Nematode-Trapping Fungi

An intriguing group of carnivorous plants inhabit the microbial world.

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Journalistic jargon includes the familiar maxim that when a dog bites a man no one is particularly interested, but when a man bites a dog, that is news. Similarly, no one is impressed when an animal eats a plant, but when a plant devours an animal, the event is a newsworthy reversal of what, from our viewpoint, is the usual condition in nature.

Green plants meet their requirements for organic matter through photosynthesis. However, there are some plants which, though green and capable of manufacturing their own food, have leaves that are fashioned to function as traps for capturing insects and other animals. Many lurid tales have been written of unwary travelers (without exception in some remote tropical jungle) who fall prey to carnivorous plants. The woman-eating species portrayed in Fig. 1 is an artist's imaginative summation of the climactic moment common to all such stories. Fortunately, small frogs are the largest animals caught by carnivorous plants, but this limitation in size of prey detracts little from the fascination of the phenomenon of predation. The ability of the pitcher plant, the sundew, and the Venus flytrap to capture insects is known to many. They are the subject of numerous popular and technical publications, including the botanical classic *The Carnivorous Plants*, by Lloyd (*1*). Of less renown, but of equal if not greater interest and importance, are the carnivores of the microbial world. The microbiologists' menagerie contains many bizarre forms of life that are ignored or, at best, regarded as curiosities by all but a few interested specialists. This has been the fate of certain fungi which are taxonomically distinct but are ecologically a natural group, united by their adaptation to the predaceous habit. These remarkable microorganisms are able to capture, kill, and consume animals of microscopic dimension. Their prey includes amoebas, rotiferans, nematodes, and springtails (*2*). This article is concerned only with those organisms that are known collectively as nematode-trapping fungi.

Fungi are filamentous plants that lack chlorophyll and develop as fine threads or hyphae. These elongate, branch, and may fuse to eventually produce a mycelium, as the network of hyphae is collectively termed. Individual hyphae that comprise a mycelium vary from 3 to 10 microns in diameter. Nematodes are ubiquitous wormlike animals. Those that live in soil average 0.1 to 1.0 millimeter in length. They are very active creatures that move sinuously. Since some nematodes are animal parasites (like those that cause trichinosis) and others are important agents of destruction of ornamental and crop plants, one should not favor the prey (the nematode) rather than the predator (the fungus) in this struggle for survival. Nematode-trapping fungi and insectivorous plants have many attributes in common, but only the fungi are "giant-killers," greatly exceeded in size by their prey. In this regard Duddington has stated (*3*), "It must be remembered that nematodes are, for their size, powerful and enormously active; they move from place to place by means of rapid threshing of their bodies, so that a vigorous specimen will cross the vision field of a microscope with the ferocious speed of a conger eel on the deck of a trawler. To capture such an animal is no mean task for a fungus that is itself composed of threads so delicate that the finest gossamer would by comparison be as a steel hawser is to a piece of string, and the means by which this is accomplished by the predaceous fungi are as extraordinary as they are efficient."

Nematode-trapping fungi are not a recent discovery. *Arthrobotrys oligospora* was described initially by Fresenius in 1852 (*4*), and in 1870 Woronin reported that the organism forms networks of hyphal slings or loops (*5*). However, the purpose served by these networks remained unknown until 1880, when Zopf (*6*) became the first to observe a fungus trap a living animal. Other workers observed this phenomenon, but there were few important additions to our knowledge of nematode-trapping fungi until 1937, when the American mycologist Drechsler published a monumental paper (*7*) that not only corrected and extended earlier accounts but also established 11 new species. It is with Drechsler's name that predaceous fungi will forever be associated; however, in recent years the torch has passed to others. The individual who has held it most high is Duddington, a prolific and talented author (*2, 3, 8*) interested in biological control.

More than 50 species of fungi that prey on nematodes are known today, and undoubtedly many others remain to be unearthed and described. Such fungi are not at all difficult to isolate. One need only place a quantity of partially decomposed organic material on the surface of a dilute medium such as cornmeal agar and observe with the microscope the sequence of organisms that develops when the preparation is incubated at 25°C. There will be growth of bacteria, and many of the common fungi will be recognizable, but their numbers will be limited by the low nutrient level of the medium. Nematodes present in the inoculum will multiply, and, eventually, fungi which prey on nematodes may be observed. Pure cultures of the fungi are obtained most readily by micromanipulation of spores. Some nematode-trapping fungi are Phycomycetes, at least one is a Basidiomycete (*9*), and many are Deuteromycetes of the order Moniliales (*8*). The genera most commonly represented are *Arthrobotrys, Dactylaria, Dactylella,* and *Trichothecium.* The cell walls of

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these fungi are chitinous (*10*), and the structures they produce for the capture of prey are remarkable. They vary greatly in design and detail, but they trap nematodes by either adhesion or occlusion.

Morphology and Morphogenesis

Some fungi capture nematodes through adhesion to virtually undifferentiated hyphae, but many fungi have for this purpose specialized organelles that include networks of adhesive branches or bails, stalked adhesive knobs, nonconstricting rings, and constricting rings.

Adhesive networks are produced by hyphal branching. In some species, networks are simple and consist mainly of short branches which fuse occasionally. In others there is considerable anastomosis to form a three-dimensional system of bails or loops that are coated with a mucilage and capture nematodes on contact by adhesion and entanglement. Certain species form one-celled sticky processes, and others produce spherical knobs on short stalks. These knobs, which have been referred to as "lethal lollipops," are also coated and capture nematodes by adhesion. There are a number of species in which the hyphal branches curl, fold, and fuse to produce clusters of rings or loops. The surfaces of these specialized hyphae are in all cases coated with an adhesive, and the fate of a nematode which in the course of its wanderings makes contact with such a surface is similar to that of a fly on flypaper.

Some organelles of capture function mechanically. They are usually fashioned from three curved cells which join to form a closed ring at the end of a short stalk. No adhesive is involved. Entrapment can be passive, in that a nematode that enters a ring and attempts to force its way through becomes firmly wedged and unable to escape. The nonconstricting ring acts somewhat like a rubber band looped tightly around one's finger. When an attempt is made to withdraw the finger, the rubber band grips tenaciously, restricting movement and escape. A number of species of nematode-trapping fungi produce constricting rings. These rings appear to be the most highly developed and in some aspects the most remarkable organelle of capture. Constricting rings are active rather than passive. When a nematode enters, the ring cells swell to approximately three times their normal size, obliterating the opening and constricting the nematode so that it cannot escape. Ring closure requires approximately 0.1 second and appears to be a thigmotropic response, triggered when the nematode touches the inner surface of any cell of the ring.

Figure 2 shows organelles of capture and worm entrapment in representative fungus species. However, neither the written word nor the photographic plate can adequately reproduce either the beauty of morphological detail in specialized hyphae or the drama of the moment when prey encounters predator. Time-lapse cinephotomicrography (*11*) permits greater appreciation of the arrangement and adroitness of nematode-trapping fungi, but a view of living preparations remains unsurpassed.

The mucilage produced by nematode-trapping fungi is of unknown composition. No attempt has been made to isolate and identify it. Moreover, the mechanism of closure by the constricting ring remains obscure. Muller (*12*) demonstrated that the time required for inflation of ring cells can be increased from 0.1 second to 10 seconds if the process is activated in sucrose and the solution is diluted gradually. With this technique, ring closure was observed in slow motion, and visual evidence was obtained that a change in the structure of the fungus wall initiates inflation of cells that comprise the ring. It was postulated that this change causes a sudden decrease in wall pressure and an increase in the permeability of the cell membrane to water. The concentration of intracellular solutes increases, and, driven by a difference in osmotic potential, water enters the cell, causing elastic extension of the wall. With time, there is plastic flow (microfibrillar slip) of wall material from the lumen to the annular region of the ring, and the deformation of inflated cells is permanent. We are indeed indebted to Muller (*12*) for a lucid description of the sequence of events that culminate in ring closure and nematode capture. However, postulations are not to be confused with explanations, and much work remains to be done before we have a complete understanding of the way in which movement of a nematode across a fungal cell can induce the wall of the fungus to change structurally.

Fig. 1. An artist's imaginative drawing of a carnivorous plant. [By Isabelle Haller, from W. H. Muller, *Botany: A Functional Approach* (Macmillan, New York, 1963), reproduced with permission]

Whatever the species of nematode-trapping fungus and whatever the trapping mechanism involved, the fate of the nematode is the same. It struggles for a time and then appears dead or moribund. Its surface is penetrated (*13*), and fungus hyphae ramify throughout the carcass and digest and absorb its content. Under favorable conditions nematodes may be captured in large numbers, especially by those fungi that form adhesive networks of hyphal loops. The actual cause of death of a trapped nematode is not certain. Death may be due to mechanical damage and to exhaustion during the struggle for liberty, but this is unlikely. The production by the fungus of a toxin (*14*) is a possibility that would better account for the observation that nematodes frequently are dead before their surface has been penetrated.

In spite of their remarkable morphological adaptation, nematode-trapping fungi are not obligate predators. They will grow as saprophytes, feeding on various complex organic substrates (as opposed to parasites, which require living tissue), and some species have been cultivated in chemically defined media (*15*). Of particular interest is the finding that in pure culture many of these fungi do not form traps. However, if nematodes are added to the culture there is hyphal differentiation and within 24 hours numerous organelles of capture are produced. This phenomenon is unique; the presence of prey *somehow* induces the predator to undergo morphological change essential to the predatory relationship. The fact that nematodes cause a change in the form of the fungus is intriguing and has been studied in our laboratory at Rutgers and in other laboratories. A detailed presentation of our progress in elucidating the biochemical basis of morphogenesis in the nematode-trapping fungus *Arthrobotrys conoides* was published recently (*16*). The work is not complete, and is, therefore, deserving of only cursory consideration.

The observation that some species of fungi do not form traps when grown in pure culture but do so in the presence of nematodes suggested that some morphogenic substance is produced by the worms. Evidence in support of this possibility (*17*) existed at the time my associates and I first became actively interested in these fungi, and it was established as fact

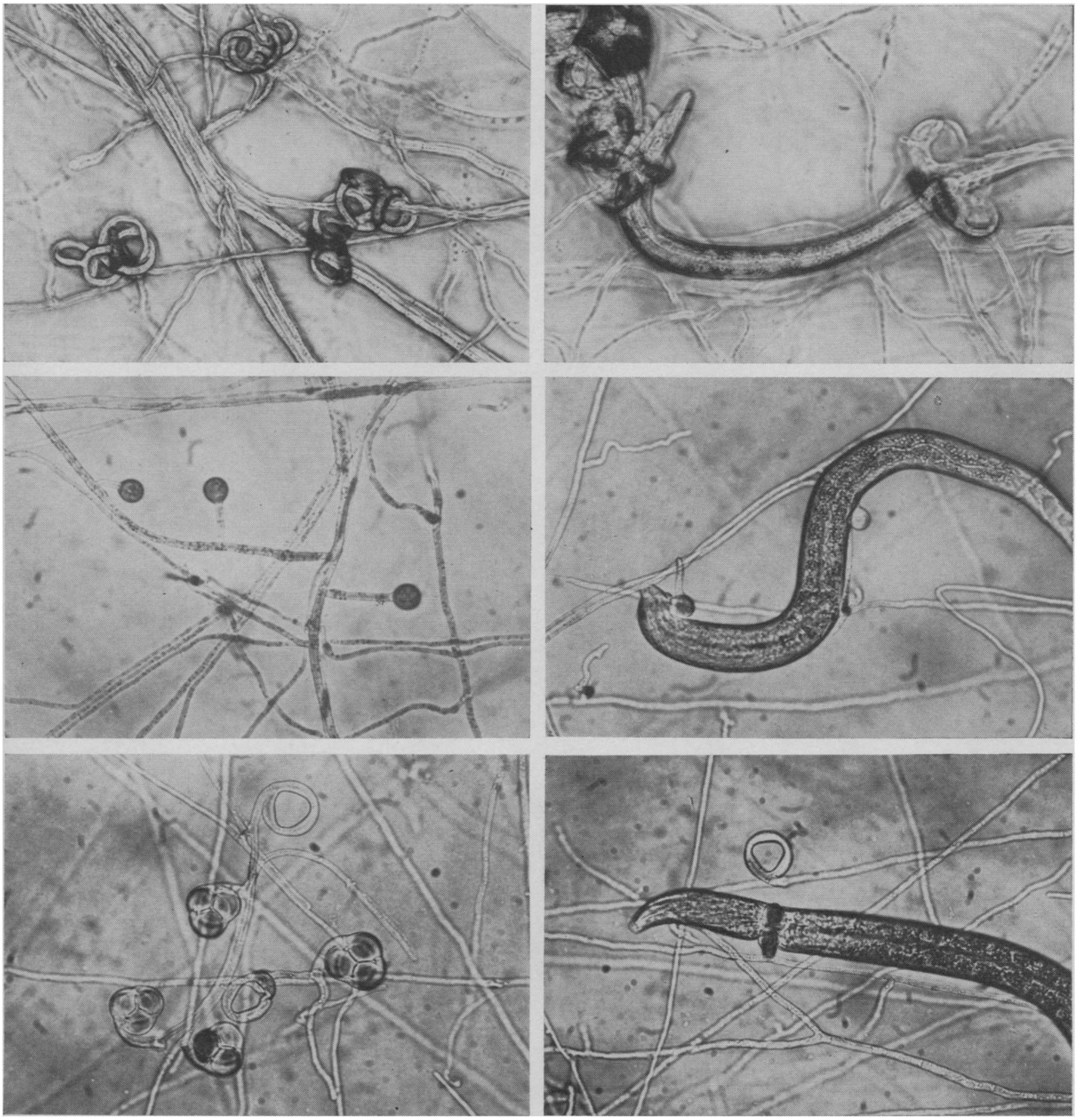

Fig. 2. (Top) *Arthrobotrys conoides* forms networks of hyphal loops (left) which are coated with a mucilage of unknown composition and which capture nematodes (right) by adhesion. (Middle) *Dactylella drechsleri* produces spherical knobs on short stalks (left). Knob surfaces are adhesive and trap nematodes (right) on contact. (Bottom) Constricting rings, as formed by *A. dactyloides*, appear to be the most highly developed organelles of capture. Each is composed of three cells (left). When a nematode enters the ring, the cells swell rapidly, obliterating the opening and gripping the worm so that it cannot escape (right); × 363.

when broth from a pure culture of the nematode *Neoaplectana glaseri* was demonstrated to induce trap formation by *Arthrobotrys conoides*. The substance causing morphogenesis in nematode-trapping fungi was designated "nemin" (*18*), and a program of research was initiated to determine its identity. Before we could proceed with purification it was necessary to develop a nemin assay and select a suitable starting material. The assay procedure employed is a simple dilution technique, based on a series of studies in which the influence of various environmental factors on growth and trap formation by the test organism, *A. conoides*, was evaluated (*19*). Ascarids were selected as starting material for chemical fractionation and isolation of nemin. These nematode worms are numerous and large, and they were collected in quantity from swine intestine at the time of slaughter.

Since the properties of nemin were completely unknown, numerous preliminary tests of a qualitative nature were performed, and it soon became apparent that we were dealing with a complex substance of high molecular weight rather than with a simple small molecule. The active principle was not extractable in any significant amount in organic solvents, and it was not dialyzable. Purified protein having nemin activity has been isolated from aqueous extracts of ascarids (*20*). One preparation that was examined in detail showed maximum absorption (A) in the ultraviolet region at 278 mμ ($E^{1\%} = 10.2$ at pH 7.3), and the ratio $A_{278\,\mathrm{m}\mu}/A_{260\,\mathrm{m}\mu}$ was 1.45. This preparation appeared homogeneous when examined by moving-boundary electrophoresis (in NaCl-phosphate buffer at pH 7.3, $I = 0.1$), by cellulose-acetate-film electrophoresis (at pH 4.0, 5.4, 7.3, and 8.6), and by disc and polyacrilamide-gel electrophoresis. The sedimentation coefficient ($s_{20,\,w}$) for a 1.0-percent solution of the preparation in 0.1M phosphate buffer (pH 7.3) was 1.92. Although the preparation sedimented as a single boundary, the ultracentrifugation pattern was polydisperse. Further purification has been attempted by means of anion-exchange chromatography (on diethylaminoethyl cellulose with gradients and eluents that differed in composition, concentration, and pH), preparative electrophoresis (with agar, starch, and polyacrylamide as supporting media), and electrophoresis on vertical columns (packed with ethanol-treated cellulose). We have had some success, but an unforeseen hindrance to progress is the regrettable fact that ascarid proteins induce allergy in the chemist as well as morphogenesis in nematode-trapping fungi. The preparations we are now studying appear to contain at least three components; these are yet to be separated and tested for biological activity.

Feder, Everard, and Wootton (*21*) demonstrated that nematode-trapping fungi do not respond uniformly to nemin. Different concentrations of an active extract of the worm *Panagrellus redivivus* were required to evoke morphogenesis in four different species of *Dactylella*. Each of the four species appeared to have a characteristic sensitivity or reactivity threshold, and nemin was likened to the semispecific organizers which induce differentiation in the embryo of vertebrates. It was recently observed (*22*) that the nemin activity of purified ascarid proteins remained unchanged when treated with pepsin, but if enzymatic hydrolysis was followed by dialysis, the digest was then incapable of inducing morphogenesis. Some, but not all, of the original activity was displayed by the dialyzed portion—a finding which indicates that the active principle (nemin) is liberated by enzymatic hydrolysis of protein and is capable of passage through cellophane film. An extensive survey established that nemin is not identical with any commercially available peptide or amino acid. In all, 62 peptides and 27 amino acids were examined empirically. Also tested were various blood fractions, animal hormones, and peptide antibiotics, but all lacked nemin activity. The identity of nemin is yet to be established.

Ecology and Exploitation

As it became increasingly evident that nematodes are destructive parasites, they began to receive the lion's share of the attention of agricultural scientists concerned with plant protection. Among the methods contrived to reduce economic losses due to nematode parasites were crop rotation, chemical treatment, and the use of resistant stock. Predaceous fungi were not ignored, and initial attempts to exploit their activity for the biological control of a nematode-caused disease were made just prior to World War II by Linford and his associates (*23*), working in Hawaii on root-knot of pineapple. In their first series of experiments, pure cultures of six different species of predaceous fungi were added to nematode-infested soil, but the fungi were apparently without effect, and no convincing evidence of a reduction in nematode damage to plants was obtained. However, a useful degree of control was achieved when soil was supplemented with organic matter (chopped green pineapple tops) rather than inoculated with fungi. In explanation of this effect it was suggested that incorporation into soil of green plant tissue provided saprophytic nematodes with food. Development of these nematodes promoted multiplication of nematode predators, including the predaceous fungi. Being indiscriminate in their taste, the fungi caught and consumed not only saprophytic nematodes but the root-knot organism as well, with the result that nematode damage to plants was lessened. In the course of these studies no evidence that control was attributable directly to nematode-trapping fungi was provided, but the food chain postulated by Linford and his colleagues (*23*) has on many occasions been erroneously cited as fact. The pioneering studies performed in Hawaii have been repeated, modified, and extended by various investigators throughout the world. Details of this work were summarized by Duddington (*8*) and need not be reconsidered here. It frequently lacked thoroughness, and the results were often indeterminate or inconclusive. Most experiments were variations on the original theme: pure cultures of predaceous fungi, organic matter, or both were incorporated into nematode-infested soil and the influence of treatment on the severity of a nematode-caused disease was evaluated. In general, addition of living fungus material alone was not effective. Irrespective of whether predaceous fungi had been added to the soils, were present naturally, or were absent, better crops were commonly, but not invariably (*24*), harvested from nematode-infested soils treated with organic materials. Moreover, damage to plants by the nematode parasites in such soils in laboratory or greenhouse trials, where conditions can be rigidly regulated, was less than the damage in field tests.

It is not surprising that inoculation

of soil with predaceous fungi failed to reduce nematode damage to cultivated crops. The potentialities of soil inoculation have not been completely explored; but, except in the case of seeds treated with legume bacteria and mycorrhizal fungi, the results of continuing studies, initiated early in the history of soil microbiology, provide no rational basis for expecting enhanced plant growth from the simple expedient of inoculating soil or seed. A beneficial effect appears all the more unlikely when the organism used as inoculum is a normal inhabitant of soil. In this regard Garrett has stated (*25*), "The population of most soils is a remarkably cosmopolitan one, and the absence or scarcity of a particular organism generally denotes that conditions in that particular soil are unfavorable for it, rather than that no attempts at colonization have been made, because of its restricted geographical distribution. Most attempts at soil inoculation have had a still smaller chance of success because the inoculant organisms had been isolated in the first place from soils in which it was desired to establish them at a higher population level. Such attempts to boost the population of an antagonistic organism by inoculation alone have been doomed to failure from their inception, because they are in flagrant contradiction to the ecological axiom that population is a reflection of the habitat, and that any change due to plant introduction without change of the habitat must be a transient one."

If predaceous fungi are to protect plants from nematode infection, they must grow and be active in the rhizosphere—the region where soil and roots make contact. Here there is an abundance of every type of microorganism, and populations are much greater than in root-free soil. This is true for all plants that have been examined, and there are qualitative and quantitative differences in the effects produced by different plants, as well as by the same plant at various stages of growth (*26, 27*). Microorganisms develop in the rhizosphere because food is available to them, and this comes from the plant. Nematode-trapping fungi can be isolated from the rhizosphere. Here prey is plentiful, but the influence of other organisms on the relationship between predator and prey is not known. If fungi are to be used for the control of nematode-caused diseases, it is not their presence but their growth and predaceous activity that must be encouraged. Organic matter may, in fact, provide such encouragement, but the effects of added organic matter on soil are legion, and activation of the food chain in favor of predaceous fungi has not yet been demonstrated experimentally. Biological control is intellectually attractive and it has popular appeal and support, but it is extremely difficult to achieve. The degree of success is frequently a direct function of available knowledge relating to the system under study. The biologist interested in using fungi for the control of plant-parasitic nematodes must base his efforts on reliable information about the prey, predator, and plant, acting individually and as an integrated unit.

The abundance of nematodes in a variety of habitats was described most vividly by Cobb (*28*): "In short, if all the matter in the universe except the nematodes were swept away, our world would still be dimly recognizable, and if, as disembodied spirits, we could then investigate it, we should find its mountains, hills, vales, rivers, lakes, and oceans represented by a film of nematodes. The location of towns would be decipherable, since for every massing of human beings there would be a corresponding massing of certain nematodes. Trees would still stand in ghostly rows representing our streets and highways. The location of the various plants and animals would still be decipherable, and, had we sufficient knowledge, in many cases even their species could be determined by an examination of their erstwhile nematode parasites." As compared to insects that are harmful to plants, nematode parasites that inhabit soil are small and lack sensory organization and mobility. They cannot locate their host over long distances, but this difficulty is overcome in any one or combination of three ways: (i) the nematode remains in a dormant or resting stage (encysted) until the host reappears; (ii) the nematode parasite does not subsist on a single species but can feed on a variety of plants; (iii) intimate association with host tissue assures that plant and parasite are dispersed as one (*29*). Although our present knowledge of the ecology and physiology of nematodes is fragmentary and at times contradictory, work in these areas is increasingly quantitative, and there is rapidly emerging an intelligible view of the interrelationships of the nematode and its environment (*30*).

Unfortunately, our knowledge of the ecology and physiology of predaceous fungi is meager. They develop readily from organic matter in contact with soil and undergoing decomposition, and they can always be isolated from manure, composted leaves, rotting wood, moss, and soil itself. However, there is no available method by which their numbers can be measured, and their abundance in these habitats is not known. Lack of a selective technique of enumeration is a formidable obstacle to ecological understanding. Until it is surmounted, no quantitative studies can be made of the influence of environmental variables on fungus growth and activity, and no conclusion is possible regarding a correlation between abundance and distribution of predator and prey in natural substrates. Of particular relevance in this regard are recent attempts by Cooke (*31*) to describe the response of saprophytic nematodes and predaceous fungi in soil when organic matter is added. The nematodes were counted directly, but the lack of an adequate method for enumerating the fungi made it necessary to evaluate their reactions by means of an "activity factor," derived from the numbers and types of organelles of capture that appeared on agar discs buried in treated and in untreated soil.

When chopped cabbage was added to soil, the fungal activity factor and the nematode count both rose sharply. Fungus activity reached a maximum in approximately 3 weeks, then declined, and was negligible at the end of an experimental period of approximately 6 weeks. At the termination of the test the nematode count was still high—higher, in fact, than it was when fungus activity was greatest. The addition of sucrose produced an increase in fungal activity that was more persistent than that caused by chopped cabbage, but the nematode population remained low, and it appeared that after sucrose decomposition reached a certain stage, the fungi ceased to trap nematodes. Cabbage tissue, but not sucrose, supported a large nematode population, yet the fungal activity factor was greater and less transient in sugar-treated soil than in soil supplemented with cabbage. An increase in concentration of organic matter caused a decrease in predaceous activity, despite a continued rise in numbers of nematodes. If, as these observations indicate, predator and prey are independent rather than affiliated variables, the concept of a food chain, as postulated by Linford and his associates (*23*), must be rejected, and an explanation of the beneficial effects of adding organic matter to nematode-infested soil must be sought elsewhere in the complex system of checks and counterchecks that tend to maintain a dynamic equilibrium among the vast and varied microbial populations of the rhizosphere. However, Cooke's activity factor (*31*) is more arbitrary and less quantitative than is desirable, and one cannot accept a lack of numerical relationship between nematode-trapping fungi and their prey as unequivocally established until it has been confirmed by additional tests, with new techniques of increased precision. It is of interest here to note Eren's (*32*) current evaluation of a fluorescent antibody staining technique (*33*) for the study of nematode-trapping fungi. Intravenous injection of *Arthrobotrys conoides* into rabbits elicited the production of antibodies, and when the gamma globulin fraction of serum harvested from sensitized animals was conjugated with fluorescein and used as a stain, there was a characteristic yellow-green fluorescence of the fungus. With this technique it was possible to identify and estimate the growth, on glass slides buried in soil, of *A. conoides* as it developed from spores in the presence of numerous other microorganisms. The specificity and quantitative aspects of the system appear promising as a means of investigating obscure microhabitats.

We know that predaceous fungi are able to capture and destroy nematodes in large number, but what is viewed in the laboratory cannot be construed as a faithful reflection of nature, and additional support is required for any conclusion regarding the ecological significance and usefulness of the phenomenon of predation. There is much to be done. First it is necessary to recognize, with Katznelson (*27*), that "soil is the habitat of an extremely complex microbiological community in which occur all the phenomena operative in the struggle for existence, and, as may be expected, by analogy with ecological events on a macroscale, certain groups and types of microorganisms eventually establish themselves as dominant forms in the community, and others are relegated to a subdominant level." The struggle for existence among the components of the soil population is intensified in the rhizosphere, but every grand design is simple when it is understood. The presence of large numbers of organisms in the rhizosphere is evidence that roots supply considerable quantities of organic matter. Many of the compounds excreted by roots are major organic nutrients, some are growth factors, and some are inhibitory substances. The localization of parasites is directed by host tissue, and there is evidence that the aggregation of nematodes in or on roots may be due to concentration gradients of compounds as simple as carbon dioxide (*34*) or ammonia (*35*). It is necessary that the amounts and kinds of compounds originating from roots be identified, and that conditions affecting their excretion be further explored. Moreover, our knowledge of the nutrition and physiology of predaceous fungi is fragmentary, and it must be expanded greatly. Growth and trap formation are prerequisites to nematode destruction, and this initial development must depend, not on predation, but, rather, on the ability of the fungi to compete saprophytically for organic nutrients and required minerals in the rhizosphere. Information must be gathered from numerous sources, in many different ways, until there is understanding of the influence of soil and rhizosphere populations, and of the effects of plant roots and soil properties on growth, trap formation, and nematode capture by predaceous fungi. With such understanding we can estimate the extent and direction of modification that is required if the rhizosphere environment is to be rendered amenable to a shift in the balance of power between prey and predator in nematode-infested soil. Unfortunately, we now lack much of the information that the strategist must have if he is to use predaceous fungi as armament in a successful attack. Empirical attempts at biological control will continue to be made, but the probability of conquering nematode parasites will be increased greatly if future operations are based on fundamental investigation and experimental fact.

Conclusion

An understanding of what was initially obscure has made possible rapid advances in many areas of human endeavor, and, in science, organisms endowed with a singular property have been frequently recognized as the key to a storehouse of information. Examples are legion; it is sufficient to recall that genetic studies of the "red bread mold," *Neurospora*, were exceedingly productive and moved biological research along a course that continues to be rewarding. Nematode-trapping fungi are unique among microorganisms, but few people have ever heard of them and still fewer have ever seen them. My present intent is to bring the nematode-trapping fungi to the attention of the scientific community and to emphasize the numerous opportunities they offer the interested investigator. Here truth is as strange as fiction. Possibly, under certain conditions, the activities of these fungi can be directed against nematode parasites that are of economic significance, but it must be recognized that this is not their sole value.

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New Problems for Surgery

Drugs that act on the cell nucleus affect the surgeon's work on cancer and on transplantation.

Francis D. Moore

Iselin, in his Newcomen Lecture "The Pathfinder of the Seas" (*1*), said:

> . . . no matter how pure the idealists among us try to keep science, there is little doubt that important advances frequently are achieved because someone realizes the practical applications that can be made of a particular course of study.

In biology, significant practical applications usually precede the completion of that "particular course of study" destined to elucidate the precise chemical or physiological mechanisms involved. The precise manner in which the digitalis leaf alters the irritability of the heart remains obscure despite 200 years of practice with clinical digitalization. A century of experience with ether anesthesia has failed to reveal to us the biochemistry of its action. Insulin therapy was used for 40 years before there was any satisfactory knowledge about its chemical structure or action. Today we are exploring the practical usefulness of drugs which affect the synthetic and mitotic activities of the cell nucleus. Although their practical usefulness is established beyond a doubt, it will increase as precise chemical and biological mechanisms are elucidated. Only then can the clinical investigator take advantage of the growing biochemical sophistication of his laboratory colleague.

It is no coincidence that the drugs used to treat cancer likewise interfere with the production of antibodies against transplanted tissues. But it is somewhat of a coincidence that the majority of patients who are treated with these drugs are under the care of surgeons. A hundred years ago the care of epithelial cancers (such as those of the esophagus, stomach, lung, rectum, bladder, kidney, breast, and thyroid) was shared by all doctors alike. There was very little compartmentalization or professional division. Indeed, very little could be done for the patient except to recognize the tumor and then to provide the simplest type of symptomatic treatment, analgesia, and compassion. This diffuse responsibility for the care of cancer changed to one of sharp focus by the rapid development of the techniques of sterile anesthetized tissue dissection, with blood transfusion and antibiotics, as a means for the total removal and thus the early cure of many malignant tumors. These events of the last 75 years have placed responsibility for the primary care of most cancers in adults squarely on the shoulders of the surgeon. He sees the patient first. If the tumor is early, he is the only person who has the golden opportunity to cure it—by removing it completely. In cases where that cannot be achieved, it remains the surgeon's responsibility to care for the patient through the long illness of recurrent and fatal malignancy. It is up to him to supervise or arrange for the other modalities of treatment, chiefly irradiation and chemotherapy.

In the field of tissue transplantation, responsibility is much more divided. Right from the start the surgeon shares his load with the physician who is expert in the management of the disease being treated by transplantation. Up to this time approximately 250 kidney transplantations have been done throughout the world; the kidney transplant, therefore, provides the model for this discussion, but the principles apply equally well to other tissues or organs. In the case of the kidney, it is the physician experienced in the study and care of patients with renal failure, renal hypertension, renal vascular disease, and degenerative cardiovascular processes who sees the patient first and helps to guide the surgeon in the preparation of the patient for operation and to assist in the management of the study and care of the patient during and after the operation.

For 75 years surgery has expanded by increasing the number of anatomical areas to which it can be successfully applied: the gut, the brain, the lungs,

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