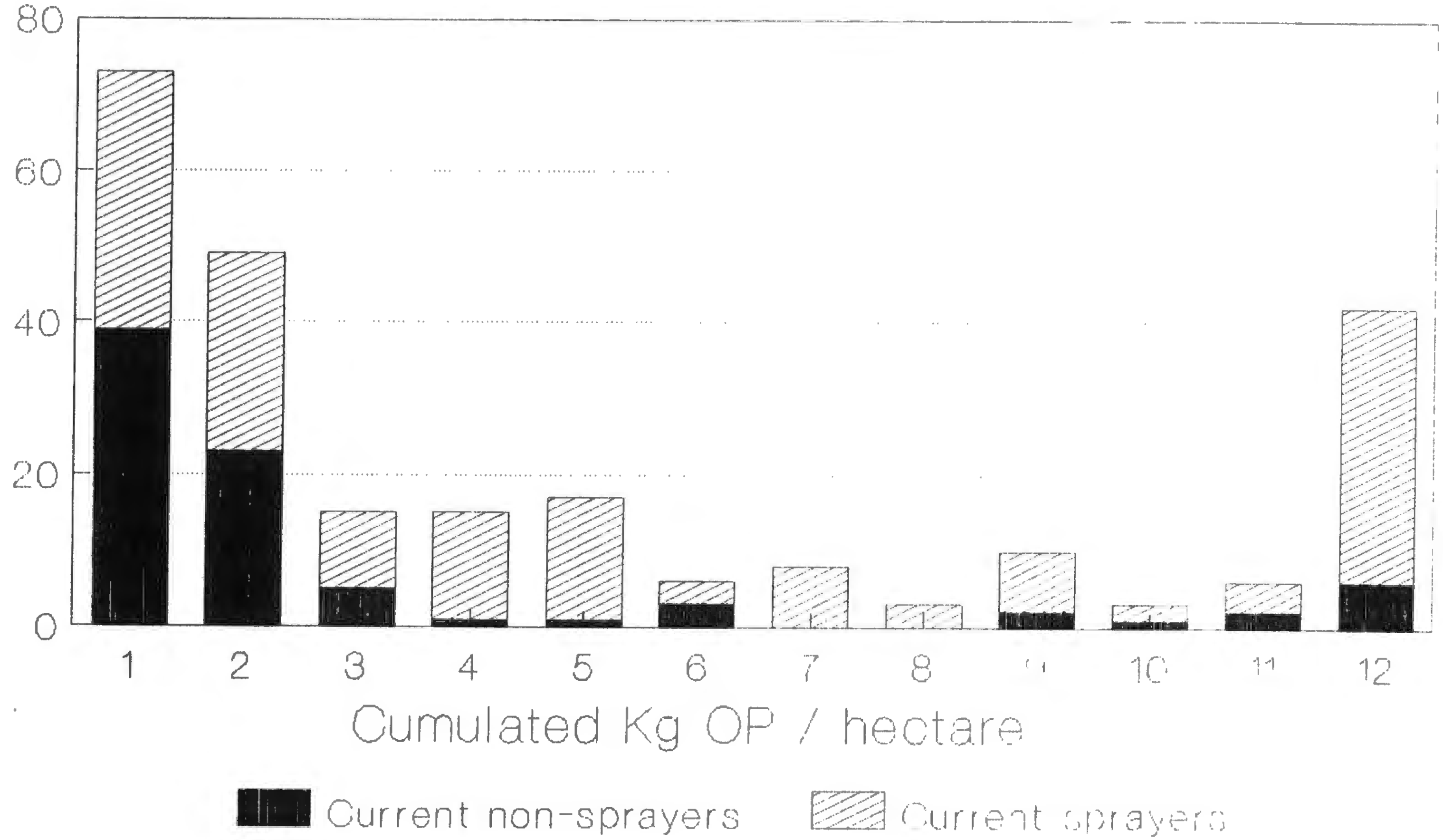
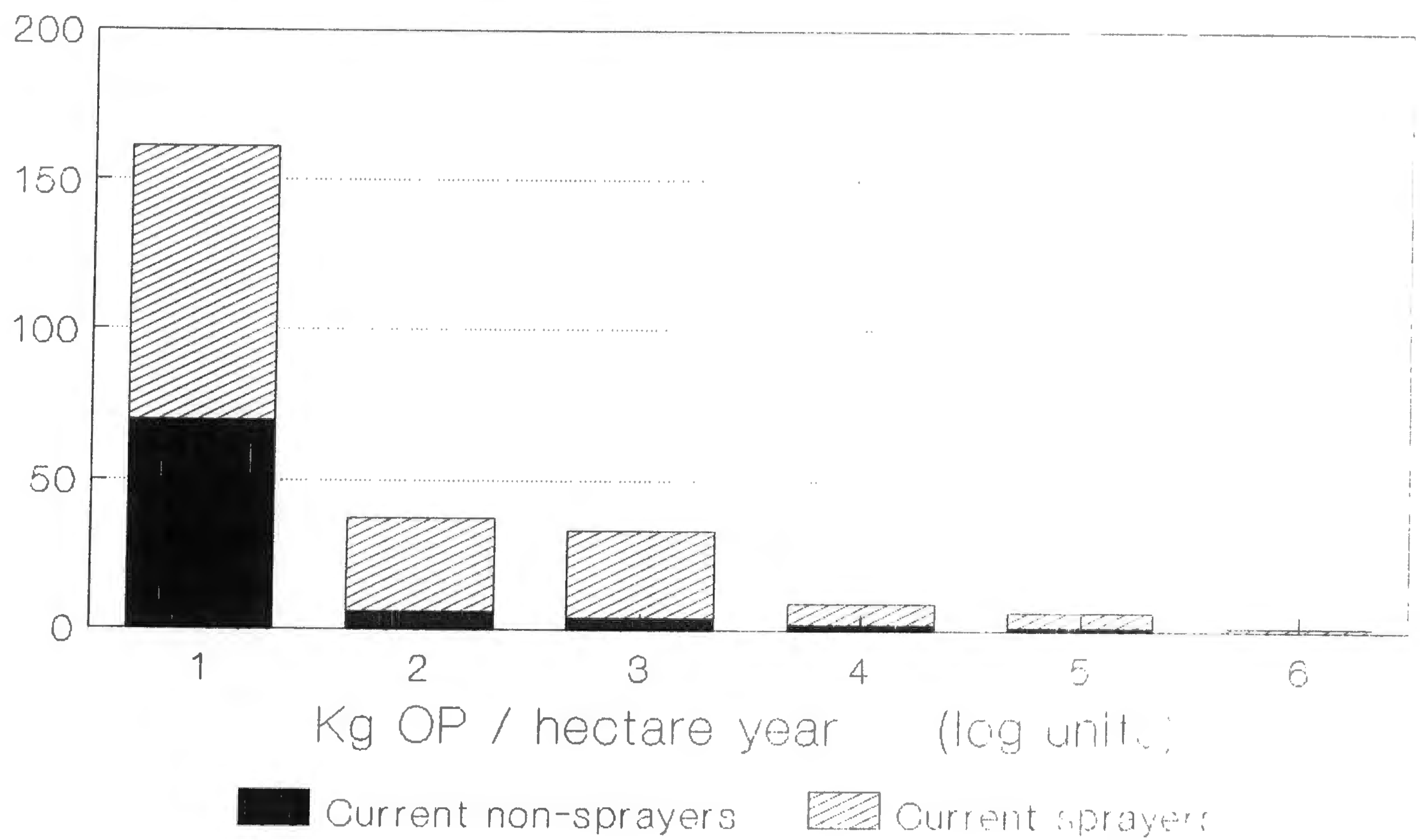


Figure 6.5 Average lifetime exposure
Weighted on job and crop sector
by current applicator status



6.5.2 Recent exposures

Recent exposure was assessed from interview and from farm records. These data are summarised in Table 6.13. Forty-five percent of subjects reported that they had applied pesticides in the preceding 10 days before examination and 22.3% had applied pesticides on either the same morning of, or the previous morning to, their attendance for examination. The estimate of exposure in the preceding 10 days based on farmer records was 36.9% but data from this source was incomplete (n=193). Agreement between these two sources of data was poor (Kappa = 0.19). For example, 9 subjects reported exposure to OPs in the preceding 24 hours which was not reflected in farmer records. These discrepancies might arise because workers may not be familiar with the types of chemicals they use, or be able to read the name, with the result that they over-report potential exposures to organophosphates. Alternatively, farmers may omit to report OP usage, a hypothesis which is supported by data supplied from the 2 local co-ops on recommended spray programmes. These data are also reflected in Table 6.13 and suggest substantial under-reporting by farmers of spraying activities, given the schedule recommended by the cooperatives programmes. Given the sensitive nature of the survey for the image of the farming community, there may have been strong incentives operating for under-reporting of exposure.

Review of agreement between different measures of recent exposure found low correlation coefficients generally. The only instances where agreement was high was when the variables were derived from a similar source. For example, the estimate of the total days OP application in the past 3 months by farmers replying to a questionnaire correlated closely with the same farmer's estimate for the equivalent days for application of azinphos-methyl (R=0.56) but poorly with an equivalent estimate by the field advisor from the local cooperative (R=0.18), or with days of exposure reported by the workers (R=-0.06). Similarly, farm workers' reports for different measures of acute exposure correlated well internally, but poorly with farmers' reports.

Table 6.13 Recent exposures to organophosphates in deciduous fruit farm workers

	N	Mean (SD)	Range	Variable name
a) Interview [a]				
Days since last exposure	190	62.8 (240.7)	1 - 2190	Daylast
Total days exposure in past season	247	47.4 (46.9)	0 - 170	Acute
Total days exposure in 3 months prior to examination	247	15.8 (16.3)	0 - 60	Acute1
b) Farm Records [b]				
Days exposure to organophosphate in past 2 months	168	0.5 (1.4)	0 - 10	Anrctrec
Days exposure to azinphos methyl in past 2 months	165	0.1 (0.3)	0 - 2	Azrctrec
c) Modelling [c]				
Days exposure to organophosphate in past 2 months	194	4.6 (4.5)	0 - 36	Anrctgrt
Days exposure to azinphos methyl in past 2 months	196	3.8 (3.6)	0 - 24	Azrctgrt

a - Exposure as reported by workers, irrespective of the nature of the job activity in which they were exposed.
b - Days of exposure experienced by mist blower operators in preceding 60 days, as from record supplied by farm management.
c - Days of exposure experienced by mist blower operators in preceding 60 days, as from modelling based on cooperative spraying programmes.

Because of the discrepancies in recent exposure data, plasma cholinesterase was used as the primary marker of recent worker exposure in the subsequent analyses rather than any of the record or history data. Plasma cholinesterase has the advantage of being an integrated measure of the biological effect of organophosphates on the human body (Minton and Murray, 1988), and thus more closely allows control for confounding by acute exposure of the effects of long-term exposure on neurological and neurobehavioural function.

The results of the blood cholinesterase tests are presented in section 6.8 with other blood chemistry results.

6.5.3 Non-farm exposures to potential neurotoxins

Few farm workers were ever employed outside of agricultural work. Of these, thirty-nine subjects reported experiencing exposures to chemicals that are potential neurotoxins in non-farming jobs. These exposures included handling petrol (25 subjects), paint (6 subjects), hydraulic fluid, welding, soldering and woodwork (each less than 2 subjects). No subject had ever previously worked in the manufacture or formulation of pesticide. Because the numbers and intensities of these non-farm exposures to potential neurotoxins were low, these variables were treated as dichotomous (present/absent) in subsequent analysis.

6.6 Knowledge, Attitude and Practices (KAPs) Relating to Personal Protective Equipment

6.6.1 Current usage of personal protective equipment

Current usage of personal protective equipment (PPE) amongst the subjects who performed high exposure jobs is summarised in Table 6.14. Only one worker reported buying his own overall.

Table 6.14 Current usage of protective equipment amongst deciduous fruit farm spray operators

Usage of:	Reported usage *	Reported reason for use **
Gloves	68%	Spraying - 90% Mixing - 9% Other - 1%
Masks	59%	Spraying - 95% Mixing - 2% Other - 3%
Overall	99%	General farm work 48% Spraying only 4% Farm work + spraying 48%
Plastic coats	81%	General farm work 19% Spraying only 48% Farm work + spraying 33%
Footgear	84%	General farm work 79% Spraying only 19% Farm work + spraying 3%

* Prevalence amongst workers in high exposure jobs; n=163.
** Percentage amongst those using the different forms of PPE.

The reason for reported usage of gloves was usually for spraying (90%) or mixing (9%) of pesticides, and that for reported usage of masks was similar. Overalls and plastic coats were widely used for both spraying and general farm work. The type of mask most frequently used was a helmeted mask (52%), sometimes with oxygen supplied (10%). Surgical-type masks (14%), or facial shields (17%) which give inadequate protection were less widely used. An overall score was developed for PPE usage which is summarised in Table 6.15.

As is obvious from Table 6.15, PPE usage was more widespread amongst workers in high exposure jobs, and little usage was present amongst the internal controls. A score for knowledge of, and attitude toward safety practices was computed and is summarised in Table 6.16 below. The manner in which the scores above were derived is described in Appendix 6.2. Knowledge and attitude as measured by the study questionnaire appeared generally to be adequate, although a reporting bias may be operative.

Table 6.15 Distribution of PPE Score amongst deciduous fruit farm workers

	Non-spraymen(n=84)	Spraymen (n=163)
0 - No items of PPE	18 (21.7%)	3 (1.8%)
1 - Less than 5 items of PPE	47 (56.7%)	40 (24.4%)
2 - Used all 5 items of PPE	18 (21.7%)	121 (74.2%)

Table 6.16 Knowledge of, and attitude towards pesticide safety amongst deciduous fruit farm workers

	Number of workers	Percentage	Mean score
Knowledge of Dangers			2.07
1 - Poor	3	1%	
2 - Adequate	209	90%	
3 - Insightful	20	9%	
Knowledge of Prevention			2.60
1 - Poor	8	3%	
2 - Adequate	212	91%	
3 - Insightful	13	6%	
Attitude score			2.60
0 - Low	27	11%	
1 - Low / Mod	38	15%	
2 - Moderate	21	9%	
3 - Mod / High	83	34%	
4 - High	78	32%	

6.6.2 Usage of personal protective equipment and demographic variables

Preliminary exploration of the relationship between educational levels, age and knowledge and attitudes regarding pesticide safety is presented below. Table 6.17 summarises the relevant data.

Amongst the currently exposed group, education (measured both by years at school and by literacy) appeared to be strongly related to reported usage of protective equipment, though there was no obvious relationship to knowledge or attitude to safety. Unlike other studies (Stone et al, 1988), age appeared to have little relationship to any of the measures of knowledge, attitude or practice.

Comparisons between currently exposed and currently non-exposed subjects for the three variables in Table 6.17 show little difference for knowledge scores and a small non-significant difference in attitude scores. This suggests that any over-reporting for knowledge and attitude that may have existed was likely to have been non-differentially distributed across exposure status. Hence, despite over-reporting, the data may still be valuable for exposure-effect investigations involving PPE knowledge and usage, although an underestimate of the extent of confounding by these factors would arise due to non-differential misclassification.

6.7 Domestic Exposures to Pesticides and Other Neurotoxins

Potential domestic exposure to agrichemicals amongst study subjects was identified from the presence of another household member involved in spray activities, the re-use of pesticide containers or the use of farm chemicals at home. Forty-four subjects reported taking agrichemicals home for gardening, and organophosphates (10) and dithiocarbamates (8) were the chemicals most usually reported. Eleven subjects reported ever living with another household member involved in spray application. Amongst workers involved in spray activities, the majority (76%) reported that after work they

Table 6.17 Knowledge of, and attitude toward pesticide safety by age and education amongst deciduous fruit farm workers

	Mean scores (SD) for :			
Currently Exposed Group (n=163)	Danger Knowledge	Protection Knowledge	Usage PPE	Safety Attitude
Schooling:				
0 - 4 yrs	2.04(0.28)	2.02(0.24)	1.52(0.57)*	2.81(1.29)
5 + yrs	2.09(0.32)	2.05(0.30)	1.82(0.41)	2.65(1.26)
Literate:				
Write -	2.06(0.35)	2.03(0.31)	1.47(0.56)*	2.50(1.35)
Write +	2.08(0.30)	2.05(0.28)	1.78(0.45)	2.76(1.24)
Age:				
< 37 yrs	2.08(0.31)	2.02(0.21)	1.71(0.50)	2.72(1.22)
37 yrs +	2.07(0.30)	2.07(0.35)	1.73(0.47)	2.69(1.33)
Currently non-exposed group (n=84)				
Schooling:				
0 - 4 yrs	2.00(0)	1.93(0.26)	1.00(0.63)	2.50(1.55)
5 + yrs	2.09(0.03)	1.98(0.35)	1.00(0.67)	2.34(1.50)
Literate:				
Write -	2.00(0)	1.94(0.24)	1.06(0.64)	2.33(1.57)
Write +	2.09(0.34)	1.98(0.36)	0.98(0.67)	2.38(1.50)
Age:				
< 37 yrs	2.07(0.35)	1.95(0.31)	0.94(0.66)	2.53(1.62)
37 yrs +	2.07(0.25)	2.00(0.36)	1.09(0.67)	2.29(1.34)

* $P < 0.001$ for difference in mean reported PPE usage score between:
a) workers with 4 or fewer years of schooling vs 5 or more
b) workers able to sign their names vs those unable to sign their names

removed their protective overalls at home. Overalls were usually (70%) washed only once a week, and no plans were made for separate washing. The majority of farm workers (90%) reported access to running water, the source of which was a covered borehole (i.e. groundwater).

Use of other chemicals with potential neurotoxic effects included wood preservatives (11 subjects) and glue for hobbies (3 subjects). These were dealt with as dichotomous variables (present/absent) in the analysis because of the small numbers involved.

6.8 Blood Chemistry Results and Clinical Findings

The results of blood chemistry amongst subjects are summarised in Tables 6.18 and 6.19.

Table 6.18 Blood Chemistry amongst deciduous fruit farm workers

Measurement	N	Mean	SD	Range
Plamsa Cholinesterase	247	6357	1232	3002 - 9398
Erythrocyte Cholinesterase	247	5271	705	2730 - 7090
Haemoglobin	247	14.76	1.33	11.0 - 17.9
Haematocrit	247	47.1	3.5	35.0 - 58.0
Serum Albumen	247	44.9	3.1	32.0 - 54.0
Serum Gamma Glutamyl Transferase	247	22.8	19.0	5.0 - 124.0
Standardised [a] Erythrocyte Cholinesterase	247	35.8	4.5	17.0 - 49.3

a - Standardised erythrocyte cholinesterase = Erythrocyte Cholinesterase / Haemoglobin

Levels below the clinical "normal range" for haemoglobin (13.5 - 17.0 g/dl) and albumen (35 - 50 g/dl) were found amongst 16.6% and 2.4% of subjects, respectively. The mean height of the subjects was 165.0 cm (SD 5.8). This is substantially lower than norms for males in the United States, and significantly lower than the mean height of a random sample of adult coloured males in the Cape Peninsula in 1990 (Mean difference = 2.5 cm; $p < 0.0001$) (Steyn et al, 1990). These biochemical and anthropometric findings may reflect the prevalence of chronic undernutrition in this population as well as the presence of other chronic diseases. Similar findings regarding chronic undernutrition have been made amongst other farm worker populations in the sub-continent (Loewensen, 1986).

Table 6.19 Comparison of plasma and standardised erythrocyte cholinesterase amongst currently sprayers and non-sprayers

Measurement	(n=164) Currently Sprayers Mean	(SD)	(n=83) Curr Non-sprayers Mean	(SD)
Plasma [a] cholinesterase (U/l)	6416	1251	6240	1194
Standardised [b] erythrocyte cholinesterase (U/g Hb)	35.6	4.0	36.2	5.3

a - t-test for difference in mean cholinesterase levels between currently exposed and non-exposed: p=0.28
b - t-test for difference in mean cholinesterase levels between currently exposed and non-exposed: p=0.33

No obvious differences in blood chemistry are noted between currently exposed and unexposed despite the high percentage of subjects reporting exposure to OPs in the preceding 5 days (45%). Five subjects (2.0%) had plasma cholinesterase levels below the reference levels for the laboratory (4000-8000 U/l), of whom 2 were not actively involved in current agrichemical application. Similarly, four subjects had erythrocyte cholinesterase levels below the equivalent laboratory reference range (4000-8500 U/l) of whom 2 were not currently applying agrichemicals. None of those with low plasma levels had simultaneously low erythrocyte cholinesterase levels. One subject with a particularly low erythrocyte cholinesterase level (more than 3 standard deviations below the mean) had a plasma cholinesterase well within the normal range, and exhibited no evidence of clinical cholinergic intoxication, or history of previous poisoning. This was probably a chance finding reflecting the high level of interindividual variability in cholinesterase levels (Coye et al, 1986). No data was available for any subject on previous cholinesterase status.

The chemistry results are explored further in section 7.2 of Chapter 7.

6.9 Neurological and Neurobehavioural Outcome Measures

Clinical examination identified one subject with a frank sensori-motor distal neuropathy and 4 subjects with lesser degrees of impairment of pinprick discrimination. On further referral and investigation, the local neurology unit at a large teaching hospital in Cape Town felt on clinical grounds that the neuropathy in the one subject was due to an inherited disorder. Nonetheless, all subjects with any evidence of neurological abnormality on clinical grounds were flagged in order to exclude possible confounding in later analyses.

Notwithstanding the clinical findings, the main outcome measures used in this study involved symptoms or subclinical test performances as outlined in Table 5.2 in Chapter 5. Univariate analyses for these outcomes are grouped into four categories for convenience: 1) Symptom outcomes, 2) Vibration sense and tremor outcomes, 3) WHO NCTB outcomes, and 4) Neurobehavioural outcomes based on the information processing model of cognitive psychology.

6.9.1 Symptom outcomes

Table 6.20 lists the prevalence of symptoms (both current and prolonged for the past 3 months) amongst the workforce. These include symptoms inserted as "dummy" symptoms with no obvious relationship to OP exposure (ear pain and chest pain). An overall symptom score is also indicated at the bottom of the table for all symptoms, for possible neurologically-related symptoms ("neurological symptoms") and for "dummy" symptoms.

The commonest symptoms reported include headache, sleepiness and tiredness. Persistent drowsiness was the most prevalent of the symptoms present for 3 months. These symptoms are relatively non-specific for neurological and neurobehavioural disorders. The "dummy" symptom of earache was relatively uncommon though chest pain was as widely reported as other neurotoxic symptoms. Reporting of either group of symptoms was intercorrelated (Spearman's correlation coefficient between symptoms scores for neurological and dummy symptoms was 0.42; p=0.0001), suggesting that sickness behaviour may have been an underlying determinant of reported symptoms.

6.9.2 Peripheral vibration sense and motor tremor

Results for the tests of peripheral vibration sense and for motor tremor are summarised in Table 6.21.

Table 6.20 Neurological and other symptoms amongst deciduous fruit farm workers

Symptom		N	Prevalence (%)
Stomach pain	current:	247	21.1
	for past 3 months:	247	2.0
Nausea	current:	247	17.4
	for past 3 months:	247	3.6
Dizziness	current:	247	30.0
	for past 3 months:	246	6.5
Gait disturbed	current:	247	6.1
	for past 3 months:	247	1.6
Numbness limbs	current:	247	7.3
	for past 3 months:	247	2.4
Parasthesia	current:	247	16.2
	for past 3 months:	247	4.0
Earache	current:	247	6.5
	for past 3 months:	247	2.0
Lameness limbs	current:	247	18.2
	for past 3 months:	247	4.4
Pain in limbs	current:	247	19.4
	for past 3 months:	247	6.1
Rhinorrhoea	current:	247	20.6
	for past 3 months:	247	3.6
Headache	current:	247	38.5
	for past 3 months:	247	8.5
Sleepiness	current:	247	36.4
	for past 3 months:	247	13.4
Chest pain	current:	247	19.0
	for past 3 months:	247	6.1
Tiredness	current:	247	33.6
	for past 3 months:	247	10.9

SYMPTOM SCORE	Median	Mean	SD	Range
* All symptoms	2	2.64	2.82	0 - 14
* Neurological symptoms	2	2.38	2.54	0 - 12
* "Dummy" symptoms	0	0.26	0.52	0 - 2

Table 6.21 Peripheral vibration sense and motor tremor amongst deciduous fruit farm workers

Test (Units)	N	Median	Mean	SD	Range
Vibratron threshold [1] (log vibratron units)	247	1.5	1.6	0.6	0.13-2.99
Tuning fork extinction[2] time (seconds)	246	12.5	12.7	3.3	4.5-20.5
Tremor score [3] dominant hand (achieved holes)	247	6	5.7	0.9	1 - 7
Tremor score [3] non-dominant hand (achieved holes)	247	6	5.4	1.0	1 - 7
Tremor intensity [4] dominant hand (counts/hole)	246	0.32	0.38	0.34	0 - 3
Tremor intensity [4] non-dominant hand (counts/hole)	246	0.32	0.39	0.41	0 - 4
Maze counts [5] dominant hand (counts)	245	2.5	4.08	5.68	0 - 44
Maze counts [5] non-dominant hand (counts)	245	4.5	6.24	6.65	0 - 40
Maze time [6] dominant hand (seconds)	245	36.0	39.1	12.8	20 - 99
Maze time [6] non-dominant hand (seconds)	245	37.5	39.9	11.9	19 - 99

1 - Average of last 8 of 9 trials per subject. Units are log transformed.
2 - Average of last 2 of 3 trials per subject.
3 - Total number of holes of descending size order sucessfully reached.
4 - Cumulated counts excluding counts of last hole divided by number of holes achieved minus 1.
5 - Average of counts from touching side of maze over 2 trials per subject.
6 - Average of time taken to complete maze over 2 trials per subject.

6.9.3 Neurobehavioural outcomes: WHO NCTB

Two hundred and forty-two (242) subjects underwent neurobehavioural assessment. Results of the first part of the neurobehavioural battery (WHO NCTB) are summarised in Table 6.22.

Table 6.22 Neurobehavioural test battery results: WHO NCTB performances amongst deciduous fruit farm workers

Test WHO-NCTB	N	Median	Mean	SD	Range
* Digit span					
Span forward	242	5	4.80	1.02	3 - 8
Span backward	242	3	3.24	1.17	0 - 7
Total span	242	8	8.04	1.84	3 - 13
Score forward	242	5	4.79	1.77	1 - 11
Score backward	242	4	3.88	1.78	0 - 11
Total raw score	242	9	8.66	3.02	1 - 16
WAIS-R Std score	242	6	5.59	2.06	1 - 10
* Benton					
Total score	242	7	6.87	2.02	1 - 10
* Santa Ana Peg Board					
Dom hand total	242	39	38.45	6.85	11 - 53
Dom hand dropped	241	0	0.29	0.68	0 - 4
Non-dom total	241	35	35.35	7.27	10 - 54
Non-dom dropped	241	0	0.51	1.04	0 - 7
* Digit Symbol					
Total Correct	231	26	25.34	10.39	0 - 57
WAIS-R Std score	227	4	4.55	1.47	1 - 10
* Pursuit Aiming					
Correct	231	94	90.48	35.04	5 - 189
Attempted	231	112	113.24	32.20	41 - 219
Wrong	231	15	22.73	21.29	0 - 112
* Simple Reaction time (ms)	232	273.4	289.4	69.6	172.7-587.3

These results are remarkably similar to findings amongst 228 African paint factory workers in 2 plants in South Africa (Colvin et al, 1993; Myers et al, 1994) with farm workers scoring slightly higher on pursuit aiming but lower on digit span, despite similar educational levels in the two groups. Scores by subjects in this study are listed in Table 6.23 alongside data from 4 other studies in Israel (Richter et al, 1992), Singapore (Chia et al, 1993), Nicaragua (Rosenstock et al, 1991) and Holland (Hooisma et al, 1990) for comparability. For digit symbol, digit span, Benton and pursuit aiming, the farm workers tended to perform slightly worse than their counterparts in developing and developed countries, but for simple reaction time, similar scores were obtained for all but the Dutch study. (Even in this case, the degree of difference between South African farm workers and Dutch volunteers for reaction time appeared smaller than the discrepancy for the more complex WHO NCTB tests.) This again reinforces the argument advanced by Myers et al, (1994) that cross-cultural effects are paramount in influencing test performance with neuropsychological test batteries, particularly for tests that are nearer the cultural end of the effect spectrum (Nell et al, 1993).

Of interest are the highly similar variances obtained for all the tests by two South African groups with very different language and cultural backgrounds. This suggests that some degree of standardisation in administration of the NBCTB is possible and this partly reflects the rigourous quality control of the neuropsychological team derived in both studies from the same institution (UNISA Health Psychology Programme).

Table 6.23 WHO NCTB scores from 4 other studies compared to farm workers

Test	Subject Group: Israeli 1	Singapore 2	Nicaragua 3	S Africa 4	S Africa 5	Holland 6
Digit span forward	-	-	6.3 (3.2)	5.2 (1.0)	4.8 (1.0)	-
Digit span total	-	13.4 (2.8)	-	-	8.0 (1.8)	12.5 (3.4)
Dig span scaled score	10.0 (2.2)	-	-	-	8.7 (3.0)	-
Benton	8.6 (1.2)	7.9 (1.4)	6.1 (2.2)	6.4 (1.7)	6.9 (2.0)	8.4 (1.3)
Santa Anna # dominant	43.6 (7.0)	36.2 (4.6)	35.6 (7.0)	35.9 (7.7)	38.5 (6.9)	41.0 (6.3) (dominant and non-dominant bracketed together)
non-dominant	44.0 (6.4)	35.8 (4.8)	-	32.5 (7.0)	35.2 (7.6)	
Digit symbol correct	51.6 (10.2)	46.5 (11.8)	25.4 (11.9)	20.9 (9.5)	25.3 (10.4)	50.7 (12.6)
Digit symbol scaled score	8.1 (2.2)	-	-	-	4.7 (2.8)	-
Pursuit aiming	-	188.8 (28.8)	94.4 (29.9)	79.9 (36.6)	90.5 (35.0)	133.6 (37.3)
Simple reaction time (ms)	284.2 (3.5)	-	308.0 (50.0)	275.3 (68.1)	289.4 (69.6)	241.4 (37.7)
Age	27.7 (range 17-45)	35.7 (12.1)	27.8 (9.3)	46.0 (9.0)	36.9 (10.0)	M:49.1 (14.2) F:50.9 (15.1)
Educ	12.7 (range 9-15)	not supplied	not supplied (34% no formal educ)	6.1 (3.5)	5.1 (2.9)	lower grade to high school

Glossary to Table 6.23: Reference sources for WHO NCTB scores for 4 other studies compared to farm workers in this study

1 - 51 residents and 39 workers on a kibbutz at peak spraying (Richter et al, 1992).
2 - 17 referrants for workers exposed to manganse ore : Chia et al, 1993
3 - 36 referrants for workers previously poisoned by organophosphates : Rosenstock et al, 1991.
4 - 228 workers from 2 paint factories in Johannesburg and Durban (Myers et al, 1994).
5 - Current study of 247 farm workers.
6 - 138 men and 49 women volunteers drawn from the general population (Hooisma et al, 1990).

- Scoring for Santa Ana testing for studies 1,2 and 6 adjusted by doubling to make test score compatible for comparison.

6.9.4 Neurobehavioural outcomes: Performance probes and Hick Box tests

Table 6.24 summarises the results of the tests based on the information processing model of cognitive psychology. The variables are explained in detail in Appendix 5.3.

Simple reaction times in this study appear fairly similar to those reported in other studies (Tables 6.23 and 6.24). For example, mean simple reaction time of a group of Dutch volunteers was 241 ms (Hooisma et al, 1990), while those of Nicaraguan men acting as controls for poisoned cases was 308 ms (Rosenstock et al, 1991), compared to the farm workers (289 ms). These data are explored further in Chapter 7. Of note is that fewer subjects completed tests of Short-term memory scanning and working memory, particularly Manipulating Numbers II and III. These are tests of working memory, and the low numbers suggest that complex multivariate analyses investigating agrichemical exposure-effect relationships will be limited in statistical power.

Table 6.23 Neuropsychological performance on information-processing test battery amongst deciduous fruit farm workers

TEST	N	Mean	SD	Range
1. DOMAIN: MOTOR SPEED (HICKBOX TESTS)				
* One Light Condition				
Simple Reaction Time (ms)	232	289.42	69.59	172.73 - 587.28
Simple Movement Time (ms)	232	313.87	70.49	180.15 - 585.20
2. DOMAIN: ENCODING (HICKBOX TESTS)				
* Two Light Condtion				
Choice Reaction Time (ms)	233	296.60	59.20	192.27 - 547.68
Choice Movement Time (ms)	233	301.88	72.21	183.18 - 570.55
* Four Light Condition				
Choice Reaction Time (ms)	227	323.11	72.01	200.98 - 714.90
Choice Movement Time (ms)	227	309.38	77.27	178.50 - 721.30
* Eight Light Condition				
Choice Reaction Time (ms)	227	385.92	104.91	239.57 - 936.50
Choice Movement Time (ms)	227	304.06	73.21	177.27 - 711.65
3. DOMAIN: APPREHENSION (HICKBOX TESTS)				
* Inspection Time				
Reaction Time (ms)	187	311.58	163.81	142.13 - 1016.80
Movement Time (ms)	187	326.27	136.78	151.82 - 1514.00
Efficiency score *	187	4.66	0.63	2.87 - 7.00
* Inspection Window				
Reaction Time (ms)	178	411.12	191.33	131.85 - 1112.30
Movement Time (ms)	178	327.31	101.83	180.40 - 768.10
Power score *	168	1862.07	21221.57	10.00 - 274877.0
4. DOMAIN: ATTENTION				
* Continous Number Checking				
Reaction Time (ms)	222	3951.39	2049.89	1606.60 - 16862.0
Speed Index (items/s)	222	0.25	0.08	0.06 - 0.45
Efficiency Index (items/s)	222	0.24	0.08	0.04 - 0.43
Transformed Accur Index *	211	1.18	0.43	-0.04 - 2.25
Work Gradient Index *	222	4.60	0.05	4.38 - 4.81
Variability Index *	222	2.95	1.12	0.80 - 8.30

Table 6.23 (Continued) Information processing battery

5. DOMAIN: SEMANTIC ACCESS				
* Animal Postures I Reaction Time (ms)	234	1596.34	644.86	814.02 - 7393.50
* Animal Postures II Reaction Time (ms)	233	1742.66	504.40	945.61 - 3806.30
* Difference I and II reaction time (ms)	233	146.78	419.37	-4223.00 - 1183.30
* Speaking Arrows				
Reaction Time (ms)	223	2632.82	1199.33	1099.00 - 11386.0
Incorrect response count *	223	2.83	5.43	0.00 - 38.00
5a. SUBDOMAIN: STIMULUS RESISTANCE				
* Echopraxis	225	3.62	1.37	1 - 6
* Pointing Arrows I Reaction Time (ms)	231	711.60	332.12	289.52 - 2094.60
* Pointing Arrows II Reaction Time (ms)	231	876.62	360.50	426.00 - 2919.30
* Difference I and II Reaction Time (ms)	231	165.03	234.56	-873.70 - 1554.70
6. DOMAIN: PASSIVE SHORT TERM MEMORY				
* STM Scanning				
Reaction Time (ms)	179	1546.49	360.77	717.65 - 2651.00
7. DOMAIN: ACTIVE SHORT TERM MEMORY				
* Manipulating Number I				
Reaction Time (ms)	169	6641.39	2409.72	3266.10 - 20791.0
Correct response count *	169	18.43	1.72	9 - 20
* Manipulating Numbers II				
Reaction Time (ms)	106	3751.79	1357.27	2108.40 - 10481.0
Correct response count *	106	30.20	6.25	3 - 36
Efficiency score *	106	981.60	7.03	929.20 - 986.49
* Manipulating Numbers III				
Reaction Time (ms)	32	3754.48	1656.00	2021.30 - 11152.0
Efficiency score *	32	977.55	5.18	965.90 - 982.60
8. GLOBAL INTELLECTUAL ABILITY				
* Anomalous Concept Test	199	14.63	4.97	1 - 24

* - Unitless

II. REPEATABILITY OF RESULTS

Reliability of some of the data was assessed from 2 sources:

- Fifty-five subjects had a second 5 ml tube of heparinised blood taken at time of examination, which was then given a pseudonym and forwarded to the laboratory to assess the degree of laboratory repeatability.

- Twenty-nine subjects were randomly chosen to have repeat neurobehavioural screening, occupational and life history questionnaires administered at a follow-up visit three months after the initial examination. One interviewer administered all questionnaires at repeat visit. The data obtained at repeat visit were compared to data obtained at initial visit. These comparisons therefore reflect an unspecified combination of inter-observer, intra-observer and instrument error. Variables chosen for comparison were those for which no temporal changes would be expected when measured three months apart.

Repeatability statistics included kappa and correlation coefficients (Tables 6.25, 6.26 and 6.27). Where data were non-normally distributed (for example count data), Spearman's correlation coefficient with a 95% confidence interval was calculated and Pearson's correlation coefficient and a similar 95% confidence interval calculated for continuous data with normal distribution (Gardner and Altman, 1989).

Kappa statistics were calculated for categorical data. Kappa is a measure of agreement between categorical variables adjusting for agreement due to chance. Values of kappa greater than 0.75 are said to reflect excellent agreement, values between 0.4 and 0.75 fair to good agreement, and values less than 0.4 poor agreement (Fleiss, 1981).

Intra-laboratory error appears low with excellent agreement on duplicate blood specimens from a random subset of subjects (Table 6.25). Given blinding of the laboratory to the true identity of the subjects, this represents excellent repeatability. Of note is the slightly poorer repeatability of the erythrocyte cholinesterase compared to the plasma cholinesterase. Our experience confirmed that the laboratory procedures for the erythrocyte cholinesterase assay were more complex than that for PCE, and involved a number of sequential technical steps in which observer error may be magnified. Nonetheless, a correlation coefficient in excess of 0.94 represents excellent agreement (88% of the variance explained).

Table 6.25 Reliability of laboratory chemistry (n=55)

Blood Test	Pearson Correlation Coefficient	95% Confidence Interval
Plasma Cholinesterase	0.996	0.993 - 0.998
Erythrocyte Cholinesterase	0.941	0.901 - 0.965
Serum Albumen	0.929	0.881 - 0.958
Gamma Glutamyl Transferase	0.998	0.997 - 0.999

Table 6.26 Reliability of Questionnaire Data

I. Categorical Variables	N	Kappa	95% Confidence Interval
Brain injury	29	0.663	0.320 - 1.000
Previous blunt head injury	29	0.458	0.107 - 0.809
Marijuana use ever	29	0.453	0.090 - 0.816
Marijuana use current	29	0.256	0.0 - 0.621
Ever previous loss of consciousness	29	0.425	0.072 - 0.778
Previously played video games	29	0.418	0.055 - 0.781
Previously watched video games	29	0.440	0.077 - 0.803
12 pt visual disturbance	29	0.463	0.096 - 0.781
Previous history of pesticide poisoning	29	0.651	0.310 - 0.992
Currently on tot system	29	0.420	0.055 - 0.785
Paternal work	29	0.752	0.576 - 0.928

Table 6.27 Reliability of Questionnaire Data

II. Continuous Variables	N	Correlation* Coefficient	95% Confidence Interval
Age	29	1.000	0.999 - 1.000
Schooling #	29	0.918	0.831 - 0.961
Cigarette pack-years	28	0.920	0.835 - 0.962
Cumulative lifetime alcohol consumption	29	0.693	0.438 - 0.845
Usual weekend alcohol consumption	28	0.600	0.312 - 0.791
Alcohol consumption regarded as normal	22	0.392	-0.036 - 0.698
Alcohol consumption regarded as abnormal	17	0.274	-0.238 - 0.639
Grams alcohol drunk at one sitting	27	0.548	0.231 - 0.765
CAGE score #	29	0.750	0.529 - 0.876
MAST score #	29	0.636	0.351 - 0.813
Lifetime experience of the tot system #	29	0.509	0.175 - 0.738
Number of brain injuries#	29	0.770	0.562 - 0.886
Number of brain injuries causing prolonged loss of consciouness #	29	0.384	0.012 - 0.656
Cumulated exposure days	29	0.674	0.409 - 0.834
Cumulated pome exposure days	29	0.665	0.395 - 0.829
Average lifetime exposure intensity	29	0.594	0.292 - 0.789
Weighted cum exp days	29	0.604	0.305 - 0.794
Weighted av lifetime exp intensity	29	0.383	0.020 - 0.657
Cumulated dipping exposure days	29	0.635	0.350 - 0.812
Cumulated marker exposure days	29	0.994	0.987 - 0.997
Cumulated years of work in deciduous fruit	29	0.524	0.195 - 0.747
Usage PPE score #	29	0.742	0.516 - 0.872
Knowledge of risk score#	26	0.348	-0.046 - 0.648
Prevention knowledge score #	26	-0.083	-0.450 - 0.315
Attitude score #	29	0.061	-0.313 - 0.418
Lifetime residential exposure years	29	0.890	0.777 - 0.947
Lifetime resid spray exposure years	29	0.668	0.400 - 0.831
Lifetime close resid exposure years	29	0.185	-0.195 - 0.516
Lifetime residential exposure years (decid)	29	0.830	0.666 - 0.917
Lifetime resid spray exposure years (decid)	29	0.649	0.371 - 0.820
Lifetime close resid exposure years (decid)	29	0.185	-0.194 - 0.516

* Pearson correlation coefficient unless otherwise indicated
\# Spearman correlation coefficient

On questionnaire data, repeatability generally appeared satisfactory for most variables. Amongst 11 selected categorical variables, kappa exceeded 0.4 for all but one variable. This low kappa (0.256) was found for admitting current marjuana use, for which one would expect low reliability and validity. The key variables brain injury and previous history of pesticide poisoning both had kappa values suggesting good agreement (>0.65).

For continuous variables, agreement ranged from excellent ($r>0.9$) for demographic variables such as age and schooling, to poor for knowledge and attitude scores for pesticide safety ($r<0.35$). Given the likelihood of subject knowledge and attitude being influenced by the entire survey process, this finding is not unexpected. In fact, it may reflect an unexpected benefit of the research process, in that participants may have heightened awareness of pesticide safety as a result of their involvement in the study. Comparison of mean knowledge, attitude and PPE usage scores at initial survey, and 3 months after the survey revealed an increase in all scores, but only that for PPE usage was statistically significant ($t=2.7$; $p< 0.02$ - Paired T-test). However, it is not possible in this study to assess whether a long-term effect in improving knowledge, attitude and usage of PPE was achieved.

Intermediate in correlation were many of the measures of chronic workplace pesticide exposure. Cumulative exposure measures appeared to have correlation coefficients of the order of 0.6, while that for average lifetime intensity of exposure was substantially lower. This is partly the result of using a variable compounded of 2 other variables, each with their own error margins. Within-subject correlation for cumulative exposure for successive 5 years periods for Dutch farmers involved in bulb-production based on a similar JEM (Brouwer et al, 1994) was slightly better ($r=0.88$) than that found here, though this was not strictly speaking a measure of repeatability.

Potential environmental exposure was well correlated on repeat questionnaire ($p=0.89$) though the strength of this correlation fell as the variable became more focussed on closeness of residence to spray site (spray years p=0.67; spray in proximity years p=0.19). Similar findings were present for environmental exposure in deciduous fruit, and presumably reflected problems of recall by subjects of the precise nature of spray activities on farms many years ago. However, the environmental exposure variables that were less specific for close exposure, while having high repeatability, were less able to discriminate between subjects. Data in Tables 6.1 and 6.3 show that average total years resident and average total years resident on a sprayed farm were very similar to the subjects' average age, limiting the value of these variables in detecting exposure effect relationships. As a result, the variable reflecting spray in proximity was chosen for multivariate analysis, notwithstanding its low repeatability.

The analysis of repeat data on a random subsample of 29 subjects demonstates adequate repeatability for a range of variables, including the key ones to be selected for multivariate modelling. Alcohol related variables exhibited inconsistent repeatability, particularly for responses regarding normal and abnormal drinking patterns. Cumulated lifetime grams of alcohol consumed, CAGE and MAST scores showed the highest kappas on repeat measure compared to other measures of alcohol intake. Other variables which showed high correlations included lifetime cigarette packyears and previous history of brain injury, though the repeatability of the variable of brain injury qualified more specifically by prolonged loss of consciousness appeared to be less reliable.

REFERENCES

Ball A. (1990). Organisating farmworkers. SA Lab Bull 14(8) : 52-61.

Berberian IG, Enan EE (1987). Neurotoxic studies in humans occupationally exposed to pesticides. J Soc Occup Med. 37 : 126-127.

Bernhadt MW, Mumford J, Taylor C, Smith B. (1982). Comparison of questionnaire and laboratory tests in the detection of excessive drinking and alcoholism. Lancet 1(8267) : 325-328.

Brouwer DH, Brouwer EJ, Van Hemmen JJ. (1994). Estimation of long-term exposure to pesticides. Am J Ind Med. 25 : 573-588.

Bourne L, Langenhoven ML, Steyn K, Jooste PL, Laubscher JA, Van der Vyfer E. (1993). Nutrient intake in the urban African population of the Cape Peninsula, South Africa. The BRISK study. C Afr J Med 39(12) : 238-247.

Chia SE, Foo SC, Gan SL, Jeyaratnam J, Tian CS. (1993). Neurobehavioural function among workers exposed to manganese ore. Scan J Work Environ Health 19 : 264-270.

Chinyadza E, Moyo IM, Katsumbe TM, Chisvo D, Mahari M, Cock DE, Mbengeranwa OL. (1993). Alcohol problems among patients attending five primary health care clinics in Harare city. Centr Afr J Med. 39 : 26-32.

Colvin M, Myers JE, Nell VN, Rees D, Cronje R. (1993). A cross-sectional survey of neurobehavioural effects of chronic solvent exposure on workers in a paint manufacturing plant. Environmental Research 63 : 122-132.

Coye MJ, Lowe JA, Maddy KT. (1986). Biological Monitoring of agricultural workers exposed to pesticides: I. Cholinesterase Activity Determinations. J Occup Med 28(8) 619-636.

Fleiss JL. (1981). Statistical methods for rates and proportions. 2nd ed. New York: John Wiley. pp212-236.

Gardner MJ, Altman DG. (1989). Statistics with confidence - confidence intervals and statistical guidelines. British Medical Journal, London.

Groenewald CJ. (1986). *Afrikaans:* Gemeenskapsontwikkeling op plase in die Weskaap (Community development on farms in the Western Cape). Geleentheidspublikasie 9, Department Sociology, University of Stellenbosch, Stellenbosch, 1986.

Hooisma J, Emmen HH, Kulig BM, Muijser H, Poortvliet D, Letz R. (1990). Factor analysis of tests from the Neurobehavioural Evaluation System and the WHO Neurobehavioural Core Test Battery. In : Advances in neurobehavioural toxicology: Applications in Environmental and Occupational Health. Ed: Johnson BL, Anger WK, Durao A, Xintaras C. pp 245-255. Lewis Publishers, Michigan.

Lowensen R. (1986) Farm labour in Zimbabwe. Health Policy and Planning 1 : 48-57.

Loewensen R, Nhachi C, Gona P, Murambiwa W. (1990). Current findings of field research on practices of use and user knowledge of pesticides in Zimbabwe. Paper presented to Research Workshop into Pesticide Safety, Zimbabwe Congress of Trade Unions, Harare.

London L, Ehrlich R, Rafudien S, Krige F, Vurgarellis P. (1994). Notification of pesticide poisoning in the Western Cape 1987 - 1991. S Afr Med J. 84 : 269-272.

Mayfield DG, Mcleod G, Hall P. (1974). The CAGE questionnaire: validation of new alcoholism screening instrument. Am J Psych 131 : 1121-1123.

Minton NA, Murray VSG. (1988). A review of organophosphate poisoning. Medical Toxicology 3 : 350-375.

Myers JE, Nell V, Colvin M, Rees D, Cronje R, Thompson ML. (1994) Neuropsychological and neurological function in paint manufacturing workers with long-term exposure to organic solvents in two South African factories. Manuscript submitted to Occupational and Environmental Health.

Nell V, Myers JE, Colvin M, Rees D. (1993). Neuropsychological assessment of organic solvent effects in South Africa: Test selection, adaptation, scoring and validation issues. Environ Res. 63 : 301-318.

Rees D, Soderlund N, Cronje R, Song E, Kielkowski D, Myers JE. (1993). Solvent exposure, alcohol consumption and liver injury in workers manufacturing paint. Scan J Work Envir Health 19 : 236-244.

Richter ED, Chuwers P, Levy Y, Gordon M, Grauer F, Marzouk J, Lvey S, Barron S, Gruener N. (1992). Health effects from exposure to organophosphate pesticides in workers and residents in Israel. Isr J Med Sci 28 : 584-597.

Rosenstock L, Kiefer M, Daniell W, McConnell, Claypole K. (1991). Chronic central nervous system effects of acute organophosphate pesticide exposure. Lancet 338 : 223-227.

Rothman KJ. (1986). Modern Epideimiology. Little, Brown and Company, Boston.

Selzer ML. (1971). The Michigan alcoholism screening test: the quest for a new diagnostic instrument. Am J Psych 127 : 1653-1658.

Steyn K, Fourie J, Rossouw JE, Langenhoven ML, Joubert G, Chalton DO. (1990). Anthropometric profile of the coloured population of the Cape Peninsula. S Afr Med J ; 78 :68-72.

Stone JF, Eichner ML, Kim C, Koehler K. (1988). Relationships between clothing and pesticide poisoning: symptoms among Iowa farmers. J Environ Health 50 : 210-215.

Waldman L. (1993a). Women on the farms speak out. SA Lab Bull 17(5) : 49-54.

Waldman L. (1993b). Here you will remain: Adolescent experiences on farms in the Western Cape. MA Thesis, Department of Anthropology, University of Cape Town, Cape Town.

Weidepoel L. (1984). Learning from a literacy project. A survey of adult literacy in South Africa. Centre for Extra-Mural Studies, University of Cape Town, Cape Town.

Whittaker S. (1987). A nutritional and socio-economic study of Phillipi farm children and their mothers during November 1986. Dissertation in fulfilment of requirements for the degree M Med (Community Health), Department of Community Health, University of Cape Town.

Wolmarans P, Langenhoven ML, Benade AJS, Swanepoel ASP, Kotze TJvW, Rossouw JE. (1988). Intake of macronutrients and their relationship with total cholesterol and high-density lipoprotein cholesterol. The Coronary Risk Factor Study, 1979. S Afr Med J 73(1) : 12-15.

CHAPTER 7

NEUROLOGICAL AND NEUROBEHAVIOURAL EFFECTS OF AGRICHEMICALS AMONG DECIDUOUS FRUIT FARM WORKERS IN THE WESTERN CAPE: BIVARIATE AND MULTIVARIATE ANALYSES

CONTENTS Page

CHAPTER 7

NEUROLOGICAL AND NEUROBEHAVIOURAL EFFECTS OF AGRICHEMICALS AMONG DECIDUOUS FRUIT FARM WORKERS IN THE WESTERN CAPE: BIVARIATE AND MULTIVARIATE ANALYSES

7.1 Bivariate Analyses

Methods for bivariate analyses have been fully outlined in Chapter 5. A brief summary of these methods is presented below:

1. The relationship between symptom outcomes and categorical variables were examined by Chi^2 tests for differences in proportions, while T-tests and Wilcoxon tests were used to compare means and medians for continuous data with normal, and non-normal distributions respectively. Symptom scores were compared by means of non-parametric tests: differences in medians (Wilcoxon tests) for comparing symptom scores across categorical variables and logistic regression for continuous independent variables after dichotomising score results into high and low.

2. Vibration sense (vibratron units and extinction time), tremor performance, WHO NCTB and Information Processing Probe results were analysed for bivariate associations using t-tests for difference in means across categorical data, and linear regression for continuous data. Where outcome data could not be transformed to normality, non-parametric comparisons of medians (Wilcoxon tests) were used for categorical data and logistic regression was used for continuous data after reducing outcome variables to dichotomous categories.

For brevity, all the analyses above are not included here. Tables A.7.1.1 to A.7.1.4 in Appendix 7.1 summarise bivariate analyses by listing only those independent variables found to have a statistically significant association (at $p < 0.05$) with each of the 4 groups of outcome measurements (symptoms, vibration sense and motor tremor, WHO NCTB results and Information Processing Neurobehavioural test battery results) on bivariate analysis. The direction of the association is indicated in parenthesis. The discussion below summarises these findings.

7.1.1 Symptom reporting - bivariate analyses

Workers currently applying organophosphates (OPs) reported symptoms more commonly than non-applicators (Table 7.1). This was statistically significant for dizziness, headache, sleepiness and for overall score for neurological symptoms, and was non-significantly increased for most other symptoms. These results may be due to agrichemical exposure, or may arise from non-chemical stresses of their work (eg: long work shifts, tractor vibration, etc.) causing increased reporting behaviour. However, their overall score for "dummy" symptoms was minimally lower than that of non-sprayers, and this specificity tends to rule out increased illness behaviour resulting from general workplace stress as an explanation. Symptoms of dizziness and parasthesia (37% and 29% respectively) were also reported in another study in Poland amongst 35 exposed male workers and this was significantly higher than in a group of 32 controls (Richter, 1993).

Data in Appendix 7.1 (Table A.7.1.1) suggest that educational level appeared to influence symptom reporting. Workers with higher schooling reported fewer "neurological" symptoms. Numeracy and visual acuity (as measured by ability to identify a gap in a 12 point circle) also appeared to be associated with symptom reporting, and may be proxies for educational level achieved.

Variables referring to past head injuries were commonly associated (in a positive direction) with a range of symptoms (nausea, dizziness, headache, drowsiness, tiredness, parasthesia, gait disturbance, rhinorrhoea and chest pain). Age was associated with symptoms such as pain in the limbs, gait disturbance and parasthaesiae, all of which may be explained by a higher prevalence of arthritic conditions in the elderly. Other medical conditions were also positively associated with weakness, tiredness and dizziness (epilepsy) and numbness of the extremities (diabetes) (Appendix 7.1).

Table 7.1 Neurological and other symptoms by current exposure status among deciduous fruit farm workers

Symptom	Prevalence (%)	Current Sprayer (N=164)	Current Non-sprayer (N=83)	Odds Ratio (95% CI	
Stomach pain	current:	23.9	15.7	1.68	(0.80-3.57)
	for past 3 months:	2.4	1.2	2.05	(0.20-102.17)
Nausea	current:	19.5	13.3	1.59	(0.72-3.57)
	for past 3 months:	4.9	1.2	4.21	(0.55-188.83)
Dizziness	current:	34.8	20.5	2.07	(1.07-4.05)
	for past 3 months:	7.9	3.6	2.30	(0.60-12.89)
Gait disturbed	current:	5.5	7.2	0.75	(0.23-2.64)
	for past 3 months:	1.2	2.4	0.50	(0.04-7.03)
Numbness limbs	current:	9.8	2.4	4.38	(0.99-40.03)
	for past 3 months:	3.7	0.0	-	
Parasthesia	current:	17.1	14.5	1.22	(0.55-2.71)
	for past 3 months:	4.9	2.4	2.08	(0.40-20.47)
Earache	current:	4.9	9.6	0.48	(0.16-1.47)
	for past 3 months:	2.4	1.2	2.05	(0.20-102.17)
Lameness limbs	current:	19.5	15.7	1.31	(0.61-2.82)
	for past 3 months:	6.1	1.2	5.32	(0.73-233.85)
Pain in limbs	current:	19.5	19.3	1.02	(0.50-2.09)
	for past 3 months:	6.7	4.3	1.42	(0.40-6.36)
Rhinorrhoea	current:	23.2	15.7	1.62	(0.77-3.45)
	for past 3 months:	5.5	0.0	-	
Headache	current:	45.1	25.3	2.43	(1.31-4.54)
	for past 3 months:	11.0	3.6	3.29	(0.92-17.88)
Sleepiness	current:	43.3	22.9	2.57	(1.36-4.89)
	for past 3 months:	17.7	4.8	4.24	(1.41-17.14)
Chest pain	current:	20.7	15.7	1.41	(0.66-3.02)
	for past 3 months:	6.7	4.8	1.32	(0.38-5.88)
Tiredness	current:	36.6	27.7	1.51	(0.81-2.79)
	for past 3 months:	12.8	7.2	1.88	(0.70-5.94)

SYMPTOM SCORE	Current Sprayer		Current non-spr		P value*
	Mean	(Std Dev)	Mean	(Std Dev)	
* Neurologic symptoms	2.71	2.65	1.75	2.18	0.002
* "Dummy" symptoms	0.26	0.52	0.25	0.54	0.834

Odds for symptom reporting among workers currently applying pesticides relative to workers not applying pesticides.
* Wilcoxon rank sum test for comparison of medians.

Past poisoning, either by chemical fumes, or specifically with pesticides, was associated with a range of symptoms, including both "neurological" and "dummy" symptoms. Given the evidence for long-term neurobehavioural effects of past pesticide intoxication, it is possible that these symptoms may reflect some degree of psychological dysfunction in workers as a result of previous chemical insult. To control for possible confounders and effect modification, these results are re-examined using logistic regression modelling later in this chapter.

7.1.2 Neurological outcomes: Vibration sense and motor tremor - bivariate analyses

The 5 subjects with clinical evidence of neurological deficit (1 with frank sensori-motor neuropathy, and 4 with loss of peripheral sensory pinprick discrimination) were all current spraymen. However, the numbers were too small to show statistically significant differences between spraymen and non-spraymen (Fisher's exact test $p = 0.13$). Those subjects with any evidence of clinical deficits appeared to be older, more poorly educated, have higher cumulative and average intensity of occupational exposure, and greater lifetime alcohol consumption, although none of these differences were statistically significant (Table 7.2).

The role of alcohol in confounding a possible relationship between long-term agrichemical exposure and gross clinical deficits is elaborated upon later in this chapter. However, the focus of the investigation throughout is on the presence of sub-clinical deficits as detected by the measurement instruments outlined in Chapter 5. The following sections deal with the results of measurement of vibration sense and motor tremor.

Table 7.2 Mean schooling, age, occupational exposure, environmental exposure and alcohol consumption by clinical status among deciduous fruit farm workers

	(n=242) No Clinical deficit	(n=5) Clinical deficit	P-value*
Schooling (yrs)	6.28 (3.71)	4.80 (4.21)	0.34
Age (yrs)	36.8 (10.1)	41.00 (8.06)	0.23
Cumulative lifetime Kg OP/hectare	5.63 (8.25)	6.62 (1.84)	0.08
Average lifetime intensity log(Kg OP/hectare-year)	0.21 (0.23)	0.26 (0.12)	0.18
Cumulative lifetime Kgs alcohol	4.15 (3.93)	5.24 (4.06)	0.39
Lifetime residence in proximity to OP spray	9.53 (12.00)	7.87 (1.56)	0.44

* Based on Wilcoxon test.

Recognized predictors of vibration sensation include age, height (Gerr and Letz, 1988; Gerr et al, 1990; Bove et al, 1989) and skin temperature (Lundstrom et al, 1992). Bivariate analyses (Appendix 7.1 - Table A.7.1.2) confirm associations of log vibratron threshold with age, and of tuning fork extinction time with both age and height. Both measures of vibration sense were also associated with education level. Height was positively associated with log vibratron threshold, but the parameter estimate in the bivariate regression model of log vibratron on height just failed to reach statistical significance (p=0.06). Nonetheless, height was included in the final model for multivariate analyses because of its known association with peripheral vibration sense.

Current status as an agrichemical applicator was also examined in relation to the vibratron and tremor tests (as in Table 7.1 for symptoms) but no significant associations were found. Moreover, none of the measures of recent agrichemical exposure or of acute biological effects (plasma cholinesterase) were found to be associated with either extinction time or vibratron threshold. In contrast, many of the measures of cumulative occupational and non-occupational exposure to pesticides were associated with poorer peripheral vibration sense (See Appendix 7.1 - Table A.7.1.2 for details). However, these latter associations are probably confounded by age, and are examined further using multiple linear regression later in this chapter..

The different measures of peripheral tremor appeared to have similar relationships to age, education and cumulative measures of occupational and non-occupational exposures. Age and cumulative exposure are associated with greater intensity of tremor, poorer score and slower performance, while the inverse is the case with increased schooling (Appendix 7.1 - Table A.7.1.2). In addition to cumulative exposure, measures of recent exposure were positively associated with tremor intensity for both dominant and non-dominant hand and for maze time for dominant hand, though a negative relationship was present for tremor score for the dominant hand (Appendix 7.1 - Table A.7.1.2).

Alcohol consumption was another variable found to be associated with tremor intensity and tremor counts (Appendix 7.1 - Table A.7.1.2). In particular, cumulative lifetime grams of alcohol consumed were (positively) associated with tremor intensity and maze counts for the subjects' dominant hand. While this would again be confounded by age, other measures of alcohol consumption were also associated with maze performance - reported quantity of alcohol consumed at one sitting was positively associated with tremor score in both dominant and non-dominant hands; opinions on quantity of alcohol regarded as normal consumption was negatively related to tremor intensity in the non-dominant hand; MAST scores were positively associated with times on the maze (though the CAGE scores were negatively related to maze counts on the dominant hand). These alcohol variables were used in later multiple linear regression analyses.

Educational level appeared to be positively related to performance on a variety of the maze tests (Appendix 7.1 - Table A.7.1.2).

Given the complexity of the instruction, and familiarity with testing situations associated with educational exposure, this phenomenon is not unexpected.

Exposure to glue and past occupational exposure to paint were found to be negatively associated with tremor intensity in the dominant hand and with vibration threshold, respectively (Table A.7.1.2 in Appendix 7.1). This may be due to these variables reflecting a level of technical proficiency and therefore acting as proxies for educational level.

Poor visual acuity, which would be expected to strongly influence maze tests, was found to be associated with tremor score, intensity and counts in both hands. Variables relating to previous head injury appeared to be (positively) associated with tremor intensity but not with the other maze test outcomes (Table A.7.1.2 in Appendix 7.1).

7.1.3 Neurobehavioural outcomes: The WHO NCTB - bivariate analyses

Consistent associations with test performance on the WHO NCTB (Table A.7.1.3 in Appendix 7.1) include age (negative), education (positive), numeracy (positive) and poor visual acuity (negative). Previous experience of video games was also positively associated with a number of the test outcomes (digit span forwards, total digit span, digit score forwards, total digit score, Benton visual retention, Santa Ana Peg Board dominant and non-dominant hands total and digit symbol WAIS-standard score). Paint exposure was found to be positively related to raw score, and glue use to Benton performance and Santa Ana peg board performance in both dominant and non-dominant hands. This is similar to the bivariate associations (Table A.7.1.2 in Appendix 7.1) involving the vibratron and tremor device reported above for paint and glue exposure respectively and may be due to these variables being proxies for skill and education. Age and education were not related to the number of pegs dropped in the Santa Ana test in either hand, and there were few variables associated with this outcome measure.

Poor visual acuity was found to be associated with poor performance on most of the WHO NCTB tests. Other associations of interest include a positive association between serum albumen (as a marker of general nutritional status) and 2 of the WHO NCTB subtests; a negative association between smoking status (ever smoked) and total span and score backwards; a positive association between marijuana use and Santa Ana peg board performance in both dominant and non-dominant hand (Table A.7.1.3 in Appendix 7.1).

Alcohol consumption was inconsistently associated with test performance on bivariate analyses (Table A.7.1.3 in Appendix 7.1). Positive associations were found for typical weekend alcohol consumption, and past week alcohol consumption with digit span (and score) forward, with the latter variable associated with the age-adjusted WAIS Standard score. Similar positive associations were found with the Santa Ana Peg Board outcomes and digit symbol subtests. A negative association was found between Benton scores and both the threshold regarded as excessive drinking by subjects, as well as the proportion of jobs in which the tot system was practiced. The latter variable is potentially confounded by age.

Current employment as a sprayer was not associated with any of the neurobehavioural outcomes on bivariate analysis. However, the possibility that spraymen are a selected group likely to be neurobehaviourally more competent than general farm workers is suggested by the positive association between the proportion of jobs held as spraymen and scores in the following WHO NCTB tests: Digit span backwards and forwards, Santa Ana Peg Board (dominant hand), digit symbol correct and Benton (Table A.7.1.3 in Appendix 7.1). Workers who are more competent to begin with may be given jobs requiring more skills such as tractor spraying. However, the confounding role of education is examined further in subsequent multivariate analyses.

Occupational and non-occupational cumulative exposures to agrichemicals were widely associated with most of the neurobehavioural outcomes, but age is an important confounder.

However, measures of intensity of agrichemical exposure were found to be positively associated with score forward and span backward, and WAIS Std score and number correct on digit symbol testing. In contrast, average lifetime intensity was positively related to the number of trials wrong in Pursuit Aiming (Table A.7.1.3 in Appendix 7.1). These conflicting relationships are analysed further in the multivariate analyses.

7.1.4 Information Processing Probes and ACT - bivariate analyses

From Table A.7.1.4 in Appendix 7.1, it is apparent that many of the measures of cumulated pesticide exposure (occupational and non-occupational) appeared to be associated with adverse outcomes on bivariate analysis. Association with measures of acute agrichemical exposure appeared rarely. However, relationships between cumulative exposure measures and probe outcomes are strongly confounded by age. Subsequent multivariate analyses take this confounding into account.

Other variables associated with probe outcomes included those pertaining to educational level, alcohol intake, (both chronic and short-term measures but with inconsistent directions of association), visual acuity, head injury and previous experience of playing video games. CAGE score appeared consistently with tests related to Continuous Number Checking in the expected direction. Nutritional status as measured by serum albumen appeared inversely related to performance on tests for Semantic Access. Smoking variables were associated with increased reaction times on a number of subtests for Short-term Memory scanning and for Manipulating Numbers. Variables pertaining to head injury appeared to demonstrate associations in a direction inverse to the expected for a number of probe outcomes.

Of interest is the presence of an inverse association between PPE score and reaction time on two of the Hick Box tests, suggesting that those who reported higher usage of PPE performed better on tests of reaction time. These associations are explored further later in this chapter.

7.2 Multivariate Analyses - Acute Biochemical Outcomes

The relationship between acute biochemical markers of OP exposure and various measures of recent exposure were analysed in tandem to the investigation of chronic neurological and neurobehavioural outcomes. To control for the effects of confounders, multiple linear regression modelling was performed using forward stepwise selection from a range of variables (total of 8 variables) that included:

a) Three non-correlated measures of recent exposure as independent variables:
   1) current status as a pesticide applicator (Yes/No),
   2) days reported by subject since last contact with organophosphates (Number of days) and,
   3) total days of contact with OPs in the past 3 months reported by the subject.

b) In addition, age, serum albumen (as a marker of nutrition), cumulated lifetime alcohol consumption, cumulated lifetime weighted Kg OP/hectare (EXWGHT) and PPE usage score were also included as independent variables based on their known association with cholinesterase levels.

The criterion for inclusion of variables in the forward selection was based on improvement in the proportion of explained variance at $p<0.15$.

7.2.1 Biochemical Outcomes - Results

The results of the analysis are presented in Table 7.3 below.

Table 7.3 Significant predictors of Plasma and standardised Erythrocyte Cholinesterase amongst deciduous fruit farm workers *

I. Plasma Cholinesterase

Model r^2	Variable (direction of association)	Partial r^2	P-value **
0.062	Serum Albumen (+)	0.051	0.003
	Age (+)	0.012	0.040

II. Standardised Erythrocyte Cholinesterase

Model r^2	Variable	Partial r^2	P-value **
0.058	Cumulated lifetime Kg OP/hectare (-)	0.045	0.006
	Age (+)	0.014	0.018

* Linear modelling using forward selection; Criteria for inclusion based on improvement in the proportion of explained variance at $p<0.15$.

** P value gives significance of the slope estimate.

None of the acute exposure variables included in the forward regression were significant predictors of either erythrocyte or plasma cholinesterase, although long-term exposure (cumulative Kg OP/hectare) was able to predict about 5% of the model variance for erythrocyte cholinesterase and this was a significant association. Of note is the failure to demonstrate any relationship between reported PPE usage and cholinesterase levels. Nutritional status appears as a predictor for plasma cholinesterase (partial r^2 = 0.05).

7.2.2 Biochemical outcomes - discussion

Little of the overall variance was explained in the modelling procedures (r^2 less than 0.1) for both plasma and erythrocyte cholinesterase. This may reflect the high levels of inter- and intra-individual variation inherent in population cholinesterase levels (Coye et al, 1986).

The lack of agreement between different measures of acute exposure (see Section 6.5.2 in Chapter 6) may reflect misclassification of acute exposure and may explain the failure to demonstrate an association between the biochemical markers and measures of acute exposure based on history and records. In contrast, the variable for cumulative lifetime Kg OP exposure/hectare appeared to significantly predict a lowered haemoglobin-standardised erythrocyte cholinesterase level. Given the apparent levels of acute exposure misclassification, cumulative exposure to OPs may be a less misclassified variable, and its superior precision may therefore allow better detection of an overall agrichemical effect, as manifested in its association with standardised erythrocyte cholinesterase.

This finding is not entirely compatible with our current understanding of the role of erythrocyte cholinesterase as a biological marker of relatively sub-acute exposure to organophosphates, though cumulative exposure to OPs has been reported to cause tolerance to low levels of enzyme activity (Coye et al, 1986; Lotti, 1992). Presumably, repeated exposures to low doses of OPs may lead to persistent lowering of red cell cholinesterase levels. While the strength of this association is relatively small (partial $r^2 = 0.05$), this result suggests that the JEM used to construct historical exposure in this study was able to discriminate between coarse levels of OP exposure and the findings warrant further exploration.

The presence of an association with serum albumen is consistent with the role of liver function in maintaining plasma enzyme levels (Coye et al, 1986). Age has also been reported as a predictor of plasma cholinesterase (Coye et al, 1986) and this finding is similarly supported by these data.

7.3 Multivariate Analyses - Chronic Neurological and Neurobehavioural Outcomes

Methods for multivariate analyses have been fully outlined in Chapter 5 and are summarised briefly below.

Variables were chosen for inclusion in regression modelling using a combination of a priori choices and selection based on bivariate analyses. The general model is outlined in the box below (see Chapter 5 for detailed explanation). For analyses of the tuning fork extinction time and vibratron thresholds, height was added to the group of a priori variables for inclusion, making a total of 8 a priori variables.

Linear regression was used for continuous data, after checking assumptions for normality of the residuals and homoscedasticity. Logistic regression was used for symptom outcomes, and for those continuous outcomes where transformation to normality was neither possible nor appropriate, in which cases the outcomes were reduced to dichotomous variables. Subjects with impaired visual acuity not improved by the use of spectacles (n=9) were excluded from analysis of neurobehavioural performance and from tests of motor tremor requiring hand-eye coordination.

$$
\begin{aligned}
\text{OUTCOME} = a &+ B_1(\text{AGE}) \\
&+ B_2(\text{EDUCATION}) \\
&+ B_3(\text{PREVIOUS POISONING}) \\
&+ B_4(\text{ALCOHOL INTAKE}) \\
&+ B_5(\text{ACUTE EXPOSURE}) \\
&+ B_6(\text{LONG-TERM OCCUPATIONAL EXPOSURE}) \\
&\quad [\text{CUMULATIVE or AVERAGE LIFETIME INTENSITY}] \\
&+ B_7(\text{CUMULATIVE NON-OCCUPATIONAL EXPOSURE}) \\
&+ B_8(\text{HEIGHT})\ ^{*} \\
&+ B_{9...N}\ (\text{VARIABLES FROM BIVARIATE EXPLORATIONS})
\end{aligned}
$$

* Height only included routinely for mean log vibratron threshold and tuning fork extinction time.

The significant associations derived from the final models are summarised in Tables 7.3 to 7.7. Appendix 7.2 gives the complete multivariate statistics for the full models on which these associations are based.

7.3.1 Symptom reporting - multivariate analyses

7.3.1.1 Symptom outcomes: results

Table 7.4 lists the independent variables associated in logistic regressions with all symptom outcomes in the study population. The full model results are listed in Appendix 7.2.

A variable that appears with consistency as predicting the presence of individual symptoms amongst farm workers is a history of previous pesticide poisoning (or fume intoxication). Less commonly, CAGE score and the presence of, or number of previous head injuries leading to loss of consciousness are significantly associated with various symptom outcomes. Odds ratios for associations with previous poisoning were statistically significant for 10 symptoms, and these odds ratios were generally large (greater than 5) though with wide confidence intervals.

No long-term occupational or environmental exposure variables appear to predict symptoms generally and none of the major environmental variables related to exposure appeared to predict symptom outcomes (except for the use of pesticide containers at home, and the duration of domestic gardening). Specific symptoms in Table 7.4 (current nausea, limb pain, rhinorrhoea and sleepiness, and chest pain, tiredness and headache for 3 months or more) appeared to be positively predicted by a few alcohol-related variables (CAGE score, gms alcohol consumed at one sitting, lifetime experience of the tot system and cumulative lifetime alcohol consumption). Positive associations between age and symptoms such as limb pain could be expected given the high prevalence of arthritis and related conditions amongst the elderly.

Table 7.4 Independent variables associated * with symptoms amongst deciduous fruit farm workers

SYMPTOM OUTCOME	Variables Associated	Odds Ratio (95% CI)
Stomach pain current	Use of pesticide container at home	5.36 (1.12-25.62)
Stomach pain 3 months	Previously poisoned by pesticides	19.33 (2.38-157.09)
Nausea current	Ever lost consciousness	2.41 (1.17-4.98)
	CAGE score	1.57 (1.06-2.31)
Nausea 3 months	Previously overcome by fumes	6.93 (1.19-40.35)
Dizziness current	Duration of domestic gardening	1.12 (1.00-1.25)
Dizziness 3 months:	History of epilepsy	10.59 (1.25-89.32)
	Previously poisoned by pesticides	5.88 (1.36-25.47)
Gait disturbed current:	Previously poisoned by pesticides	12.39 (2.42-63.40)
	Clincal sensory deficit	4.84 (1.15-20.30)
Gait disturbed 3 months:	Previously poisoned by pesticides	14.39 (1.17-177.67)
Numbness limbs current	none	
Numbness limbs 3 months	Previously poisoned by pesticides	9.28 (1.22-70.61)
Parasthesia current	Clinical sensory deficit	2.78 (1.05-7.34)
	Duration of domestic gardening	1.10 (1.02-1.20)
Parasthaesia 3 months:	Lifetime cigarette pack-years	1.04 (1.01-1.08)
Earache current	Non-numeracy	10.58 (1.26-88.59)
	Previously poisoned by pesticides	5.65 (1.33-23.98)
Earache 3 months	Previously poisoned by pesticides	14.28 (1.23-166.03)

Table 7.4 (Continued) Independent variables associated * with symptoms amongst deciduous fruit farm workers

SYMPTOM OUTCOME	Variables Associated	Odds Ratio (95% CI)
Lameness limbs current:	Schooling years	0.87 (0.78-0.98)
	Previously played videos	0.09 (0.01-0.69)
	Previously overcome by fumes	3.42 (1.17-10.00)
Lameness 3 months	History of epilepsy	18.96 (2.16-166.74)
Limb pain current	Previously poisoned by pesticides	6.61 (1.56-28.03)
	Quantity alcohol drank at one sitting	0.996 (0.992-0.999)
Limb pain 3 months	Age	1.07 (1.01-1.14)
	Ever used marijuana	4.97 (1.50-16.48)
Rhinorrhoea current:	Lifetime experience of the tot system	1.32 (1.02-1.72)
Rinnorhoea 3 months:	None	
Headache current	Proportion of jobs held as sprayman	3.94 (1.24-12.52)
	Number past head injuries	1.44 (1.09-1.91)
Headache 3 months	Previously poisoned by pesticides	8.61 (1.05-39.17)
	CAGE Score	2.83 (1.38-5.77)
Sleepiness current	Cumulative lifetime alcohol consumption	1.00 (1.00-1.00)
	Previously overcome by fumes	8.00 (1.98-32.34)
Sleepiness 3 months	None	
Chest pain current	Number past head injuries	1.56 (1.18-2.06)
	Duration of domestic gardening	1.10 (1.02-1.19)
Chest pain 3 months:	CAGE score	2.67 (1.27-5.63)
Tiredness current	Previously poisoned by pesticides	4.35 (1.21-15.63)
	Number past head injuries	1.67 (1.27-2.19)
Tiredness 3 months	Previously poisoned by pesticides	6.17 (1.57-24.25)
	CAGE score	2.01 (1.08-3.73)

* - Only variables with an odds ratio significantly different from 1 at $P<0.05$ presented. The full model statistic are listed in Appendix 7.3.

In order to summarise the symptom outcomes, symptoms were reduced to scores for "neurological" symptoms and "dummy" symptoms, and dichotomised as high versus low scores for each category of symptoms. A high score was taken as the presence of 2 or more "neurological" symptoms, and the presence of 1 or more "dummy"

Table 7.5 The association between independent variables and symptom scores amongst deciduous fruit farm workers

I. Score for neurological symptoms

Variables Associated	N#	Odds Ratio	(95% CI)
Previously overcome by fumes	28	5.71*	(1.43-22.76)
Current pesticide applicator	164	2.15*	(1.10-4.23)
Past pesticide poisoning	15	2.14	(0.47-9.82)
Average lifetime intensity of exposure		1.88	(0.47-7.52)
Number of past head injuries causing loss of consciousness		1.55*	(1.04-2.31)
High lifetime alcohol users [b]	123	1.39	(0.69-2.81)
CAGE Score		1.30	(0.99-1.69)
Residence in proximity to spray		1.01	(0.98-1.03)
Age		1.01	(0.97-1.05)
Schooling years		0.98	(0.90-1.10)
Past head injury	170	0.71	(0.28-1.80)
Past experience playing video games	44	0.59	(0.26-1.33)
Low plasma cholinesterase [a]	5	0.41	(0.03-4.87)

II. Score for "dummy" symptoms

Variables Associated	N#	Odds Ratio	(95% CI)
Past pesticide poisoning	15	3.37*	(1.07-10.62)
Average lifetime intensity of exposure		2.20	(0.54-8.96)
Number of past head injuries causing loss of consciousness		1.56*	(1.19-2.04)
Low plasma cholinesterase [a]	5	1.16	(0.11-11.86)
Residence in proximity to spray		0.99	(0.96-1.02)
High lifetime alcohol users [b]	123	0.98	(0.48-2.04)
Age		0.98	(0.94-1.02)
Schooling years		0.92	(0.83-1.02)

* $P < 0.05$

\# - Number of subjects for whom the categorical variable was present - does not apply to continuous variables.

b - Plasma cholinesterase less than 4000 U/l (laboratory reference range).

a - Cumulative lifetime alcohol consumption greater than 3267 Kg ethanol (median).

symptoms. Table 7.5 presents the results of multiple logistic regressions of high "neurological" and "dummy" symptom scores on predictor variables. Unlike other tables, statistics for all the variables included in the model are presented. Previous poisoning by pesticides is significantly related to reporting of dummy symptoms and is associated with a non-significant increase in reporting neurological symptoms. Fume intoxication which may include poisoning events not reported as pesticide poisoning (the two variables were not well correlated - Spearman's r = 0.08, Chapter 6) is significantly associated with reporting of neurological symptoms, as is present work as a pesticide applicator. The number of head injuries resulting in loss of consciousness are strongly related to both group of symptoms. Plasma cholinesterase is weakly associated with increased "dummy" symptom reporting. CAGE scores are weakly and non-significantly predictive of neurological symptoms.

7.3.1.2 Symptom outcomes: discussion

The presence of affective changes and subjective symptoms amongst survivors of acute OP pesticide poisoning has been reported (Levin et al, 1976; Coye et al, 1986; Rosenstock et al, 1990; Rosenstock et al, 1991) as have the presence of long-term neurobehavioural deficits (Savage et al, 1988; Steenland et al, 1994). Conspicuous in this study is a strong association between previous poisoning with pesticides and "dummy" and, to a lesser extent "neurological" symptoms. One explanation for this is that the subtle neurobehavioural changes resulting from pesticide (specifically organophosphate) poisoning may result in increased symptom reporting behaviour. While data in this study on the specific chemical agent responsible for the poisoning were not available, it may be reasonably inferred that these events usually involved organophosphates as the experience of notifications of pesticide poisoning in the Western Cape has shown (London et al, 1994).

A second, but possibly less plausible explanation for the association between symptom reporting and previous poisoning may be that workers with illness-reporting personalities may be more likely to expose themselves to agrichemicals, or to be involved in poisoning events. Given the international literature on neurobehavioural function amongst survivors of acute poisoning (Savage et al, 1988; Rosenstock et al, 1991; Steenland et al, 1994), this explanation appears unlikely. Inaccurate description of poisoning resulting in systematic misclassification of the independent variable (previous poisoning) is also unable to explain away this association given the consistency within different symptoms, and the acceptable repeatability achieved for previous pesticide poisoning on repeat questionnaires (Table 6.24). In any event, such misclassification of previous poisoning would be more likely to be non-directional and thus underestimate the strength of exposure-effect relationships.

However, a third and probably most likely explanation for the apparent association may lie in systematic overreporting of symptoms by agrichemical-exposed workers and those workers with brain injury and loss of consciousness. In the preparation for the study and in the consent procedures, farm workers may have been aware of the investigation of pesticide-related effects, and this may have influenced their reporting of symptoms or their recall of poisoning. This bias may account for the substantially increased odds ratios in Tables 7.3 and 7.4. This explanation is supported by the finding of an association between past pesticide poisoning and "dummy" symptoms which would not have been anticipated had there been a specific relationship between previous poisoning and neurological symptoms. This illustrates the main limitations of subjective information. Symptom outcomes accordingly are considered to carry relatively less weight in the interpretation of possible causal effects of chemicals in neurotoxicity assessment (Simonsen et al, 1994).

The association between previous head injury and symptoms is hardly surprising given the literature on brain damage following head injury. The odds ratios for "dummy" and neurological symptoms were remarkably similar in strength and direction. This finding may suggest that the categorisation of symptoms into "dummy" and neurological may not have been sufficiently specific to discriminate between symptom outcomes resulting from global central nervous system damage. This might reduce the impact of the reporting bias described above for the variable for previous pesticide poisoning.

A striking feature of the data is that there appears to be little relationship between measures of acute agrichemical exposure and symptom outcomes. Previous research in Southern Africa (Bwititi et al, 1987; Innes et al, 1990) and India (Kashyap, 1986) has not demonstrated associations between plasma cholinesterase lowering and the presence of neurological symptoms amongst OP exposed workers. In contrast, others have reported the association of non-specific symptoms with low plasma cholinesterase (Coye et al, 1986; Peedicayil et al, 1991) and with the presence of urinary organophosphate metabolites (Richter et al, 1992).

If minor exposures to organophosphates (that are too small to result in overt clinical intoxication) were related to increased symptom reporting, one could expect plasma cholinesterase as a biological marker of OP exposure to be related to symptom outcomes. In this study, the data are doubtful. Plasma cholinesterase was not associated with any individual symptoms but was related to overall scores for "dummy" symptoms. However, the fact that current spraymen reported more neurological symptoms but not "dummy" symptoms compared to non-sprayers (Table 7.1), and that current spraying activity was independently related to neurological symptom score tends to support a role for current low-dose exposures in leading to adverse symptom morbidity. Moreover, the fact that current spraying activity was not related to "dummy" symptom scores tends to minimise the likelihood of any reporting bias based on current sprayer status being present.

It may well be that the two variables in question, current spray activity and previous pesticide poisoning, are associated with symptoms by means of different mechanisms. For example, symptoms associated with current exposure may be mediated by sub-acute effects of organophosphates on neurotransmitter function, while those associated with previous poisoning may be due to long-term neurobehavioural changes arising from mechanisms yet to be elucidated. Nonetheless, the associations with current spray activity are small and those with previous pesticide poisoning are potentially subject to substantial reporting bias, and these require further investigation in appropriately designed studies.

7.3.2 Vibration sense and motor tremor - multivariate analyses

While subclinical outcomes were the focus of the study, it is worth noting that five subjects were found to have some evidence of clinical deficit on neurological examination. All 5 were current spraymen. However, this association was not statistically significant and neither were any of the differences in mean exposures presented in Table 7.2 above. A multiple logistic regression model with clinical deficit as outcome was run using the variables outlined in the box at the start of Section 7.3 as explanatory variable (i.e. the "basic model" plus current status as spray operator or not). Again, none of the variables were found to be significant predictors of clinical outcome (data presented in Appendix 7.3).

Despite the lack of significant association, these findings may suggest some effect of agrichemical exposure since the direction of association between clinical outcome and current status as an applicator remained positive after controlling for age and other confounders in the model. However, the study was not directed at detecting clinical effects, and power calculations were based on anticipated abnormalities on sub-clinical tests. The discussion that follows therefore concentrates on the results of the tests of motor tremor and vibration sense threshold, and their relationship to long-term agrichemical exposure.

Subjects with clinical deficit were included in the following multivariate analyses for neurological and neurobehavioural outcomes. However, the anticipated effect of including subjects with clinical deficit in tests of subclinical outcome would have been to overestimate a possible effect. For this reason, if significant associations were found with occupational exposure variables, the analyses were re-run excluding these subjects to see if the strength or direction of association were changed. In none of the cases where associations were demonstrated with occupational exposure factors, did the exclusion of the 5 subjects with clinical deficit make any substantive difference to the results.

7.3.2.1 Vibration sense and motor tremor: results

Results of multiple linear and multiple logistic regression involving vibration sense and motor tremor outcomes are presented in Tables 7.6 and 7.7.

Table 7.6 Independent variables associated * with vibration sense loss and motor tremor intensity

NEUROLOG OUTCOME	Model r^2	Variables (Direction of assoc)	Partial r^2
Vibratron threshold (Log Vib U)	0.263	Age (+)	0.205
		Height (+)	0.034
		Serum albumen (-)	0.017
Tuning fork extinction time (sec)	0.176	Age (-)	0.086
		Serum GGT (+)	0.042
		Height (-)	0.028
Tremor intensity domin hand	0.198	Height (+)	0.062
		Ever smoked (+)	0.040
		OP exposure in past 10 days (+)	0.035
Tremor intensity non-domin hand	0.065	Schooling years (-)	0.027

* Multiple linear regression: Only variables with a B-slope significantly different from 0 at P<0.05 presented. The full model is listed in Appendix 7.2.
Nine subjects with visual acuity problems excluded from the analysis of tremor intensity.

Table 7.7 Independent variables associated * with motor tremor score and count, and maze count and maze time among deciduous fruit farm workers

	Variables Associated	Odds Ratio (95% CI)	
Tremor score [1] dominant hand (achieved holes)	Schooling (yrs)	1.18	(1.05 - 1.32)
	Lifetime close residential exposure (yrs)	0.95	(0.92 - 0.98)
Tremor score [1] non-dominant hand (achieved holes)	Gms alcohol consumed at one sitting (gms)	1.002	(1.0005-1.004)
	Height (cm)	0.95	(0.91-0.999)
Maze counts [2] dominant hand	Schooling (yrs)	1.16	(1.07 - 1.27)
Maze counts [2] non-dominant hand	Age (yrs)	0.95	(0.92 - 0.99)
Maze time [3] dominant hand (seconds)	-		
Maze time [3] non-dominant hand (seconds)	-		

1 - Subject reached 6th hole in series of descending size order vs did not reach (i.e. reached 5th or fewer). Nine subjects with visual acuity problems excluded from the analysis.
2 - Average counts from touching side of maze over 2 trials per subject less than 4.6 vs greater than 4.5. Nine subjects with visual acuity problems excluded from the analysis.
3 - Average time taken to complete maze over 2 trials per subject less than 36.6 vs greater than 36.5. Nine subjects with visual acuity problems excluded from the analysis.
* - Logistic regression model: Only variables with an odds ratio significantly different from 1 at $P<0.05$ presented. The full model is listed in Appendix 7.2.

None of the measures of chronic exposure appear as significant outcome predictors. Age and schooling are the most consistently associated, the former with vibration sense and maze counts in the non-dominant hand, and the latter with tremor score (dominant hand) and maze counts (dominant hand), and with tremor intensity in the non-dominant hand. The association with schooling is not surprising, given the complex nature of the instruction procedures attached to the administration of the test and familiarity with testing situations induced by schooling exposure. Height, a known covariate of peripheral vibration sense, appears as predictive of both log vibratron score and of tuning fork extinction time. Of interest is the association between serum albumen and log vibratron score, suggesting that chronic undernutrition in adults may be associated with subclinical sensory impairments.

Despite many alcohol-related variables having associations with the vibration sense and tremor outcomes on bivariate analyses (Appendix 7.1), hardly any of these associations persist after controlling for other covariates in the multivariate models above. Subjects with higher CAGE scores and higher reporting of alcohol consumption at a single sitting appear to perform better on tests of tremor for score and for holes achieved, while subjects with high MAST scores perform slower on the maze tests (Appendix 7.2). However, only the association between tremor score in the non-dominant hand and reported quantity of alcohol consumed at one sitting was statistically significant. The direction of this association was opposite to expected but it was a very weak association.

7.3.2.2 Vibration sense and motor tremor: discussion

Tremor intensity in the dominant hand was found to be related to a history of OP exposure as reported by the farmer in the preceding 10 days, suggesting some acute agrichemical exposure effect, but was not related to any of the measures of long-term exposure. Findings of increased tremor using a clinical measure were reported amongst production workers chronically exposed to organophosphates and other agrichemicals when compared to textile workers (Otto et al, 1990). However, to date this hypothesis of increased tremor being an effect of long-term agrichemical exposure has not been explored amongst the few studies of survivors of acute poisoning, nor has quantitation of tremor been widely used in studies of workers exposed to organophosphates.

In this study, height was associated with tremor intensity in the dominant hand and tremor score in the non-dominant hand, and this relationship is similar in direction and strength to the association with height exhibited by vibration sense measures. Given the recognised value of tests of peripheral vibration sense in the early detection of the effects of exposure to chemical neurotoxins, this association between height and motor tremor may indicate grounds for developing further the use of tremor measurement as a survey device in occupational neurotoxicity. Smoking status may be an important confounder, given the physiological effect of nicotine on neurotransmitter function, and the association between smoking and tremor intensity in the dominant hand confirms the need to take this variable into account when using this test. However, the biological plausibility of an association between height and tremor is not obvious, and the association may be artifactual in that the method of conducting the test, whereby the subject is not allowed to rest his elbow during the test, may favour subjects with shorter stature. Nonetheless, this finding may warrant further study, as a valuable survey device for early detection of neurological function may be developed.

None of the environmental measures of exposure showed any relationship to the outcomes above except for tremor score in the dominant hand, with poorer performance on the test being associated with longer lifetime residence in proximity to a sprayed farm. Few studies have examined the impact of non-occupational agrichemical exposure in studies of rural workers, and this finding may suggest that this route of exposure needs further investigation. However, this finding was also an isolated one and may well have arisen due to the chance effects of multiple comparisons.

Exposure misclassification as suggested from poor correlations between different alcohol variables (Table 6.6 in Chapter 6) may contribute to the failure to demonstrate associations between alcohol and vibration sense and motor tremor. A more likely explanation is that the alcohol intake levels in this population are homogeneous and relatively high (see Table 6.5 - usual alcohol intake in this study was more than double that found for other

South African populations in two recent studies). As a result of the absence of an alcohol exposure gradient, it is difficult to demonstrate dose-response relationships for alcohol.

*7.3.3 **Neurobehavioural outcomes: WHO NCTB - multivariate analyses***

7.3.3.1 Neurobehavioural outcomes: WHO NCTB - results

Results of multiple linear regression are presented for the WHO NCTB in Table 7.8. Age and schooling are consistent predictors for most of the NCTB outcomes above, and their effects are in the expected direction. In addition to schooling, non-numeracy is an independent predictor of performance on a number of NCTB tests (Digit span, Santa Ana, Benton). The two variables were not well correlated (Spearmans r=-0.32) and thus their inclusion simultaneously in the regression model was justified. Alcohol related variables also appear frequently, but their associations are inconsistent, and frequently in a direction contrary to expected. However, unlike the cases for age, schooling and non-numeracy, the strength of these associations with alcohol measures are small as judged from the partial r^2 (of the order of 2 to 5%).

Table 7.8 Independent variables associated* with WHO NCTB outcomes amongst deciduous fruit farm workers

WHO NCTB OUTCOME	Model r^2	Variables (Dir assoc)	Partial r^2
* Digit span			
Span forward	0.281	Schooling (+)	0.171
		Age (-)	0.073
		Lifetime Gm of alcohol consumed (+)	0.044
Span backward	0.242	Schooling (+)	0.100
		Non-numeracy (-)	0.086
Total span	0.350	Schooling (+)	0.188
		Non-numeracy (-)	0.075
		Lifetime Gm of alcohol consumed (+)	0.043
Score forward	0.296	Schooling (+)	0.181
		Age (-)	0.078
		Lifetime Gm of alcohol consumed (+)	0.043
		Non-numeracy (-)	0.019
Score backward	0.225	Schooling (+)	0.100
		Non-numeracy (-)	0.053
Total score	0.339	Schooling (+)	0.188
		Age (-)	0.102
		Non-numeracy (-)	0.052
		Lifetime Gm of alcohol consumed (+)	0.034
WAIS-R Std score	0.278	Schooling (+)	0.174
		Lifetime Gm of alcohol consumed (+)	0.037
		Non-numeracy (-)	0.036
* Benton			
Total score	0.283	Schooling (+)	0.149
		Age (-)	0.127
		Non-numeracy (-)	0.024
* Santa Ana Peg Board			
Dom hand total	0.292	Schooling (+)	0.054
		Age (-)	0.128
		Ever used dagga (+)	0.028
Dom hand dropped	0.017	-	

Table 7.8 (Continued)
Independent variables associated* with WHO NCTB outcomes amongst deciduous fruit farm workers

WHO NCTB OUTCOME	Model r^2	Variables (Dir assoc)	Partial r^2
Non-dom total	0.248	Age (-)	0.135
		Lifetime Gm of alcohol consumed (+)	0.043
		Previously played videos (+)	0.022
		Non-numeracy (-)	0.018
Non-dom dropped	0.081	Gm of alcohol consumed in past week (+)	0.041
		Plasma Cholinesterase(+)	0.025
* Digit Symbol Total Correct	0.469	Schooling (+)	0.342
		Age (-)	0.171
WAIS-R Std score	0.303	Schooling (+)	0.283
* Pursuit Aiming Correct	0.547	Age (-)	0.317
		Schooling (+)	0.316
		Lifetime Kg OP per hectare (-)	0.014
Attempted	0.326	Schooling (+)	0.226
Wrong	0.248	Age (+)	0.207
		Schooling (-)	0.010
		Years worked on a farm (-)	0.034
* Simple Reaction Time	0.104	Height (-)	0.038
		Lifetime residential exposure (-)	0.029

* Multiple linear regression: Only variables with a B-slope significantly different from 0 at $P<0.05$ presented. The full model is listed in Appendix 7.2.
Nine subjects with visual acuity difficulties excluded from analyses.

Neither occupational nor environmental exposure variables appeared as significant predictors for most NCTB tests. This was no different using cumulative or average lifetime intensity of occupational exposure (full results reflected in Appendix 7.2).

Cumulative lifetime exposure was significantly associated with the number of correct trials on Pursuit Aiming, but the strength of this association was small (partial $r^2 < 0.02$).

7.3.3.2 Neurobehavioural outcomes: WHO NCTB - discussion

The lack of numeracy reflects the particularly low educational levels of the group. The ability to demonstrate an independent effect of non-numeracy on WHO NCTB performance, despite the low prevalence of non-numeracy (3.7% in the survey group), is striking. These data suggest that application of the WHO NCTB tests to other worker populations in developing countries may need to consider non-numeracy as a potential confounding factor, particularly in settings of low education, as is commonly found in developing countries.

It is of interest that Pursuit Aiming was one of the tests found to be most likely to be sensitive to occupational exposure based on findings concerning construct validity in the study of South African paint workers referred to previously (Colvin et al, 1993; Myers et al, 1994), even though the strength of the association was likely to be small. In that study, both Pursuit Aiming and the Santa Ana tests were strongly associated with known covariates of neuropsychological performance (schooling, age and alcohol) and the researchers anticipated that these tests would be most sensitive to adverse chemical neurotoxic effects.

Results in this study confirm the association with covariables age and schooling but demonstrate little association with measures of occupational exposure other than for Pursuit Aiming. Similar to the findings among South African paint workers (Myers et al, 1994), the bulk of the variance explained in the regression models for the WHO NCTB outcomes were due to age and education variables. Moreover, for many of the WHO NCTB subtests, the proportion of overall variance explained by the model was also similar for both study samples (Table 7.9). Given the findings of similarities between such diverse groups as African factory workers and Coloured farm workers on scores and score variance (Table 6.22)

Table 7.9 Comparison of WHO NCTB results * : South African Farm workers and Factory workers #

WHO NCTB OUTCOME	FARM WORKERS (N=242) Model Variance	FARM WORKERS (N=242) Proportion Explained	FACTORY WORKERS (N=228) Model Variance	FACTORY WORKERS (N=228) Proportion Explained
* Digit span				
Span forward	0.28	+Educ (0.17) -Age (0.07) +Cum alc (0.04)	0.21	+Educ (0.12)
Span backward	0.24	+Educ (0.10) -Innum (0.08)	0.25	+Educ (0.23)
Score forward	0.30	+Educ (0.18) -Age (0.08) -Innum (0.02) +Cum alc (0.04)	0.20	+Educ (0.12)
Score backward	0.23	+Educ (0.10) -Innum (0.05)	0.29	+Educ (0.25) -Factory (0.02)
* Benton Total score	0.28	+Educ (0.15) -Age (0.13) -Innum (0.02)	0.26	+Educ (0.15) -Factory (0.09)
* Santa Ana Peg Board				
Dom hand total	0.29	+Educ (0.05) -Age (0.13) +Dagga (0.03)	0.19	-Age (0.09) +Educ (0.02)
Non-dom total	0.25	-Age (0.14) +Cum alc (0.03) -Innum (0.02) +Video exp (0.02)	0.19	-Age (0.07) +Educ (0.04)
Total Correct	0.47	+Educ (0.34) -Age (0.17)	0.52	+Educ (0.30) -Age (0.15)
* Pursuit Aiming Correct	0.55	-Age (0.32) +Educ (0.32) -Cum exp (0.01)	0.45	-Age (0.31) +Educ (0.05) +Expos (0.03) -Alcoh (0.03) -Factory (0.02)

- Myers et al, 1994.
* - Results of multiple linear regression: Only variables with a B-slope significantly different from 0 at P<0.05 presented.

Glossary: Alcoh = High alcohol intake
Cum alc = Cumulative lifetime alcohol intake
Cum exp = Cumulative lifetime OP exposure
Dagga = Ever used dagga (cannabis)
Educ = Schooling
Expos = Average lifetime solvent exposure
Factory = Source factory of subjects
Innum = Non-numeracy
Video exp = Ever played video games

and the proportion of variance explained by expected predictors (Table 7.9) for a range of WHO NCTB sub-tests, there appear to be substantial grounds for anticipating the development of normative values for local use.

7.3.4 Neurobehavioural outcomes: Information Processing Probes - multivariate analyses

7.3.4.1 Neurobehavioural outcomes: Information Processing Probes - results

Results of multiple linear regression are presented for the Information Processing Probes in Table 7.10. For the majority of the information processing probe outcomes, distributions were transformed to normality by appropriate log, square root and other transformations prior to analyses. Full details of these transformations are given in Appendix 5.3.

For the Hick Box test results schooling did not predict performance, except in the case of Power Score in the Inspection Window. Age was commonly associated with Movement Time in these tests. Little association with any occupational exposure measures was evident. In particular, measures of cumulative and average intensity of OP exposure were not associated with reaction time or movement time under any of the test conditions. Of note, however, was the association of Inspection Time Efficiency score with duration of OP exposure in the preceding 3 months and that of Inspection Window Power Score with the standardised erythrocyte cholinesterase, suggesting an adverse effect of recent / sub-acute exposure on these test outcomes. Duration of work on a farm was also associated with prolonged movement time on the Inspection Window.

Performances on the tests of attention (Continuous Number Checking) were strongly influenced by schooling and, to a lesser extent, age. Alcohol measures were associated with lower speed, efficiency and accuracy indices. Again, measures of occupational exposure were unimpressive. The Anomalous Concept Test which

Table 7.10 Independent variables associated* with the information processing neurobehavioural battery outcomes amongst deciduous fruit farm workers

BATTERY OUTCOME	Model r^2	Variables (Direction assoc)	Partial r^2
HICKBOX TESTS			
1. DOMAIN: MOTOR SPEED (HICKBOX TESTS)			
* One Light Condition			
Simple RT	0.104	Height (-)	0.038
		Lifetime residential exposure (-)	0.029
Simple MT	0.107	-	
2. DOMAIN: ENCODING (HICKBOX TESTS)			
* Two Light Condition			
Choice RT	0.099	PPE Usage score (-)	0.042
		Use of pesticides at home (-)	0.018
Choice MT	0.115	Age (+)	0.067
* Four Light Condition			
Choice RT	0.073	Use of pesticides at home (-)	0.019
Choice MT	0.091	Age (+)	0.056
* 8 Light Condition			
Choice RT	0.114	Use of pesticide containers at home (-)	0.045
		Height (-)	0.039
Choice MT	0.124	Age (+)	0.087
		Lifetime close residential exposure (-)	0.035
3. DOMAIN: APPREHENSION (HICKBOX TESTS)			
* Inspection Time			
RT	0.086	Ever severely head injured (-)	0.043
MT	0.100	-	
Efficiency Score	0.153	Days organophosphate exposure in past 3 months (-)	0.101
		Cumulative lifetime Gms alcohol (+)	0.020
* Inspection Window			
RT	0.064	-	
MT	0.110	Years worked on a farm (+)	0.044
Power Score	0.112	Schooling years (+)	0.040
		Haemoglobin adjusted Erythr Cholinesterase (+)	0.028
		Farm size > 25 ha (-)	0.028
4. DOMAIN: ATTENTION			
* Continous Number Checking			
Reaction Time	0.363	Schooling years (-)	0.205
		Age (+)	0.137
		Cumulative lifetime Gms alcohol (-)	0.036

Table 7.10 (Continued) Information processing battery

BATTERY OUTCOME	Model r^2	Variables (Direction assoc)	Partial r^2
Speed Index	0.366	Schooling years (+)	0.193
		Age (-)	0.139
		Cumulative lifetime Gms alcohol consumption (-)	0.033
		Ever smoked (-)	0.030
Effic Index	0.389	Schooling years (+)	0.209
		Age (-)	0.150
		Cumulative lifetime Kg alcohol consumption (-)	0.035
		Ever smoked (-)	0.033
Transformed Accuracy Index	0.214	Schooling (+)	0.061
		Cumulative lifetime cigarette packyears (+)	0.044
		PPE usage score (+)	0.042
		Gms alcohol consumed at one sitting (-)	0.029
Work Gradient Index	0.072	Lifetime residential exposure (+)	0.025
Variability Index	0.140	Age (-)	0.086
5. DOMAIN: SEMANTIC ACCESS			
* Animal Post I Reaction Time	0.303	Age (+)	0.202
		Schooling years (-)	0.073
		Cumulative lifetime Kg alcohol consumption (-)	0.050
* Animal Post II Reaction Time	0.198	Age (+)	0.123
		School (-)	0.039
		Cumulative lifetime alcohol consumption (-)	0.039
* Diff I and II = Semantic Access	0.132	Age (-)	0.077
		Lifetime Kg OP per hectare (+)	0.016
* Speaking Arrows Reaction Time	0.380	Age (+)	0.277
		School (-)	0.100
		Days Organophosphate exposure in past 3 months (+)	0.037
Count Incorr	0.157	School (-)	-0.052
5a. SUBDOMAIN: STIMULUS RESISTANCE			
* Echopraxis	0.177	Schooling (+)	0.113
* Point Arrows I Reaction Time	0.114	Schooling (-)	-0.066
		Years lived on a farm (+)	0.018

Table 7.10 (Continued) Information processing battery

BATTERY OUTCOME	Model r^2	Variables (Direction assoc)	Partial r^2
* Point Arrows II			
Reaction Time	0.157	Schooling years (-)	0.072
		Previous experience playing video games (-)	0.020
		Plasma cholinesterase (-)	0.016
* Difference in Reaction time for I and II	0.098	Lifetime experience of the tot system (-)	0.060
6. DOMAIN: PASSIVE SHORT TERM MEMORY			
* STM Scanning			
Reaction Time	0.101	-	
7. DOMAIN: ACTIVE SHORT TERM MEMORY			
* Manipulating Numbers I			
Reaction Time	0.306	Age (+)	0.128
		Schooling (-)	0.084
		GGT (-)	0.076
		Cumulative lifetime ethanol consumption (-)	0.032
Count Correct	0.212	Ever seriously head injured (-)	0.053
		Schooling years (+)	0.031
		Cumulative lifetime alcohol consumption (+)	0.026
* Manipulating Numbers II			
Reaction Time	0.267	Schooling (-)	0.123
		Cumulative lifetime alcohol consumption (-)	0.083
		Age (+)	0.066
Count Correct	0.171	Age (-)	0.101
		Lifetime close residential exposure (-)	0.050
Effic Score	0.272	Age (-)	0.121
		Schooling years (+)	0.094
		Lifetime residence in proximity to sprayed farm (-)	0.067
* Manipulating Numbers III			
Reaction Time	0.106	-	
Effic Score	0.138	-	
8. GLOBAL INTELLECTUAL ABILITY			
* Anomalous Concept Test	0.304	Schooling (+)	0.130
		Non-numeracy (-)	0.046
		Right handed dominance (+)	0.032

* Multiple linear regression: Only variables with a B-slope significantly different from 0 at $P<0.05$ presented. The full model is listed in Appendix 7.3.
Nine subjects with visual acuity problems excluded from the analyses.

indirectly measures cognitive planning functions and is a global test of intellectual functioning, was strongly predicted by education and other cultural variables.

For tests of long-term semantic memory (Semantic Access - Animal Postures I and II), age appeared as a more important covariate than education, and there were also some occupational variables that appeared significant in the modelling - Recent exposure for Reaction Time on Speaking Arrows and cumulative OP exposure for the difference in RT between the two conditions (Animal Posture I and II). The modelling of results of other tests of long-term semantic memory (Stimulus Resistance and Echopraxis) appeared to explain less of the variance than models of Animal Postures. For example, the variances explained by models used for results of Stimulus Resistance ranged from 10% to 18% in contrast to those of Semantic Access (20 to 40%). In most cases, schooling was the most important and consistent predictor of performance even though the proportion of model variance explained by schooling was small ($r^2<0.1$). Previous experience of playing video games came up as an association with pointing arrows II (Stimulus Resistance) though the proportion of model variance explained by this variable was, once again, small ($r^2=0.02$).

Among the tests of short-term memory, reaction time on short-term memory scanning was not found to have any significant covariates, although the parameter estimate for a past history of fume intoxication was borderline in this model (p=0.054; Appendix 7.2). Tests of working memory (active short-term memory) were commonly related to age and schooling which contributed most of the explained variances in the models. Non-occupational exposure appeared to be related to performance on Manipulating Numbers II, with longer lifetime residential exposures being associated with poorer performance on the test.

7.3.4.2 Neurobehavioural outcomes: Information Processing Probes - discussion

The Hick Box test results measuring apprehension and encoding showed an interesting pattern in that schooling was relatively unimportant in predicting performance, while age was commonly associated with Movement Time on most Hick Box tests. This is to be expected, given that tests of simple and choice reaction time are on the more physiological end of a spectrum of neurobehavioural performance. However, tests of inspection time, which reflect information apprehension rather than encoding in the model of information processing (Figure 5.1 in Chapter 5), appeared to differ somewhat in showing no relationship to age, and having some evidence for a schooling effect, and for an effect of recent OP exposure. However the size of these effects are small as evidenced from the small partial r^2s for all variables (0.1 or less).

In contrast to the Hick Box tests, the tests of attention (Continuous Number Checking) and planning (ACT) were much more strongly influenced by schooling. This is partly to be anticipated, given the influence of cultural factors on these modalities of cognitive performance (Taylor and Nell, 1993). Of note is that, even though the models explained a substantial proportion of the overall variance for these tests (model r^2 generally of the order of 30%), occupational exposure, both acute and long-term, were not associated with performance outcome on any of these tests. This may reflect an absence of an exposure effect, or may be another example of the masking of a small exposure effect by an overwhelming cultural effect (Myers et al, 1994).

This situation is to be contrasted with results for tests of long-term semantic memory (the difference in Reaction Times for Animal Postures I and II is a measure of the extra cognitive demand for semantic access in addressing the task, and Speaking Arrows which is also a direct measure of semantic access) where age appeared as a more important covariate than education. In this setting, there were some occupational variables that appeared significant in the modelling - Recent exposure for Reaction Time on Speaking Arrows and cumulative OP exposure for the difference in RT demanded by the semantic access in the task. While these associations are small ($r^2<4\%$), their presence in tests where education effects appear to be minimised may signify an ability of these tests to detect small neurobehavioural effects due to chemical exposure, without the masking effects of education.

Other tests designed to measure output from long-term semantic memory (Stimulus Resistance and Echopraxis) appeared less helpful. The modelling of results of these tests explained less of the variance, and what was explained was commonly due to education.

Tests measuring output from Short-term Memory would be expected, in terms of the theoretical constructs outlined in Chapter 5 regarding information processing theories, to be key tests for bypassing the effects of culture. Unfortunately, their performance in detecting possible occupational exposure effects appears limited. Active Short-term Memory or Working Memory (as measured in tests of Manipulating Numbers) was generally very sensitive to schooling, and test results for Manipulating Numbers III were not helpful because of the small numbers of subjects who completed the test. This was largely because of the increasingly complex nature of the series of tests for Manipulating Numbers - if subjects failed to score 15 correct out of 36 trials, they did not receive the subsequent test as their results would be meaningless. Short-term Memory Scanning had no associations and modelling explained little overall variance.

How consistent are these findings with hypotheses outlined in Chapter 5 that these cognitive tests are able to measure psychological functions below the level of culture? In general, it appears that these tests do not improve much on the WHO NCTB. Particularly, tests of Short-term Memory fail to demonstrate a clear independence from the effects of education. However, there appears to be some limited evidence that tests of Apprehension and of Semantic Access (Long-term Memory) have some consistency with the hypotheses in that they appear less sensitive to the effects of education, and the latter tests show a few small exposure effects. This is illustrated in Table 7.11 which summarises the relative contributions of age, schooling and long-term occupational exposure and other explanatory variables to regression models for the different test domains in the information processing probes compared to the WHO NCTB.

Of note in the results are associations with alcohol consumption that contradict anticipated directions - cumulative lifetime alcohol consumption is associated with higher efficiency score on inspection time and shorter reaction times on a range of tests (Continuous Number Checking, Animal Postures I and II and Manipulating Numbers I and II). However, this contrasts with the findings of slower, less efficient and less accurate performance on the CNC. The effect of alcohol consumption on the outcomes of the information processing tests has not been investigated to date and this warrants further attention if these tests are to gain wider currency.

The fact that similar contradictory findings regarding alcohol were made with the WHO NCTB tests reported above, suggests that there may be an information bias operating with low test performers reporting lower alcohol consumption. Alternatively, those high alcohol consuming workers who are pesticide applicators and who suffer from alcohol-related neurotoxic effects may be more likely to lose their work than non-applicators whose job tasks are less demanding. The possibility of a selection effect operating is discussed in more detail in the following section. A further factor to consider is the problem of a generally high alcohol intake level in this population causing a lack of sufficient alcohol contrast with which to demonstrate any exposure effect relationships for alcohol. This has been discussed earlier for other neurological and neurobehavioural outcomes.

Table 7.11 Contributions of age, schooling and other explanatory variables to linear regression modelling of neurobehavioural outcomes in the information processing battery by domain compared to the WHO NCTB among deciduous fruit farm workers

INFO-PROCESSING DOMAINS	Percentage of overall variance explaned by: Model r^2	Age	School	Occup exp
Attention	14 - 39	4 - 15	2 - 21	0.04 - 0.7
Encoding	7 - 11	0.3 - 5	1 - 6	0.01 - 0.5
Apprehension	6 - 15	0.3 - 5	0.1 - 4	0.001 - 0.2
Passive STM*	10	2.5	0.2	1.1
Active STM*	11 - 31	0.5 - 13	0.02 - 12	0.01 - 4.0
Semantic Access				
- Speaking Arrows	16 - 38	9 - 28	5 - 10	0.2 - 0.6
- Animal Postures	13 - 30	8 - 20	1 - 7	0.03 - 2
- Stimulus Resistance	10 - 16	1 - 4	0.1 - 7	0.001 - 1
GLOBAL INTELLECTUAL FUNCTION (ACT)	30	12	13	1
WHO NCTB BATTERY DOMAINS				
Dexterity	25 - 55	11 - 32	1 - 32	0.1 - 1
Clerical Speed	30	0.2	28	0.1
Visuospatial	28	13	15	0.3
Attention	23 - 35	5 - 10	1 - 19	0.1 - 0.6
Motor speed	11	0.1	1.2	0.01

* - STM = Short term memory

Another feature of the results is the relative absence of head injury variables as covariates in most of the neurobehavioural modelling. This is despite the high levels of head injury reported, particularly stemming from interpersonal violence.

Table 7.12 Effect of varying occupational exposure variable on analyses of vibration sense, tremor and neuropsychological function.

Outcome:-		EXWGHT	EXWGHTI	EXWGHTB	EXWGHTBI
Logvib	Model r^2	0.263	0.262	0.263	0.262
	Partial r^2	0.0006	0.0003	0.0005	0.0002
TFK	Model r^2	0.176	0.173	0.176	0.174
	Partial r^2	0.005	0.004	0.005	0.006
Tremintd	Model r^2	0.198	0.198	0.198	0.198
	Partial r^2	0.002	0.002	0.002	0.003
Tremintn	Model r^2	0.065	0.066	0.065	0.098
	Partial r^2	0.003	0.005	0.003	0.013
Pursuit	Model r^2	0.547	0.542	0.546	0.542
Aimng	Partial r^2	0.014 *	0.003	0.015 *	0.003
St Anna	Model r^2	0.292	0.293	0.292	0.294
dom tl	Partial r^2	0.001	0.004	0.001	0.003

* - Significance of the parameter estimate for the slope differing from 0
in multiple linear regression modelling : $P < 0.05$

7.4 Use of Other Agrichemical Exposure Indices

Similar analyses to those presented here were re-run using alternative indices of exposure. In particular, average lifetime intensity of Kg OP per hectare (EXWGHTI) was used in place of cumulated lifetime Kg OP per hectare (EXWGHT) for all the analyses presented above. This did not improve the fit of the overall models substantially, nor were there explicit exposure-effect relationships detected using this measure of exposure. Similarly, analyses were run using equivalent cumulative (EXWGHTB) and average intensity (EXWGHTBI) occupational exposure variables for BE OP per hectare, with little improvement.

Table 7.12 summarises these analyses by presenting the equivalent estimates for overall model r^2 and the estimates of partial r^2 attributable to the each of the 4 possible exposure variable of choice, for analyses of results for the Vibratron, the Tuning fork extinction time, Tremor intensity and 2 selected WHO NCTB outcomes (Santa Ana total pegs for dominant hand and Pursuit Aiming correct). The full model results for these variables are presented in Appendices 7.2 and 7.4.

In a similar fashion to the above, analyses were re-run using alternative variables for alcohol consumption, in order to address the contradictory effects of alcohol on neurological and neurobehavioural outcomes. In particular, GGT was used in place of ETHANOL (Cumulative lifetime grams alcohol consumed), but the results gave similar inconsistencies (data not presented). Other strategies of excluding high alcohol consumers (top 5%), and of investigating alcohol-outcome relationships only among those workers who had never previously worked as a pesticide applicator (n=74) were utilised but did not yield results that were any more consistent with the expected effects of alcohol.

A likely explanation for this anomaly may be that with a relatively high prevalence and median alcohol intake among the population (only 4% were non-drinkers), there is insufficient contrast in alcohol exposure to demonstrate any alcohol effects. This phenomenon appears to have been present for most of the other neurological and neurobehavioural outcome-exposure relationships investigated in this study. Differential misclassification of reported alcohol intake may occur if the neurotoxic consequences of high alcohol intake affect the subject's memory and recall, but at this gross level of impact, one would anticipate other clinical and peripheral sensory signs. Moreover, the fairly good correlations on repeat interview for a number of the quantitative measures of alcohol consumption (Table 6.24 in Chapter 6) also make this an unlikely explanation.

7.5 Neurological and Neurobehavioural Effects of Long-term Agrichemical Exposure - An Appraisal of the Data

Despite careful attention to the characterisation of exposure status in the study group, few associations were found between long-term agrichemical exposure and adverse neurological and neurobehavioural outcomes. One out of the 17 WHO NCTB outcomes measured in this study, number correct on Pursuit Aiming, was associated with cumulative OP exposure, as was one out of the 23 Performance Probe tests - Difference in Reaction Times for Animal Postures I and II (Reaction time given a demand for Semantic Access in the test task). The strength of these associations were small (partial $r^2 < 0.02$; $p=0.043$ and $p=0.027$ respectively) and the presence of these 2 associations may be the result of chance given multiple comparisons, and the evidence for chronic effects of low-dose long-term occupational agrichemical exposure therefore appears limited.

7.5.1 Exposure misclassification

Exposure misclassification may have played some role in this failure to demonstrate occupational exposure effects. Such misclassification may have arisen in the process of measurement - the kappa statistic for average lifetime intensity of exposure was less than 0.4 (Table 6.26 in Chapter 6), or in the modelling of exposure used to construct the job-exposure matrix (Table 3.11 in Chapter 3), which may have weighted job activities incorrectly in the absence of empirical data on which to base estimates of activity-specific agrichemical exposures. Nonetheless, one would have anticipated a priori that direct application or mixing of pesticides would have the greatest exposures, yet separate analyses of these job activities (using the same models as outlined above controlling for known confounders) failed to demonstrate any significant associations between these measures of exposure with adverse outcomes. (Analyses for 4 selected outcomes using the variable CUMULTR (Cumulated lifetime days of mist blower operator application of pesticides) are included in Appendix 7.5. Moreover, given the significant (but weak) association demonstrated between cumulative Kg OP/hectare exposure and standardised erythrocyte cholinesterase, the JEM appears not to have been substantially affected by significant exposure misclassification. If such misclassification was present, its impact would have most likely been to underestimate any association described.

Because most of the outcome assessments were of such a nature that they did not give direct feedback to subjects as to how good their outcome performance was, it appears unlikely that there was an incentive operating for those with poor outcomes to over- or under-report past or present agrichemical exposures. Moreover, the assessment of exposure and outcome was done by separate observers blinded to the status of the subject, and exposure assessment was done prior to outcome assessment. Thus the nature of misclassification that would have occurred is likely to have been non-differential, and would have underestimated any exposure-effect relationships that may have been present. Outcome misclassification may also have been operative, but given the strict quality controls outlined in Chapter 5, this is less likely to have been an important factor.

The key problem with exposure characterisation in this study probably lies in the extremely heterogeneous chemical exposures experienced by subjects over a lifetime, as outlined in Chapter 5. In the pilot studies, subjects were generally unable to recall specific chemicals they had used, and this was born out by the difficulties subjects experienced in this study when trying to recall chemicals they took home for domestic use (less than half the respondents were able to name the chemical they had taken home - section 6.7, Chapter 6), or the chemicals with which they had been poisoned (none of the subjects could name the agent - section 6.4, Chapter 6). The result of this heterogeneity is that exposure characterisation lost its chemical specificity, notwithstanding the ability of the JEM to detect biochemical effects of overall OP exposure (as measured by standardised erythrocyte cholinesterase). Given that the literature indicates that a limited number of organophosphates are responsible for OPIDN, and that the mechanisms for the development of chronic neurotoxic effects from low-dose OP exposure are as yet undefined, it may be that neurotoxic effects from low-dose OP exposure are specific to particular chemicals, or subgroups of OPs. Any possible dose-effect relationships that may have been present in this study would therefore have been substantially diluted.

The choice of cumulative and average lifetime intensity of exposure were measures of exposure chosen for use after careful review of the literature regarding chronic health effects of agrichemical exposure. Was it possible that any other parameters of exposure were better indicators of biological dose? To address this, analyses were run using a) peak exposure as being the maximum number of exposure days in a single given year in a lifetime, and b) cumulative lifetime days of OP exposure experience prior to 1984. The latter variable was explored on the basis that exposures experienced more than a decade ago may have been qualitatively different in intensity, particularly in light of the absence of data on safety behaviour in the industry historically. These analyses are not presented in the text (they are included in Appendix 7.6) but showed no substantive difference in the patterns with that using the JEM-derived variables as outlined in the sections above.

7.5.2 Selection effects

To what extent is the failure to demonstrate an exposure-effect relationship between long-term agrichemical exposure and neurological and neurobehavioural outcomes attributable to a selection effect inherent in the cross-sectional design? In other words, are workers with poorer neurological and neurobehavioural performance likely to drop out of employment before the cross-sectional study samples them? Two factors would militate against this. On the one hand, the nature of adverse effects being sought are subtle and often subclinical, and are unlikely to result in gross disability leading to job loss or to death, and therefore loss to the study population. Only one subject was found to have a clinical neuropathy (not attributed to agrichemicals), and 4 had minor degrees of sensory deficit. Secondly, farm workers who lose their farm work jobs, tend to remain as farm workers but on other farms in less demanding jobs (Waldman, 1993) and may have appeared in our study as currently non-exposed subjects with a history of past exposure. They would therefore have been accounted for because all workers in the region were included in the study population.

Indeed, in our study 9 subjects selected as current non-applicators were former pesticide spraymen. To investigate this further, their performance for a sample of vibration sense, tremor and WHO NCTB outcomes are presented below in Table 7.13 compared to results for current applicators. Equivalent results for workers who had never worked as applicators are also presented as background. Past applicators appeared to perform worse for tremor intensity in the dominant hand and for Pursuit Aiming, Digit Symbol score and score on the Santa Ana Peg Board (dominant hand) for the WHO NCTB. However, they also appeared to have more years of schooling and reported consuming less alcohol. Because the numbers involved are small, these differences did not reach statistical significance, except in the case of tremor intensity in the dominant hand.

In order to control for age and other confounders, the linear modelling for 6 of the variables in Table 7.13 were rerun incorporating a dichotomous variable (PAST1=0 if subject was current sprayman; PAST1=1 if subject was past sprayman) as an additional variable to the model and the results are summarised in Table 7.14 (full models in Appendix 7.7). These analyses suggest that, at least for some outcomes, previous status as a sprayman was associated with poorer performance on neurological and neurobehavioural assessment. However, whether this was a cause (poor performance leads to loss of job and change in exposure status) or an effect of exposure status (exposure leads to poor performance and loss of job) is not resolvable without longitudinal follow up of a suitable cohort of exposed workers. Only if the latter phenomenon is widespread could this result in a selection bias in this study and available evidence does not

Table 7.13 Selected vibration sense, tremor and WHO NCTB outcomes by spray applicator status

TEST	SPRAYMAN STATUS Current (n=164) Mean (SD)	Past (n=9) Mean (SD)	Never (n=74) Mean (SD)
Age (yrs) aa	36.9 (9.8)	35.9 (8.8)	37.0 (10.9)
Schooling (yrs) aa	6.0 (3.7)	8.1 (3.2)	6.5 (3.8)
Cumulative Kg aa alcohol (Kg)	4.4 (4.3)	3.5 (3.5)	3.8 (3.1)
Tuning Fork # extinction time (sec)	12.8 (3.4)	13.1 (3.5)	12.6 (3.2)
Vibratron # threshold (log vib units)	1.6 (0.6)	1.6 (0.4)	1.5 (0.6)
Tremor Intensity * domin hand #	0.36 (0.30)	0.56 (0.31)	0.41 (0.40)
Tremor Intensity nondom hand #	0.38 (0.33)	0.34 (0.27)	0.45 (0.54)
Pursuit Aiming # score correct	89.3 (35.4)	83.5 (37.9)	94.0 (34.1)
Benton Visual aa score correct	6.9 (2.0)	6.7 (1.2)	6.8 (2.2)
Digit Symbol # score correct	25.0 (10.6)	22.6 (9.9)	26.5 (10.0)
Santa Ana Peg aa Board total domin hand	39.3 (6.7)	36.0 (7.9)	37.1 (6.8)

aa - Means of current and past spraymen compared by Wilcoxon test.

Means of current and past spraymen compared by Paired T-test test.

* P < 0.05 for difference between mean log transformed tremor intensity in the dominant hand for current (-0.05 log transformed counts/sec) vs past (-0.97 log transformed counts/sec) sprayers.

Data on workers never spraying included as background information.

suggest that job loss due to subclinical illness is common on farms in the Western Cape (Du Toit, 1992; Waldman, 1993). Moreover, all 5 of the subjects with any evidence of clinical deficits (4 with decreased peripheral sensation and 1 with frank neuropathy) were still currently employed as sprayers, which, again, tends not to support the presence of a selection effect operating to a substantial extent.

Table 7.14 The contribution of previous vs current status as a pesticide applicator to model variance in linear regression for selected vibration sense, tremor intensity and WHO NCTB outcomes.

TEST	Model r^2 (n=164)	Partial r^2 due to past1	Signif of param estim
Tuning Fork extinction time (sec)	0.184	<0.0001	NS
Vibratron threshold (log vib units)	0.278	0.001	NS
Tremor Intensity domin hand	0.236	0.06	0.01
Tremor Intensity nondom hand	0.141	<0.0001	NS
Pursuit Aiming score correct	0.644	0.030	0.04
Santa Ana Peg Board total domin hand	0.399	0.013	NS

Full models presented in Appendix 7.7.

The Healthy Worker Effect (selection of healthy individuals into the farm worker workforce) as another source of confounding is also unlikely to operate in the South African agricultural setting to a significant effect, given the lack of alternative employment opportunities, the low levels of unemployment in rural areas relative to urban areas (Donaldson and Roux, 1994) and the low-skill requirements of agricultural labour. While there is little data available on this issue, there may well be migration of healthier (and more neurologically and neurobehaviourally competent) workers to the industrial (urban) labour market and out of the farming community, resulting in an inversion of the healthy worker effect amongst farm workers.

7.5.3 Effects of pesticide exposures other than long-term: Previous poisoning and acute exposure

In contrast to the lack of association with low-dose long-term occupational exposure measures, a history of past pesticide poisoning was strongly related to adverse symptom outcomes for both "neurological" and "dummy" symptoms. A significant exposure effect relationship involving past poisoning did not appear for any of the neurological or neurobehavioural outcomes, although the parameter estimates for past poisoning in all the linear regression models involving vibration sense and tremor differed non-significantly from 0 in a direction to suggest a positive association (Appendix 7.2). This was not the case for the neurobehavioural outcomes where the direction of the parameter estimates for pesticide poisoning showed no consistency in direction. This may reflect an insensitivity of the testing instruments to the neurological and, particularly, behavioural effects stemming from previous OP intoxication. However, given published reports (Savage et al, 1988; McConnell et al, 1994; Steenland et al, 1994), this explanation appears unlikely, especially for the more physiological tests of tremor and vibration sense which would be expected to be less sensitive to cultural confounders.

However, the small numbers involved (only 15 subjects were counted as previously poisoned) would reduce the power of any hypothesis testing involving this variable. The study was not designed to evaluate past poisoning as the exposure of interest, and a different study design could have generated appropriate numbers for such an investigation. Moreover, the nature of the diagnostic process, i.e. retrospective and self-reported, may result in wide heterogeneity of diagnosis, and the resultant imprecision would dilute exposure-effect relationships. For example, hospital admissions were included with doctor visits for which time off was prescribed, but not included were cases where the worker absented himself or received no sick leave from the doctor.

The failure to find associations between previous poisoning and non-symptom outcomes is thus a problem of internal validity, as distinct from poor reliability resulting in exposure misclassification, since the repeatability kappa statistic for previous poisoning was high - 0.65 (Table 6.25 in Chapter 6). The presence of subjective reporting bias is a key limitation of these data and may be the reason for the presence of symptom effects but lack of other effects.

Although not the main focus of the investigation, acute exposure effects were evident in this study for a few outcomes. This included tremor intensity in the dominant hand and three of the Performance Probes (Inspection Window, Speaking Arrows and Pointing arrows II). However, the size of these associations were small with partial r^2s generally less than 0.05, and the effect of multiple comparisons may also play a role.

Haemoglobin-adjusted erythrocyte cholinesterase was also found to be related to cumulative Kg OP/hectare exposure although not to measures of acute exposure. What this suggests is not clear. The greater precision of the cumulative exposure variable relative to acute exposure variables may make it more correlated with a "true" acute exposure status and therefore enable it to predict an acute or sub-acute effect. Alternately, the erythrocyte cholinesterase may be directly related to a long-term exposure effect. Its utility as a marker of long-term OP exposure needs further exploration.

7.5.4 The role of environmental exposure

How important could environmental exposure be as a confounder for a long-term occupational exposure-effect relationship? A number of outcomes were found to be related to interview-based measures of non-occupational exposure. For example, 2 symptoms were related to domestic use of pesticides or of containers, and the Efficiency score for Manipulating Numbers II in the Performance Probes were inversely related to years of residence in proximity to agrichemical spray, while some of the Reaction Times for the Performance Probes were positively associated with close residential exposure. However, a number of associations were in contradictory directions and most outcomes showed no significant relationship to variables measuring environmental exposure. Moreover, the size of the effects that were present were small (partial r^2s < 0.07) and the associations may again simply be the result of multiple comparisons.

However, the strategies to measure environmental routes of exposure in this study may have missed more subtle but substantial routes of exposure (eg: in drinking water, in food). The only published research to date suggests that water table contamination due to agrichemicals in rural areas is not common (Weaver, 1993). Data in another survey (London, 1994), and from the farmers in this study, confirmed that almost all farm workers obtain their drinking water by closed borehole or reticulated from urban sources. For this reason, environmental routes of exposure involving ingestion are unlikely, although the possibility of consumption of contaminated fruit cannot be entirely excluded. Further research into the routes and extent of potential environmental exposure to agrichemicals in rural farming communities is needed to clarify this possibility.

7.5.5 Outcome measurement in neurobehavioural research

The performances of the testing instruments used in this study appear to confirm the role of many of the known covariates of neurological and neurobehavioural function. Age and education were the strongest predictors of outcome overall for a range of the neurobehavioural tests. Previous research into chemical neurotoxicity among South African workers (Bachmann et al, 1993) found that the use of tuning fork extinction time appeared to be more sensitive than the Vibratron II, but this study showed little difference between the two methods, with age and height being common predictors of vibration sense by both methods. The Vibratron linear regression modelled slightly more of the overall variance, but there appears little to choose between the two tests and the tuning fork's utility may confer significant logistical advantages for studies measuring peripheral vibration sense in settings where electric power is unavailable, or where high-technology instrumentation is unaffordable, as may be commonly encountered in developing countries.

Other new issues of relevance to neurobehavioural testing generated in this study include: 1) The independent association of non-numeracy with many of the WHO NCTB outcomes, and the implication of this factor as a possible confounder in low-education populations in developing countries; 2) The use of tremor testing appears to show promise in the detection of relatively acute / sub-acute effects of OP exposure and this requires further study; 3) The range of performance probes based on cognitive psychological theory do not appear as promising for detection of subtle neurobehavioural effects "free of the effects of culture" as their theoretical rationale had suggested (Chapter 5). However, in analysing the test results of different domains, there is some suggestion that those tests that were less sensitive to education (Tests of Attention: Inspection Window and Inspection Time, and tests of Long-term Memory: Semantic Access) were able to detect agrichemical exposure effects, although these effects were small, sporadic and related to acute or sub-acute rather than long-term exposure. Nonetheless, these results do indicate that these tests may yet prove to be useful additions to neurobehavioural assessment methods and warrant further investigation.

7.5.6 Generalisability of study results

Another key issue to consider is the external validity of the study. To what extent are workers on farms belonging to two large cooperatives exporting fruit to international markets likely to be representative of farm workers exposed to OPs in general in South Africa? The high levels of reported usage of current protective clothing relative to other studies in South Africa (Emanuel, 1993; London, 1994) suggest that these workers are, in some sense, a selected workforce. However, their demographic and educational profiles appear similar to farm workers generally. Available evidence suggests that past exposures of workers over many years in South Africa are unlikely to differ substantially (London and Myers, 1993). Thus, while the current scenario may reflect a "best-case" situation with regard to safety practices, enough evidence exists in the descriptive data presented in Chapter 6 to confirm that lifetime exposures were substantial and that sufficient exposure contrast was present to have been able to detect any clear effects.

7.5.7 Conclusion

In summary, it appears that an optimally designed investigation into the possible adverse effects of long-term agrichemical exposure on neurological and neurobehavioural function in a typically less developed setting has not demonstrated consistent exposure-effect relationships. Various possible reasons for this have been explored above, including most importantly the possibility of exposure misclassification and effect dilution, design constraints and the presence of confounding. Given a critical assessment of the study methods, it may be reasonably argued that, had there been a true exposure-effect relationship of sufficient magnitude, this would have still have emerged in the analysis, albeit in a diluted form. Prior power calculations made use of a relatively low level of Beta error and should have ensured that any real association would have been detected. The inference to be made is that there is either no relationship between long-term low-dose agrichemical exposure and neurological and neurobehavioural effects, or, even if this relationship exists, the size of the effect is slight, and too small to have been detected in this study. Based on the preceding discussions, the next and final Chapter addresses some of the policy implications and recommendations flowing from this study.

REFERENCES

Bachmann O, De Beer Z, Myers JE. (1993). n-Hexane neurotoxicity in metal can manufacturing workers. Occup Med. 43 : 149-154.

Bove FJ, Letz R, Baker EL. (1989). Sensory thresholds among construction trade painters: A cross-sectional study using new methods for measuring temperature and vibration sensitivity. J Occ Med. 31 : 320-325.

Bwititi T, Chikuni O, Loewensen R, Murawambiwa W, Nchachi C, Nyaezema N, (1987). Health hazards in organophosphate use among farm workers in the large-scale farming sector. C Afr J Med. 33(5) : 120-126.

Colvin M, Myers JE, Nell VN, Rees D, Cronje R. (1993). A cross-sectional survey of neurobehavioural effects of chronic solvent exposure on workers in a paint manufacturing plant. Environmental Research 63 : 122-132.

Coye MJ, Lowe JA, Maddy KT. (1986). Biological Monitoring of agricultural workers exposed to pesticides: I. Cholinesterase Activity Determinations. J Occup Med 28(8) : 619-627.

Donaldson A, Roux A. (1994) Education, employment and income of black South Africans in 1985. Development Southern Africa 11(1) ; 131-143.

Du Toit A. (1992). The farm as family. Paternalism, management and modernisation on Western Cape wine and fruit farms. Centre for Rural Legal Studies, Stellenbosch.

Emanuel K. (1992). "Poisoned pay: Farmworkers and the South African Pesticide Industry." Group for Environmental Monitoring and The Pesticide Trust, Johannesburg.

Gerr FE, Letz R. (1988). Reliability of a widely used test of peripheral cutaneous vibration sensitivity and a comparison of two testing protocols. Br J Ind Med. 45 : 635-639.

Gerr FE, Hershman D, Letz R. (1990). Vibrotactile threshold measurement for detecting neurotoxicity: Reliability and determination of age- and height-standardised normative values. Arch Envir Health 45(3) : 148-154.

Innes DF, Fuller BH, Berger GMB. (1990). Low serum cholinesterase levels in rural workers exposed to organophophate pesticide levels. S Afr Med J. 78, 581-583.

Kashyap SK. (1986). Health surveillance and biological monitoring of pesticide forumulators in India. Toxicology Letters 33 : 107-114.

Levin HS, Rodnitzky RL, Mick DL. (1976). Anxiety associated with exposure to organophosphorus compounds. Arch Gen Psych 33 : 225-228.

London L, Myers J. (1993). "Agrichemical Hazards and the Work Process in Agriculture in the Western Cape." Occupational Health Research Unit Report number 1. Department of Community Health, University of Cape Town, Rondebosch, Cape Town.

London L, Ehrlich R, Rafudien S, Krige F, Vurgarellis P. (1994). Pesticide poisoning notification in the Western Cape 1987 - 1991. S Afr Med J ; 84 : 269-272.

London L. (1994). Agrichemical safety practices on farms in the Western Cape. S Afr Med J 84 : 273-278.

Lotti M. (1992). Central neurotoxicity and behavioural effects of anticholinesterases. In: Clinical and experimental toxicology of organophosphates and carbamates. Eds Ballantyne B, Marrs TM, Aldridge WN. Butterworth, Stoneham, MA.

Lundstrom R, Stronberg T, Lundborg G. (1992). Vibrotactile perseption threshold measurements for diagnosis of sensory neuropathy. Int Arch Occup Environ Health 64 : 201-207.

McConnell R, Keifer M, Rosenstock L. (1994). Elevated quantitative vibrotactile threshold among workers previously poisoned with methamidophos and other organophosphate pesticides. Am J Ind Med. 25 : 325-334.

Myers JE, Nell V, Colvin M, Rees D, Cronje R, Thompson ML. (1994) Neuropsychological and neurological function in paint manufacturing workers with long-term exposure to organic solvents in two South African factories. Manuscript submitted to Occupational and Environmental Health.

Otto D, Soliman S, Svensgaard D, Soffar A, Ahmed N. (1990). Neurobehavioural assessment of workers exposed to pesticides. In : Advances in neurobehavioural toxicology: Applications in Environmental and Occupational Health. Ed: Johnson BL, Anger WK, Durao A, Xintaras C. pp 305-322. Lewis Publishers, Michigan.

Peedicayil J, Ernest K, Thomas M, Kanagasabapathy AS, Stephen PM. (1991). The effect of organophosphorus compounds on serum pseudocholinesterase in a group of industrial workers. Human and Experimental Toxicology 10 : 275-278.

Richter ED, Chuwers P, Levy Y, Gordon M, Grauer F, Marzouk J, Lvey S, Barron S, Gruener N. (1992). Health effects from exposure to organophosphate pesticides in workers and residents in Israel. Isr J Med Sci 28 : 584-597.

Richter E. (1993). Organophosphorus pesticides. A multinational epidemiologic study. European Occupational Health Programme, World Health Organisation, Copenhagen, Denmark.

Rosenstock L, Daniell W, Barnhart S, Schwartz, Demers PA. (1990). Chronic neurological sequalae of occupational exposure to organophosphate insecticides. Am J Ind Med 18 : 321-325.

Rosenstock L, Keifer M, Daniell W, McConnell R, Claypole K. (1991). Chronic central nervous system effects of organophosphate pesticide intoxication. Lancet 338 : 223-227.

Rosner B. (1990). Fundamentals of Biostatistics. 3rd edition. PWS Kent, Boston, Massachusetts.

SAS Insitute Inc. (1989). SAS/STAT User's Guide, Version 6.08. Fourth edition. Cary.

Savage EP, Keefe TJ, Mounce LM, Heaton LM, Lewis JA, Burcar PJ. (1988). Chronic Neurological Sequaelae of Organophosphate Pesticide Poisoning. Arch Envir Health. Jan/Feb 43(1) : 38-45.

Simonsen L, Johnsen H, Lund SP, Matikainen E, Midtgard U, Wennberg A. (1994). Methodological approach to the evaluation of neurotoxicity data and the classification of neurotoxic chemicals. Scand J Work Environ Health 20 : 1-12.

Steenland K, Jenkins B, Ames RG, O'Malley M, Chrislip D, Russo J. (1994). Chronic neurological sequelae to organophosphate pesticide poisoning. Am J Public Health 84 : 731-736.

Taylor TR, Nell V. (1993). Bypassing culture: An approach to neuropsychological assessment informed by cognitive theory. Manuscript submitted for publication. Human Sciences Resource Council and Health Psychology Unit, University of South Africa, Johannesburg.

Waldman PL. (1993). Here you will remain: Adolescent experience on farms in the Western Cape. MA Thesis, Department of Anthropology, University of Cape Town, Cape Town, South Africa.

Weaver JMC. (1993). "A Preliminary Survey of Pesticide Levels in Groundwater from a selected area on intensive agriculture in the Western Cape." Report to the Water Research Commission by the Division of Water Technology, CSIR. Water Research Commission Report 268/1/93. Pretoria.

CHAPTER 8

NEUROLOGICAL AND NEUROBEHAVIOURAL EFFECTS OF LONG TERM AGRICHEMICAL EXPOSURES: POLICY IMPLICATIONS AND RECOMMENDATIONS

CONTENTS

CHAPTER 8

NEUROLOGICAL AND NEUROBEHAVIOURAL EFFECTS OF LONG-TERM AGRICHEMICAL EXPOSURES: POLICY IMPLICATIONS AND RECOMMENDATIONS

Farm workers remain amongst the most underserved and under-researched occupational groups in South Africa. This study has investigated a key aspect of the occupational health of farm workers, namely the health effects of agrichemical exposure. In terms of the main hypothesis under investigation, evidence for chronic neurological and neurobehavioural health effects due to long-term low-dose exposures in the absence of acute poisoning was not demonstrated in the study. However, despite this "negative" result, a number of factors point to the need to examine critically the implications of the findings for farm workers' occupational health.

Firstly, in the broad spectrum of agrichemical toxicity, some evidence emerged for biochemical effects of long-term agrichemical exposures, and of "softer" symptom outcomes arising from previous pesticide poisoning. This may suggest that a small exposure-effect relationship for long-term exposure may be demonstrable under circumstances of improved exposure characterisation, and this possibility is elaborated upon further below.

Secondly, the recognised hazards posed by acute agrichemical exposures, as well as the less easily quantifiable hazards for other non-neurological chronic disease (such as carcinogenesis and chronic respiratory morbidity) remain unanswered public health issues in South Africa, and data from this study provides useful pointers for the control of these hazards.

Thirdly, much of the descriptive data in this study provides us with unique insights into the working and living conditions for farm workers in South Africa, which have immediate relevance to possible policy planning for agricultural health. For these reasons, the implications of the study's findings for public health practice and the control of chemical hazards in the farming workplace are discussed below.

In doing so, the approach adopted is informed by the debate in the epidemiological literature regarding the role of epidemiology in policy development (Rothman and Poole, 1985; Teret, 1993; Rothman, 1993; Coughlin, 1994). While it has long been traditional for epidemiologists to make assertive policy recommendations flowing out of their findings, it is increasingly being recognised that policy development is an extremely complex endeavour requiring skills in and grasp of social and political determinants of resource allocation (Segall, 1983; Makhoul, 1984; Walt, 1994). As such, epidemiology may play a key role in informing policy planners, but does not have the necessary grounding in social and political science to do justice to policy development in a comprehensive manner. Accordingly, the discussion that follows aims to identify the key problem areas for agrichemical safety that emerge from the data and possible solutions that may be fed into the policy process, rather than to prescribe policy recommendations in a linear fashion.

8.1 Improving Agrichemical Exposure Characterisation at the Workplace

Despite the development of indirect forms of exposure estimation by means of a job-exposure matrix, the level of detail in exposure characterisation achieved in this study using the best available data appears to have been limited for the evaluation of dose-effect relationships involving specific neurological and neurobehavioural effects. This scenario reflects the lack of surveillance data in the sector as a whole, and requires that serious consideration be given to improving the quality of data available both for epidemiological investigation as well as workplace monitoring. Various options for achieving this are examined below:

8.1.1 Improving the quality of secondary data

Statutory reporting of manufacture, distribution and usage of potentially hazardous chemicals has been successfully implemented in other countries to identify hazardous industries and to assist epidemiological investigations (Heikkila and Kauppinen, 1992). Such strategies comprise an essential element of a public health approach to the control of chemical hazards at the workplace. Recent changes in occupational health legislation in South Africa (Department of Manpower, 1993a) may facilitate this type of exposure surveillance by making mandatory a workplace health and safety audit where any of a number of hazardous chemicals listed by regulations are in use.

However, the farm as a workplace in South Africa has little culture of state regulation, and current personnel constraints in the Department of Manpower inspectorate render the enforcement of these regulations in remote rural areas particularly fraught with logistic problems. Moreover, given the history of labour relations in this sector, enforcement resources are most likely to be devoted to the securing of basic working conditions and collective bargaining rights, with little left over for the fairly detailed and abstruse requirements of chemical registers at every farm. In addition, it is likely that small-scale entrepreneurial farming will be encouraged in the restructuring of agriculture in South Africa (African National Congress Department of Economic Planning, 1994), and that the State will be reluctant to impose regulations on new (Black) entrants to the market, who have previously been excluded because of past apartheid policies and practices.

For this reason, an alternative strategy would be to utilise the agrichemical industry infrastructure and expertise to produce detailed and comprehensive reports on the distribution of agrichemicals with which to guide preventive, promotive and research interventions. These reports could be made to comply with minimum quality standards without the major financial or human resource inputs required by a specific inspectorate or equivalent organisational structure. Quality control could preferably be built into the functions of State infrastructure entrusted with the implementation of various related aspects of occupational health and safety legislation. For example, the National Centre for Occupational Health could be charged with the auditing of chemical industry data for the country with a particular brief to address the needs of the agrichemical sector.

Industry data could therefore generate the macro-level of secondary data necessary to evaluate trends, identify high-risk areas and to investigate preliminary ecological hypotheses.

For further detailed epidemiological investigations such as conducted in this study, these data need to be complemented by accurate first-hand industrial hygiene assessment of exposures specific to particular job activities. Such data need not be routinely collected, nor would it be desirable to do so, given the considerable financial and human resources needed for such investigations. (For example, the costs of the technical analyses for residues on skin patches alone for evaluation of 4 job activities was estimated in our study to be close to R20 000 [$6 000].) Critical areas for further research to characterise agrichemical exposure have therefore been identified.

However, a significant source of data for such investigations is the agrichemical industry itself. If the process for registration of all agrichemicals were modified by including a requirement for empirical data on the extent to which different field conditions and job activities impact on exposures experienced by humans working with the chemicals, considerable useful data would be generated. At present, the registration process in South Africa is considerably more perfunctory than in many developed countries where, for example, data on contaminants, and on methods for biological monitoring, as well as data on long-term health effects, are required as part of initial registration, and where ongoing review of existing products in response to new information are part of the regulatory process (Ormrod, 1989; Somogyi, 1989; Rodericks and Rachman, 1990).

Most pesticide companies have ample access to international databases and scientific research of considerable complexity. It is recommended that these technical resources are fully utilised in the process of registering chemicals so that ongoing evaluation and monitoring of the health implications of pesticide use are facilitated. The registration process should ensure that these data are publically available to researchers, academics and public health practitioners.

8.1.2 Primary workplace data

Direct environmental measurements of the concentration of hazardous chemicals at the workplace is clearly a superior method of exposure assessment than extrapolation from secondary data. Requirements of the new OSH Act include just such environmental monitoring requirements for substances listed in the regulations (Department of Manpower, 1993b). Such surveillance will help considerably in reducing potentially hazardous exposures in South African industry and in mapping the long-term exposure of worker cohorts. If applied to agriculture, such measures will make it possible to link individual farm workers to workplace environmental measurements for purposes of both epidemiological investigation and hygiene interventions.

However, despite the listing of many agrichemicals in the OSH regulations, the action levels indicated are largely airborne thresholds and therefore apply mainly to indoor industrial settings. In the farming sector, there are few situations other than indoor mixing, or greenhouse application of chemicals, where these situations pertain, and these apply to relatively few workers. For this reason, greater attention needs to be paid to developing dermal thresholds or to using biological monitoring as a method of estimating exposure among farm workers.

8.2 The Role of Biological Monitoring

Biological monitoring has the advantage of reflecting more accurately the internal dose of agrichemicals likely to result in human health effects, and integrates many different routes of exposure. It also allows for direct estimation of an individual's exposure. Medical monitoring is one of the responsibilities in terms of the OSH Act imposed on employers using chemicals listed in the regulations, and it follows that farmers are required to introduce such monitoring for their workforce.

For practical purposes, this implies the introduction of a monitoring programme for cholinesterase measurement since OPs are the most ubiquitous of the biologically active agrichemicals. Data in this study support the need for such a programme in a variety of ways: 1) previous poisoning was reported by 6 to 9% of workers in the sample and was strongly associated with adverse current symptom outcomes; 2) cumulative lifetime organophosphate (OP) exposure was a significant predictor of standardised erythrocyte cholinesterase levels even when controlled for other exposure variables and confounders. Ongoing workplace monitoring would be invaluable both for the prevention of clinical disease and for the characterisation of exposure in the investigation of potential long-term health effects of OP exposure. Moreover, biochemical data would be useful in defining possible cohorts of subjects for studies investigating long-term health effects of acute intoxication with OPs.

Excellent examples of cholinesterase monitoring programmes exist elsewhere (Ames et al, 1989) and these need to be adapted to South African conditions. Field methods are available for cholinesterase estimation (Coye et al, 1986; Magnotti et al, 1988) and their application in biological monitoring programmes will greatly facilitate low-cost and technically simple surveillance at the agricultural workplace. However, these methods still need to be adequately evaluated for validity and reliability (London et al, 1994).

Nonetheless, it should still be borne in mind that other agrichemicals may well warrant biological monitoring, especially if they are known to be particularly dangerous (eg: penatachlorophenol), or have chronic adverse health effects (eg: arsenic), or have wide usage despite an apparently low acute toxicity profile (eg: sulphur).

However, shortcomings of the South African OSH legislation include its failure to specify clear indications for implementation of workplace (cholinesterase) testing, and much discretion is left to the attending medical officer. Doctors are often poorly trained and motivated to play this role in the rural setting (Hartye, 1990), and an alternative approach, as outlined in the California regulations, is to set administrative guidelines for indications for testing frequency and action protocols. Such standards would go a long way towards preventing acute, and possibly chronic morbidity and mortality arising from workplace OP exposures.

8.3 Improving Safety Practices on South African Farms

For the deciduous fruit industry in South Africa, Integrated Pest Management (IPM) has become a key strategy for reducing dependence on chemical pest control, with the benefit to workers of reduced occupational chemical exposure risks. These developments need to be encouraged and investment directed at developing new methods of pest control that combine cost-effectiveness, environmental sensitivity and worker safety. Data in this study suggest that, even if individual workers are relatively mobile between fruit farms, there is limited mobility beyond the fruit industry overall. The implication of this homogeneity is that IPM policies developed for the industry may have greater capacity for impacting on the long-term occupational health of the industry's workers.

While usage of Personal Protective Equipment (PPE) plays an important role in reducing workplace exposure, the data in this study did not allow adequate evaluation of its role in reducing long-term agrichemical morbidity. The estimates of PPE practices in Chapter 6 were based on self-reported usage and did not reflect the quality of PPE or whether the items were really worn, nor under what conditions PPE was used. For this reason, it is difficult to assess whether PPE usage was really effective in reducing acute exposures or adverse acute effects, and historical data on PPE usage needed for assessing PPE impact on long-term exposures, was likely to be even more misclassified.

Further investigation into PPE practices and their impact on acute and chronic agrichemical morbidity is therfore warranted. However, many behavioural, social and organisational obstacles exist with regard to the consistent use of protective clothing and these require appropriate methodologies for assessment of attitudes and behaviours relevant to chemical safety.

Evidence from other studies suggest that exclusive emphasis on PPE usage is not effective in the prevention of poisoning due to pesticides (Loewensen et al, 1990). PPE should form one part of a comprehensive workplace strategy for reducing chemical exposures, which should include the reorganisation of workplace practices to improve chemical safety. For example, the practice of using human markers is almost non-existent in developed countries, yet almost 10% of subjects in this study reported being expected to act as a marker for aerial spray application in their current job. In this case, replacing human labour with mechanical markers is clearly a superior strategy to improving personal protective equipment for the human marker concerned. In general, simple measures such as job rotation and administrative controls may be more beneficial than reliance on protective equipment.

At the same time, widespread mechanisation of pesticide application in the agricultural sector may have an adverse effect on employment and should only be implemented within a satisfactory labour relations framework. In any event, the high costs involved are likely to be prohibitive to all but the biggest producers, whose establishments may be sufficiently large to manage the changes with redeployment rather than retrenchment.

Although not a conclusion that arises explicitly from this study, it is nonetheless evident that IPM practices need to be extended to agricultural sectors other than the deciduous fruit industry in South Africa.

8.4 The Social Context of Farm Worker Occupational Health

Notwithstanding the main focus of the investigation on possible neurotoxicity, the study has highlighted the extremely poor social conditions and related morbidity experienced by farm workers. High levels of alcohol use (and abuse), interpersonal violence and low education are all part of the milieu in which farm workers live, and which impact on their vulnerability to workplace chemical and other hazards. These factors all need to be addressed within a comprehensive rural development framework and, while there is some evidence that such initiatives are being implemented, huge backlogs are still apparent. The fact that ongoing use of the tot system was reported by almost a fifth of the sample is a matter for concern, and warrants preventive action. No doubt, the removal of alcohol as a medium of exchange and of social discourse in the farming community is an extremely difficult and complex challenge, but it is a challenge that must be met.

Education is a key component of any primary health care strategy, no less so than in addressing chemical safety on farms. Extremely low levels of education were encountered with approximately one-fifth of workers functionally illiterate. With these education levels, it becomes impossible to expect that workers will be able to read safety precautions and other critical information printed on chemical labels. Evidence was also present in the study that the more schooling workers had, the more likely they were to report usage of PPE, suggesting a directly beneficial effect of general education on safety practices. Clearly, inputs in the form of adult education and basic literacy will have a major contribution to make in both improving workers' capacity to cope better in their lives in general, but also make them less vulnerable to workplace hazards.

A further concern relates to the role of adult and childhood malnutrition, and it's impact on the long-term health of farm workers and their families. Given the association between lowered serum albumen, as a marker of nutritional status and peripheral vibration sense, and the stunting of the sample as a whole, the nutrition of farm workers appears to warrant further attention. In particular, the role of childhood undernutrition in the development of adult neurotoxicity and other disease is an area for further research, and appropriate intervention programmes need to be developed.

8.5 Research Tools for the Investigation of Neurological and Neurobehavioural Effects of Agrichemicals

In terms of established methods of outcome assessment in neurotoxicity research, the Vibratron II and the WHO NCTB performed as well as previous research has indicated. However, some additional findings of this study suggest that:

(i) The tuning fork extinction time, using the standardised protocol developed for this study, may be adequate for measurement of peripheral vibration sense in field settings where electricity is unavailable.

(ii) The measurement of motor tremor may be a useful method of assessing neurotoxicity, but requires more thorough investigation.

(iii) The WHO NCTB results showed remarkable similarity to data from a previous study among African paint workers, and investment of research resources into the development of normative values for South African use appears warranted.

(iv) Neurobehavioural tests based on the information-processing model of cognitive psychology did not show demonstrable superiority over the established WHO NCTB in terms of their sensitivity to possible neurotoxic effects of agrichemical exposure. However, in some areas, Performance Probes did appear less sensitive to cultural confounders, and gave slight indication of being able to detect small chemical dose-response effects. This suggests that further refinements of these tests may be warranted before their validity as a new method for neurobehavioural assessment is argued.

In addition, the development of a job-exposure matrix for estimation of workplace OP exposure in agriculture appears to have been robust enough to detect biochemical effects of OP exposure, but not specific enough to detect any chronic neurological or neurobehavioural effects had such a small effect been present. With this understanding, it appears that the JEM may be applicable for research use in other agricultural settings. However, further refinement to include accurate estimation of usage at the level of specific chemicals is needed if the JEM is to be applied to research questions where the outcome effect under investigation may be associated with only one agent in a particular class of chemicals, such as appears to be the case with OPIDN.

8.6 Long-term Low-level Agrichemical Exposures and Neurotoxicity

In terms of an an understanding of the relationship between the long-term low-dose exposure to agrichemicals and chronic neurotoxic morbidity among farm workers, this study suggests that, if such an effect is present, its size is small. Moreover, the exposure data fail to show a relationship at aggregate level (OPs), and suggest that there may be a dilution effect operating if only specific OPs were implicated in the neurotoxic process. Exposure characterisation in future studies must therefore be made down to the level of specific chemicals if they are to be able to answer this question. Such data should preferably be collected prospectively.

Whether an approach using a JEM (as in this study) can achieve this level of precision is critically dependent on considerable additional data being made available, either by the agrichemical industry itself, or by a multitude of small industrial hygiene investigations. Given the crucial importance of exposure characterisation for studies of long-term health effects of agrichemicals, not only for the field of neurotoxicity, but for a range of other health effects, particularly cancer, this investment of research resources may well be justified. Such data would be indispensable in assisting the process of standard setting for agrichemical practices in general and for individual chemicals in particular.

Many of the strategies for improving farm workers health and safety outlined above require some degree of coordination of a range of research, standard-setting and enforcement activities. Whatever elements of these strategies exist at present, are scattered across a range of government departments and non-statutory organisations. An obvious step is to rationalise these into one multidisciplinary functional structure that is able to marry the diverse and complex requirements for the integration of farm worker health and safety, environmental and consumer protection and sustainable agricultural development. Such a structure may be modelled on, for example, the Environmental Protection Agency (EPA), and recent policy pronouncements from the African National Congress suggest that such an option is gaining ground (reported in the Cape Times 16/6/94: "ANC calls for new environment laws".) Linked to appropriate Department of Manpower and Department of Health infrastructure, and supported by targeted and high-quality research, this may go a long way to identifying, controlling and preventing the burden of chemical morbidity among rural working populations.

Many questions relating to the identification and control of adverse health effects of pesticides remain unanswered. This study has highlighted a few key areas in chronic morbidity investigation and the need for improved surveillance. However, additional resources will have to be made available if the full spectrum of chemical-related disease control is to be adequately effected.

REFERENCES

African National Congress Department of Economic Planning. (1994). Agricultural Policy. Land and agriculture desk. Johannesburg.

Ames RG, Brown SK, Mengle DC, Kahn E, Stratton JW, Jackson RJ. (1989). Protecting agricultural applicators from overexposure to cholinesterase-inhibiting pesticides: Perspectives from the California Programme. J Soc Occup Med. 39 ; 85-92.

Coye MJ, Lowe JA, Maddy KT. (1986). Biological Monitoring of agricultural workers exposed to pesticides: I. Cholinesterase Activity Determinations. J Occup Med 28(8) 619-636.

Coughlin SS. (1994). A ban on policy recommendations in epidemiology research papers? Surely, you jest! Epidemiology 5 : 257-258.

Department of Manpower. (1993a). Occupational Safety and Health Act 85/93. Government Printers, Pretoria.

Department of Manpower. (1993b). Draft Regulations for Hazardous Chemical Substances. Notice 270 of 1993. Government Printers, Pretoria.

Hartye J. (1990). Physicians as the weak link in Agricultural Health services: Defining the agenda for action. Am J Ind Med 18 : 421-425.

Heikkila P, Kauppinen T. (1992). Occupational Exposure to Carcinogens in Finland. Am J Ind Med 21 : 467-480.

Loewensen R, Nhachi C, Gona P, Murambiwa W. (1990). Current findings of field research on practices of use and user knowledge of pesticides in Zimbabwe. Paper presented to Research Workshop into Pesticide Safety, Zimbabwe Congress of Trade Unions, Harare.

London L, Thompson ML, Sacks S, Fuller B, Myers JE, Bachmann OM. (1994). Validity and repeatability of a field method for whole blood cholinesterase estimation. Manuscript submitted to Occupational and Environmental Medicine.

Magnotti RA, Dowling K, Eberly P, McConnell RS. (1988). Field measurement of plasma and erythrocyte cholinesterases. Clinica Chemica Acta 176 : 315-332.

Makhoul M. (1984). Assessment and implementation of health care priorities in developing countries: Incompatible paradigms and competing social systems. Soc Sci Med 19 : 373-384.

Ormrod SW. (1989). Regulation of pesticides in Canada under the Pest Control Products Act. In: Principles of Health and Safety in Agriculture. pp 211-213. Ed: JA Dosman, DW Cockcroft. CRC Press, Boca Raton, Florida.

Rodericks JV, Rachman NJ. (1990). Some issues in risk assessment for agricultural chemicals. Am J Ind Med 18 : 467-475.

Rothman KJ, Poole C. (1985). Science and policy making (editorial). Am J Public Health 75 : 340-341.

Rothman KJ. (1993). Policy recommendations in epidemiology research papers. Epidemiology 4 : 94-95.

Segall M. (1983). Planning and politics of resource allocation for Primary Health Care: Promotion of meaningful national health policy. Soc Sci Med 17 : 1947-1960.

Somogyi A. (1989). Regulation of pesticides in the Federal Republic of Germany. Food Additives and Contaminants. 6(suppl) : s123-s124.

Teret S. (1993). So what?. Epidemiology. 4 : 93-94.

Walt G. (1994). Health policy: An introduction to process and power. (In press) Zed Books, London.