

PESTICIDE RESIDUES IN THE TOTAL ENVIRONMENT: RELIABLE DETECTION AND DETERMINATION, MITIGATION, AND LEGISLATIVE CONTROL AND SURVEILLANCE PROGRAMMES

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ABSTRACT

During the past few years much has been learned about modes of introduction of pesticide chemicals into all niches of the human environment, and their nature and distribution in various substrates. There can be no question that all widely used pesticides have become broadly dispersed from the points of initial pest-control application, yet it is only recently that widespread concern over the probable ecological sequelae and more immediate effects on man and his food supply has arisen. This concern has now been abundantly justified, for many of our modern pesticide chemicals are long-lived under almost all environmental conditions. Numerous massive efforts have been undertaken, or are being contemplated, in several countries hopefully to evaluate both qualitatively and quantitatively the probable significance of both short and long-term contamination of foods and feeds, soils, waters, aquatic habitats, forests, rangelands, fibre-producing plants, wildlife, rain, snow, air, and people.

Analytical contributions are basic to these efforts, but their value is directly proportional to their reliability; either falsely negative or falsely positive residue characterizations and measurements could adversely influence important conclusions and decisions about this global problem and its future mitigation. Many legislative bodies around the world have recognized or are recognizing the absolute necessity to control both the nature and the amount of pesticide residues in our food and feeds in the interests of public health. Some of these bodies are also recognizing that the uncontrolled, widespread, and repeated uses of certain pesticide chemicals so essential to adequate agricultural production and to even partial suppression of invertebrate-borne diseases can have consequences on and in the environment far more serious than a momentary hazard from excessive residues in a particular crop or crop product.

INTRODUCTION

As even the most unobservant child quickly learns from direct, unpleasant, and unavoidable experience, the entire land surface of the earth is generously shared by man with an immense variety of biting and sucking insects. As the child grows older, he learns to his dismay and often to his extreme discomfort that most of these flying or crawling pests can also transmit virus

and other dreadful diseases ranging in severity from mere annoyance to total incapacitation and often to death (*Table 1*). Further, he soon learns that social and economic status, ethnic background, cultural plateau, adequacy of diet, intellectual level, physical maturity, and even stature of scientific advancement of his culture are of no really significant importance

Table 1. Partial list of insect-borne diseases of man and domestic animals⁵

<i>Disease</i>	<i>Vector</i>	<i>Animal affected^a</i>
African sleeping sickness	Tsetse flies	Man
Anthrax	Horse flies	All mammals
Bubonic plague	A rat flea	Man, rodents
Cattle tick fever	Several ticks	Cattle, horses
Chagas' disease	Assassin bugs	Man, rodents, dogs
Dengue	Two mosquitoes	Man
Dysentery	Several flies	Man
Encephalitis	Several mosquitoes	Man, horses, birds
Endemic typhus	Oriental rat flea	Man, rodents
Epidemic typhus	The human louse	Man
Filariasis	Several mosquitoes	Man
Fowl pox	Two mosquitoes	Avian species
Fowl spirochetosis	A fowl tick	Chicken, turkey, goose
Louping illness	Castor bean tick	Man, sheep
Malaria	<i>Anopheles</i> mosquitoes	Man, birds
Nagana	Tsetse flies	All mammals
Onchocerciasis	Several black flies	Man
Pappataci fever	A psychodid fly	Man
Piroplasmosis	Several ticks	Domestic animals
Q fever	Ticks	Man
Relapsing fevers	Several ticks	Man, rodents, fowl
Rocky Mountain spotted fever	Two ticks	Man, rodents
Scrub typhus	Chigger mites	Man, rodents
Swamp fever	Horse flies, deer flies	Equine species
Texas fever	A cattle tick	Cattle
Trypanosomiasis	Several flies	Man, many animals
Tularemia	Several flies, fleas, lice, ticks	Man, rodents, rabbits, ground birds
Verruga peruana	A psychodid fly	Man
Yellow fever	Several mosquitoes	Man, animals

^a Man is susceptible to 23 of the 29 diseases in this partial listing.

to these vicious predators. As his early education progresses, he then learns that numerous species of insects also transmit great varieties of diseases to animals, to birds, and even to plants. From casual but poignant observation, he then learns that the non-aquatic world is also generously inhabited by other insects intrinsically totally destructive to all forms of food, fibre, and wood. Similarly, the unmistakable role of fungi as effective destroyers of large shares of man's food, fibre, and wood soon becomes obvious. Less obvious to our maturing student, perhaps, are the equally serious depredations of the equally omnipresent numerous species of rodents with their associated and often deadly parasites; still less obvious are the insidious effects on useful plant life of destructive nematodes, for these tiny pests require microscopic examination to be seen. On the other hand, encroaching weeds as unwanted plants are again abundantly but not so forcibly evident to our observer, probably even if he is a city dweller.

The chronology of man's attempts to coexist with these multitudinous deterrents to evolving civilization—with its required grouping of both human and domestic animal populations and concomitant development of intensive agriculture—surely began with the insects as such unpleasant violators of both person and food supply; the rodents probably represented the second for, but as insatiable destroyers of food rather than as conveyors of disease in these early days of unawareness of bacteria and viruses; the third pest to receive defensive attention then must have been the fungi as slower but equally formidable destroyers of food supplies and clothing; among these stages came the inevitable recognition that surely there must be better ways to control unwanted small plants than by laborious pulling by hand or by hoeing.

Thus, man and animals have always been annoyed, made ill, and killed by insects and insect-borne diseases; these effects were usually immediate and obviously serious, and their attempted mitigation has occupied a very large part of man's attention for thousands of years, with almost total reliance upon the physical destruction of those annoying insects large enough to be seen and apprehended until the prehistoric discovery of the insect-repellent properties of smoke. The insecticidal properties of burning sulphur were apparently discovered early in historical times, for Homer in *The Odyssey* (*circa* 750 B.C.) mentions the fumigant action of burning sulphur, and Pliny the Elder (*circa* 60 A.D.) wrote of "pest-averting sulphur"; Pliny also recommended arsenic to kill insect pests. In addition to their nuisance and disease-causing values, it has also long been recognized with abundantly justifiable alarm that insects, rodents, and fungi pose serious and very direct threats to man's food supply, and thus to his continuing existence in even elementary states of congregation. There can be no question that the social anthropological evolution of man through band, clan, tribe, chiefdom, state and present-day 'international community, has been seriously and sometimes undoubtedly disastrously retarded by these pests, for even today—with our modern arsenal of effective agricultural pest-control chemicals—losses attributable to pests amount to at least one-third of the world food production. For example, it has been estimated⁵ that worldwide losses in agricultural production from insects alone amount annually today to at least nine dollars per arable acre, or about 21 billion dollars for the world's 2,287 million acres under cultivation, despite modern pest-control measures.

Contrariwise, the larger insects have often been important portions of the diet of man from prehistorical times to the present; many primitive cultures have relied upon beetles, locusts, caterpillars and other larvae, ants, bees, and other insects as major items of the normal food supply. Their nutritive value cannot be questioned, for in general insects are excellent sources of fats, proteins, roughage, and especially the B-complex vitamins.

In the agricultural sense, then, 'pests' are any animals or plants detrimental to man's food production, storage, and transport. There are several ways to kill or otherwise minimize ravages from pests, but the most generally and immediately effective measure is through the intelligent and guided use of pesticides, those carefully selected chemicals designed to kill pests without—at the same time—presenting undue hazard in agricultural use to man and his domestic animals, to any useful wildlife, and to

beneficial soil microorganisms. Some pesticide chemicals may persist for years in the total environment, and their indiscriminate use on the same area over long periods can have pronounced but local detrimental effects on subsequent crops, on water supplies, on wildlife and on aquatic and soil organisms.

Chemical pest-control agents have been used by man in his agricultural endeavours ever since he began actively resenting the inroads made by these diverse pests on his crops and stored products. Thus, the extensive use of vinegars to preserve many foods, of honey to preserve cooked fruits, of smoking to preserve fish and meats, and of numerous evil-smelling concoctions to repel plant-feeding and animal-biting insects and rodents and to suppress moulds date from antiquity. Sulphur, burning sulphur (sulphur dioxide), and phenols and acids in smoke were probably the first strictly pesticide chemicals, undoubtedly dating back many thousands of years. Arsenic (probably as the oxides) as both insecticide and herbicide was known to Pliny the Elder, as mentioned earlier, and the Chinese used an arsenic sulphide in the late sixteenth century⁷. Other inorganic pesticides subsequently used included salts of antimony, arsenic, boron, copper, fluorine, lead, manganese, mercury, selenium, sulphur (various oxidation states), thallium, and zinc. Most of these chemicals affected chewing animal pests only, but a few of them were effective herbicides. Insecticides that killed insects by contact date back into Chinese history with use of the wilforine alkaloids from crushed Thundergod vine, followed in several parts of the world by the discovery that some of the botanical fish poisons (e.g., the rotenoids) were also effective insecticides against some species. The use of nicotine-type compounds dates back about 300 years, when crude tobacco preparations were used in France; other botanicals included paipa roots (China), the pyrethrins (East and South Africa, Brazil, India), the Peruvian ground cherry (China, Europe, South America), camphor (probably originally from Asia), turpentine (Asia, Europe, the Americas), ryanodine (South America), the veratrine alkaloids (the Americas), and others⁸.

The so-called modern synthetic organic pesticide chemicals for agricultural use have been developed since about 1935. Their remarkable and prompt acceptance around the world stems from their long-lasting effectiveness at low dosages, as contrasted with the inorganic pesticides, and from the fact that they were essential and timely in helping provide food for a world population that now doubles every 40 years. At present there are nearly 1,000 different pesticide chemicals in use around the world, but only about 250 are major pesticides in agricultural production, including nearly 100 insecticides and acaricides, about 50 herbicides, about 50 fungicides, about 20 nematocides, about 10 rodenticides, and about 20 defoliants, plant growth regulators, desiccants, and others. Very substantial amounts of the leading 12 insecticides, 12 fungicides, and 7 herbicides are used around the world wherever modern agriculture is practised¹¹. The annually increasing sales (domestic and export) of pesticide chemicals in the United States are shown graphically in *Figure 1*^{9, 11}; similar increases must exist for all other countries producing these chemicals for agricultural applications.

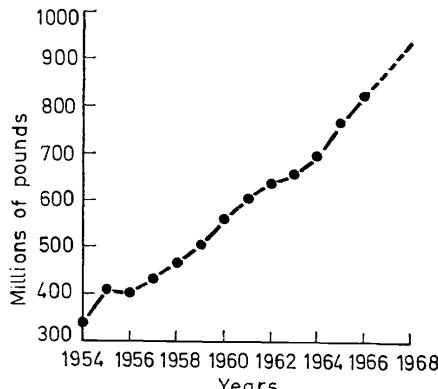


Figure 1. Combined domestic and export sales of pesticide chemicals in the United States; dashed line extrapolated^{9, 11}

PERSISTING PESTICIDE RESIDUES

Most of the pesticides applied directly to plants before about 1940 were inorganic; their deposits on plant parts remained on the plant surfaces and could largely be removed by commercial washing, as with dilute hydrochloric acid or sodium silicate solutions for the calcium and lead arsenates. By about 1950, however, it was broadly realized that the modern, synthetic, contact, organic insecticides generally possessed a potentially serious disadvantage in terms of the public health. Their deposits could penetrate treated plant parts and remain as internal residues, often for long periods. These residues were sometimes altered by the plant cellular environment into various products, often of unknown toxicology, as illustrated in *Table 2*. The systemic pesticides, deliberately designed to penetrate rapidly throughout treated plant and animal tissues, were also soon found to form various metabolites and other alteration products, sometimes in such extremely small amounts as to present a truly exciting challenge to the analyst. Pesticide chemicals admixed with soils can also be degraded or otherwise altered by both the soil environment itself and the microorganisms present and may therefore be of concern.

The few residue analytical chemists then available to work in this area soon realized the seriousness of these slowly unfolding problems associated with pesticide residues in foodstuffs, for there could be no question that the maintenance of modern agricultural production requires extensive and continuing use of these and many other agricultural chemicals. Shortly these few residue chemists began informally to organize their efforts and to exchange experiences and ideas at scientific meetings; there were no textbooks or analytical manuals for this new area in 1950, and the only publication outlets were the analytical journals and the several journals of the biological disciplines involved. Clearly, in a field where the analytical requirements became almost daily more fastidious, specific publication outlets were essential for maximum effective communication; in this atmosphere of urgency, I conceived the *Journal of Agricultural and Food*

Table 2. Illustrative metabolic and other alteration products associated with aged pesticide residues within plant and animal tissues and soils (from the general literature)

Pesticide	Substrate	Major metabolic and other products
Aldrin	Animal, plant, soil	Dieldrin and others
Amiben	Soybeans	Amiben N-glycoside
Amitrole	Plants, soils	Several
BHC (lindane)	Animals, plants, soils	Pentachlorocyclohexene, trichlorobenzenes
Bidrin	Animals, plants, soils	Series of compounds
Captan	Plants	Thiophosgene
Carbaryl	Animals, plants	Alpha-Naphthol
Colep	Plants	Colep oxon
Coral	Animals	Coral oxon
DDT	Animals, plants, soils	DDE and others
Demeton	Animals, plants	Sulphoxide, sulphone
Diazinon	Animals	Diazoxon
Dibrom	Animals	DDVP and others
Dichlobenil	Plants	2,6-Dichlorobenzoic acid
Dimethoate	Animals, plants, soils	Dimethoxon and others
Di-Syston	Animals, plants	Sulphoxide, sulphone, and others
Endosulfan	Plants	Sulphate and others
Fenthion	Animals, plants	Sulphoxide, sulphone
Heptachlor	Animals, plants, soils	Heptachlor epoxide
Malathion	Animals, plants, soils	Malaoxon and others
Methyl bromide	Plants (wheat)	N-Methylated proteins
Nicotine	Animals, plants	Cotinine and others
Parathion	Animals, plants	Paraoxon and others
Phosphamidon	Plants	Desethyl compound and others
Schradan	Animals, plants	N-oxide and others
Simazine	Plants, soils	Hydroxsimazine
Thimet	Animals, plants, soils	Sulphoxide and sulphone
Trithion	Plants	Sulphoxide and sulphone
Zectran	Animals, plants	Several

Chemistry in 1950 and sponsored by the American Chemical Society in 1952. Prior to this time, centres around the world for the chemical investigations of pesticide residues in foodstuffs existed at a few United States state experiment stations, and the U.S. Department of Agriculture research centres, as listed in Table 3. By 1950, additional residue research was being conducted by the U.S. Food and Drug Administration laboratories, the agricultural research centres of perhaps six major chemical companies around the world and a few segments of the food industry; these early efforts were almost exclusively centred around insecticides because the persisting residue problem was first recognized in our laboratories with insecticides. Now it is a major issue in every advanced country.

The enthusiastic acceptance by agriculture of modern organic pesticides, plus their escalating importance in the world economy, is attested by the rate at which books on their chemistry and on their residues have appeared. Only one of these books had been published prior to 1940; four appeared between 1940 and 1950; 16 appeared between 1950 and 1960; and 62 have been published since 1960, (including to date the 29 volumes of *Residue Reviews* and the seven volumes of *Advances in Pest Control Research*). These books are listed³ in Table 4; eight countries are represented by the authors or sponsors. *In toto*, these books and the many other technical

PESTICIDE RESIDUES IN THE TOTAL ENVIRONMENT

Table 3. Pesticide^a residue research laboratories in the United States prior to about 1940

<i>Organization</i>	<i>Location</i>	<i>Residue chemist</i>
Cornell University	Ithaca, N.Y.	L. B. Norton
Oregon State College	Corvallis, Ore.	R. H. Robinson
Pennsylvania State College	State College, Pa.	D. E. H. Frear
State of California, Bureau of Chemistry	Sacramento, Calif.	Alvin Cox
University of California Citrus Experiment Station Berkeley	Riverside, Calif. Berkeley, Calif.	F. A. Gunther W. M. Hoskins
U.S. Department of Agriculture Fruit Insect Investigations	Moorestown, N.J. Vicennes, Ind. Yakima, Wash. Beltsville, Md. Pullman, Wash.	R. D. Chisholm J. E. Fahey C. C. Cassil H. L. Haller J. L. St. John
Agricultural Research Centre Washington State College		

^a Pesticides involved were anabasine, arsenic, cryolite, the DN compounds, lead, nicotine, petroleum oils, rotenone, sulphur, and tartar emetic.

Table 4. Published books containing pesticide residue information
[updated from Gunther (1966)³]

<i>Year published</i>	<i>Author</i>	<i>Country</i>	<i>Title</i>
1939	Shephard	United States	<i>The Chemistry and Toxicology of Insecticides</i>
1942	Frear	United States	<i>Chemistry of Insecticides and Fungicides</i>
1946	West and Campbell	England	<i>DDT, The Synthetic Insecticide</i>
1948	DeOng	United States	<i>Chemistry and Uses of Insecticides</i>
1949	American Chemical Society	United States	<i>Agricultural Control Chemicals</i>
1951	Brown	Canada	<i>Insect Control by Chemicals</i>
1952	Martin	Canada	<i>Guide to the Chemicals Used in Crop Protection</i>
	West <i>et al.</i>	England	<i>Chemical Control of Insects</i>
1955	Frear	United States	<i>Chemistry of the Pesticides</i>
	Gunther and Blinn	United States	<i>Analysis of Insecticides and Acaricides</i>
	Holmes	England	<i>Practical Plant Protection</i>
	Metcalf	United States	<i>Organic Insecticides</i>
	Rose	England	<i>Crop Protection</i>
1956	Horsfall	United States	<i>Principles of Fungicidal Action</i>
	Perkow	Germany	<i>Die Insektizide</i>
1957	Internatl. Commission Ind. Agr., Permanent Internatl. Bur. Anal. Chem.	Italy	<i>Les Substances Etrangères dans les Aliments</i>
1957	Metcalf, ed.	United States	<i>Advances in Pest Control Research</i> (book series to date)
	Zbirovsky and Myska	Czechoslovakia	<i>Insecticides, Fungicides, Rodenticides</i>
1958	Souci	Germany	<i>Fremdstoffe in Lebensmitteln</i>
1959	Internatl. Union of Pure and Appl. Chem.	Germany	<i>Lebensmittel-Zusatzstoffe and Rückstände von Schadlingsbekämpfungsmitteln in Lebensmitteln</i>
	Rosival, Vrbousky, and Selecky	Czechoslovakia	<i>Toxicology and Pharmacobiodynamics of Organophosphorus Compounds</i>
1960	Dormal and Thomas	Belgium	<i>Répertoire Toxicologique des Pesticides</i>
	Gunther and Jeppson	United States	<i>Modern Insecticides and World Food Production</i>

Table 4. continued on page 362

Table 4—continued from page 361

Year published	Author	Country	Title
1960	Longgood O'Brien USDA	United States United States United States	<i>The Poisons in Your Food</i> <i>Toxic Phosphorus Esters</i> <i>The Nature and Fate of Chemicals Applied to Soils, Plants, and Animals</i> <i>Instrumental Methods for the Analysis of Food Additives</i>
1961	Butz and Noebels, eds. Crafts	United States United States	<i>Instrumental Methods for the Analysis of Food Additives</i> <i>The Chemistry and Mode of Action of Herbicides</i> <i>Organophosphorus Poisons</i>
1962	Heath Schuphan Ayres <i>et al.</i> , eds. Carson	England Germany United States United States	<i>Zur Qualität der Nahrungspflanzen</i> <i>Chemical and Biological Hazards in Food</i> <i>Silent Spring</i>
1963	Gunther, ed. FDA Zweig, ed. Klimmer	United States United States United States Germany	<i>Residue Reviews</i> (book series to date) <i>Pesticide Analytical Manual</i> <i>Analytical Methods for Pesticides, Plant Growth Regulators, and Food Additives</i> <i>Pflanzenschutz- und Schädlingsbekämpfungsmittel</i>
1964	Hayes Rudd	United States United States	<i>Clinical Handbook on Economic Poisons</i> <i>Pesticides and the Living Landscape</i>
1965	Chichester, ed. Gudzinowicz	United States United States	<i>Research in Pesticides</i> <i>The Analysis of Pesticides, Herbicides and Related Compounds Using the Electron Affinity Detector</i>
	Maier-Bode McMillen Public Health Service	Germany United States United States	<i>Pflanzenschutzmittel-Rückstände</i> <i>Bugs or People</i> <i>Guide to the Analysis of Pesticide Residues</i>
	AOAC	United States	<i>Official Methods of Analysis of the Association of Official Agriculture Chemists (every 5 years)</i>
	Environmental Pollution Panel, President's Silence Advisory Committee	United States	<i>Restoring the Quality of Our Environment</i>
1966	Natl. Acad. Sciences Crosby, ed.	United States United States	<i>Scientific Aspects of Pest Control</i> <i>Natural Pest Control Agents</i>
1967	Whitten Weed Society of America	United States United States	<i>That We May Live</i> <i>Herbicide Handbook of the Weed Society of America</i>
1968	Melnikov Bailey and Swift	U.S.S.R. United States	<i>Chemistry of Pesticides</i> <i>Pesticide Information and Safety Manual</i>
1969	Hassall Kearney and Kaufman Torgeson, ed.	United States United States United States	<i>World Crop Protection, vol. II</i> <i>Degradation of Herbicides</i> <i>Fungicides: An Advanced Treatise</i>

publications on pesticide residue matters are reassuring evidence for everyone everywhere that the world's food supply in its entirety will soon be under competent and alert surveillance to prevent abuses involving excessive pesticide residues; some countries are already in excellent command of this situation as will be shown later, and most major crops are under at least token 'market-control' scrutiny. Some of these books raised questions to which there were no answers at the time. Subsequent books and other technical publications have provided answers for most of the earlier questions about pesticide residues and their effects, and have abundantly demonstrated at the technical level that properly involved government agencies, the

PESTICIDE RESIDUES IN THE TOTAL ENVIRONMENT

world wide agricultural chemicals industry, the organized food industries state experimental stations and similar non-profitmaking research institutions have long been aware of the many problems associated with pesticide residues in the total environment and that solutions are being systematically found. These research efforts require time, money, and effective manpower, but it is important to realize that the research priorities involved in both these short- and long-term investigations of the consequences and of the amelioration of pesticide chemical behaviour in the environment should be agreed upon by experts representing public health, chemistry, biochemistry, toxicology, pharmacology, ecology, and internal medicine.

Uninformed individuals everywhere, who are deeply and vociferously concerned that man is callously poisoning his entire world with insidious chemicals, must be reassured that this eventuality was recognized long ago within the chemical and associated industries, in agriculture, in the home, in the cosmetics industry, in the food preservation industry, and in many other areas, as illustrated in *Table 5*. Most of these instances were recognized as localized problems, and were rectified as promptly as possible when the hazard was realized, usually through legislation acknowledging the rights of the individual to employment, to nourishment, and to an environment as free from chemical hazard as realistically achievable in our present society. The history of man has been that he promptly adopts a new means of

Table 5. Some early instances of concern over the direct poisoning of man by advancing civilization

<i>Approximate date</i>	<i>Effect</i>	<i>Causative agent</i>	<i>Source of agent</i>
B.C.	Cancer	Polynuclear hydrocarbons	Smoking of foods
1775	Scrotal cancer	Polynuclears	Chimney soot
1775	Cardiac stimulant	Digitalis	'Dropsy' medicine
1880	Silicosis	Crystalline silica	Quartz mining
1890	Abortions	Ergot	Cereal grain infested with <i>Claviceps purpurea</i>
1900	Heavy metal poisoning	Lead ^a , chromium, etc.	Pottery and pewter cooking utensils
1900	Cancer	'Radium' paints	Watch and clock dials
1910	Selenium poisoning	Selenium compounds	The first systemic insecticides
1920	Skin cancer	Ultraviolet radiation	Sunlight
1925	Thallium poisoning	Thallium acetate	Depilatory cream
1930	Goiter, optic nerve damage	DN-compounds	Weight-reducing agents
1930	Barium poisoning	Barium salts	Some cosmetics
1930	Nervous Tissue destruction	Triorthocresyl phosphate	Jamaica ginger extract
1940	Liver cancer	Thiourea	Food preservative
1940	Bladder cancer	β -Naphthylamine	Aniline dyes
1950	Kidney poison	Lithium chloride	Salt substitute
1950	Lung cancer	Various carcinogens	Tobacco smoke
1950	Vitamin E antagonist	β -Phenylenediamine	Hair dyes
1960	Liver cancer	Safrole	Root beer flavour
1965	Chronic bronchitis	Various	Smog

^a The lead water pipes of the Romans undoubtedly contributed to the usually short lives and decreased fertility of the wealthy class in the cities.

securing something desirable, often overlooking possible undesirable side-effects and, also, often being incapable of anticipating some eventual side-effects because of lack of knowledge at the time. Some classical examples of this possible shortsightedness are the over-refinement of foods as in the milling of grains, Nobel and his hopes for dynamite, the aeroplane in warfare, lead compounds in gasoline, boron additives in some rocket fuels, elemental phosphorus in stick matches, the ionizing radiations from radium, mercury compounds in factory wastes, the internal combustion engine in areas of atmospheric inversion layers, the use of oleander and castor-bean plants as ornamentals, and many others. These and even more recent developments or practices have now focused more scientific attention on the environment as a whole, for it has become obvious that this massive infiltration of the total environment by foreign chemicals must be curtailed in its entirety, in some instances, and stopped altogether in others. This realization has arrived because the past hazards have been recognized, experiences of many previously unanticipated side effects have been assimilated, and scientific attention in this area has been simultaneously possible and available.

This sort of attention in agriculture has been strongly focused on pesticide chemicals, for they are required in large amounts wherever intensive agriculture is practised and they are usually chemicals that in small amounts are also toxic to mammals, amphibians, birds, and fish. Arsenic compounds were long used for codling moth control in deciduous fruit orchards, and after many years it was found that many orchard soils had accumulated enough arsenic to become phytotoxic. DDT, an organic chemical, inevitably replaced the arsenic insecticides because of greater efficiency and consequent requirement of fewer applications at lower dosages. Based upon existing knowledge at that time, it was felt that DDT falling upon the soil could not long survive the living soil environment, and that the extremely low solubility of DDT in water precluded its movement by leaching from the area of application. It has taken ten years of broad experience to demonstrate that both presumptions are only partial truths, but this recognition plus medical and pharmacological concern over the total body burden of DDT and other organochlorine compounds have resulted in increasing voluntary and sometimes government curtailment of the agricultural uses of the more persistent of these materials except in emergency pest-control situations.

The point behind these bits of the history of chemicals dispersing into environmental niches is that these possibilities are no longer ignored, but rather are anticipated as probabilities, and are quietly but systematically evaluated. Their occurrence, prevalence, mitigation, and curtailment to minimum standards, commensurate with probable hazard to any segment of the environment, are of great concern to responsible agencies and individuals, and are under aggressive investigation by more than enough qualified research groups. In fact, these interests and concerns are so well established now that some investigators are even guilty of seeking new niches and new possible contaminants to investigate. Information along these lines that has accumulated over the past 25 years clearly demonstrates that a very few pesticide chemicals (e.g., DDT, dieldrin) are major long-term contaminants of our total environment, and that several of them (e.g., endrin) are localized contaminants to the point of jurisprudential

interference with the production of certain root crops and of unquestioned interference with some of the local wildlife. As Gunther³ has stated, a "qualified (pesticide) residue analyst with proper equipment could find measurable DDT in any nonfossil sample presented to him, and with enough time and patience could find several other pesticides as well."

According to present indications, the need for chemical pest-control agents will continue in emergency situations in agricultural production, as their effects are sufficiently immediate and final to save a crop; other existing and postulated pest-control measures are slower in action (biological control, insect hormones, chemosterilants, chemical interruption of diapause) and more expensive (poisoned baits, attractants and repellents, radiation sterilization). Adequate non-chemical control of pest fungi does not seem to be a realistic possibility at present. It is certainly clear, however, that steady efforts will continue to be made to develop and refine any practicable method of non-chemical pest control to substitute wherever and whenever possible non-persistent pesticides for those established to be persistent, to 'rotate' pesticide chemicals in a local area when possible, to confine pesticide chemicals to the target areas, and to use the least persistent chemical when pesticide treatment is required. Unfortunately, for the foreseeable future, the economics of various effective pest-control measures available will usually dictate the treatment utilized, as with the continuing extensive use of dieldrin for grasshopper control on the cattle rangeland pampas areas of Argentina despite possible excessive residues of this versatile insecticide in the resulting beef.

LEGISLATIVE CONTROL OF PESTICIDE RESIDUES

Those countries that have enacted comprehensive pesticide residue legislation are listed in *Table 6* with a few typical tolerances to illustrate the

Table 6. Examples of countries with comprehensive legislation to control pesticides and their residues in foodstuffs, with selected illustrative tolerances.

Insecticide	Austria	Canada	Italy	Japan	The Netherlands	Germany	EEC ^a	U.S.A.	U.S.S.R.
Carbaryl	—	2.0	3.0	—	3.0	3.0	3.0	10	—
Chlordane	—	0.3	0.2	—	0.1	zero	0.1 ^b	0.3	zero
DDT	—	7.0	1.0	½ & 1	1.0	1.0	1.0	1.0	0.5
Malathion	—	4 & 8	3.0	—	3.0	0.5	—	8	8
Parathion	—	1.0	0.5	0.3	0.5	0.5	0.5	1.0	1.0 ^c
Dieldrin	zero	0.1	0.2	—	0.1	zero	0.1 ^b	0.05	zero
Lindane	—	10	2.0	0.5	2.0	2.0	2.0	10	—
Heptachlor	—	0.1	0.2	—	0.1	zero	0.1 ^b	zero	zero
Aldrin	zero	0.1	0.2	—	0.1	zero	0.1 ^b	0.05	zero
Rotenone	—	safe	—	—	—	0.04	—	safe	—

^a Proposed; about 35 tolerances will be adopted summer 1969, with 60 in 1970.

^b Individually or combined.

^c Including metabolites.

^d Some exceptions at 0.1 ppm.

still existing divergences of opinion among pharmacologists, toxicologists, and legislative bodies around the world. Many other countries are actively considering the establishment of this type of legislation, to control the 'residue quality' of their own agricultural production for both domestic consumption and for export purposes, to control imports of foodstuffs, and to assure the quality of foodstuffs in international trade. Among those countries

with some tolerance restrictions are Australia, Austria, Belgium, Canada, Denmark, England, Finland, France, Peru, Poland and Sweden; countries actively involved in establishing pesticide residue research and evaluation centres and in the outside training of qualified pesticide residue analysts include Argentina, Brazil, India, Norway, Spain, Thailand, the Philippines and the United Arab Republic. Those countries which have not initiated any activities in this area will be forced to do so by internal and international compulsion originating from individuals, agencies, and foodstuff distributors concerned with the maintenance of public health and also from the realization that pesticide residue tolerances could serve as very effective trade barriers. Numerous individuals have expressed fears that tolerances will sometimes be exploited as trade barriers; such a situation would indeed be deplorable, for the tolerance concept is based upon the best available scientific evidence of safety in use, and political prostitution of this concept would make a hollow mockery of the vast scientific effort underlying realistic tolerance values.

The imposition of these legally permitted amounts of pesticide residues in foodstuffs in any country implies market-control implementation of the legislation. In the absence of adequate governmental laboratories and residue analysts, recourse can be had to 'certificates of residue compliance' required of the producer or importer of the foodstuff, a situation requiring residue analyses of that particular lot somewhere between production and distribution to retail markets. Another recourse is to impose the often-used 'minimum intervals' required between application of the pesticide and harvest of the crop, on the philosophy that a few pilot analyses of crops from the local area, or that experiences and residue data accrued elsewhere, can be broadly applied to a particular pesticide and a particular crop in the local situation adequately to protect the consumer. In general, this 'minimum interval' concept is tenable and dependable, for it is based upon the time required after application for a pesticide deposit to attenuate or otherwise lose its original identity sufficiently to be well below the tolerance value for that pesticide chemical on and in that crop. A 'minimum interval' must accommodate the time required for the maximum initial deposit achievable under the extant 'good agricultural practice' to decrease to the desired level. Several countries utilize both tolerance and 'minimum interval' requirements, whereas some other countries currently utilize only the 'minimum interval' requirement, probably as an interim measure awaiting some sort of international agreement on tolerances for major-use pesticide chemicals on at least the major (basic food) crops (*Table 7*).

These alternate recourses to establishing compliance with tolerances are not a satisfactory permanent substitute for governmental-sponsored monitoring and surveillance programmes to assure continuing protection of the public health from possible over-tolerance amounts of pesticide residues in foodstuffs. Even though it is internationally generally agreed by toxicologists and pharmacologists that all tolerance levels should incorporate elaborate safety factors (as much as 100 times in some instances), the variety of pesticide chemicals in daily use, the fact that a given pesticide may appear as a residue in a number of prepared foods, the ever-present possibilities of pesticide-pesticide or pesticide-drug interactions, and the possibly exaggerated

PESTICIDE RESIDUES IN THE TOTAL ENVIRONMENT

Table 7. Examples of legislative control of pesticide residues in foodstuffs
 [updated from Gunther and Ott (1966)¹⁰]

Country	Residue control programme	Timing restrictions	Sources of residue data
Australia	State jurisdiction ^a	Optional ^b	State
Austria	Federal law	Occasional ^c	State
Belgium	Regulated by decree ^a	Regulated	State, institutes
Brazil	State jurisdiction	Occasional ^c	State, institutes
Canada ^d	Compulsory, comprehensive ^a	Regulated ^c	Applicant, state
Denmark	State jurisdiction	None	Ministry of Agriculture
Finland	State jurisdiction	Occasional ^c	State
France	Restricted by decree ^a	Regulated ^b	State, universities
Great Britain	Voluntary, new chemicals	Regulated ^b	Government chemists
Greece	Compulsory ^a (olives, citrus)	Regulated	State, institutes
India	State jurisdiction	Optional ^b	State
Indonesia	State jurisdiction	Occasional ^c	State
Israel	State jurisdiction	Regulated	State, institutes
Italy	Compulsory, comprehensive ^e	Regulated	Provinces
Japan	Compulsory, partial ^f	Regulated	State
Lebanon	State jurisdiction ^a , ^b	Occasional ^c	Institute
New Zealand	Regulated by law	Regulated	State
Norway	Partial ^a , ^b	Probable ^g	Institutes
Peru	Partial ^a , ^b	Probable ^g	State
Poland	Compulsory	Regulated	State, industries
Spain	Partial ^a , ^b	Probable ^g	Institutes
Sweden	State jurisdiction ^g	Regulated ^c	State
Switzerland	Regulated ^a , ^b	Regulated ^c	Cantons
Thailand	Partial ^a , ^b	Probable ^g	Institutes
The Netherlands	Comprehensive	Regulated	State, institutes
The Philippines	Partial ^a , ^b	Probable ^g	Institutes
Turkey	Government advisors	Occasional ^c	State
United Arab Republic	Comprehensive	Probable ^g	Ministry of Agriculture
United States ^h	Compulsory, comprehensive	Regulated	Various
U.S.S.R.	Compulsory, comprehensive	Regulated	National Commission
W. Germany	Comprehensive	Probable ^g	States, institutes, industry

^a Certain materials prohibited.

^b Extensive revision anticipated or in progress.

^c Not by statute, but minimum interval is often recommended on the label.

^d Tolerances for aldrin, dieldrin, and heptachlor revoked.

^e P. de Pietri-Tonelli¹³.

^f Fukunaga and Tsukano¹⁴.

^g DDT prohibited after 1 January 1970.

^h Several tolerances in the organochlorine group recently revised downwards.

responses to pesticides of the very young, of the very old, and of those other individuals on special diets, dictate the wisdom of adhering rather closely to scientifically established tolerances.

In the United States, about 50,000 samples of harvested crops have been analyzed by state and federal agencies for pesticide residues each year for several years, with the conclusion that only about 2.5% of both our domestic and our imported foodstuffs bear illegal residues, and these are usually only 'slightly illegal'. Among other requirements, realistic tolerances that will permit the continuing safe use of pesticide chemicals must be based upon the maximum amounts of the parent chemicals (or sometimes including major toxic metabolites or other *in situ* alteration products) that could persist to harvest (or sometimes sale) resulting from the biologically-established 'good agricultural practice'. On an international basis, just what constitutes

'good agricultural practice' for a particular crop is somewhat controversial, for different countries and even different growing areas within one country may have different pests and pest-complexes, cultural practices, meteorological conditions during growth of the crop, pesticide application equipment and techniques, and other factors which preclude the internationally uniform establishment of pesticide type required, timing, formulation, dosage manner of application, and minimum intervals before harvest. Also, in so countries many commodities are commercially washed, brushed, trimmed, or otherwise cleansed of dirt and exterior blemishes and decay before entering trade channels, and these practices will often substantially reduce a total residue on and in the freshly harvested commodity. Nonetheless, in most instances it should be possible by scientific arbitration among the biologists, toxicologists, and pharmacologists involved to arrive at a 'tolerance range' that would bracket the maximum, safe residues that could occur from the numerous 'good agricultural practices' around the world. Conceivably, this range could be either large or small, according to many biologists. If small, there is no problem; if too large, compromises in the 'good agricultural practices' that resulted in generally agreed unsafe residues would be indicated.

Despite much argument to the contrary, these same considerations should be applicable to the so-called basic foods such as milk, wheat, rice, potatoes, yams, and maize. Since any one of these basic foods may comprise the major part of the total diet of a large number of people, it has been felt that adequate protection of these people arises only from the lowest possible tolerance for a particular pesticide-chemical necessary in the production of that crop, whereas higher tolerances could safely apply when that crop represents a lesser proportion of the diet. This argument is scientifically tenable only if there are enough residue data to support it in terms of establishment of the proposed international 'tolerance range', and will be further weakened by the present wholesome trend to less persistent pesticides in all of agriculture and to the continuing development of alternate choices of pesticide chemicals for a given emergency pest infestation.

On the other hand, enforcing recommended 'good agricultural practices' is difficult except through the tolerance mechanism, with seizure of crops bearing illegal residues. To be effective, this mechanism implies that there must be seizures, that these seizures must be publicized and that the violators of 'good agricultural practice' must be penalized into conformity. The adequate promotion of the intent of tolerance restrictions is not met by waiting for this penalty approach to become fully effective, however. It is also clear from experiences in the United States and some other countries that detailed application instructions and warnings on the pesticide container are not always followed by the applicator or farmer. Obviously these labels cannot be completely comprehensive nor can they be technically adequate, but rather must be designed for the level of a lay education in specialized crops production. Pesticide container labels can and generally do admonish following certain dosage, timing, and coverage restrictions but cannot include sufficient details to indicate how deviations from these details might affect ultimate residue loads. In addition, the applicator (especially if he is the farmer) is rarely informed of the significance of harvest-time residues or how

they might be affected by dosages, timing, adjuvants, weather, and the other parameters that affect magnitudes of persisting residues; he is concerned about adequate pest control, and in the face of a possible lost crop he may be inclined to overtreat unless he is somehow made to realize the probable equally serious economic consequences of illegal residues from overtreatment.

Regulating actual uses of pesticides represents a complex problem. Direct approaches are to impose licensing and registration restrictions for quality and labelling, and to license applicators on a renewable basis. The indirect approach is represented by the tolerance concept, with seizure and destruction of the shipment the normal penalty for violations, rather than the imposition of criminal penalties. This indirect approach obviously provides only a partial deterrent to the improper use of pesticides in agriculture, for it involves completely voluntary compliance by the user. Too often the user is poorly informed and thus unable to make a reasoned judgment of proper use in unusual circumstances; also, it is not always possible to anticipate drift to adjoining agricultural areas and biota. Strong, enforceable restrictions on merchandizing pesticides may therefore be necessary for this essential effective tolerance compliance in any country.

Probably the most realistic assurance of the continuing conformity of foodstuffs to tolerance requirements is through both private and governmental residue monitoring and surveillance programmes, although the latter can easily assume gigantic proportions. These two quality assurance programmes for foods and feeds have been defined as follows⁴:

Surveillance programme—to assure legal safety of the item with guided selection of marketed samples (or just harvested samples). Samples are selected based upon suspicion they may contain residues of illegally used pesticides or above-tolerance residues of particular permitted pesticide chemicals.

Monitoring programme—to assure legal safety of the item with random selection of marketed samples (or just harvested samples). Samples are objectively selected with no suspicion factor, and perhaps with several possible pesticide chemicals in mind. This programme is often called 'food control', 'market control', or 'compliance programme'.

Since there are available today about 1,000 registered pesticide chemicals and more than 2,500 commercially standard food items, the resulting number of analytically conceivable combinations would appear to represent an impossible situation. Several factors reduce this situation to statistical practicability.

In the United States, for example, the latest available⁹ agricultural-use figures are for 1964 and indicate that 12 insecticides accounted for 85% of the total volume of all agricultural insecticides, that DDT and toxaphene accounted for 46% of this total, and that 67% of this total was applied to cotton, corn, and apples; similarly, 12 herbicides accounted for 85% of the total volume of all agricultural herbicides and half of this total was applied to corn, wheat, and cotton acreages; among the agricultural fungicides, the inorganic materials (mostly sulphur) accounted for nearly 86% of the total volume used in 1964. These leading pesticides are listed in *Table 8*. These figures clearly indicate that 12 organic insecticides, 10 organic herbicides, and 3 types of organic fungicides would be those pesticides most commonly

Table 8. Leading agricultural pesticides in the United States in 1964 according to volume consumption by the farmer⁹

Insecticides		Herbicides		Fungicides	
Active ingredient	Total use (× 1,000 lb)	Active ingredient	Total use (× 1,000 lb)	Active ingredient	Total use (× 1,000 lb)
Toxaphene	38,911	2,4-D compounds	34,454	Sulphur ^a	136,823
DDT	33,543	Atrazine	10,899	Dithiocarbamates	12,814
Carbaryl	14,946	Borax	4,828	Copper salts ^a	6,715
Aldrin	11,146	Calcium cyanamide	3,906	Phthalimides	5,840
Methyl parathion	9,985	Propanil	3,852	Zinc salts ^a	1,294
Parathion	6,426	CDAA	3,665	Quinones	1,044
Malathion	4,768	2,3,6-TBA	2,215	Others ^a	5,549
TDE (DDD)	3,387	Dalapon	2,062		
Strobane	2,715	2,4,5-T	1,655		
Diazinon	2,310	MCPA	1,516		
Azinphos methyl	2,273	Amiben	1,212		
Endrin	2,169	Diuron	1,124		

^a May include uses other than as a fungicide.

encountered among any residues present in the foodstuff. The U.S. Food and Drug Administration² lists in order the 10 most commonly encountered residues as in *Table 9*; it is not clear why this table contains only organochlorine insecticides and only five out of the six organochlorine compounds listed under 'insecticides' in *Table 8*.

Table 9. Most commonly encountered pesticide residues in domestic and imported foodstuffs²

Domestic samples	Import samples
DDT	DDT
DDE	DDE
Dieldrin	Dieldrin
TDE (DDD)	TDE (DDD)
Heptachlor epoxide	BHC
Lindane	Lindane
BHC	Aldrin
Endrin	Keithane
Aldrin	Heptachlor epoxide
Toxaphene	Endrin

Furthermore, any practising economic entomologist, horticulturist, or plant pathologist should be able to advise the residue analyst which few of the total number of commercially available pesticides would probably have been used in the production of the crop, especially if the growing area and season were known. If neither of these rationales is pertinent to a particular sample, the latter specialists could certainly eliminate all but a few candidate residue analytical targets. The oft-used pathetic argument that 'we must look for everything in all commodities' is therefore scientifically untenable. On the other hand, the periodic so-called 'market basket surveys' ('total diet surveys') of the U.S. Food and Drug Administration do present a complex residue analytical problem in that the constituent 82 food items from each of five regions of this country are pureed into 12 classes of similar foods for ultimate analytical aliquots, thus losing their identities as crop

PESTICIDE RESIDUES IN THE TOTAL ENVIRONMENT

items and thus incorporating into the mixture probable pest-control treatments from many production areas within one or more regions; advice from agriculturalists, plus years of experience in encountering residues in both surveillance and monitoring programmes, plus unusual public health interest in only a few chemicals, plus certain restrictive residue analytical capabilities, have resulted in the following alphabetical list of pesticide chemicals sought in these very informative and expectedly encouraging surveys²:

Aldrin	Kelthane
BHC	Lindane
Bulan	Malathion
Chlorbenside	Methoxychlor
Chlorobenzilate	Methyl parathion
Chlordane	Ovex
Chlorthion	Parathion
CIPC	PCNB
2,4-D esters and ethers	Perthane and olefin
Dacthal	Prolan
DDE	Ronnel
DDT isomers	Strobane
Diazinon	2,4,5-T esters
Dichloran	TCNB
Dieldrin	TDE
Dilan	Tedion
Dyrene	Telodrin
Endrin	Tetraiodoethylene
Ethion	Thimet
EPN	Thiodan I
Folpet	Toxaphene
Heptachlor	Trithon
Heptachlor epoxide	Vegadex
Hexachlorobenzene	

Certain additional pesticides such as a few carbamates and some of the 2,4-D type compounds are looked for only occasionally because of limited analytical resources.

Another factor reducing this analytical impossibility to practicability is that there are comparatively few major food items in the 12 classes comprising the average diet; for example, the U.S. Food and Drug Administration has concluded that 82 food and drink items are sufficient to be typical of the four major regions in the United States and will include considerations of economic status as well¹. It is obvious that exotic and luxury foods need not require the frequent residue analytical attention accorded those more standard items of daily diet and especially those consumed in quantity by any dietary group.

ENFORCEMENT OF TOLERANCES

As mentioned in the preceding section, the long-term enforcement of pesticide residue tolerances is undoubtedly best conducted through government-sponsored periodic residue analyses of foods, rather than by means of 'certificates of conformity to residue requirements'. Both of these enforcement devices may place ultimate responsibility for illegal residues upon either the farmer or the applicator, if different; the average farmer can hardly be expected to be thoroughly informed on the many field factors that influence the magnitudes of harvest residues, yet licensed applicators must be

knowledgable in this area if they are to continue to provide satisfactory pest-control while still meeting the imposed limitations of natures and amounts of residues permitted on and in the crop. Occasional violations of 'good agricultural practice' will occur in any event, and it is these occasional illegal residues that by law must be kept off the market; as stated earlier, about 2.5% of the more than 125,000 crop samples officially analyzed in the United States over the past five years was found to exceed legal tolerances or other administrative guides for excessive residues.

If governmental agencies conduct these residue analyses, there is the strong probability that the sampling and analytical methods used will be more uniform and standardized in important details from government laboratory to government laboratory than would be likely among the very large number of private and industrial laboratories that would otherwise be involved. Nonetheless, in the United States several producing and processing segments of the food industry have commendably established their own pesticide residue 'quality assurance' programmes not only to assure continuing safe pesticide residues in their products but also to permit the useful establishment and maintenance of changing pesticide residue patterns within their areas of supply, for particular pest-control problems are often highly localized and seasonal. Some of these food processors will not purchase crops without analytical assurances that any residues present are below permitted tolerance levels, whereas others rely largely on accurate and detailed pest-control records, maintained by the grower, to assure compliance with 'good agricultural practice' and thus very practical compliance with tolerance restrictions, as discussed earlier.

To be effective and reliable, any residue surveillance or monitoring analytical programme must meet a number of very stringent requirements, with emphasis on suitably rapid accumulation of final residue data to stop the shipment or sale of the commodity:

Sampling. Someone must decide what constitutes adequately sized and reproducible samples of each commodity and how to select them to represent the mean residue burden in the lot, the probable maximum residue burden in the lot, or the range of residues present in the lot; depending upon the pesticide present, the major location of the residue on or in parts of the commodity, and the unit size of the commodity, at least duplicate samples are always required for the present purposes. Similarly, it must be decided where to sample in the production scheme of the commodity, as in the field at harvest, after any packing-house operations normally involved, or in the wholesale or retail markets. These decisions must be defensible.

Preparation of sample for analysis. Someone must decide whether the sample units are to be washed (and if so, how?), trimmed, brushed, seeded, freed of any decayed parts, etc. In the United States, tolerances are based by law upon the raw agricultural commodity as shipped, and the U.S. Food and Drug Administration¹⁰ directs "Remove only obviously decomposed leaves, berries, etc. Do not wash (except root crops should be rinsed free of adhering soil), cull, strip, or otherwise use procedures which might be used in preparing the food for consumption". Some obviously required exemptions by regulation have been established, however, such as removing shells from nuts, caps from strawberries, stems from melons, crowns from pineapple, and

extraneous material from garlic cloves. In this connection, it must be remembered that in this country most raw agricultural commodities are processed in packing houses before being packed for entry into market channels. Depending upon the commodity, this processing may include brushing (carrots, potatoes, etc.); dusting (dates), washing (apples, pears, etc.), washing and waxing or oiling (citrus fruits, cucumbers, etc.), partial trimming (cabbages, celery, etc.), and other treatments. Some commodities are packed without being treated in any of these ways (melons, tomatoes, etc.).

Storage of samples. Even frozen samples should not be stored longer than 30 days without analytical proof that the sought chemical does not undergo storage alteration under such conditions. Frozen storage in glass or plastic containers often causes sweating, with possible consequent transfer of some of the sought chemical to the walls of the container.

Processing of samples. Acceptably rapid processing procedures for transferring the sought chemical(s) from the analytical aliquot of the parent sample into a suitable solvent may vary markedly from crop to crop and from chemical to chemical. Probably the nearest approach to a universal solvent for this purpose (except for dry products) is acetonitrile, but there are many exceptions in the voluminous literature on this broad subject. Sample 'extracts' should be cleaned up and analyzed as promptly as possible unless proof of non-deterioration during this storage is available.

Cleanup. This literature is also voluminous, but the well-known Mills procedure and its several modifications are nearly generally applicable for most pesticide chemicals destined for further gas chromatographic segregation and estimation. For surveillance and monitoring purposes, a single reasonably rapid, basic type of cleanup adequate for the determinative technique(s) is almost mandatory.

The analysis. Again, suitably rapid methods are legion, depending upon desired accuracy, reliability, reproducibility, and minimum detectability. Besides establishing these parameters, someone must also decide if the residue analyst should look only for the parent compound or also for certain metabolites or other alteration products, and at what levels. Samples clearly below tolerance maxima are presumably of no further interest, but samples at or above tolerance levels should be examined further with an independent back-up or buttressing method, for a claim of illegal residues may represent a large loss to grower or shipper and result in a lawsuit. Back-up residue analytical methods generally need not be rapid ones, but they must be as specific and as reliable as possible and defensible in a courtroom. By consensus among many residue authorities around the world, the following limits of accuracy for most of these analyses seem to be realistic:

$$\begin{aligned}
 10 \text{ ppm} &\pm 10\% \\
 1 \text{ ppm} &\pm 10\% \\
 0.1 \text{ ppm} &\pm 20\% \\
 0.01 \text{ ppm} &\pm 50\% \\
 0.001 \text{ ppm} &\pm 100\%
 \end{aligned}$$

Some authorities feel the last value should be $\pm 200\%$.

Multiple residue methods. In principle, these methods¹⁵ utilize a single 'extraction' (this usage of this word is incorrect for it implies quantitative transfer

of the desired solute from substrate to solvent) and a single laboratory cleanup, followed by gas or thin-layer chromatography for final segregation of sought compounds before apparent identification and quantitative measurement. Multiple methods extant for most organochlorine pesticides and few organophosphorus pesticides utilize partitioning from acetonitrile or isopropyl alcohol-hexane as preliminary cleanup, followed by gas chromatographic segregation and detection by both electron-capture and thermionic or other more specific detectors. Thus, in a few hours about 60 pesticides (including some metabolites) can be recognized, measured, and reasonably characterized in the extractives from a large variety of foodstuffs. For adequacy of results, however, these multiple residue methods must be supervised closely by a qualified and experienced residue analyst, for available procedures and supplies (e.g., the Florisil in the Mills procedure) are not yet standardized for completely consistent results without elaborate internal standards and other guides to establish aberrant behaviour in the total method.

Gas chromatography and thin-layer chromatography are excellent mutually buttressing techniques in those instances where unusual care must be taken to assure illegality of residues present. For maximum reliability, each should be applied to separate aliquots of the parent 'extract' after suitable and different preliminary cleanup (if required) because analytical results depend upon the total method from sample to readout. With a standardized 'extraction' and preliminary cleanup and partial segregation as in the Mills procedure, however, both can realistically be applied to aliquots of the Mills procedure fractions to achieve support of the final segregative and determinative technique. Proper gas chromatography accomplishes both operations, whereas thin-layer chromatography can also achieve excellent segregation but must be followed by other quantitation, as by gas chromatography, polarography, spectroscopic behaviour, etc. It should also be borne in mind that the gas chromatographic detector only reports the degree and maintenance of segregation achieved and amplitude of stimulus received¹².

AUTOMATED RESIDUE ANALYSES

These programmes involve the routine analysis of large numbers of the same or different types of samples of foodstuffs for a variety of pesticides, or 'screening' in this usage. There are at least three types of screening¹²:

Segregative screening—separating above-tolerance (or other sought parameter) from below-tolerance samples, with an acceptable quantitative latitude, as discussed earlier, and with usually only one sought pesticide in mind.

Constituent screening—detecting a variety of sought pesticides in the samples, with previously established limits of minimum detectability.

Quantitative screening—determining or otherwise adequately establishing the amounts of sought pesticides present in the samples, again with previously established limits of detectability but also with previously established reliability and reproducibility.

With sharply increasing emphasis around the world on pesticide chemical tolerances and the consequent necessity to analyze, on a continuing basis,

large numbers of samples of foodstuffs for tolerance conformity, it has belatedly been realized in many countries that there is an acute shortage of trained residue analysts; to be of any value whatsoever all of these analyses are necessarily complex and demanding and require the direct attention of qualified and experienced residue analysts, even with the multiple residue methods. It is clear, then, that routine screening procedures to demonstrate the tolerance-level 'presence' or 'absence' of groups or categories of pesticide chemicals will become increasingly important everywhere¹⁶. Thus, with a tolerance as an analytical target value, partially or totally automated screening would partition a set of samples into those comfortably below tolerance *vs.* those at or above tolerance, within the acceptable deviation guidelines presented earlier; the available expert attention could then be directed to those few percent of the samples requiring close and careful scrutiny for enforcement action. The inherent advantages of reliability, reproducibility, and speed of the automated analytical system are essential to the successful production of adequate numbers of routine residue analyses in these escalating international residue monitoring and surveillance programmes⁶.

The available pesticide chemicals may be loosely categorized into sometimes overlapping groups according to their contents of elements other than carbon, hydrogen, and oxygen:

Antimony	Mercury
Arsenic	Nitrogen
Bromine	Phosphorus
Chlorine	Sulphur
Copper	Tin
Lead	Zinc
Manganese	

Most pesticide residues occur in marketed foodstuffs within the range 0.01 to 10 ppm. Totally automated residue analyses are not yet directly adaptable to the lower ranges, yet there are possible some immediate applications to the present problem for tolerances ranging from about 0.2 to 100 ppm. For example, screening operations of the types described could be considered trifacially: analyses for characteristic elements, analyses for characteristic functional groups or moieties, and analyses for certain achievable types of biological activity. With the current exception of nitrogen, the elements listed above could be determined in organic and inorganic pesticide residues in automated assemblies of unit-operation modules in the above approximate range. Functional group analyses merely await automation, as for aldehyde, ketone, phenol, trichloromethyl, etc., moieties in the same range. Achievable automated measurements of biological activities of interest here would include cholinesterase activities before and after oxidation of any thionophosphates present to phosphates (oxons), with minimum detectabilities below 0.1 ppm.

In addition, automated combinations of modules are capable of performing almost any laboratory operation, excluding centrifugation; they may be likened to unit processes, as distillation, hydrolysis, steam distillation, evaporation (concentration), dialysis, extraction, partition distribution, homogenization, and others. Determinative automated modules include visible colorimetry, ultraviolet spectrometry, fluorometry, polarography, coulometry, flame photometry, and others.

Where minimum detectability requirements are not too severe, totally automated procedures are achievable, starting with 10 to 30 g of foodstuff or soil sample carried through automated modules to chart record. In other instances, automated procedures could be used to homogenize and 'extract' samples, then clean them up and present them as concentrates for manual or automatic injection into a gas chromatograph. In still other instances, split-stream techniques could be used to determine on a single sample such useful parameters as total organic chloride, phosphorus, and sulphur values and their ratios, plus cholinesterase activity both before and after mild oxidation.

In the pesticide residue field, several examples of these three basic types of automated analyses, as well as direct applications of isolated unit-operation techniques, have already appeared in the literature.

References

- 1 J. G. Cummings. *Pesticides in the total diet. Residue Rev.* **16**, 30 (1966).
- 2 R. E. Duggan and K. Dawson. *Pesticides—A report on residues in food. NAC News Pest. Rev.* **25**(6), 3 (1967).
- 3 F. A. Gunther. *Advances in analytical detection of pesticides*. In: *Scientific Aspects of Pest Control*, pp. 284-285. Nat. Acad. of Sci.-Nat. Res. Council, publ. No. 1402, Washington, D.C. (1966).
- 4 F. A. Gunther. *Insecticide residues in California citrus fruits and products. Residue Rev.* **28**, 1 (1969).
- 5 F. A. Gunther and L. R. Jeppson. *Modern Insecticides and World Food Production*. Chapman and Hall, London (1960).
- 6 F. A. Gunther and D. E. Ott. *Automated pesticide residue analysis and screening. Residue Rev.* **14**, 12 (1966).
- 7 W. Perkow. *Die Insektizide*. Alfred Hüthig Verlag, Heidelberg (1956).
- 8 A. Stefferud (editor). *Insects, The Yearbook of Agriculture*. U.S. Superintendent of Documents, Washington, D.C. (1952).
- 9 U.S. Dep. of Agriculture. *Pesticide Rev.* Washington, D.C. (1968).
- 10 U.S. Food and Drug Administration. *Pesticide Analytical Manual*, periodically revised. Washington, D.C. (1968).
- 11 W. E. Westlake and F. A. Gunther. *Occurrence and mode of introduction of pesticides in the environment. Adv. Chem. Series* **60**, 110 (1966).
- 12 W. E. Westlake and F. A. Gunther. *Advances in gas chromatographic detectors illustrated from applications to pesticide residue evaluations. Residue Rev.* **18**, 175 (1967).
- 13 P. de Pietri-Tonelli. *The regulation of pesticides in Italy. Residue Rev.* **27**, 1 (1969).
- 14 K. Fukunaga and Y. Tsukano. *Pesticide Regulations and residue problems in Japan. Residue Rev.* **26**, 1 (1969).
- 15 J. A. Burke. *Development of the Food and Drug Administration's method of analysis for multiple residues of organochlorine pesticides in foods and feeds. Residue Rev.* **34**, (in press) (1970).
- 16 U.S. Dept. of Health, Education and Welfare. *Report of Secretary's Commission on Pesticides and their relationship to environmental health* p. 174. Washington, D.C. (Dec. 1969).