plement sexual reproduction methods in our squash-breeding studies in Puerto Rico. Vigorous 5- to 7-node cuttings with swollen root buds at several nodes have rooted and successfully established normal plants under field conditions; under favorable soil-moisture conditions in the field, successful propagation in as high as 90 per cent. of the cuttings was not unusual. All leaves on each cutting were left intact, the youngest leaf being usually approximately one third full grown. On planting, the entire cutting was covered with soil except the youngest leaf and the vegetative growing point subtended by it. No shading was required nor was the application of growth-promoting substances or other special growth aids necessary. It was observed that plants thus propagated grew more rapidly and fruited earlier than plants produced from seed.

This vegetative propagation permits the rapid and easy establishment of clonal lines of squash and facilitates physiological studies for which plants with a high degree of uniformity are essential. By making possible the immediate propagation of superior commercial types of greater uniformity and higher quality this method of propagation has an economic application in the tropics and subtropics, where heterogenous populations of squash exist.

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BOOKS AND LITERATURE

Sulfanilamide Therapy of Bacterial Infections. By R. R. MELLON, PAUL GROSS and FRANK B. COOPER. Charles C Thomas Company, Springfield, Ill., 1938.

THE background of the discovery of prontosil in 1935 by G. Domagk remains clouded in obscurity. Of the many prior compounds that must have been studied by Domagk, in collaboration with the chemists Mietzsch and Klarer at the I. G. Dye Works in Germany, we have no record.

The entire development has been characterized by hasty application of laboratory findings to clinical practice, a fault partially justified by the life-saving nature of the therapy in many cases. Soon after Domagk's announcement of prontosil, Tréfouel, Nitti and Bovet at the Pasteur Institute demonstrated that sulfanilamide was an active fraction of the prontosil molecule, and subsequent work has shown it to be more active and less toxic than prontosil.

Originally believed by Domagk to be specific for streptococcic infections, work from various laboratories showed that the following experimental infections could to varying extents also be influenced by this type of therapy: Meningococcus, pneumococcus, staphylococcus, typhoid bacillus, Welch bacillus. Clinical trial, followed by laboratory studies, brought the gonococcus and *B. abortis* within the pale of curative action. Slight action has been found upon animals infected with choriomeningitis virus, canine distemper virus, influenza virus and the virus of lymphogranuloma inguinale. Much optimism for the future of chemotherapy can be drawn from this imposing start and from the fact that some sulfonamide compounds exhibit special activity against certain of these infections. The infections against which the most marked action can be shown in the laboratory—streptococcus and meningococcus—have been the ones yielding the most favorable results in the clinic.

It was inevitable that a wide-spread search would be begun for new compounds, and a baffling number have already been reported in the scientific and patent literature. Drs. Mellon, Gross and Cooper list several pages of them, including the more active diphenyl sulfones.

Considerable space is devoted by the authors to the various phases of mechanism of curative action. Bacteriostatic effects of sulfanilamide have been demonstrated both in culture media and in body fluids. This effect, although definite, is weak. The rôle of neutralization of bacterial toxins and of interference with capsule formation remains to be established. There is general agreement that the drug acts on the organism in some way whereby the natural defense forces of the body are rendered better able to cope with the infection. Potentiation by the drug of the action of antiserum has been demonstrated both in culture and in the infected animal. More satisfying evidence is needed to clarify the mechanism of action, although it must be remembered that the problem of mechanism in the case of most other chemotherapeutic drugs has resisted attempts at solution. Interesting is the demonstration *in vivo* of the "antitoxin" action of some of these sulfur compounds.

Pharmacological and pathological studies of these new compounds have regrettably lagged behind therapeutic investigations, and such important issues as chronic toxicity effects and metabolic studies remain to be more fully explored. It has been established that excretion of sulfanilamide is chiefly through the urine, partially in the free state, and in some species (including man) partially acetylated. Excretion is rapid, and the major part of the drug can be recovered from the urine within 12 hours after an oral dose.

Experimental evidence of curative action for strepto-

coccal infections has been obtained largely from mice. As the authors point out, comparison of results is difficult because of the many variable factors in such experiments which have not been standardized. However, this demonstration of curative action from many laboratories under many different conditions affords a solid experimental foundation for the future progress in this field. As evidence that the drug does not kill the organisms in the body, viable streptococci can be recovered from animals apparently cured; delayed death is also frequent after cessation of therapy. Unexplained is the evidence that drug therapy is more effective against organisms of high virulence than against those of low virulence. It is also to be noted that relatively large doses of sulfanilamide (approximately one fifth of the tolerated dose) are required to bring about high percentages of cures in infected mice.

The authors review the various reports dealing with hemolytic streptococcal infections in man treated with sulfanilamide and related compounds. Included are their own experiences in this field. While the early enthusiasm will undoubtedly suffer some later discount, the striking results obtained in erysipelas, streptococcal septicemia and puerperal sepsis testify to a therapeutic effect, and the recovery of the majority of cases of streptococcal meningitis, hitherto highly fatal, must carry conviction even to the doubters.

The results in cases of alpha streptococcus (viridans) infections have unfortunately shown no curative action.

Experimental work upon meningococcal infections in mice showed sulfanilamide to have marked curative action. This action was independent of immunological type, but varied with different strains. The best laboratory results have come from the combined use of drug and specific antiserum. Clinical experience, while favorable, is as yet insufficient for an evaluation of this therapy.

The action of sulfanilamide in pneumococcal infections in mice is much weaker than upon streptococci. Curative effects are pronounced in rats, however, either when infected intraperitoneally or when a pulmonary lesion is produced by intratracheal injection of the organisms. Experiments indicate a synergism between drug and serum therapy in this infection also. No comment can be made on the few cases of pneumococcus infections in humans on which information is available concerning this therapy. Significant, however, are the recent results reported with drug plus serum in pneumococcal meningitis. Also promising are the results with a pyridine compound of sulfanilamide in pneumococcus infections, recently reported.

Staphylococcal infections in animals respond slightly to sulfanilamide therapy. Some of the newer compounds were found more active, but those derivatives studied (sulfanilyl sulfanilamide) possess neurotropic side actions in man that discourage their clinical trial. Results with sulfanilamide in staphylococcal infections in man have not been promising.

Clinical evidence indicates that sulfanilamide therapy offers hope in the treatment of undulant fever, another disease for which no effective therapy previously existed.

Perhaps the widest use of sulfanilamide has occurred in the treatment of gonorrhea. Many reports are available, unfortunately poorly controlled or uncontrolled. The many favorable reports speak for a beneficial effect, the limitations of which must be established by further experience. Similar remarks can be made in reference to its use as a urinary antiseptic.

The wide-spread use of sulfanilamide soon brought to attention that the drug was not harmless. It was also found that the symptoms of toxicity in man differed considerably from those in mice and rats. In these animals 1.0 gm per kilo is tolerated for weeks without ill effects. In man the usual daily doses of 0.02 to 0.1 gm may cause (1) cyanosis, the exact nature of which remains to be determined, (2) fever, often delayed several days from onset of therapy, (3) acidosis, the mechanism of which is unexplained, (4) dermatitis of various types, one of which follows exposure to sunlight, (5) blood changes, particularly hemolytic anemia and neutropenia; a few instances of agranulocytosis have been attributed to this drug, (6) dizziness and digestive symptoms, common but not serious.

With the development of methods for the determination of sulfanilamide, attempts have been made to correlate the concentration reached in the body fluids, with therapeutic results or with toxic manifestations. As it has not yet been established whether these effects are the result of sulfanilamide itself, or other products formed from it in the body, the limitations of such investigation must be borne in mind. Important, however, is the rapidity with which the drug penetrates to all parts of the body, even when administered orally.

The authors describe experiments from their laboratory whereby accessory factors of body fitness are of importance in the fight against infection. A beginning has been made in this direction.

There is justifiable optimism from the experimental results with new compounds. Compounds with many times the activity of sulfanilamide are being obtained. Derivatives with specialized action against certain infections have been found. The field is still in its infancy, but the outlook for better and safer compounds and for new conquests in the field of infectious diseases is indeed bright.

From the context of this review it is evident that most phases of this subject can be treated with little finality at the present time. In a field as rapidly mov-

ing as bacterial chemotherapy a book is necessarily at a disadvantage in that important developments are prone to follow closely upon its heels. The authors have attempted in some way to offset this disadvantage by adding an addendum to the book. However, for those interested it is desirable to have the pertinent facts in this important field collected together at frequent intervals. The authors are well suited to this task because of their experience both in the laboratory and in the clinic.

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SPECIAL ARTICLES

HYDROSOLS AND ELECTROLYTIC IONS

WHILE electrodialyzing some solutions of clay in water and in dilute acids and alkalies, a curious relation has appeared which throws light on the association of the electrolytic ions with certain of the hydrosols which may be present.

If a montmorillonite clay be brought to equilibrium with a dilute acid solution (say 1 per cent. hydrochloric) and then filtered and the solution electrodialyzed, it will be found that the silica is carried *equally* in both directions. Other ions present are usually found unequally in anode and cathode liquors, but the silica is strictly amphoteric, it either consists of equal numbers of anions and cations or is a carrier of equal numbers of such ions. After the effect was first noted, other experiments (25 in all) were made at different acid and alkali concentrations and on various clays including soil, all confirming the original findings or indicating necessary conditions.

The dialyzer used was an ordinary Mattson with the electrodes supplied replaced by others of sheet platinum. Cellophane membranes enclose the cell 1×10×15 cm. Electrode compartments are 3×10×15 cm. The current used was from a 116-volt line and held to below one ampere by a 100-watt lamp in series. Anode and cathode liquors were replaced by fresh distilled water four times at hourly intervals and each analyzed separately.

The clay solutions were prepared by digesting about 30 grams of 150 mesh (0.1mm) clay in two liters of acid solution for fifty hours at about 90° C. with frequent stirring. A few acid clays and acid-treated adsorbent bentonites require twice as long to bring to equilibrium. About 400 cc of the filtrate was evaporated to 150 cc for the dialysis. The total recoverable solids is from 1.5 to 5 grams per liter of solution according to acid concentration. At equilibrium, there is always free and adsorbed acid present as well as salts in solution.

Electrodialysis of a solution that has not come to equilibrium with a clay or soil shows an unequal partition of silica; an acid clay shows an excess of silica transported as cations, while a slightly alkaline soil gives a slight excess of silica as anions.

The first ions removed are H^+ and Cl^-. After the first hour the cations are largely the R_2O_3 bases. If an electrodialysis of an equilibrium solution is stopped at an early stage and the three solutions analyzed, the silica will be found in equal amounts in anode and cathode liquors as though run to completion. When a pure silica gel solution is electrodialyzed, the silica is equally divided. An alkaline solution of a neutral clay (Florida fuller's earth) gave four times as much anion silica as cation silica. The same solution neutralized with HCl just before dialysis showed an equal division (49 vs 51 per cent.) of silica. A water solution of an alkaline bentonite (Wyoming swelling, 1.2 grams per liter) dialyzed 64.6+ vs 33.5− without and 48.1 vs 43.7− with HCl added before dialysis. But the same solution with NaCl added before dialysis gave for +silica 95.5 vs −4.5. When insufficient ions are present electrodialysis gives a precipitate of silica in the cell.

It seems hardly possible that silica in solution can consist of equal numbers of anions and cations. The alternative seems to be that other charged ions are adsorbed in equal numbers on the silica and supply the motive power in a potential gradient. Anions and cations are present in necessarily equal numbers, hence in equilibrium clay or soil solutions they must also adsorb in equal numbers on the silica hydrosol micellae with which the cations were previously associated. Certain added ions prevent equal adsorption, others do not.

These results will be given in more detail in a later paper. It would be of interest to know whether similar relations obtain in other fields, say in the relation of the silver halides to the gelatine in photographic emulsions, of ions to hydrosols in sugar solutions, in plant saps and the like.

P. G. NUTTING
U. S. GEOLOGICAL SURVEY

THE ASEXUAL LIFE CYCLE OF THE AVIAN MALARIA PARASITE, PLASMODIUM CIRCUMFLEXUM[1]

EVIDENCE has been accumulating for some time that the life-cycle of the malaria parasite in the vertebrate is less simple than has been thought and that the plasmodia are able to parasitize not only the erythrocytes

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