Proceedings 8th British Insecticide and Fungicide Conference (1975)

CROP PROTECTION: FUTURE DEMANDS OF WORLD AGRICULTURE

E.H. Roberts

Department of Agriculture and Horticulture, University of Reading

Summary Extrapolation of existing trends suggests that a steady increase in the use of crop protection chemicals will occur to reach a level 1.3 to 1.6 times the present usage by the early 1980's, without any marked changes in systems of crop protection. Over this period the overall geographical pattern of consumption is unlikely to change significantly with only about 10% of the total being used in developing countries, in spite of the fact that it is these countries which have the greatest need for their increased use. The overall pattern as to types of crop protection chemical used is also unlikely to change significantly with herbicides being dominant in developed countries and insecticides being dominant in the developing countries. Forecasts of technical and economic changes which are likely to affect agriculture by the end of the 1980's imply a slower rate of development of novel crop protection chemicals and a greater emphasis on integrated crop protection, with the possibility of chemical manufacturers widening their activities to include such services. Particular attention may need to be given to the development of chemicals for use in the grass crop, for grain legumes, and for use in produce stores.

INTRODUCTION

The main purpose of this paper is to attempt to discern the changes in crop production which may occur in the 1980's, and the impact these may have on crop protection. Clearly this is not a one-way process and developments in crop protection will have their impact on developments in crop production. Accordingly some attempt is made to foresee developments in crop protection and the influence that these may have on crop production.

In attempting to forecast the future the most useful approach will depend on the time-scale envisaged. For the beginning of the 1980's, which is only 5 years away, it is probably sufficient to extrapolate from existing trends. But for the end of the 1980's, 15 years from now, it is probably necessary to attempt some technological forecasting.

THE EARLY 1980's - CURRENT TRENDS IN USE OF CROP PROTECTION CHEMICALS

A recent assessment of the current world allocation of the agrochemical market (herbicides, pesticides, fungicides and growth regulators), based on user cash value, suggested about 45% in the U.S.A., 25% in West Europe, and 12% in Japan, leaving 18% for the rest of the world including the Communist countries (Mendelsohn, 1973). From this it would seem that not more than 10% of the market is in developing countries. There is little doubt, however, that it is the developing countries which are in greatest need of more crop protection chemicals. These countries contain 49% of the world population and 46% of the cultivated land area of the world (Duckham, Jones and Roberts, 1976) and it is in these countries where crop losses due to pests, disease and weeds seem to be greatest. On a world scale it has been estimated that 34% of the total value of crops is lost because of the depredations of pests, diseases and weeds - each group contributing roughly equally to this loss; in developing countries, however, total losses appear to be over 40% as compared with values of 25-30% for developed countries (FAO, 1969).

In spite of this extra need of the developing countries it is improbable that the short-term position will change significantly. One estimate of market growth suggested 10% per year for the whole world, 12% in the U.K., 14% in France, 10% in West Germany and 11% in the U.S.A. (Mendelsohn, 1973). Thus it would appear from this that the current growth rate in developing countries as a whole must be less than 10%. Some more recent estimates for market growth rates in developed countries, however, are lower; for example, a figure of 6% has been suggested for the U.S.A. (Anderson, 1975). One of the most recent estimates, based on a confidential survey of leading international markets, suggests a 4.5% growth rate per year for West Europe, 5% for North America and a higher figure of about 9% for most developing countries, all resulting in a figure of 6.4% for the world as a whole (Anon, 1975). Even on this estimate, which gives a growth rate in developing countries of almost double that of developed countries, the overall position will change very little, at least in the short term. The market in developing countries as a proportion of the whole could increase from 10% at present to 12% by 1980 (Fig. 1) and, if the trend were to continue at the same rate, to 16% by the end of the 1980's.

From all these estimates it follows that world consumption by the beginning of the 1980's is likely to be about 1.3 to 1.6 times the present consumption and possibly, if present trends continue, 2.4 to 4.2 times present consumption by the end of the decade.

In terms of the various categories of crop production chemicals, the present world consumption is about 43% herbicides, 35% insecticides and 19% fungicides (leaving 3% for growth regulators and other miscellaneous products) (Anon, 1975). Inevitably there are differences from country to country. In the U.K., for example, the relative sales to the farming industry are 66% herbicides, 10% insecticides, 20% fungicides and 3% miscellaneous (Mendelsohn, 1973). However, it is clear that herbicides hold the dominant position in the developed countries, and in the short-term this position is likely to remain the same. Indeed on a world basis it is estimated that the dominant position of herbicides will increase further, at least in the short-term, since the annual percentage increase on a world scale has been estimated at 7.7% per annum for herbicides as compared with 4.8% for insecticides and 6.2% for fungicides (Anon. 1975) (Fig.2). Obviously the proportions used by the world at large are dominated by the developed countries, but this conceals the very different pattern of usage in the developing countries where the major demand is for pesticides, particularly insecticides. It has been suggested that the relative importance of herbicides could rapidly change in the developing countries to a position nearer to that in the developed countries (Furtick, 1975), but there are social and economic constraints which I believe will tend to maintain the present balance. These will be dealt with in greater detail in considering the position towards the end of the 1980's.

In summary, then, present trends of sales suggest that at the beginning of the 1980's we shall see an increase in the world usage of crop protection chemicals to about 1.3 to 1.6 times the present usage. There will be little change in the general geographical pattern of consumption with developing countries accounting for 10-12% of the world market. In developing countries the emphasis will still be on insecticides. But herbicides will continue to be dominant overall because of their current importance, which is likely to be maintained, in developed countries.

Fig. 1

World Consumption of Crop Protection Chemicals

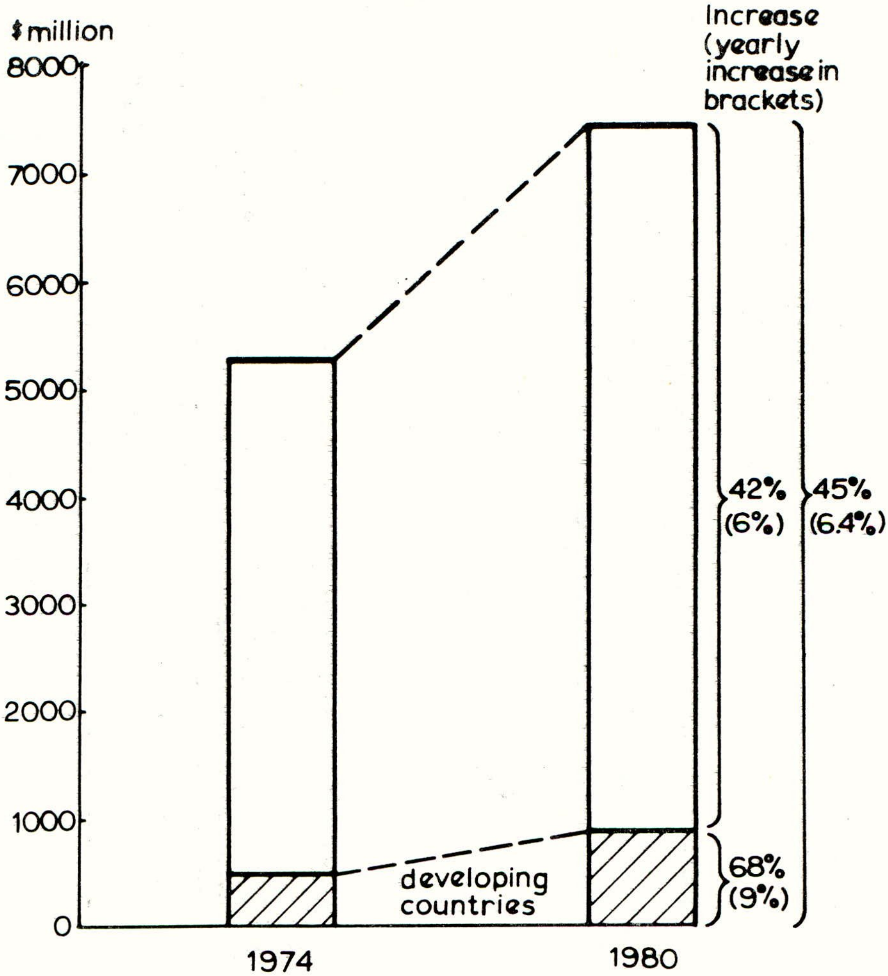
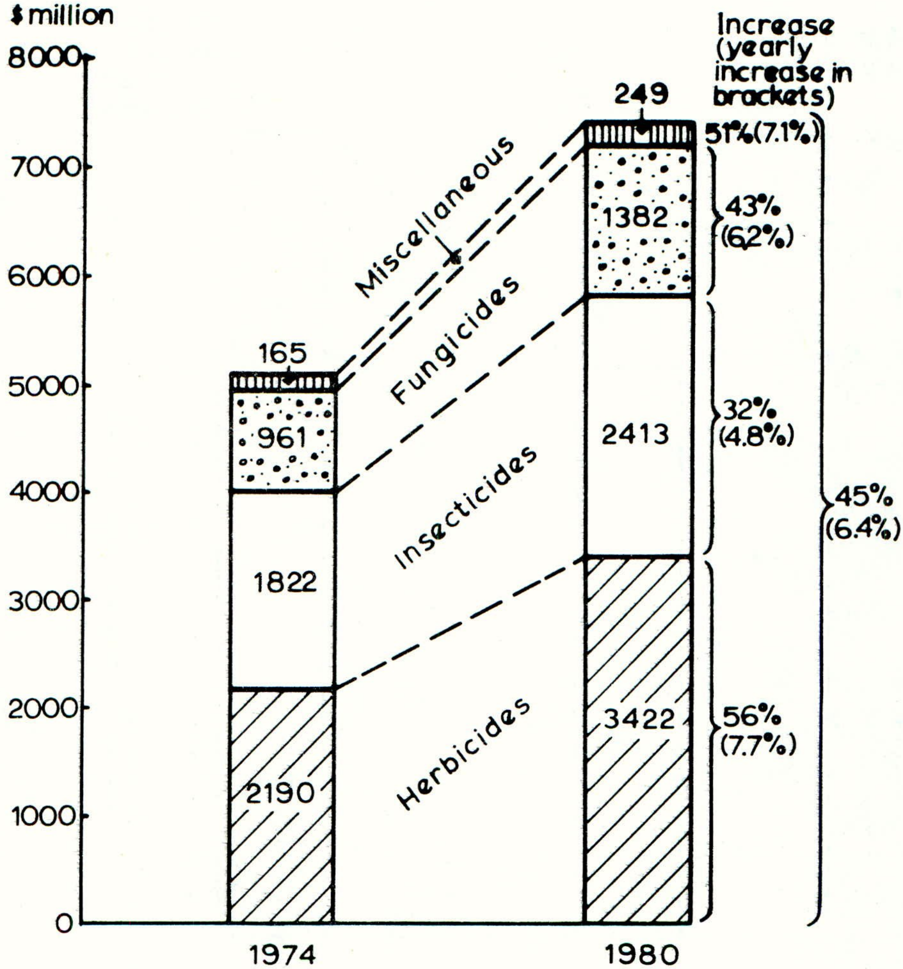


Fig. 2

World Consumption of Crop Protection Chemicals



THE LATE 1980's - POSSIBLE CHANGES IN AGRICULTURE AND THEIR INFLUENCE ON CROP PROTECTION

Certain agricultural trends seem inevitable and will certainly continue until the end of the 1980's. First of all there is likely to be an increasing intensification of production on existing agricultural land in order to meet increasing demands for food and other agricultural products. Secondly, the relative costs of some of the raw materials in agriculture are likely to increase since they depend on non-renewable resources which will become discernably more scarce and the limited distribution of which makes them vulnerable to monopolistic and political activities. Chief amongst these are oil or gas based products - e.g., fuel, nitrogen fertilizer and crop protection chemicals (where petroleum products are used as feedstocks, solvents and emulsifiers). Little more needs to be said here about the direct effects of oil prices on production costs since this problem is topical and well publicised. However, so far as crop protection chemicals are concerned it is worth pointing out that not only are production costs likely to rise but development costs are also likely to continue to escalate. There are a number of reasons for this many of which have been discussed recently by Furtick (1974). First the number of products in the crop protection armoury has risen at a very rapid rate since the early 1940's. Initially the accumulative growth of marketable products was probably exponential but is now linear (Lewis, 1974). Thus any new product has to compete with an increasing large number of well-tried and satisfactory products. Secondly, many of these older products become cheaper because of loss of patent rights and this increases their competitive advantage. Thirdly, the increased concern with the environment means that the number of tests required to ensure that a product is 'safe' has increased. This, itself, has three consequences: fewer products per number screened are successful because of the more stringent rules; the cost of development is greater because of the longer development period and the lower number of successful products; and finally, the period of protected exploitation rights under patent is reduced, thus increasing the initial market price in order to obtain a reasonable return on the investment. Fig. 3 puts these considerations together and suggests that the rate of uptake of new products by farmers may well decrease.

These considerations are not entirely speculative because there is some indication that the trends already exist: Lewis (1974) has quoted evidence which indicates that research and development costs of pesticides had increased from $2.9 per marketable product in 1964 to between $7 and $15 million in 1972/3; over the period 1956-1972 the number of compounds screened per successful product rose gradually from 1,800 to 10,000; and it has been estimated that it now takes 8 years of effort to produce one marketable product of which 5-6 years are spent on safety problems, and that safety problems account for 40-60% of development costs (Slade, 1975).

In addition to increased relative costs of fuel, nitrogen fertilizer and agro-chemicals, one of the most significant items which is almost certain to become even more expensive is phosphate. Major deposits are limited to a few areas, mainly in North Africa and North America. Evans (1975) has pointed out that world use of phosphatic fertilizer has trebled in the last 20 years; reserves are large, but if its use continues to increase exponentially, workable deposits will be exhausted in about 100 years. Even at current rates of use Josephson (1974) estimates that supplies at current costs of extraction will be depleted in 50 years.

All these factors seem to point in the same direction. Increased costs in the major fertilizers, particularly nitrogen, suggest there will be a greater emphasis away from continuous monoculture and towards rotations which make use of biological nitrogen fixation. Increased costs of agrochemicals together with increased environmental concern, and concern about resistant strains of insects and fungi, imply a greater emphasis on crop protection methods which depend on using them less intensively. These new developments will include more emphasis on genetical

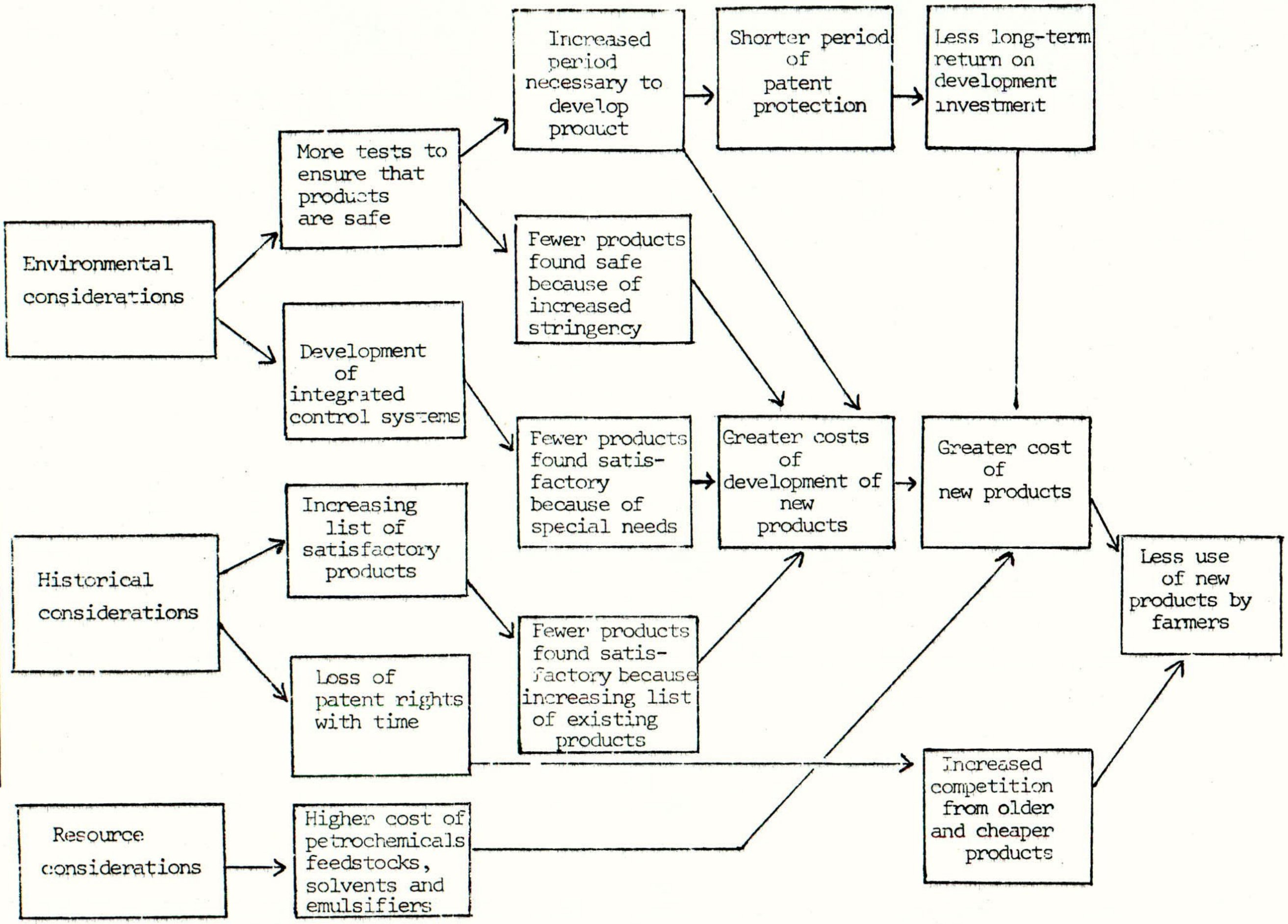


Fig. 3 Factors detracting from the development of new pesticides

resistance including possibly mixtures of genotypes, use of rotations, biological and cultural techniques and combinations of all these with agrochemicals - in other words integrated control.

If these projections materialise then it may be that the industries providing crop protection chemicals might develop a rather wider role in crop protection - to their advantage, and to the advantage of agriculture and the community. The wider role would be to provide a service to agriculture encompassing investigation, advice and possibly implementation of crop protection measures, including all forms of crop protection and not simply those depending on the simple use of agrochemicals. Furtick (1974) suggests there are already some signs of such development in the U.S.A. There are parallels currently to be seen in the other industries which serve agriculture, for example in the animal feed firms which not only supply feeds but also supply management and monitoring services, or in the food industries which integrate farm production systems for the provision of canned vegetables.

Increased costs of fuel imply some additional changes of emphasis. There will be increased advantages in spraying rather than ploughing which suggests an encouragement to minimum cultivation techniques, providing the cost of herbicides do not increase unduly. They also imply there would be considerable advantages in reducing crop protection sprays to a minimum number of passes of spray machinery over the crop.

These influences, which it is suggested will affect crop protection activities towards the end of the 1980's apply to agriculture in general. In order to discuss some other possible influences it will be clearer if the arguments are applied to developed and developing countries separately.

In the developed countries there is some possibility that by the end of the decade the emphasis in agriculture will be beginning to shift slightly more to crop production at the expense of animal production. There are a number of reasons for this. First, some hold the opinion that there is greater potential for improvements in crop production than in animal production since current levels of production are probably nearer the biological ceiling in the case of animal husbandry; if this is the case then animal products are likely to become relatively more expensive. Secondly, there will be some further development of the use of analogues of animal products manufactured directly from crops, such as the so-called meat and milk analogues manufactured currently mainly from soya beans and field beans. Many food experts in Britain predict that new proteins of this type will penetrate 10% of the meat market by 1981 (Hudson, 1971). Similarly, the U.S. Department of Agriculture predicts that textured vegetable proteins will penetrate 10-21% of the meat market in that country by 1980; and these levels of penetration are estimated to reduce cattle, sheep and pig production 4-8.5% and poultry production by 1.7-3.6% (M.A.F.F. 1972). Thirdly, there may be increasing resistance to the notion of using products like grain for animal production which could be used more directly for human food. In this context it is interesting to note that more than three-quarters of the land in the U.K. is currently used for animal production and 80% of cereal production used is for animal feed (Hutchinson, 1975). Finally, there are minor influences, which are nevertheless taken seriously by many concerned with animal production - ethical resistance to intensive animal production, and the human health hazards associated with it.

Although people generally have a preference for animal products, the food technology of analogues is only in its infancy and it is possible that there will therefore be further inroads into the traditional meat and dairy markets continuing beyond the projections mentioned for the early 1980's. In order to supply this new market it seems that soya beans, the primary plant protein material used for this purpose at present, will become increasingly important where they can be grown satisfactorily. In other countries we may well see the increased development of other leguminous crops, such as lupins and beans, not only to provide material for the new foods but also because of their ability to fix nitrogen and to be useful components in rotations. Consequently, the agrochemical manufacturers may need to anticipate these new possibilities in their development of agrochemicals.

The effect of these developments on animal production in the short-term however should not be exaggerated. In Great Britain, for example, it has already been pointed out that the current proportion of agricultural land used for animal production is more than 75% and, on an area basis, grass is the most important crop. This situation is likely to continue to the end of the 1980's and beyond. Although the technology of grass production has improved a great deal, it is only recently that the problems of insect and other pests in grassland have been taken seriously.

Recent evidence suggests that considerable yield improvements, sometimes up to 30%, can sometimes be obtained in apparently healthy crops by the application of pesticide cocktails (Henderson and Clements, 1974). The reasons for the increases remain to be elucidated, but there seems little doubt that there is a great potential for improving the grass crop by applying crop protection practices.

As mentioned earlier, the greatest potential for the use of crop protection chemicals lies within the developing countries. It is in such countries that reported losses due to pests, weeds and diseases are often extremely high. However the rate at which these problems are dealt with will depend on the general rate of economic development, and the types and relative proportions of agrochemicals used will depend on the agricultural systems which are developed.

One of the major differences between the developing and developed countries is the proportion of the population directly employed in agriculture. Whereas, for example, the figure in the U.K. is about 3% and the U.S.A. about 5%, in most developing countries the proportion of the working population directly employed in agriculture is usually more than 80%. Although many consider that industrialisation is an important part of the development process, the rate which this can be achieved is severely limited by the capital investment required per head employed in industry. I have not seen any recent figures but possibly £10,000 per worker would represent quite a modest investment for many industries. If for no other reason than this then it would seem probable that the population employed in the agricultural sector at the end of the 1980's will still be very large. Thus, agriculture in such countries will still need to be very labour-intensive, otherwise a drift of population to the cities, where there would be considerable unemployment, would lead to grave social and political problems. The need for labour-intensive systems may partly account for the current greater use of insecticides than herbicides in the tropics which, as we have seen, contrasts with the situation in the developed countries. For although herbicides have many advantages in weed control it is often possible to use alternative labour-intensive methods; whereas in the case of pest and disease control it is less easy and usually impossible to substitute physical work for chemical methods. Undoubtedly there will be expansion of the use of herbicides in the tropics, especially for weeds difficult to control manually (e.g., rice and wheat weeds) and many believe that herbicides willconsequently become extremely important (Mendelsohn, 1973). But the social and economic factors just described may well inhibit the rate at which that market expands. In the case of pesticides, studies have suggested that the level of their use in developing countries will need to expand by a factor of 4 to meet minimum food production requirements by 1980 (Furtick, 1975); but whether such targets will be achieved is entirely another matter.

There are, however, two factors which will encourage an expansion of the use of crop protection chemicals in developing countries. In the case of peasant agriculture the new varieties of rice, wheat, maize and potatoes, produced by the International Agricultural Institutes are having a considerable impact and attention is now being given to grain legumes, sorghum, millet and other crops. The philosophy behind many of the breeding programmes adopted so far has been to produce varieties which are physiologically adapted to a wide range of environments; and 'outreach' programmes include supplying fertilizers and crop protection chemicals as well as seed. The consequence of the breeding philosophy is that large areas are covered by a single genotype, and these conditions provide ideal environments for disease and pest problems of potentially epidemic proportions. While such a philosophy is pursued then there will be a great need for crop protection chemicals. It may mean however, that as these problems become more apparent there may be a greater emphasis on growing more varieties or even mixtures of varieties which will provide greater biological safeguards.

The second factor in developing countries which will encourage large-scale and increasing use of agrochemicals is the further development of cash crops. Cotton, for example, is already one of the heaviest users of crop protection chemicals accounting for a quarter of the world market in agricultural pesticides (Anon. 1973). But more generally it should be pointed out that many cash crops are perennial and often depend on vegetative propagation; even those which do not, very often have a very narrow genetic base. Simmonds (1961) has shown that, as one might expect, in general disease losses in self-seeded crops are about twice as great as in outbred crops, and that disease losses in clonal crops are about three times as great as in self-seeded crops. Thus many large-scale cash crops in the tropics which can afford high inputs will continue to need more and probably new agrochemicals.

Finally, there has been a growing awareness that there is little point in concentrating all the development effort on crop production if much of the harvested products are subsequently lost in storage. Estimates of losses vary widely, but certainly losses in the tropics are generally higher than in temperate latitudes. In West Africa it has been estimated that losses between harvest and the consumer may amount to 25%; in India it has been estimated that storage losses are 5-7.5% in cereals and about 8.5% in pulses (F.A.O., 1969).

Storage losses and spoilage are caused mainly by rats, insects, mites and fungi. It is possible to prevent all these by physical methods: stores can be constructed to exclude rats; the activities of fungi and mites can be prevented by controlling grain moisture content at 13% or less. Insects are more difficult since it is necessary to control grain moisture at 9% or less (which is difficult to achieve) to prevent their activities; alternatively they are not active at temperatures less than 12^{o}C. (Roberts, 1972). Such physical controls in the case of insects would be particularly expensive to achieve. There therefore seems to be a good opportunity for the further development of safe chemicals for use in storage, particularly for the control of insects.

References

ANDERSON, E.V. (1975). Steady growth pegged for pesticide use. A and EN, May 19, pp 15-16

ANON (1973). Where are the markets? Farm Chemicals, January 28-32

ANON (1975). World pesticide markets. Farm Chemicals, September 45-48

DUCKHAM, A.N., JONES, J.G.W., and ROBERTS, E.H. (1976). Food Production and Consumption: Human Food Chains and Nutrient Cycles. In press

EVANS, L.T. (1975). The physiological basis of crop yield. In Evans, L.T. ed. Crop Physiology. Cambridge University Press, 327-355.

F.A.O. (1969). Provisional Indicative World Plan for Agricultural Development Vol. I, 207-209

FURTICK, W.R. (1974). Insecticides and food production. Reprint of paper presented to the International Conference, Insecticides for the future: needs and prospects, Bellagio, Italy.

FURTICK, W.R. (1975). International research needs on control of pests in agriculture. Paper prepared for Technical Advisory Committee of the Consultancy Group for International Agricultural Research.

HENDERSON, I.F. and CLEMENTS, R.O. (1974). The effects of pesticides on the yield and botanical composition of a newly-sown ryegrass ley and on an old mixed pasture. Journal of the British Grassland Society, 29, 185-190

HUDSON, J.F. (1971). The production and utilisation of new proteins in the United Kingdom. In New Protein Foods, 13-18. Report of a Conference, Department of Food Science, University of Reading.

HUTCHINSON, J. (1975). Agriculture and nutrition. Nature, 254, 92

JOSEPHSON, G. (1974). Fertilizer and mineral supply and outlook. In The Mining and Benefication of Fertilizer Minerals, Central Treaty Organisation, Ankara, Turkey, 27-54

LEWIS, C.J. (1974). Uncertainties in crop protection chemicals. ECMRA Conference, Geneva. October

MENDELSOHN, R. (1973). World market assured despite the critics. Chemical Age International, 107 (2831), 9-10

MINISTRY OF AGRICULTURE, FISHERIES AND FOOD (1972). Novel Protein Intelligence Unit, Bulletin No. 1

ROBERTS, E.H. (1972). Storage environment and the control of viability. In Roberts, E.H. ed. Viability of Seeds, Chapman and Hall, London, 14-58.

SIMMONDS, N.W. (1961). Mating systems and the breeding of perennial crops. Advances of Science, 18, 183-186

SLADE, P. (1975). Seminars on efficient and safe use of pesticides and other pesticide work of the FAO Industry Co-operative Programme. Outlook on Agriculture, 8, 178-183

Proceedings 8th British Insecticide and Fungicide Conference (1975)

THE FUTURE OF PESTICIDE TECHNOLOGY: OPPORTUNITIES FOR RESEARCH

I. J. Graham-Bryce

Department of Insecticides and Fungicides, Rothamsted Experimental Station, Harpenden, Hertfordshire, AL5 2JQ

Summary The use of chemical agents, including novel substances such as pheromones and hormones, is likely to remain the most rewarding field for crop-protection research in the next decade. The opportunities for advance are discussed by comparing existing materials with the requirements for an ideal crop protection agent. Fundamental considerations suggest that there is much scope for increasing activity and selectivity and for regulating persistence and improving the efficiency of transfer to the target organism by devising more sophisticated pesticides and better formulations and methods of application. Exploitation of chemical and biochemical transformations occurring in the environment has great potential as a means of providing the often conflicting properties required for improved treatments. Many of the suggested improvements might appear unprofitable for industry as organised at present. A possible solution would be for industry to market a comprehensive crop protection service, enabling best use to be made of all methods of control.

Résumé L'emploi des agents chimiques, y compris les substances nouvelles telles que les phéromones et les hormones restera probablement le domaine le plus productif de recherche pour la protection des plantes pendant la prochaine dizaine d'années. Les possibilités de progrès en ce domaine sont discutées en comparant les propriétés des substances actuels avec celles d'un agent idéal. Des considerations fondamentales suggèrent qu'il y a beaucoup d'opportunités pour augmenter l'activité, la selectivité, contrôler la persistance et atteindre une plus grande efficacité dans le transfert de l'agent à l'organisme nuisible en inventant des pesticides plus specialisées et des formulations et des méthodes d'application améliorées. L'exploitation des transformations chimiques et biochimiques dans l'environnement même peut fournir les propriétés souvent incompatibles mais nécessaires pour des traitements plus efficaces. Il se peut que beaucoup de ces améliorations proposées paraissent peu profitables à l'industrie chimique dans son organisation actuel. Il serait souhaitable que l'industrie offre un service compréhensif pour la protection des plantes pour assurer le meilleur emploi possible de toutes les méthodes de contrôle.

INTRODUCTION

Prophesying is notoriously hazardous, particularly in relation to an activity such as research which is essentially creative and unpredictable. As implied by the title, the emphasis of this paper will therefore be on identifying the opportunities for advances in pest and disease control, although some specific ways in which these opportunities might be realised are also suggested.

Any consideration of the future of pesticide technology can start from the safe assumption that the growing world demands for food and materials will make it increasingly important to minimise losses due to pests and diseases. Although the rapid development of modern synthetic pesticides represents a remarkable technological achievement which has provided acceptable solutions for many crop protection problems, new methods and materials are needed to treat damaging organisms not yet satisfactorily controlled or to overcome deficiencies in existing methods. These deficiencies include undesirable side effects, inappropriate stability and mobility in soils and plants and diminished effectiveness due to resistance. Improvements are becoming progressively more difficult and expensive, particularly as regulatory requirements increase. However there seems no prospect that strictly non-chemical methods such as resistant varieties, cultural control, genetic methods or the use of natural enemies will take over the main burden of crop protection currently achieved by pesticides in the foreseeable future. While we should undoubtedly be extending the range of practicable crop protection methods, and while non-chemical methods offer considerable scope for research, the use of chemical agents, broadly defined, is therefore likely to remain the most rewarding field for industrial research in the 1980's. This does not imply an unexciting adherence to the traditional types of pesticidal product: such research should embrace not only new toxicants, but also new formulations and methods of application and novel approaches such as the use of behaviour controlling chemicals and hormones, all within the framework conveyed by the term "integrated control".

The opportunities for advance may be discussed by comparing existing materials with the requirements for an ideal crop protection agent. Detailed specifications would vary, but there would probably be general agreement that such an agent should be very potent at low cost, should act selectively against the target organism(s), should not persist for longer than needed for its intended effect and should be transferred efficiently from the point of application to the target without the risk of contaminating non-target areas. It will be apparent that existing materials fall far short of these ideals; in the following sections the potential for improvement will be discussed in relation to each type of requirement.

ACTIVITY

Damaging organisms not yet satisfactorily controlled

In considering pesticidal activity reference should first be made to those organisms for which there are at present no satisfactory treatments. The outstanding classes in this category are the viruses and related organisms such as mycoplasmas. The search for anti-viral agents is proving difficult, but unquestionably provides a major opportunity for future research. All the present indications are that successful materials will probably exert their effects by interaction with the host plant. Bacterial diseases also offer much scope for the discovery of entirely new toxicants. Other classes of damaging organisms as a whole are better served, but there are notable exceptions within certain classes. For example many nematodes are not well controlled and in the case of fungicides, there are relatively few products active against phycomycetes. In such cases where traditional methods of discovery have proved relatively unsuccessful, it would seem desirable to undertake fundamental research to discover why the organisms involved have proved particularly invulnerable.

The search for greater insecticidal activity

For many pests and diseases, we are more concerned to find better and more active toxicants to replace those already available, with the objective of reducing rates of application. However research has already provided some very potent pesticides; it is therefore prudent to ask what sort of upper limit to activity might be expected and thus how far further efforts to increase potency are likely to be worthwhile. Circumstantial evidence may be obtained by comparing the activity of pesticides with that of the most active toxicants from other classes (see for example Elliott *et al.*, 1974a). Because of variations in methods of application and conditions of assessment, conclusions from such comparisons must necessarily be limited, but Table 1 illustrates that only the most effective pesticides approach the activity of the most potent other toxicants.

Table 1

Activity of some potent pesticides compared with other biologically active compounds

Compound	Species	Approximate ED_{50} mg kg^{-1}	Reference
Tetradotoxin	rat	0.01	Ogura, 1971
Tetrachlorodibenzo-p-dioxin	guinea pig	0.0006	Schwetz *et al.*, 1973
Botulinum toxin	human	0.00002	Simpson, 1971
DDT and analogues	housefly	7-14	Elliott *et al.*, 1974
Parathion	housefly	2	Elliott *et al.*, 1974
Paraoxon	asparagus beetle	0.03	Krueger and Casida, 1957
Synergised NRDC 161	housefly	0.002	Elliott *et al.*, 1974
Carbendazim	bread mould (neurospora)	1-2	Clemons and Sisler, 1971
Cycloheximide	yeast	0.38	Wescott and Sisler, 1964

An alternative approach is to attempt to estimate the minimum amount of chemical needed to inactivate vital biochemical processes within target organisms. This approach is more direct, but the essential information for such calculations is only available for certain well characterised target sites such as acetylcholinesterase (AChE). For example, from measurements of rates of substrate hydrolysis and estimates of the catalytic centre activity, it can be calculated that houseflies (*Musca domestica*) probably contain approximately 5×10^{-14} moles AChE per insect. The toxicity of organophosphate insecticides to houseflies is typically in the region of 10^{-10} moles per insect. The difference is attributable to degradation within the insect and attenuation of the applied dose during transport from the outside of the organism to the target site. The calculations thus suggest that the maximum theoretical improvement which could be obtained by eliminating the effects of these processes would be about 2000 fold assuming a mole for mole irreversible inhibition of enzyme by insecticide and that 100% inhibition is needed for kill (A.L.Devonshire, personal communication). The possibilities of obtaining increased activity by improving the molecular fit at less well defined sites of action or by attacking more sensitive or critical sites are more problematical. The most active toxicants would be those which attacked a system present in small amount but essential to the organism. As a very broad generalisation there has been a trend as crop protection has developed towards the introduction of classes of insecticides and fungicides attacking increasingly specific sites, and this has tended to be accompanied by progressive increases in activity. The purpose of this paper is to consider the potential for further improvement rather than to discuss in detail biochemical approaches to the design of new pesticides, which are considered more fully by Corbett (1975). However, biochemical considerations suggest that there is still considerable scope for continuing this trend towards increasingly specific modes of action. Acetylcholinesterase, the principal target for existing synaptic poisons is distributed throughout the central nervous system: it should be possible to find more specific transmitters than acetylcholine, or ones located in more restricted sites. For example, it has been suggested that transmission in the locust heart may involve relatively specific amine transmitters (see review by Lunt, 1975) although the effect of inhibiting such a site is not known.

The ultimate in specificity and sensitivity among biologically active chemicals is probably reached by pheromones. While reports that even quantities in the region of 50 molecules per insect can produce responses (e.g. Jacobson et al., 1963) may appear extreme, there is no doubt that these compounds are effective at very small concentrations. The remarkable sensitivity of sensory receptors prompts the question as to whether compounds which blocked sensory processes rather than stimulating them as in the case of pheromones might prove to be outstandingly active control agents. Pheromone inhibitors have been considered in this connection but there would seem to be wider possibilities, for example, compounds acting via the eyes. The accessibility of sensory receptors to externally applied compounds could greatly decrease the effects of penetration and metabolism which reduce the activity of conventional toxicants. Other general approaches which would seem in principle to offer potential for devising more potent compounds, include the development of inhibitors which act catalytically and are thus not consumed or inactivated in the toxic reaction. The bipyridal herbicides provide a well known example in the related field of weed control.

The search for greater fungicidal activity

It seems more difficult to suggest specific unexploited avenues to the design of substantially more toxic fungicides. At present there is much interest in the chemical basis of disease resistance in plants. While this field clearly holds much promise, some of the chemicals which have been identified are not outstandingly active and the exact role of others needs to be clarified. It would be wise not to overlook other less intensively explored areas; for example the differential biochemistry of host plants and their pathogens or the field of germination inhibitors where various natural compounds with an unequivocal and potent action have already been identified (e.g. Macko et al., 1970; Leppik et al., 1972). Better understanding of the mode of action of existing fungicides might also suggest ways to increase activity.

While it thus seems reasonable to expect substantial increases in potency of both insecticides and fungicides during the next decade, recent practical experience, particularly with some systemic fungicides sounds a note of warning. The results of widespread use in the field have given some support for the view that organisms are more likely to develop resistance to chemicals having very specific modes of action; if this principle were to be generally valid, it could be an important consideration in deciding future policies for pesticide development.

SELECTIVITY

Selectivity has many aspects, which vary in importance according to the type of agent and the use to which it is being put. First, to ensure safety, selectivity between the target species and man, domestic animals and wildlife is essential. The second aspect which is assuming increasing importance in the context of integrated control concerns preservation of beneficial insects, both pollinators and natural enemies of pests. Thirdly pesticides should ideally leave the crop undamaged, a particularly demanding requirement for herbicides which are not considered here and for the control of fungi which live in intimate association with the crop.

Selectivity is achieved either by arranging that a much larger proportion of the toxicant reaches the target than reaches non-target organisms (which was defined as "ecological selectivity" by Ripper et al., 1951) or by using compounds intrinsically more toxic to the target organism, which Ripper et al. termed "physiological selectivity". The relative contribution of each approach depends on the type of selectivity being considered.

Safety to man, domestic animals and wildlife

In relation to safety, it is preferable that selectivity should not depend solely on the conditions of application so that a reasonable measure of physiological selectivity is desirable. Estimating toxicological risks is difficult and complex. No single factor should be considered in isolation, but one important property which can be used for illustration in the present discussion is the ratio of the acute toxicity against mammals to that against pest species: the absolute toxicity to mammals is only a partial guide because differences in efficacy result in different rates of application and consequently different hazards to non-target organisms. Table 2 shows that this ratio can vary greatly for different compounds.

Table 2

Relative toxicity of insecticides to insects and mammals

(Graham-Bryce, 1975a)

Insecticide	LD_{50} to rats, mg kg^{-1} (acute oral)	LD_{50} to houseflies (M. domestica) mg kg^{-1} (topical)	Ratio rats:houseflies
Parathion	3 - 6	0.9	5
DDT	118 - 250	10	18
Dieldrin	40	0.5	80
Dimethoate	200 - 300	0.7	357
Fenitrothion	800	1.4	572
Malathion	1400 - 1900	18	917
Bioresmethrin	8600	0.2	43000

Toxicities against rats from Martin (1972) and from technical data supplied by manufacturers; toxicities to houseflies from R. Sawicki and A.W. Farnham (personal communications)

Some organophosphorus insecticides such as parathion are particularly unfavourable on this basis of comparison, while the synthetic pyrethroid, bioresmethrin, is outstandingly safe (Elliott, 1971). Such favourable selectivity should be more than sufficient to eliminate risk in any normal operation and in considering future developments, the question arises as to how far such a property could be deliberately incorporated into other pesticides. Several recent lines of work suggest that this would be a promising field for future research. Physiological selectivity arises from differences in the rate at which the toxicant is transported to the site of action in different organisms, differences in the rates and nature of metabolism of the toxicant and differences in the sensitivity at the site of action. Intensive research has done much to show how these factors determine the differential toxicity of the pyrethroids and to show how this knowledge might be exploited in the design of future synthetic compounds (Elliott, 1976). The possibilities of utilising differences in the nature and rate of oxidation and hydrolysis reactions between mammals and insects to design selective organophosphorus and carbamate toxicants have also been explored (e.g. Fahmy et al., 1970; Black et al., 1973). In detail, the relative toxicities of some of the compounds and the effects of synergists have been difficult to interpret, but the results give considerable encouragement to this type of approach. In general, the concept of using metabolic processes to obtain the properties required by the more sophisticated crop protection methods which will be required in the future seems capable of much greater exploitation, and other examples will be given later.

The discovery of compounds acting on a site exclusive to the target organisms would of course provide an even more fundamental basis for physiological selectivity. In this connection the work in many laboratories on insect growth regulators and chemicals influencing metamorphosis, on neurotransmitters specific to insects and on microbial pesticides is of great importance.

Selectivity between beneficial and harmful arthropods

It would be fortuitous if such toxicants designed to attack sites exclusive to insects were active on other classes of organism, so that in principle they should be relatively safe to mammals. However, they can often also provide an even narrower degree of selectivity, being especially active against particular species of insect. They may thus be considered in relation to the second aspect of selectivity distinguished above, the preservation of beneficial insects. However, it should not be forgotten that, contrary to popular belief, conventional chemical pesticides also show considerable selectivity. The aphicide pirimicarb (Baranyovits, 1970) and various acaricides such as chlorbenside, tetradifon and tricyclohexyltin hydroxide are well known examples of favourable selectivity, but most insecticides vary considerably in their relative toxicity to different species. Data at present available on the relative susceptibility of pests and their natural enemies are reviewed by Croft and Brown (1975). In the present context we are concerned with the opportunities for further research; Table 3 therefore summarises some of the most advantageous examples calculated from the lists given by Croft and Brown, and illustrates their general conclusion that predators are less likely to be damaged than parasites. Another important consideration is toxicity to pollinating insects;

Table 3

Relative toxicity of selected pesticides to pests and their predators and parasites. Values calculated from data summarised by Croft and Brown (1975)

Crop	Application method	Pest	Predator/ Parasite	Compound	Toxicity ratio Pest/ Predator
Cotton	topical	Lygus bug	green lacewing	trichlorphon	12500
Cereals	direct spray	oat aphid	convergent ladybird	parathion	650
Cotton	topical	tobacco budworm	green lacewing	trichlorphon	260
Sugar beet	direct spray	bean aphid	seven-spot ladybird	thiometon	60
Citrus	topical	oriental fruit fly	braconid parasite	isopropyl parathion	29
Citrus	topical	oriental fruit fly	braconid parasite	parathion	2

Table 4 shows the relative toxicity of several representative insecticides to three pest species compared with that to honeybees (Apis mellifera, L).

Table 4

Toxicity of representative insecticides against three pest species relative to their toxicity against honeybees (Apis mellifera, L.)

Compound	Toxicity relative to that against honeybees		
	Musca domestica	Anopheles stephensi	Glossini austeni
Endosulfan	-	592	1578
p,p'-DDT	102	72	43
dimethoate	9	5	3
malathion	0.5	34	1
bioresmethrin	1	5	2

Relative toxicities calculated from LD_{50} values expressed as µg/insect using data kindly made available by F. Barlow, M. Elliott, A. Hadaway and J.H. Stevenson

Tables 3 and 4 indicate that in the most favourable cases it is quite possible to obtain a degree of physiological selectivity sufficient to avoid harmful effects in practice. This again poses the question as to how far such selectivity can be obtained by design. As with selectivity between different classes of organism, differential toxicity to various arthropods depends on differences in penetration, metabolism and sensitivity at the site of action. Such differences are likely to be relatively small between closely related species. However, a key point in considering the design of toxicants acting selectively between different insect species, which emerges clearly from studies on the causes of resistance (Sawicki, 1973) is that individual mechanisms which are likely to confer only slight selectivity alone can greatly potentiate each other when combined. By obtaining sufficient knowledge of these three basic processes determining relative activity in selected pests and their natural enemies, it should therefore be possible to suggest molecular structures in which the appropriate properties would be assembled to optimise selectivity (Graham-Bryce, 1975b). While in principle it thus seems that there are no insuperable difficulties in designing selectivity more rationally, the effort involved would be very considerable and it could certainly be argued that, under present arrangements, for industry to add this further constraint in searching for new products would make the odds against success unacceptably long, however desirable the objective.

In seeking to minimise damage to beneficial insects, however, ecological selectivity too offers many possibilities. In practice ecological selectivity is obtained by adjusting the timing, the method of application or the formulation of the pesticide treatment to match the behaviour of the pest as opposed to non-target species. These principles are implicit in many established pest control practices, but the potential of the approach is far from fully realised. There is a general need for much better understanding of the biology and behaviour of target organisms and of the much neglected subject of dosage transfer to enable the distribution of the toxicant to be related much more precisely to the behaviour of the target species. The potential benefits are considerable: for example theoretical calculations for a simplified model system (Graham-Bryce, 1975b) suggest that applying pesticides to receiving organisms by direct spray could be ten times less selective than when the toxicant is taken up as vapour from surface deposits. Formulation offers many ways for manipulating the relative amounts of pesticide reaching different organisms.

The advantages of seed treatments, granules and, more recently, microcapsules are well recognised, but other techniques merit more consideration. For example, the addition of amine stearates to wettable powder formulations of DDT, not only increases the persistence of the insecticidal deposit on leaf surfaces but also decreases the contact action without affecting stomach poison activity against chewing insects such as lepidopterous larvae (Phillips and Gilham, 1968). Much earlier Ripper et al. (1948) showed that selectivity could be obtained by coating DDT particles with hemicelluloses which were only effective against phytophagous chewing insects possessing the appropriate hemicellulases to degrade the coating, thus providing another example of the exploitation of metabolic processes to augment the range of properties available in the original materials.

The approach to pest control which offers the greatest degree of selectivity is the use of behaviour controlling chemicals, notably pheromones. Modern structure-determining techniques have made it possible to identify an impressively large number of structures influencing insect behaviour, and very many more will undoubtedly be found in the future. So far however there have been disappointingly few examples of successful practical use of such chemicals, other than for monitoring pest populations to enable conventional pesticides to be applied more effectively. Our ability to identify the active materials has clearly outstripped our knowledge of how to use them and the priority for future work in this very fascinating and promising field, as for other approaches to selectivity, must be for studies of dosage transfer and of the behavioural factors which determine the response of the pest.

Selectivity of fungicides

While the two types of selectivity discussed so far are also required with fungicides to which many of the same arguments therefore apply, selectivity between the damaging organism and the crop tends to be a much greater problem in disease control. Traditional protectant fungicides are general toxicants and achieve their selective fungicidal activity by remaining on the plant surface. The relatively recent development of systemic fungicides translocated within the plant represents a remarkable achievement. It appears that most of these compounds act by affecting biosynthetic processes, rather than those involving energy production and many probably owe their selectivity to the more damaging effects of such action on fast growing pathogens compared with the generally slower growing plant cells (Kaars Sijpesteijn, 1972). Although relatively few essential metabolic differences between higher plants and fungi have been identified so far, disruption of processes exclusive to fungi would provide an alternative basis for designing selective fungicides.

TRANSFER TO THE TARGET ORGANISM

It is widely recognised that present methods of applying pesticides under practical conditions are inefficient, with only a very small proportion of the applied dose reaching the target. However, estimates of the extent of the scope for improvement may still cause surprise. Table 5 gives calculations of the proportion of applied pesticide actually needed to control the damaging organisms for two representative crop/pest situations. In both cases almost all the applied dose enters the environment where it can cause undesirable side effects with no benefit in terms of pest control. Estimating the efficiency of collection by fungal pathogens is more difficult, but leads to broadly similar conclusions. Even in more favourable cases, such as when systemic compounds are applied as seed treatments for uptake by the growing plant or ULV formulations are applied to swarms of locusts in flight (which is probably the most efficient of all practical pesticide application methods) the amounts taken up by the receiving organisms are likely to be only a few per cent of that applied at best. If the potential for improvement in efficiency of utilisation is coupled with that for increasing biological activity discussed earlier, it can be concluded that in theory it should be possible to reduce rates of application by several orders of magnitude, a very challenging prospect.

Table 5

Utilisation of pesticides

Crop	Pest	Infestation level causing significant yield loss (insects per hectare)	Pesticide and normal application rate, kg ha^{-1}	Approximate LD50 per insect (μg)	Proportion of applied dose required for control, %
Field beans[1]	Aphis fabae	1.5×10^8	dimethoate 0.35	0.0007	0.03
Cocoa[2]	Capsids	2×10^4	lindane 0.2	< 2	0.02

1 Data calculated from various experiments at Rothamsted.
2 Data from Winteringham, 1974

Novel formulations

Some general approaches to improving utilisation have already been discussed in considering ecological selectivity, which clearly depends on optimising the transfer of chemical to the target organism. The plea for a more imaginative approach to formulation made in connection with selectivity may be repeated here. Various areas of neglect may be cited. For example, it is increasingly recognised that the volatility of many pesticides, although relatively small by conventional laboratory standards, is sufficient to be of considerable significance in the field at typical rates of application. This is not only an important factor in their loss from the intended region, but also provides a mechanism for redistribution within the canopy and for transfer to receiving organisms. The prospects of exploitation seem particularly attractive for fungicides to be used within a dense crop canopy. Various application and formulation devices, including particles with unconventional shapes, could be suggested to improve the initial location of the sources. Other novel formulations, such as fibres, or even threads of viscous liquids could also have advantages in other situations where special localised distributions or prolonged contact with foliage are required.

Downward translocation in plants

Soil systems provide an extreme example of the difficulties of dosage transfer so that it is not surprising that many of the outstanding problems in crop protection involve the control of soil-inhabiting organisms: these include nematodes, slugs and soil-borne diseases. For controlling these pests, the advantages of active compounds which were translocated downwards in plants and could therefore be applied to the foliage of crops at risk need no emphasis. The discovery of such compounds has been a major goal of pesticide research for many years, but very few insecticides and fungicides with the appropriate properties have been found, in contrast with the significant number of herbicides and plant growth regulators. There is thus great opportunity for comprehensive studies of the basic requirements for penetration and translocation in the symplast. In view of the difficulty of finding downward moving pesticides, it can be concluded that these requirements are not simple. Indeed the properties needed for pesticide activity, penetration and translocation could be conflicting, so that only compounds with some sort of compromise of properties have had any success. In such a situation there is however an approach with far greater potential; this is to exploit the metabolic processes in the plant to modify the properties of a precursor at appropriate stages in its passage from the point of application to the target. There are well established precedents for this "trojan horse" type of approach in the case of acropetally translocated pesticides. For example, the organophosphorus insecticides demeton, disulfoton and phorate are relatively lipophilic and as such tend to penetrate plant surfaces well. However largely because of their lipophilic nature they are not appreciably systemic. Within the plant they are oxidised at the thio-ether group to the sulphoxide and sulphone, making the molecule much more hydrophilic and hence much more readily transported in the translocation stream. The application of precursors and exploitation of metabolic processes in the plant for the development of pesticides translocated basipetally has been advocated by Crisp (1971) who suggested various specific reactions which might be utilised. Whatever the prospects for these particular examples, the general concept appears of considerable interest and deserves much more attention than it has received so far.

PERSISTENCE

The degree of persistence needed for different pest or disease control problems covers a wide range, but except for some preharvest clean-up procedures almost all crop-protection treatments must have some measure of residual effect. For any given problem, the period required for control can vary with the behaviour and response of the pest population while the persistence of the treatment will depend greatly on the environmental conditions. Some margin must always be allowed therefore to obtain consistent control under the variable conditions in the field. The ideal requirement that a pesticide should not persist for longer than required for its biological effect is thus in some ways the most utopian of those listed in the introduction and there seems little prospect of achieving it completely, at any rate until we can predict or control the weather much better than at present. Nevertheless various avenues for further advance can be suggested.

Design of molecules with appropriate persistence

The most direct approach is to design chemical structures which have the appropriate stability for each crop protection problem, while retaining the required biological activity. Such design may be attacked from two ends. First, attempts may be made to decrease the stability of excessively persistent compounds. This approach was adopted by, for example, Holan (1971) and by Metcalf et al., (1972) who showed that by replacing some or all of the chlorine atoms in DDT by functional groups such as alkyl, alkoxy, nitro etc., which can be more easily attacked, much more degradable compounds can be obtained, in some cases without loss of insecticidal activity. Such approaches therefore offer good prospects for the development of more acceptable pesticides in the future. The alternative method of attack is to increase the stability of very transient compounds which have favourable properties in the environment. This can be illustrated by the recent development of photostable synthetic pyrethroids by Elliott and co-workers (Elliott et al., 1974b). The natural pyrethrins and earlier synthetic compounds, although very potent against insects and safe to mammals decomposed so rapidly in air and sunlight that their use was largely restricted to the control of pests indoors and in the glasshouse. By systematically eliminating the centres susceptible to photodecomposition while retaining the features essential for activity, persistence was greatly increased while the other favourable features of the group were retained. The more stable compounds should therefore find many more uses in agriculture and horticulture.

Persistence also depends on the physicochemical properties of the compound which determine its mobility and volatility. As with stability in principle it should be possible to design structures with suitable physicochemical properties. This would clearly be of interest not just for controlling persistence but also in connection with optimising dosage transfer as discussed in the last section. Designing structures with the appropriate mobility in the environment has received relatively little attention, but the possibilities are illustrated by investigations such as those of Briggs (1969) who showed that the extent of adsorption by soil could be related to free energy substituent constants within a related series of compounds. Influencing persistence by modifying chemical structure is a very attractive and fundamental but difficult approach. A more immediately practicable line of attack is by formulation and to a lesser extent adjustment of the method of application. It would seem best to concentrate on extending the life of compounds which have desirable properties in the environment, but which are too transient to give the extended control often wanted in practice. What is required is a method of protecting the chemical until it is needed, when it can be released, achieve its intended effect and then disappear quickly. For the reasons already given it is difficult to see such a specification ever being completely realised, but several of the formulation techniques such as microencapsulation discussed in relation to dosage transfer, could give a considerable measure of control over release rates.

GENERAL CONSIDERATIONS AND CONCLUSIONS

The picture of the middle-term future which emerges from the considerations discussed in this paper indicates a continued dependence on the use of chemicals for pest and disease control, but with important changes in the types of chemicals involved and possibly of even greater significance, in the ways they are used. It has only been possible to consider a few examples, but in relation to the needs which have been identified several major trends can be distinguished:

(1) A trend towards the development of more sophisticated chemicals. This includes conventional pesticides with additional properties such as mobility in the symplast or selective activity. It also includes new types of toxicant such as insect growth regulators and chemicals needed for new approaches to control such as pheromones. This last group particularly is likely to require synthesis on a much smaller scale than traditional commodity pesticides, that is on a scale more typical of the pharmaceutical industry.

(2) Much more exploitation of chemical and biochemical transformations occurring in the environment and within receiving organisms to obtain the often conflicting properties required for improved treatments.

(3) A much better understanding of the behaviour of pesticides in the environment and of the behaviour and biology of receiving organisms so that dosage transfer to intended targets can be optimised and harmful side effects minimised.

(4) A much broader approach to formulation and methods of application based on the information obtained under (3).

Although the emphasis of these suggestions is on chemical control, they should be considered in conjunction with parallel developments in breeding for host plant resistance which is certain to contribute very significantly to reductions in losses in the future. Such developments are bound to influence the use of pesticides and there are many interacting problems requiring investigation. There would be great advantages if research programmes in the two fields could be integrated. Another major factor which must be stressed in any consideration of the future of crop protection is resistance of the target organism to the toxicant. Resistance is a most intractable problem which is becoming progressively more serious throughout the world and eliminating an increasing number of compounds for some uses. As resistance mechanisms proliferate, it is becoming clear that the traditional solution of changing to an alternative compound is unlikely to succeed indefinitely and those involved in crop protection must consider pesticide management policies, as discussed by Sawicki (1975) if the future of chemical control is to be safeguarded.

The trends outlined above should also be seen against possible future changes in agricultural practice. The importance of certain protein and oil crops such as oil seed rape and lupins seems almost certain to increase, leading to new requirements for crop protection. Changing circumstances may encourage pest control measures on crops where traditionally they have been considered uneconomic. Grass is an obvious example where it has already been shown that spectacular increases in yield can be obtained by applying crop-protection treatments (Henderson and Clements, 1974). The problems of applying pesticides to such a crop which is largely perennial and is often consumed directly by livestock appear formidable and would require much research. Freer speculation suggests other areas where pest and disease control could become much more important. Fish farming is one such example which would provide even more challenging requirements for selective toxicants and retention of toxicant in the required area than agriculture. Other novel methods of food production would also have specialised needs for eliminating damaging organisms.

The suggested trends would have some very fundamental implications for industry and industrial research. It could well be maintained that many of the suggested improvements, such as the development of pheromones, selective pesticides and more elaborate formulations, however desirable, would be unprofitable for industry. This seems hard to refute assuming existing marketing policies and in a situation where treatments are applied on the localised scale of individual fields. However the pressures to develop more discerning methods of control should not, and probably cannot be resisted. Under present arrangements, industry is probably the only sector with the necessary resources and organisation to develop these methods in practice and it seems vital therefore that they recognise and take full advantage of the trends and opportunities, as it might be claimed that they were rather slow to do when the original environmental objections to pesticides, however much overstated, began to receive attention. One possible solution to this apparent dilemma would be for industry to market a complete crop protection service, possibly developed partly in collaboration with the public sector, which would enable them to make use of all methods of control and to justify research on some which at present appear unprofitable. This proposal would envisage the existence of highly trained practitioners who would operate the service. Such a scheme would also ensure a continuing bright future for the agrochemical industry and the future of crop-protection whatever changes from traditional methods are introduced.

Acknowledgements

I thank many colleagues at Rothamsted Experimental Station and elsewhere, particularly Dr. A.L. Devonshire, Dr. M. Elliott, Dr. D.W. Hollomon, Mr. P.H. Needham, Dr. R.M. Sawicki and Dr. L.R. Taylor for helpful discussions and permission to quote results.

References

BARANYOVITS, F. (1970) Pirimor: a new aphicide for the control of resistant aphids and its use in integrated control programmes, FAO Plant Protection Bulletin, 18, 64-6

BLACK, A.L., CHIU, Y.-C., FAHMY, M.A.H. and FUKUTO, T.R. (1973) Selective toxicity of N-sulfenylated derivatives of insecticidal methyl-carbamate esters, Journal of Agricultural and Food Chemistry, 21, 747-751

BRIGGS, G.G. (1969) Molecular structure of herbicides and their sorption by soils, Nature, London, 223, 1288

CLEMONS, G.P. and SISLER, H.D. (1971) Localization of the site of action of a fungitoxic benomyl derivative, Pesticide Biochemistry and Physiology, 1, 32-43

CORBETT, J.R. (1975) Biochemical Design of Pesticides, Proceedings 8th British Insecticide and Fungicide Conference, (in the press)

CRISP, C.E. (1971) The molecular design of systemic insecticides and organic functional groups in translocation, Proceedings 2nd International Congress of Pesticide Chemistry, Israel (1971) 1, 211-64

CROFT, B.A. and BROWN, A.W.A. (1975) Responses of arthropod natural enemies to insecticides, Annual Review of Entomology, 20, 285-335

ELLIOTT, M. (1971) The relationship between structure and the activity of pyrethroids, Bulletin of the World Health Organisation, 44, 315-24

ELLIOTT, M. (1976) Properties and applications of pyrethroids, Environmental Health perspectives, (in the press)

ELLIOTT, M., FARNHAM, A.W., JANES, N.F., NEEDHAM, P.H. and PULMAN, D.A. (1974a) Insecticidally Active Conformations of Pyrethroids in Mechanism of Pesticide Action, ACS Symposium Series, No.2 , 80-91

ELLIOTT, M., FARNHAM, A.W., JANES, N.F., NEEDHAM, P.H., PULMAN, D.A. and STEVENSON, J.H. (1974b) NRDC 143, a more stable pyrethroid, Proceedings 7th British Insecticide and Fungicide Conference, 1973, 721-28.

FAHMY, M.A.H., FUKUTO, T.R., MYERS, R.O. and MARCH, R.B. (1970) The selective toxicity of new N-phosphorothioylcarbamate esters, Journal of Agricultural and Food Chemistry, 18, 793-96

GRAHAM-BRYCE, I.J. (1975a) Influence of Pesticide Properties, Environmental Factors and formulation on residues in soils, water and crops, Proceedings CENTO Conference on Toxicology of Pesticides, Tehran, 1974, (in the press)

GRAHAM-BRYCE, I.J. (1975b) Selective insecticidal action, Comptes Rendues 5e Symposium Lutte intégrée en vergers OILB/SROP, 315-326

HENDERSON, I.F. and CLEMENTS, R.O. (1974) The effects of pesticides on the yield and botanical composition of a newly-sown ryegrass ley and of an old mixed pasture, Journal of the British Grassland Society, 29, 185-190

HOLAN, G. (1971) Rational design of Insecticides, Bulletin of the World Health Organisation, 44, 355-362

JACOBSON, M., BEROZA, M. and YAMAMOTO, R.T. (1963) Isolation and identification of the sex attractant of the American cockroach, Science, 139, 48

KAARS SIJPESTEIJN, A. (1972) Effects of fungal pathogens, Systemic Fungicides, ed. R.W. Marsh, Longman Ltd., London, 151.

KRUEGER, H.R. and CASIDA, J.E. (1957) Toxicity of fifteen organophosphorus insecticides to several insect species and to rats, Journal of economic Entomology, 50, 356-8

LUNT, A.A. (1975) Synaptic Transmission in Insects, Insect Biochemistry and Function, ed. Candy, D.J. and Kilby, B.A., London, Chapman and Hall.

LEPPIK, R.A., HOLLOMON, D.W. and BOTTOMLEY, W. (1972) Quiesone: an inhibitor of the germination of Peronospora tabacina conidia, Phytochemistry, 11, 2055-63

MACKO, V., STAPLES, R.C., GERSHON, H. and RENWICK, J.A.A. (1970) Self-inhibitor of bean rust uredospores: methyl 3,4-dimethoxycinnamate, Science, 170, 539-40

MARTIN, H. (1972) Pesticide Manual, third edition, British Crop Protection Council

METCALF, R.L., KAPOOR, I.P. and HIRWE, A.S. (1972) Development of persistent biodegradable insecticides related to DDT in Degradation of synthetic organic molecules in the biosphere, Proceedings of a Conference, San Francisco, 1971 (National Academy of Sciences, Washington) 244-59

OGURA, Y. (1971) Fugu (Puffer-Fish) poisoning and the pharmacology of crystalline tetrodotoxin in poisoning, in Neuropoisons, their pathophysiological actions, Vol.1, Plenum Publishing Corporation, New York and London, 139-158

PHILLIPS,F.T. and GILLHAM, E.M. (1968) Effect of formulation on persistence of deposits of DDT on foliage, Report of Rothamsted Experimental Station for 1967, 170-171

RIPPER, W.E., GREENSLADE, R.M. and HARTLEY, G.S. (1951) Selective insecticides and biological control, Journal of economic Entomology, 44, 448-59

RIPPER, W.E., GREENSLADE, R.M., HEATH, J. and BARKER, K. (1948) New formulations of DDT with selective properties, Nature, London, 161, 484-5

SAWICKI, R.M. (1973) Recent advances in the study of the genetics of resistance in the housefly, Musca domestica, Pesticide Science, 4, 501-12

SAWICKI, R.M. (1975) Effect of sequential resistance on pesticide management, Proceedings 8th British Insecticide and Fungicide Conference,(in the press)

SCHNETZ, B.A., NORRIS, J.M., SPARSCHU, G.L., ROWE, V.K., GEHRING, P.J., EMERSON, J.L. and GERBIG, C.G. (1973) Toxicology of chlorinated dibenzo-p-dioxins, in Chlorodioxins, origin and fate Advances in Chemistry Series, No.120, ed. E.H. Blair, Washington, American Chemical Society, 55-69

SIMPSON, L.L. (1971) The neuroparalytic and hemagglutinating activities of botulinum toxin, in Neuropoisons, their pathophysiological actions, Vol.1, Plenum Publishing Corporation, New York and London, 303-323

WESCOTT, E.W. and SISLER, H.D. (1964) Uptake of cycloheximide by a sensitive and resistant yeast, Phytopathology, 54, 1261-64

WINTERINGHAM, F.P.W. (1974) Fate and significance of chemical pesticides: an appraisal in the context of integrated control, Proceedings EPPO Conference on Integrated Control in Horticulture, Kiev, 1974

Proceedings 8th British Insecticide and Fungicide Conference (1975)

PROSPECTS AND PROBLEMS FOR THE PESTICIDE MANUFACTURER

C. A. I. Goring

Dow Chemical U.S.A., P. O. Box 1706, Midland, Michigan 48640

Summary A three-fold increase in food production by the end of this century is needed to feed the world. This will probably require a five-fold increase in the use of pesticides. Pesticide needs will be met primarily by currently available products although additional materials could be developed for newly emerging or previously unsolved problems.

There is a real danger that extremists in the environmental movement and medical research establishment, especially in the United States, will cause the unjustifiable elimination of many products now in use and stifle the development of valuable new materials through overregulation.

Problems of special concern are (1) The excessive time required in some countries to bring a product from the discovery stage to the market-place (over 10 years in the United States); (2) The need for a benchmark system of evaluating the environmental acceptability of new pesticides; (3) The lack of agreement between countries on uniform test procedures and tolerances; and (4) The lack of a workable policy for products reputed to be carcinogenic.

Résumé Une augmentation triplée de la production alimentaire sera nécessaire à la fin du siècle pour nourrir l'univers. Cela nécessitera une augmentation quintuplée de la production des pesticides. La demande des produits pesticides sera satisfaite principalment par les produits actuels, bien que de nouveaux pesticides pourraient être développés pour les problèmes qui émergeront ou ceux qui n'ont pas été résolus.

Il y a un danger réel que les extrémistes des mouvements pour l'environnement et la recherche médicale, spécialement aux Etats Unis, causeront l'élimination unjustifiable de beaucoup de produits de valeur par l'excès de la réglementation.

Les problèmes impliqués sont (1) le temps exorbitant, dans quelques pays, associé à la procedure bureaucartique qui est nécessaire pour qu'un produit soit introduit du stage de la découverte au marché (plus de dix années aux Etats Unis); (2) le besoin d'un système de point de repère pour évaluer l'acceptabilité environnementale de nouveaux pesticides; (3) le manque d'accord entre les differents pays sur les procedures d'investigation et les tolerances uniformes; et (4) le manque de politique viable à l'égard de produits qui sont estimés cancerigéneux.

INTRODUCTION

Barring a miracle in population control or a catastrophe in population reduction, world population will double in the next 25 years. Hundreds of millions of people now live on the edge of starvation. Chronic malnutrition on a large scale, primarily in the developing countries, was amply documented at the recent United Nations Food Conference (14). These hungry people and their progeny are not going to be fed adequately unless food production is tripled by the end of this century. Massive agricultural inputs will be required to achieve this goal. One of these inputs is a very substantial increase in the use of pesticides.

PROSPECTS

The use of pesticides should increase more than the three-fold growth projected for food production. Table 1 shows estimated crop areas, total expenditures for pesticides, and pesticide expenditures per hectare for some of the agriculturally advanced regions in comparison with all other regions combined (2, 3, 4). The United States, Japan and W. Europe spend considerably more per hectare for pesticides than the rest of the world. Expenditures for pesticides in other countries are therefore expected to increase at a far greater rate than increases in agricultural productivity. Existing trends in sales suggest a two-fold overall increase by the mid-1980's and as much as a five-fold increase within two to three decades.

Use Trends - Important pesticides will probably continue to dominate the markets they currently serve. It is a misconception that replacement of older pesticides with newer materials is an ordained phenomenon. The fact is, farmer expenditures for most major pesticides continue to increase. Newer materials usually impact on emerging or previously unsolved problems, but in some instances do provide satisfactory alternatives to older products, particularly when insect or fungi resistance has developed. Some of the important older and newer pesticides are shown in Table 2 (10). Many of the major pesticides discovered in the 1940's and 1950's are still with us.

Table 1

Crop hectares and pesticide expenditures in different parts of the world

Area	Estimated Crop Hectares (Millions)	Estimated Pesticide Expenditures at User Level (Millions of U.S. Dollars)	Estimated Pesticide Expenditures Per Hectare in U.S. Dollars
Japan	5.3	450	84.9
Western Europe	50.6	1,301	25.7
U.S.A.	80.2	1,732	21.6
All Other countries (excluding China)	503.2	1,655	3.3

Table 2

Some organic pesticides of major current and future economic importance

Pesticide 1/	Approximate Year of Introduction	Use
Methyl bromide	1932	Space and soil fumigant
2,4-D	1942	Postemergence herbicide
Dichloropropane-dichloropropene mixture	1942	Soil fumigant
Zineb	1943	Foliar fungicide
Dinoseb	1945	Pre and postemergence herbicide
Methyl parathion	1947	Foliar insecticide
Captan	1949	Foliar fungicide
Parathion	1949	Foliar insecticide
Maneb	1950	Foliar fungicide
Malathion	1950	Foliar and premise insecticide
Diazinon	1952	Soil and foliar insecticide
Dalapon	1953	Postemergence herbicide
Azinphosmethyl	1953	Foliar insecticide
Phorate	1954	Soil and Systemic insecticide
Diuron	1954	Preemergence herbicide
EPTC	1954	Preemergence herbicide
Dicofol	1955	Acaricide
Dibromochloro propane	1955	Soil fumigant
Disulfoton	1956	Soil and systemic insecticide
Carbaryl	1956	Foliar insecticide
Simazine	1956	Preemergence herbicide
Atrazine	1958	Preemergence herbicide
Chloramben	1958	Preemergence herbicide
Paraquat	1958	Postemergence herbicide
Fenitrothion	1959	Foliar insecticide
Trifluralin	1960	Preemergence herbicide
Linuron	1960	Pre and postemergence herbicide
Fluometuron	1960	Preemergence herbicide
Tri-allate	1961	Preemergence herbicide
Butylate	1962	Preemergence herbicide
Pyrazon	1962	Pre and postemergence herbicide
Chlorthalonil	1963	Foliar fungicide
Picloram	1963	Postemergence herbicide
Bromacil	1963	Preemergence herbicide & soil sterilant
Aldicarb	1965	Nematicide and systemic insecticide
Dicamba	1965	Postemergence herbicide
Propachlor	1965	Preemergence herbicide
Chlorpyrifos	1965	Soil, foliar and premise insecticide
Chlordimeform	1966	Foliar insecticide and acaricide
Alachlor	1966	Preemergence herbicide
Methomyl	1966	Foliar insecticide
Carbofuran	1967	Soil insecticide and nematicide
Benomyl	1967	Systemic foliar fungicide
Cyanazine	1968	Preemergence herbicide
Cyhexatin	1968	Acaracide
Bentazon	1968	Postemergence herbicide
Tridemorph	1969	Systemic foliar fungicide
Orthene	1971	Foliar insecticide
Metribuzin	1971	Preemergence herbicide
Glyphosate	1973	Postemergence herbicide

1/Pesticides that are in danger of being completely banned such as DDT and other chlorinated hydrocarbons are not included.

Insecticides and Acaricides - Restrictions on DDT and other chlorinated hydrocarbons have created a void that is not easily filled. They are being replaced with carbamates and phosphates that are often more acutely toxic to humans. Efforts are being made to safen hazardous products by appropriate formulation (encapsulated methyl parathion) and use practices (minimal re-entry times after application).

Programs to discover novel types of insect control agents are being accelerated. Chlordimeform, the juvenile hormone analogue methoprene, and PH 60-40 are examples of materials that are relatively low in mammalian toxicity and appear to have different modes of action than the carbamates and phosphates. Hopefully they will be less susceptible to development of resistance. A unique group of pyrethroids, typified by permethrin have improved stability under outdoor conditions and are extraordinarily active against a wide range of insects. Pheromone, bacterial, and viral insect control agents are being actively developed. Special emphasis is being placed on integration of cultural practices and insecticide use in an effort to optimize crop production with minimal environmental impact.

Because of the novel nature and lack of background information to support judgment of some of these products, the United States Environmental Protection Agency (EPA) may require more data than for conventional products. Furthermore, their survival in the marketplace will only be achieved if their cost relative to their performance is competitive with entrenched materials. Who would wish it any other way? Certainly not the farmer, nor the consumer.

Nematicides and Fungicides - Nematode control used to be almost exclusively the domain of soil fumigants. Phosphates and carbamates are now extensively applied to certain crops such as tobacco and will become more widely used on peanuts, soybeans, cotton and sugar beets, carving a growing slice out of the expanding soil fumigant market.

Few systemic nematicides are being developed in contrast to the torrent of systemic fungicides. Benomyl is the most effective and widely used. Triarimol is more active but has been withdrawn from the marketplace for toxicological reasons. Nevertheless, its unique activity is indicative of the opportunity for further advances.

One of the problems with benomyl is the potential for development of resistant strains of fungi, a phenomenon not observed for protectant materials such as dithiocarbamates and captan. In some markets, where resistance has developed, such as peanut leaf spot, benomyl is being replaced by chlorthalonil, a protectant fungicide. For both insecticides and fungicides more attention will be given in the future to using mixtures of compounds and to rotating those compounds in order to minimize the development of resistance.

Pyroxychlor (11) is the most recent important advance in chemical control of soil fungi. It has unique selective and systemic action on root diseases caused by Pythium and Phytophthora. Currently it is the only systemic fungicide known to translocate in effective concentrations from the foliage to the roots of plants.

There is still a need for unique fungicides. Table 3 shows production losses due to weeds, insects, and fungi for major crops in the United States and the use of herbicides, insecticides and fungicides on these crops in 1966 (15, 16). By 1974 over 80% of the corn, soybean and cotton acreage and 40% of the wheat acreage was being treated with herbicides although there was little increase in the acreage being treated with insecticides and fungicides. The need for effective fungicides is obvious.

Herbicides - The emphasis on weed control in the last decade has uncovered many new types of herbicides although continued domination of the markets by the triazine, acetanilide, urea, thiolcarbamate, nitroaniline, benzoic acid, phenoxy acid, and pyridine herbicides is expected.

Table 3

Estimated production losses and pesticides use on major crops in the U.S.A. in 1966

	Weeds		Insects		Diseases	
Crop	% Crop Loss 1/	% Area Treated	% Crop Loss 1/	% Area Treated	% Crop Loss 1/	% Area Treated 2/
Corn	10	57	12	33	12	<0.5
Soybeans	17	27	3	4	14	<0.5
Cotton	8	52	19	54	12	2
Wheat	12	28	6	2	14	<0.5

1/ Average annual losses from 1951 to 1960

2/ Percent of crop area treated in 1966 excluding fungicide seed treatment

Nevertheless, materials such as metribuzin, bentazon, and glyphosate will have a significant impact because of their unique activity. Metribuzin, applied pre-emergence, selectively controls hard-to-kill broadleaf weeds in soybeans. Bentazon is similarly effective when applied post-emergence. Glyphosate is highly active through the foliage on perennial grass and broadleaf weeds.

The search for improved herbicides is likely to continue unabated because the markets are large. Decreases in cultivation, and development of weed populations resistant to materials currently being used, will continue to trigger the need for new herbicides.

Plant Growth Regulators and Plant Nutrition Control Agents - Plant growth regulators are receiving special attention although current markets for materials such as maleic hydrazide and chlormequat are small. Newer chemicals such as ethephon and glyphosine could capture larger markets. The opportunities for useful chemical manipulation of plants and plant processes are enormous. Hopefully, the ingenuity of the pesticide industry and the incentive to achieve this goal will flourish, and wide scale success will eventually be achieved.

Unique developments are occurring in plant nutrition (8). Compounds such as nitrapyrin are being commercialized for control of nitrification. This practice will become important for reducing losses of nitrogen, improving nitrogen uptake and the growth and quality of crops, and mitigating plant diseases.

Production Trends - A continuing world-wide shortage of capital could restrict the funds available for expanding pesticide production to meet market demand, but it is probable that manufacturers will continue to give top priority to the pesticide business providing regulations do not become unbearably stringent. Developing countries are pressing for local manufacturing or formulating facilities so that these capital funds are expended in the countries in which the pesticides are to be used. India, Malaysia and several other countries are following this policy.

PROBLEMS

It is evident that there is a rapidly expanding need for chemicals in agriculture and that manufacturers can meet this need. I am not certain they will have the opportunity if present trends in pesticide regulation persist. The pesticide manufacturer was, unfortunately, the first target of the environmental movement that is now engulfing the entire chemical industry. Some people blame Rachel Carson because of her exaggerated environmental concerns. I think the problem is more fundamental.

Origins of the Pesticide Controversy - Malthus was right. Earth's resources are limited and cannot support human population growth without end. We must stabalize our numbers at a level commensurate with our resources or excessive growth will eventually be corrected by catastrophic population reduction. Unfortunately, because of the pervasive environmental impact of humans, some higher species could be snuffed out in the process.

Environmentalists warned of this possibility a long time ago, but Rachel Carson dramatized the problem. All of us would like to avoid environmental catastrophes and welcome reasonable regulation directed towards improving the quality of our environment and protecting our health. Regrettably, regulation of pesticides has advanced beyond all reason.

Impact of Overregulation - Scientific rationality is not very popular with much of the urban press, many politicians and the extreme environmentalist demagogues. The public is confused and fearful because of the indiscriminate attacks on pesticides. EPA and environmental agencies of many other countries are developing, implementing, and enforcing a myriad of rules and regulations that almost by design stifle the creation of new products and threaten the survival of older products.

Table 4 shows that discovery and development of major pesticides accelerated rapidly between 1930 and 1960, leveled off between 1961 and 1970 and may now be in a downtrend although the complete picture will not be known until the end of this decade. Furthermore, many major older pesticides might eventually be eliminated by government fiat.

It is not relevant to discuss DDT, aldrin, dieldrin and the mercurials which have already been banned or greatly restricted. Nor need I discuss the current attacks on chlordane, heptachlor and 2,4,5-T. There certainly should be rational examination of cost versus benefit for these materials, indeed all pesticides, but this is a difficult goal in the present political climate.

I am alarmed at the mounting attacks on pesticides by extremists in the environmental movement and the medical research establishment using such inflammatory buzz words as carcinogenic, oncogenic, mutagenic, and teratogenic to intimidate a fearful and poorly informed public into support of even more repressive regulation. In the end the public pays the bill for these regulatory excesses.

Costs of Overregulation - The cost to the public shows up mainly as increased prices and decreased availability of food. Additional costs are increased public health problems associated with disease vectors and decreased value of recreational and forest lands.

The question is, will pesticide manufacturers continue to stay in business? Companies need to make a satisfactory return on their investment if they are to continue spending large sums of money on pesticide research and development. Some have already jumped ship, others will follow. The ones that survive could eventually deem it prudent to get out of the business if regulation becomes too extreme.

Recently Dow, and other companies, were asked by a consulting firm retained by the EPA for information on the added cost of regulation associated with the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). Our estimates are shown in Table 5. They are probably conservative.

Table 4

Rate of discovery and development

of major pesticides from 1931 to date

Decade	Number of Major Pesticides Introduced
1931-1940	1
1941-1950	9
1951-1960	18
1961-1970	19
1971-date	3

Table 5

Estimated current economic impact of the Federal insecticide, Fungicide and Rodenticide Act (FIFRA) on Dow Chemical U.S.A.

Section	Description	Estimated Additional Costs Per Year $ Millions	Estimated Loss of Sales Per Year $ Millions
5	Experimental use permits	-	12
6	Administrative review	1	-
8	Books and records	1	-
12	Unlawful acts	-	1
19	Storage and disposal	5	-
24	Authority of states	-	4
	TOTAL	7	17

The increased costs are due to our struggles with the EPA to save our products, politely called administrative review (Section 6), record keeping (Section 8), and requirements for storage and disposal (Section 19). Losses in sales are caused by delays in the registration process (Sections 5 and 24) and harassment of our customers by a sometimes overzealous enforcement division (Section 12). Substantial additional costs and losses in sales due to delays in registration and loss of products is certain to occur with the full implementation of Section 3 which covers the rules and regulations for registration, re-registration and classification. Some of the delays and increased costs are an inevitable outgrowth of necessary and desirable pesticide regulatory procedures but many of the procedures are counterproductive.

Continued overregulation will certainly strangle the inventive genius of the pesticide industry. As the costs of defending current products and developing newer materials continue to mount, pesticide manufacturers will be forced to allocate a decreasing proportion of their research and development expenditures to the discovery phase. The experience of The Dow Chemical Company in the United States is shown in Table 6. This trend comes at a time when the need for improved pesticides and the opportunities for creative breakthroughs were never greater.

Most unfortunately, some of the research effort diverted away from discovery is devoted to satisfying whimsical regulatory requests that contribute little to the assessment of the possible environmental impact of potential products.

The high costs of research have prompted companies to seriously consider increased collaboration and shared costs in world-wide evaluation and development of major products.

Table 6

Trend in expenditures for discovery research on pesticides for

Dow Chemical U.S.A. in recent years

	Distribution of Pesticide R&D Expenditures	
Year	Discovery Research %	Product Registration & Development %
1970	53	47
1971	48	52
1972	43	57
1973	42	58
1974	39	61
1975	38	62
1976 (projected)	34	66

Regulatory Problems of Special Concern - Discussion of all of these regulations and how to make them reasonable is beyond the scope of this talk, but I would like to focus on several key issues.

Currently it is almost impossible to reduce the time from discovery to submission for tolerances and registration to less than seven years for a major pesticide use in the U.S.A. Table 7 shows that it takes an additional 2-1/2 years to obtain the first major registration. This period could become even longer when FIFRA exerts its full effect. Nor is it likely that pesticide regulation has reached its zenith. Regulator fiefdoms often seem to feel compelled to expand their domains and this goal is sometimes accomplished by creating more regulations. So there may be even further delays in obtaining registrations and an astronomical level of sunk costs (9) before new products are ever sold in the U.S.A. Fortunately more enlightened approaches to pesticide regulation have been adopted by many countries, particularly the United Kingdom so that the time required to obtain registration is more reasonable. Hopefully EPA can eventually improve their procedures and reverse the present alarming trend.

A second cause for concern is certain key deficiencies in the guidelines especially in the areas of toxicological and environmental requirements. The guidelines do not provide a clear concept of how toxicological and environmental acceptability is being judged. Nor has a list of toxicologically and environmentally acceptable chemicals been officially designated as a guide for the development of new products. Such a group of chemicals could serve as "benchmarks" in judging the suitability for registration of a potential product. The behavior of new materials in an appropriate number of critical environmental and toxicological tests would be compared with the behavior of "benchmark chemicals" in these same kind of tests and the acceptability of the new materials judged (6,7).

A third problem of global significance is the slow rate of progress in getting agreement between countries on uniform acceptable test procedures and tolerances (12, 13).

Table 7

Average length of time from first submission to completion for Dow Chemical pesticide registrations and tolerances in the United States 1970-1975

Type of Regulatory Action	Number of Dow Applications	Time Required From First Submission To Completion - Weeks
Miniscule[1/]	175	18
Minor[2/]	61	51
Major[3/]	40	131

1/ Minor change in formulation or label

2/ New relatively minor use

3/ First registration of a new product or a major new use

Perhaps the most serious problem is the recent list of cancer principles promulgated by the EPA. Nine were initially developed but soon after multiplied to 17. Incredibly, the EPA seems to believe that by legal means it can shut off national debate on the scientific validity of these alleged principles.

No one can argue with public health goals designed to prevent human exposure to concentrations of carcinogens known to be unsafe. But EPA seems to be moving towards a ban of all chemicals which in any test appear to increase benign or malignant tumors in animals given the chemicals for their lifetime at daily dosages just below those required to cause death. This is a ludicrous goal that appears to encompass enormous numbers of manmade and naturally occurring chemicals.

The U.S. Department of Health, Education and Welfare recently published an extensive list of suspected carcinogens (1) including many of the major polymers and chemical intermediates, drugs such as penicillin and sulfanilide, and metals such as gold, zinc and cobalt. Also included were such naturally occurring materials as paraffin, cholesterol, testosterone, ethyl alcohol, petroleum, histamine, fructose, ozone, glutamic acid, lactic acid and ammonia. Many of the natural materials listed are essential to living systems.

Obviously, if this attitude towards cancer is to be the basis for judgment, the chances for a high percentage of current and future potential pesticides being banned or refused registration is excellent. What manufacturer is willing to continue to assume this kind of risk in a search for new products?

It seems certain that non-significant environmental levels of suspected carcinogens will eventually be established. The alternative is the mind-boggling concept of eliminating most chemicals from an environment that consists essentially of chemicals.

There are at least three good reasons why non-significant effect levels can be estimated. The human body is a splendidly organized mass of many different kinds of cells that somehow are prevented from growing out of control by some marvelous mechanism. Sooner or later this mechanism breaks down and if nothing else kills us we die of cancer. There is therefore a substantial natural incidence of cancer which is part of the human and animal aging process. Tumor induction caused by chemicals can be extrapolated to allowable intake levels that would not add significantly to natural cancer incidence.

Secondly, many chemicals may be eliminated from the body by entirely different metabolic mechanisms when given to animals at low versus high levels, often with tumor formation being caused by metabolites created at the high but not at the low level. Pharmokinetic studies can reveal the qualitative and quantitative nature of these differing metabolic pathways (5).

Lastly, there is increasing likelihood that tumor formation can be caused indirectly by stress, presumably by lowering the natural defenses of the body against cancer. In particular, such general metabolic stress might be caused by very high dosages of chemicals very low in mammalian toxicity. When the stress is removed by lowering the dosage, tumor formation would not occur.

EPILOGUE

The United States frequently carries its crusades to extremes and the environmentalist movement is no exception. Furthermore, because of its important position in world science and politics some countries are likely to follow its example. Fortunately, responsible effort in some of the other major pesticide using countries will help moderate regulatory excesses perpetrated in the United States and eventually we will have a world-wide system that combines the best features of all of the systems now being used in the various countries.

The world is headed for a horrendous food crisis in the next 25 years, although the industrialized countries will probably be the last to really suffer and this tends to make them complacent. Pesticides, along with other agricultural inputs, are not going to solve the long-term food problem, only population control will do that. However, these inputs will buy us time. We must get the extremists in the environmental movement, the medical research establishment, and the regulatory agencies, to recognize the real horror of widespread starvation, and develop some perspective on the largely imaginary horror of a silent spring and the minute amounts of pesticide chemicals that occur in our food.

References

1. Department of Health, Education and Welfare, Center for Disease Control, Occupational Safety and Health (1975). Request for information on certain chemical agents, Vol. 40, No. 121, pp 26390-26496.

2. Farm Chemicals (1975) World pesticide markets, September issue, pp 45-48.

3. Farm Chemicals (1975) Japan - expanding pesticide production. September issue, pp 64-65.

4. Food and Agricultural Organization of the United Nations, Production Yearbook (1968) pp 1-814.

5. GEHRING, P.J., et al (1975) Pharmokinetic studies in evaluation of the toxicological and environmental hazard of chemicals (In press). Advance in Modern Toxicology - Newer Concepts in Safety Evaluation. Hemisphere Publishing Corporation, Washington, D. C.

6. GORING, C. A. I. (1972) Agricultural chemicals in the environment: A quantitative viewpoint. In Organic Chemicals in The Soil Environment (C. A. I. Goring and J. W. Hamaker, eds.) Marcel Dekker, New York, N. Y., pp 793-863.

7. GORING, C. A. I., et al (1973) A proposed approach to PR 70-15 guidelines. In Chemicals, Human Health and The Environment, Vol. 1 (E. H. Blair and C. E. Otis, eds.) The Dow Chemical Company, pp 7-14.

8. HAUCK, R. D. (1972) Synthetic slow release fertilizers and fertilizer amendments. In Organic Chemicals in The Soil Environment (C.A.I. Goring and J. W. Hamaker, eds.) Marcel Dekker, New York, N.Y. pp 633-690.

9. JOHNSON, J. E. (1971) Safety in the development of herbicides DOWN TO EARTH* 27 (No. 1): 1-7.

10. MARTIN, H. (1972) Pesticide Manual, 3rd Edition. British Crop Protection Council.

11. NOVEROSKE, R. L. (1975) DOWCO* 269: A systemic fungicide for control of Phytophthora parasitica on tobacco. Phytopathology 65: 22-27.

12. VAN TIEL, N. (1975) Principles and problems of pesticide legislation. Pestic. Sci. 6: 189-197.

13. WAITT, A. W. (1975) Pesticide legislation and industry. Pestic. Sci. 6: 199-208.

14. United Nations World Food Conference (1974) Assessment of the world food situation - present and future.

15. U.S.D.A. Agricultural Research Service (1965) Losses in agriculture. Agricultural Handbook No. 291.

16. U.S.D.A. Economic Research Service (1968) Extent of farm pesticide use on crops in 1966. Agriculture Economic Report No. 147.

* Trademark of THE DOW CHEMICAL COMPANY LIMITED