The Role of Epidemiology in Modern Phytopathology

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I gratefully acknowledge the manyfold suggestions and critical comments made by colleagues and students at the Laboratory of Phytopathology.

I am very thankful to the technical and secretarial staff who have assisted me in many ways, working at times under high pressure.

Scholars gather in scholarly assemblages to hear in elegant statement what all have heard before. Yet it is not a negligible rite, for its purpose is not to convey knowledge, but to beatify learning and the learned.—J. K. Galbraith: The Affluent Society, 1958.

As a matter of fact all epidemiology, concerned as it is with the variation of disease from time to time or from place to place, *must* be considered mathematically, however many variables are implicated, if it is to be considered scientifically at all.—R. Ross: The Prevention of Malaria, 1911.

1. *What is modern in phytopathology?*.—

Phytopathology came of age towards the end of the 19th century (Orlob, 1964; Whetzel, 1918), and graduated as a specialized science around 1900, when the early phytopathological societies and journals were founded: e.g., The Netherlands Phytopathological Society in 1891 and The American Phytopathological Society in 1908. The development of phytopathology was so gradual that the beginning of a 'modern' phytopathology, another zero hour, cannot easily be found in any specific event within phytopathology, but rather has to be sought for in events moving science and society in general.

One such event is the rising of the 'critical generation' in the sixties, which voiced its opinions loudly in contrast to the 'silent generation' of the fifties. Criticism on social systems, and sneering at the affluent society with its pollution problems were negative symptoms, the emergence of the 'ecology drive' was a positive one (Mok and Westerdiep, 1974). Student revolts spread like an epidemic all over the world in the years 1964 to 1969. But The Food and Agriculture Organization of the UN, an establishment institution in the eyes of the criticasters, embarked upon a highly 'relevant' study of crop losses in 1967 (F.A.O., 1967). Horsfall (1969) addressed the membership of The American Phytopathological Society in a banquet speech at Spokane, 1969, and summarized the change in attitudes in one ominous sentence: 'basic science is dead'.

What is the criterion for 'modern' in phytopathology, or in any science? The answer is twofold. (i) There must be a change in the attitude of scientists towards their science. (ii) There must be a new paradigm, a new set of concepts, definitions, and examples (Kuhn, 1970). The criterion will be tested in the realm of phytopathology.

2. *Levels of integration*.—

The sciences work different levels of integration, which go from the subatomic to the atomic, molecular, cellular, individual, and population level. Biology is a well differentiated science at all levels of integration. To explain and predict a phenomenon at any one level, the next lower level should be known (De Wit, 1968). Unfortunately, one individual scientist masters usually two, or at best three integration levels.

Phytopathology, representing only a small segment of biology, comprises all levels of integration, but these have not yet been differentiated so sharply. Actually, there are only two main groups of phytopathologists, which as groups have little in common because of differences in training, research techniques, and scientific outlook. One group works mainly at the cellular level; the other group works largely at the population level. The two groups meet at the level of common interest, the intact plant, which is the end point for the former and the starting point for the latter group.

The phytopathologists of the latter group I want to call epidemiologists, whether they study soil-borne root-invading, or airborne shoot-invading, organisms (Zadoks, 1972a). This to avoid a common misconception that only students of foliar diseases should be called epidemiologists. Later, arguments will be given for the lumping together of the two sub-groups that separate whenever they can, even here at this congress.

3. *Epidemiology and ecology*.—

The foregoing characterized people but not their subject: epidemiologists, but no epidemiology. Epidemiology is a section through the life sciences that singles out 'disease in populations' (Van der Plank, 1963). In this sense, the word 'epidemic' was used for the first time by Hippocrates (Jones, 1972), over two thousand years ago.

Epidemiology has a medical, veterinary, and botanical branch (Zadoks, 1967a). The medical and veterinary branches study disease in populations, whether it is infectious or not (MacMahon and Pugh, 1970). The distinction is hardly relevant: cholera is caused by an infectious agent, but this was not known during the early investigations in the city of London leading to a remedy. The epidemiology of cancer is well developed, though conclusive evidence for an infectious agent is still not available. There is an epidemiology of coronary disease, psychiatric affections (Tsung-Yi Lin and Standley, 1962), nutritional disorders, and air pollution-induced illnesses (Lawther *et al.*, 1962; Van der Lende, 1969), though there are no infectious agents.

The botanical branch of epidemiology has restricted itself traditionally to diseases caused by infectious agents (lastly: Van der Plank, 1963). But this is only a matter of convention, and not always a useful one, as in the case of chemical air pollutants and airborne spores, both subject to the same rules of aerobiology, or the case where nutritional disorder makes the crop more susceptible to infectious disease.

In a wider perspective, epidemiology can be seen as a form of applied ecology (Oort, 1971; Weltzien, 1971). Classical phytopathology was just that, applied ecology, though it has never been called so. Ecology has several facets, among which autecology, synecology, and population dynamics. Autecology studies the relation between a species and the physicochemical aspects of its environment. Many phytopathologists diverged in autecological studies of the pathogen, but more rewarding is the autecology of disease, that close association of two organisms resulting in something new for which Loegering (1972) coined the word 'aegricorpus', or 'sickbody'. The autecological approach was quite productive and yielded scores of disease warning systems.

The synecological approach contains great promise. It looks at disease as the result of an interaction between at least two populations: those of the plant host and of the pathogen. Usually, the effect of a third population, that of man, must be considered. Often, additional populations are involved: those of the vector(s) and the reservoir(s) (Zadoks, 1967a). More and more it is realized that populations of antagonists, competitors and predators can interfere with that of the pathogen. Reconsidering the distinction between the root and the shoot pathologists, it must be admitted that, apart from differences in techniques, the root pathologists mainly used a synecological approach whereas the shoot pathologists largely used an autecological approach to disease. This difference of emphasis, due to considerations of quantity rather than of quality, seems to be a temporary one.

The third facet of ecology is populations dynamics. It describes the growth and decline of populations in quantitative terms. The malaria specialist Ross stated in 1911, that "As a matter of fact, all epidemiology, concerned as it is with the variation of disease from time to time or from place to place, *must* be considered mathematically, however many variables are implicated, if it is to be considered scientifically at all." Thus, he fired the starting shot for mathematical epidemiology in medicine. The break-through in botanical epidemiology was brought about by Van der Plank (1963), when he published his famous book on "Plant diseases, epidemics and control." When computer simulation models came forth in 1968 (Waggoner, 1968; Zadoks, 1968), the system was extended to numerical integration of autecological and synecological aspects of disease. Simulation models can handle about 10 times as many variables as differential models, thus fulfilling the requirements of Sir Ronald Ross (Waggoner and Horsfall, 1969; Waggoner *et al.*, 1972; Zadoks, 1971; Zadoks and Rijsdijk, 1973).

4. *Fashions in phytopathology.*—

New tools, of which the computer is but one, change the face of phytopathology. The developments in organic chemistry after World War I, culminating in the use of sulphonamides as chemotherapeutants in medicine around 1935, channeled phytopathological thinking into new beddings. After World War II, biochemistry spread its wings. New technology led to rapid advances, as illustrated by the example of ethanol. In a hundred years the time needed to determine the structure of good old alcohol has been reduced by a hundredfold (Den Hertog, 1967). Phytopathologists turned to biochemistry, where they expected to find the 'stone of wisdom'. Alas, such a stone does not exist, but the experience gained in the search is a valuable treasure.

Neither the glitter of technology nor the glamor of basic science fully explain the height of the biochemical wave in phytopathology. The research funding system was out of balance, at least in the U.S.A., where science is largely funded by agencies spending grants. The scientist in receipt of grant has to repay: by means of publications. His success is in part measured by the number of his publications. In the biochemical approach to phytopathology, the equipment was turned to speed, the field was new, a vacuum had to be filled, and great numbers of new findings (and publications) streamed forth. The productivity blinded the gate-keepers, who did not escape the charm of biochemistry as a basic or fundamental contributor to phytopathology. Do not blame them; the field was ripe for exploitation (Weinberg, 1963).

The situation in Europe was less extreme, partly because of the system of government funding through existing institutions (Mok and Westerdiep, *in press*). Epidemiological research was continued on a modest scale, but the American pattern of preferences within phytopathology could hardly be avoided. In this context it is noteworthy, that in the U.S.A. epidemiology was mainly government-funded: by the U.S. Department of Agriculture and the U.S. Army. Much epidemiological information was distributed by the government-issued Plant Disease Reporter.

Technological developments have added new zest to epidemiology. The level of sophistication was stepped-up by the application of growth cabinets, electronic data collection equipment, remote sensing techniques, and computers. It is gradually realized that the collateral sciences of greatest use to epidemiology are physics and mathematics, not chemistry (Zadoks, 1963). In addition, the social merit (Weinberg, 1963), in present-day terminology the relevance of epidemiology is reappraised. A recent revival of interest in epidemiology took place in several European countries. The tide of fashion is turning. A combination of some gadget-appeal and much social motivation now leads many fresh and eager minds to epidemiology.

There are, however, serious impediments. The subject of epidemiology is the epidemic, and an epidemic roughly has the duration of a growing season. The research effort may be fruitless because no epidemic appears. Often, a large body of data has to be collected and studied, at a low level of automation, with a high investment of labor. Consequently, the annual number of publications to be expected from the epidemiologist is low. This case is extreme, but illustrates the point: the evaluation system of scientists has to be changed in order to be fair.

5. *Monocyclic and polycyclic studies.*—

The progress of science is determined by two concurrent thought processes, analysis and synthesis. This pair of contrasting processes is of paramount importance (Zadoks, 1972b), because many epidemics are built up of a large number of consecutive and identical infection cycles.

Most epidemiological studies examine phenomena occurring within the time span of one infection cycle: they are essentially monocyclic studies (Zadoks, 1972c). Such studies are easy to perform, but they have little merit unless they help to explain and predict phenomena at the next higher integration level, the epidemic as a whole.

Easygoingness, and the 'publish or perish' mentality, generated scores of irrelevant publications recording what could be measured easiest. Analysis at the monocyclic level is a necessity, but it seems that there is a large amount of ill-directed effort (compare: Weltzien, 1971).

Until recently, there was no quantitative method of knitting the small pieces produced by analysis at the monocyclic level together into a series of consecutive or overlapping infection cycles, resulting in a picture of the epidemic as a complete unit. This process is synthesis at the polycyclic level. Computer simulation techniques provided the long-awaited tool. The polycyclic, synthetic approach adds depth and relevance to analytical studies at the monocyclic level. It is no longer the available instrumentation which dictates what is to be measured and at what accuracy, but the needs of the simulator as seen from the viewpoint of systems analysis. The epidemiological relevance of any single element, and *a fortiori* the measuring accuracy needed, can be assessed by sensitivity tests (Smith, 1970), within the limits of predetermined constraints. It is a matter of prudence to state that the tool described has not yet been sharpened. Here lies a challenge for the present generation of students in epidemiology.

The polycyclic approach leads epidemiology to its real subject: to the epidemic as the unit of study, which has a beginning, a climax, and an end. As Gaumann (1951) indicated, every epidemic has a character of its own; it is an individual different from other individuals. Simulation models can demonstrate the individuality of epidemics *ad oculos* (Zadoks and Rijsdijk, *in press*).

6. *The epidemiology of change.—*

Epidemics by any cause sometimes come in groups of successive years, and then they can be a symptom of some basic change in agriculture. The nature of the change can be manyfold, e.g. (i) gradual improvement, (ii) intensification, and (iii) irrigation.

Gradual improvement is so much part of our life, that we hardly recognize it as change. Gradual improvement leads to slow but steady growth of yields. There is no single specific factor responsible for this growth, but in retrospect one specific factor can be held responsible for one specific type of damage. The recent epidemics of southern corn leaf blight in the U.S.A., caused by *Helminthosporium maydis*, have opened our eyes for one such factor, genetic uniformity leading to genetic vulnerability (APS, Committe on Epidemiology, 1972). In Europe, the increasing use of chlormequat (Cycocel®, Chloroethyltrimethyl-ammonium chloride) for the improvement of straw stiffness in winter wheat, which permits higher dosages of N fertilizer, is said to lead to more severe epidemics of glume blotch caused by *Septoria nodorum* (Dilz, 1971). In tropical countries, gradual improvement started later but proceeded faster. In rice, the poor man's disease was *Helminthosporium oryzae*; when tillage, water control, cultivars, and fertilization improved, the rich man's disease, *Pyricularia oryzae*, took over. If there is a general rule for the change in the types of epidemics during gradual improvement, it might be this: 'weak parasites yield to perthotrophics, and perthotrophics yield to biotrophics'.

Intensification of agriculture takes two major forms: (i) loss of rotation, and (ii) year-round cultivation. A shortening of the crop rotation period takes place in northwest Europe as a result of specialization on the farm, which is at present an economic imperative. The barley-beef system in Great Britain led to continuous cropping of spring barley. One result was a period of severe *Rhynchosporium secalis* epidemics. In northwest Europe, where winter wheat predominates over spring wheat, the classical eye-spot disease caused by *Cercosporella herpotrichoides* and the Fusarium foot rots are on the increase due to shortening of the rotation period, and the increasing concern with *Septoria nodorum* (which is certainly in part a matter of fashion) may be also related to increasing severity due to the same causes.

Year-round cropping is another form of intensification which can lead to severe epidemics. A recent east-Europen example is that of *Phytophthora infestans* on tomatoes. In the traditional field crops, this disease was of little importance. From 1965 onward, programs were launched for the building of glasshouses to grow autumn and spring crops under glass. As soon as tomatoes were grown all the year round, later blight became a major problem (Turkensteen, 1973). The pattern repeated itself in three countries: Rumania, Bulgaria, and Hungary. Similar patterns are known in other crops, e.g. *Puccinia horiana* of chrysanthemum (Zadoks, 1967b).

The introduction of irrigation is a decisive change, with profound influence on epidemiology. The crop is not only more luxuriant, but also cooler, so that even downy mildews can thrive in semi-arid areas. The effect of irrigation has been thoroughly studied by an Israeli group (Rotem, *et al.*, 1971). But also yellow stripe rust and powdery mildew on wheat can be favoured by irrigation, and possibly the various Septoria diseases of wheat.

The lesson to be drawn from this short and incomplete survey of change in agriculture is, that change often is accompanied by an unexpected set of epidemics lasting during a series of years, until agriculture has built up its defences. This phenomenon will be called the 'polyetic epidemic' (*το ϵτοζ* = year). A 'polyetic epidemic' is an abstraction; and the complexity of its causation is accordingly. It may be a matter of availability of inoculum (*Rhynchosporium* on barley, *Septoria* on wheat, *Phytophthora* on tomatoes) a change in the general weather pattern (*Helminthosporium* on maize, *Fusarium* on wheat), an artificial change in microclimate by irrigation, or just the appearance of a new pathogen or physiologic race. One constraint is the presence of genetic vulnerability, sometimes in a perverse form, as with *Phytophthora* in tomatoes that could become severe only where spraying against *Cladosporium fulvum* stopped after the introduction of *Cladosporium*-resistant cultivars.

The problem of the polyetic epidemic is actual because of the great changes in the agriculture of the third world. It is, in Waggoner's words, 'the green revolution's second generation problem'. Can polyetic epidemics be predicted? The answer is: not yet. We are engaged in model studies to assess regional or climatic risks, including the carry-over of inoculum, as an introduction to polyetic studies. There is no ready-made methodology for experimental research in polyetic epidemics, except perhaps in the case of some soil-borne diseases. A systematic historical analysis of known cases could provide a good starting point.

7. *Uniform, differential, and environmental crop protection.*—

Notwithstanding occasional or even polyetic failures, crops are protected rather adequately by genetical, chemical, or environmental means.

Genetical protection by means of the manipulation of genes for resistance, influences the course of epidemics and of epidemiology. In the Stakmannian era, the emphasis was on what is now called differential or vertical protection; today, breeders all over the world are searching for uniform or horizontal protection (Van der Plank, 1963; 1969).

The epidemiological approach to the study of uniform resistance is the 'components analysis' (Zadoks, 1972d), in which uniform resistance is split up in measurable units that fit into epidemiological theory. But epidemiological theory can also contribute to the knowledge of differential protection: in tomatoes, a new gene for differential resistance against *Phytophthora infestans* was recently discovered by analyzing the inheritance of disease progress curves (Turkensteen, 1973).

The concepts of uniform and differential protection are also applicable, in a metaphoric way, to chemical protection. Heavy metal salts and dithiocarbamates are protectants effective against a large number of pathogens. Their generalized protoplasmic toxicity gives them a broad action spectrum, and causes not more than a mild selection pressure for resistant strains of the fungi (Dekker, 1972). This is uniform (or horizontal) chemical protection. In contrast, the effect of systemic fungicides with their highly specific biochemical modes of action could well be called differential (or vertical) chemical protection. Some systemics happen to exert a strong selection pressure on fungal populations, just like differential genes for resistance do.

Physiologic races appear with differential resistance to chemicals, the old story in a new form. Whereas, in the past we studied the epidemiology of single physiologic races with differential virulence to resistance genes, we shall soon start to investigate the epidemiology of single physiologic races with differential resistance to systemic fungicides (Dekker, 1972). This has already been attempted for benomyl-resistant cucumber mildew (Kooistra *et al.*, 1972). I want to push the comparison one step further. The appearance of resistance in some fungi against 'uniform' fungicides may contain a warning that the physiologic races can appear with uniform virulence against the presently highly desired uniform resistance of the host plant. Nilsson's (1969) findings on *Ophiobolus graminis* could be interpreted in this sense.

The situation, in which uniform and differential resistance occur together in one host plant (Van der Plank, 1963), has been called two-dimensional (Zadoks, 1972c) protection. Two-dimensional protection can also be given by fungicides. The simple way is just mixing a uniform and a differential fungicide. A far more subtle way seems to exist. The benomyl molecule has no fungicidal effect in compounds. One is MBC (methyl-2-benzimidazole carbamate), the active differential chemical; the other is or can be butylamine (Hammerschlag and Sisler, 1973), that has a phytoalexogenic effect (Reilly and Larman, 1972), and thus conditions uniform protection.

In genetical crop protection there has been a trend towards high selection pressure for differential genes, with such neglect for uniform genes, that the selection pressure for these genes was negative. The phenomenon has been named the "Vertifolia effect" (Van der Plank, 1963). In chemical crop protection there is a comparable situation. To understand this, the concept of environmental resistance should be introduced. It is known among entomologists, who encountered difficulties in introducing a foreign insect into a new environment. Medical bacteriologists experimented with the recolonization of the digestive tract of mice by various orally introduced bacteria (Van der Waaij *et al.*, 1971); they found and measured recolonization resistance. Recolonization resistance is well known in pasteurized soils, and again can be expressed in a measure (Evans, 1955).

Recolonization resistance is only a specific phenomenon of a more generalized environmental resistance, an old experience with respect to soil-borne pathogens. New examples of environmental resistance have been found after the introduction of systemic fungicides. In the Netherlands, cyclamen was spray-treated with benomyl against *Botrytis cinerea*; after a short period of good control, disease severity increased. A benomyl-resistant physiologic race of *B. cinerea* had been selected, which was no longer antagonized by the benomyl-suppressed microflora of the petioles (Bollen and Scholten, 1971). Final proof came when a benomyl-resistant physiologic race of *Penicillium brevicompactum* came to the fore, which was highly antagonistic to *Botrytis*, and partly restored the environmental resistance (Van Dommelen and Bollen, 1973). Systemic fungicides can interfere with populations and their interactions in many ways. Soaking of cucumber seeds in diazouracil changed the subsequent rhizosphere flora, giving protection to *Pythium debaryanum* (Stankova-Opocenska and Dekker, 1970). Leaf treatment of rye with benomyl changed the rhizosphere flora with a subsequent change in disease pattern (Van der Hoeven and Bollen, 1972). The interference can go so far as to cause new epidemics, like the catastrophic epidemic of *Penicillium corymbiferum* on bulbs of lilies during storage after treatment with benomyl (Rattink and Beuzenberg, 1972).

I emphasized the point of environmental resistance, not because of its newness, but because of its interest. Its most intriguing aspect is its normality, its ever-presence, in the phyllosphere (Leben, 1965; Sinha and Kapooria, 1966) as well as in the rhizosphere. Environmental protection is gradually opening itself to the techniques of systems analysis, with its relation diagrams, and the quantification of the relations therein. Finally, artifical enhancement of rudimentary environmental protection comes into reach as a new field of research, with the possibility of biological control of fungal diseases far away in the perspective.

8. *Epitome.*—

Let us reconsider what epidemiology contributes to modern phytopathology, the paradigms and the attitudes. The paradigms are a system of concepts, relations, and integrators, embedded in a unifying philosophy, and presented by way of example rather than in an explicit statement.

A. A set of basic concepts leads to unambiguous working definitions, to expression in simple physical dimensions, to counting and measurement; in short: to quantification.

B. A set of relations between these concepts and environmental data leads to the quantification of their interactions.

(1) Some relations are obvious and well-known, those with weather data;

(2) Other relations are being studied presently, those with resistance data;

(3) Some relations are coming into focus just now, those with chemical control data;

(4) Other relations are in a phase of conceptualization preceding actual modeling and measurement, those with biotic data.

C. A set of mathematical techniques integrates concepts and relations over time into polycyclic and maybe even into polyetic pictures: regression analysis, calculus, analog and digital simulation.

D. A unifying philosophy, of which this paper is only a preliminary study, welds together hitherto unrelated areas, like etiology, genetical protection, chemical protection, and environmental protection in one system of concepts, relations, and integrators, in short: one scientific language.

The attitudes also change. There is a unifying viewpoint: ecology, aiming at pest management rather than pest control (Symp. Agric. Board, 1972). There is a unifying purpose: the strategy of crop protection (Butt, 1972). And there is a unifying motivation, rooted in a revival of interest in professional ethics (De Wilde, 1968).

A group of plant pathology students in Wageningen, The Netherlands, studied ethics (and not content) until they arrived at operational terms, and developed a Code of Honor for plant pathologists (Anonymous, 1969). These students followed in the steps of Hippocrates and Targioni. Hippocrates, the godly doctor, our earliest colleague, was not only interested in epidemics but also in ethics. In our days, physicians still swear the 'Hippocratic oath' before being licensed. Giovanni Targioni-Tozzetti, and idealistic botanist, can be regarded as the first 'modern' botanical epidemiologist. He published his studies on the epidemiology of wheat rusts in 1767, as a 'means of rendering less serious the dearth, proposed for the relief of the poor'.

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PHYTOPATHOLOGY for June (64:765-906) was issued 12 June 1974.