unconjugated ferritin, or of inactive conjugates, and incomplete penetration into the depths of cells. Techniques whereby thin sections, suitable for electron microscopy, can be stained directly with antibody conjugates remain to be developed. In the methods hitherto used, antibody conjugates were applied to suspended cells or to thick sections; this was followed by preparation for electron microscopy. Singer demonstrated some encouraging results obtained by modifying current techniques for processing tissue and by use of a new embedding process.

That ferritin is particularly suitable for studies relating to uptake of proteins by cells was demonstrated by J. B. Caulfield (Harvard Medical School). He has studied the uptake of ferritin by Ehrlich ascites tumor cells in vitro. The ferritin molecule, roughly spherical and measuring about 120 Å in diameter when hydrated, is a globular protein. However, it contains 23-percent iron in the form of ferric hydroxide micelles, which, in electron micrographs, have a characteristic and specific appearance. These are situated in the centers of the molecules and can be considered as labels of the protein, apoferritin. Caulfield found that uptake of ferritin by cells can occur in two ways. In one of these, single ferritin molecules are adsorbed on the cell surface within 5 minutes, particularly when serum albumin or horse serum are present in the incubating media. Later there is invagination of the plasma membrane and eventually formation of pinocytic vesicles. Stages in the evolution of these vesicles into larger vacuoles were inferred from serial electron micrographs which also indicated that the macromolecules are eventually concentrated into a few intracellular compartments. The second form of uptake of ferritin molecules by the cells appears to be less specific; it is connected with adsorption on extracellular debris derived from dead cells. In regions of cell surfaces close to debris a wavy plasma membrane can frequently be seen, thus indicating considerable surface activity. Large numbers of ferritin molecules enmeshed in such debris are taken up by cells. Ingestion of such aggregates may be a response of the entire cell by involving large-scale modification of cell surface activity, and resembling phagocytosis. By contrast, uptake of single ferritin molecules involves quite localized modifications of the cell surface.

The importance of checking such qualitative findings against quantitative data obtained by other methods was pointed out by H. J. P. Ryser (Harvard Medical School). In collaborative work with Caulfield, Ryser studied uptake of I^{131} serum albumin by Ehrlich ascites tumor cells in suspensions in vitro. Recently, he has extended this work to include Sarcoma 180 cells, thus combining methods of isotope analysis with cell culture methods. The I^{131} serum albumin becomes fixed to the cells in two phases: an initial, rapid, temperature-independent adsorption and a subsequent slow fixation that increases linearly with time and that can be diminished by lowering the temperature of incubation. The nature of this second phase suggests uptake by means of pinocytosis. Control experiments indicated that biosynthetic incorporation of labeled I^{131} mono- or diiodotyrosine from the medium into cell protein was unlikely during the periods of observation. In both cell systems, uptake at 37°C was of the same order of magnitude, that is, 1.2 to 1.7 $\times$ 10^5 molecules per cell in 2 hours; these values are smaller than other reported estimates. Though probably insignificant as a source of nitrogen for the cell, the ingested protein may be important as a carrier of other substances.

G. W. Richter (Cornell University Medical College) presented observations on the quaternary structure of apoferritin and on the production of ferritin and apoferritin by two cell lines derived from human cancers and growing in vitro in defined media. Using modifications of the staining procedure with uranyl nitrate, he has found that the apoferritin shell of the ferritin molecule is composed of 20 equal subunits with diameters in the neighborhood of 20 Å, and situated at the vertexes of a regular dodecahedron. This is in agreement with recent chemical findings of British investigators.

Sequential changes in fine structure of HeLa and KB cells, associated with the production of apoferritin and ferritin during the first hours after administration of iron, were demonstrated. Both types of cells synthesize ferritin within 4 hours after administration of iron, and ferritin molecules are first encountered within discrete cytoplasmic organelles. While there are several kinds of such bodies, previously termed siderosomes, those which are seen within 4 hours after administration of iron appear to be associated with production of ferritin and may play a role in the insertion of iron hydroxide micelles into apoferritin shells. However, the final assembly of the apoferritin molecule, that is, construction of the dodecahedral shell, may also take place in these organelles.

Ferritin obtained post-mortem from livers or spleens of humans, horses, and rats was fractionated by disk electrophoresis in acrylamide gels to yield five fractions termed α-, β-, γ-, δ-, and ϵ- ferritins. Fractions from each species have characteristic electrophoretic mobilities. The fractions produced by HeLa cells differ from those obtained from human livers or spleens. Only an α-ferritin was obtained from KB cells and this had the same mobility as HeLa α-ferritin, thus differing from α-ferritin in human liver or spleen. That the fractions separated by electrophoresis are indeed ferritins was shown by electron microscopy but as yet no differences in their fine structure have been discerned, presumably because the electrophoretic determinants are too small to be revealed by methods now in use. In serological studies HeLa ferritin had the same specificity as ferritin from human liver or spleen, but KB ferritin lacked an antigenic determinant.

The discussion was led by G. Majno (Harvard Medical School). The proceedings of the symposium, which was supported by U.S. Public Health Service grant 2G313, will be published in *Laboratory Investigation*.

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Root Diseases Biologically Controlled

A first of its kind, an international symposium on factors determining the behavior of plant pathogens in soils, was held on the Berkeley campus of the University of California during the week, 7 to 13 April. A principal purpose of the symposium was to bring together investigators from divergent disciplines to focus attention upon the problems of biological control of root diseases. Representatives were invited from the fields of bacteriology, mycology, nematology, virology, soil science, entomology, zoology, anatomy, physiology, biochemistry, and ecology, in addition to plant pathology. Over 300 participants from 18 countries attended.

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Lively and continuing discussions took place as the delegates joined in the exploration of the highly involved interactions of plant roots, soil, saprophytic soil microorganisms, and plant pathogens. The ultimate objective of the symposium was the subjugation by biological means of soil-borne pathogenic viruses, bacteria, fungi, and nematodes. In essence, this was a search for new approaches and new ideas on how to attain control of such groups of soil-borne plant pathogens through biological techniques and an attempt to define the areas where additional research is most needed.

The underlying encouragement which motivated the symposium has come from instances of biological control which have proven successful and, more than this, sometimes spectacular. This has been especially true where chemical control has not been economically feasible and suitable resistant varieties of plants have not been available.

One of the oldest biological approaches to control disease on pathogen-infested land has been to resort to different crop successions or to turn under various green manure crops to allay damage from diseases anticipated in a succeeding crop. This technique has met with notable success in certain regions against specific diseases. For example, it is reported that phymatotrichum root rot of cotton in the Southwest is being successfully combated by disking into the soil an immature crop of peas in the spring, prior to planting cotton. Ophiobolus root rot ("take-all") of wheat may be controlled by rotating a crop of oats with the wheat.

In California streptomyces scab of potato is effectively kept in check where the crop is grown on the same land year after year by growing a crop of soybeans in the fall after the potato harvest and turning it under before the crop matures. Sclerotium rot of peanuts is prevented in the South by avoiding the presence of undecomposed organic litter in the top few inches of soil. A serious Fomes rot of rubber tree crowns and roots in the tropics is being kept under control cheaply and rather spectacularly by biological means. A particular variety of legume is grown as a ground cover in rubber plantings where the disease has appeared. The pathogen appears to dissipate its energy on the legume without doing any real damage to either the legume or the rubber trees.

On the other hand, many crop rotation and cover-cropping systems either fail in disease control or actually make the disease worse.

An objective of the symposium was to seek out the mechanisms involved in biological control in soil and to understand the circumstances which make for success on one hand and failure on the other. Knowledge of the mechanisms involved in the soil-pathogen-host relationships would enable a more intelligent approach to the control of soil-borne diseases through biological means.

Several aspects were selected for greater research emphasis. It was brought out, for instance, that the behavior of the host plant in terms of root diseases may be manipulated to some extent by sprays, fertilization, time of planting, and so forth. Since root exudates are known to be important in initiating the activity of root parasites, it follows that cultural practices which influence the amounts and quality of these exudates are important in the inception of disease and in its avoidance.

Since most pathogens in soil are in a resting rather than a vegetative condition, it is clear that the manipulation of soil likewise may be important. More information is needed on the factors which influence the survival, multiplication, and parasitic activity of the pathogens in soil. Stimulation of the pathogen into activity in the absence of its host may waste the reserves of the organism and decrease its population in soil. Certainly it became clear that the specific roles of plant exudates and plant residues in nature need clarification.

Many discussions centered about the role of natural openings in roots in relation to pathogen entry. Ruptures at the point of root emergence, the senescence of transient roots, and certain features of the root surfaces themselves were considered as possible portals of entry. It is surprising how little information is available on root anatomy and physiology in relation to pathogen entry and development.

Investigators from different disciplines were made aware of the overall problems in the biological control of root diseases and most had valuable suggestions to offer.

Critically deficient lacunae in our knowledge of the interactions of soil, plant, and soil microorganisms in relation to the activity of root pathogens were pinpointed.

It became apparent that although biological control, as treated here, could be and at times is accomplished by di-

rect attack on the pathogen by some element of the soil fauna or flora, perhaps the major mechanism is of an indirect nature, or through the creation of greater stresses for the pathogen in its competition for moisture, air, food, and space. It also seemed clear that even slight modifications in crop culture could greatly improve the effectiveness of biological control. This in itself struck a note of hope.

Enthusiasm and interest ran high throughout the sessions, a fact which attests to the promise and optimism felt for the future of biological control. In the minds of the organizing committee this alone was evidence of success for one of the prime objectives of the symposium—to stimulate research in what seems now to be a potentially rewarding approach to plant disease control.

The program was supported by grants from the National Institutes of Health, National Science Foundation, and the Agricultural Research Service; the other sponsor was the Agricultural Board of the National Academy of Sciences–National Research Council. The meeting was organized by its Committee on Biological Control of Soil-borne Plant Pathogens whose members include W. C. Snyder (chairman), K. F. Baker, R. R. Baker, F. E. Clark, A. W. Dimock, W. A. Kreutzer, J. D. Menzies, L. I. Miller, and Z. A. Patrick. The Department of Plant Pathology at the University of California in Berkeley served as host for the symposium.

In order to make available the invited papers and discussions, it is planned to publish the proceedings of the symposium.

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Forthcoming Events

September

9–11. **Weak Interactions**, intern. conf., Brookhaven, N.Y. (G. C. Wick, Brookhaven Natl. Lab., Long Island, N.Y.)

9–11. **Soils**, Laboratory Shear Testing, Ottawa, Ont., Canada. (American Soc. for Testing and Materials, 1916 Race St., Philadelphia 3, Pa.)

9–12. **Production Engineering** Research, intern. conf., Pittsburgh, Pa. (Carnegie Inst. of Technology, Pittsburgh)

9–12. **Instrument** Soc. of America, conf. and exhibit, Chicago, Ill. (T. A. Abbott, American Oil Co., 2400 New York Ave., Whiting, Ind.)

9–13. International Union against **Cancer**, conf., Amsterdam, Netherlands. (H. G. Kwa, UICC Cancer Conf., c/o Congresdienst Gemeente Amsterdam 4, St. Agnietenstraat, Amsterdam-C)

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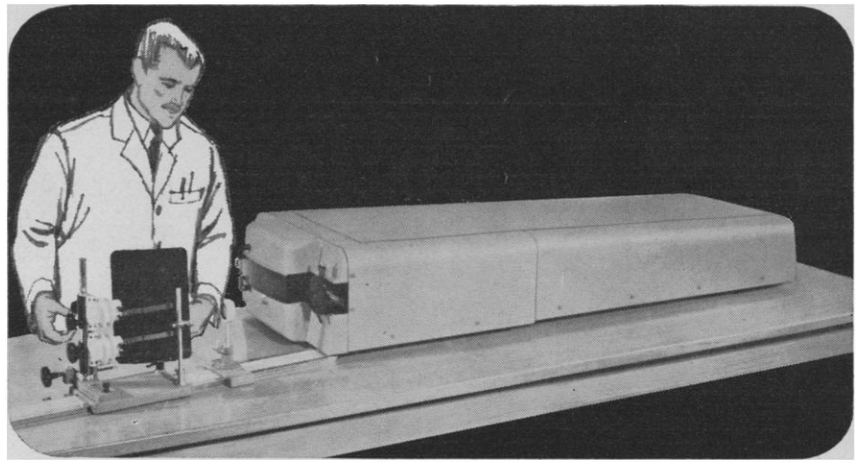

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