



Fig. 4. NITRITE OXIDATION IN THE PRESENCE OF CHLORATE (SOIL ENRICHED WITH NITRITE-OXIDIZING ORGANISMS).

taining therefore but few nitrite-oxidizing organisms) shows on subsequent perfusion with nitrite a lengthy time lag before the nitrite undergoes oxidative change (see Fig. 3).

### Rate of Nitrite Oxidation in Soil in Presence of Chlorate

It would be expected that if the main effect of chlorate, at low concentrations, is to prevent proliferation of nitrite-oxidizing organisms, the velocity of nitrite oxidation in a soil enriched with these organisms would be a constant in the presence of chlorate. The velocity would be proportional to the number of cells initially present; it would not increase with time, in the presence of chlorate, as it should if proliferation were taking place.

The results of four separate experiments are included in the data given in Fig. 4, in which the nitrite content of the perfusion fluid at any moment is plotted against time. The soils were enriched with nitrite-oxidizing organisms by initial perfusion with sodium nitrite, and then they were perfused with  $M/280$  sodium nitrite solution containing potassium chlorate. Three concentrations of chlorate,  $M/10,000$ ,  $M/20,000$ ,  $M/40,000$ , were used, but much the same results were obtained with all three.

Fig. 4 should be a straight line if the velocity of nitrite oxidation is constant. It will be seen that there is a close approximation to linearity, indicating the largely bacteriostatic action of chlorate.

TABLE 3. RATES OF NITRITE OXIDATION ON PERFUSION OF 200 ML.  $M/280$  SODIUM NITRITE CONTAINING  $M/2000$  POTASSIUM CHLORATE THROUGH 50 GM. GARDEN SOIL, IN THE PRESENCE AND ABSENCE OF NITRATES.

Concentration of sodium nitrate added initially to perfusate	Time in days from start of perfusion									
	0	3	5	7	10	12	14	17	19	
	Nitrite N, γ/ml. perfusate									
Nil	50	54	51	55	55	56	52	52	50	0
$M/400$	50	54	50	54	51	48	45	25	0	0
$M/200$	50	53	50	50	48	45	36	14	0	0
$M/100$	50	56	47	40	20	0				
$M/50$	50	39	29	20	0					

### Effects of Nitrate on Chlorate Bacteriostasis

The action of chlorate in inhibiting the oxidation of nitrite in soil is partially or completely eliminated by the presence of nitrate. If a solution of sodium nitrite containing potassium chlorate is perfused through soil containing initially a relatively high concentration of nitrate, little or no retardation of nitrite oxidation is exhibited. Results given in Table 3 show how increasing concentrations of sodium nitrate in the perfusion fluid have increasingly large effects in neutralizing the action of chlorate.

This result demonstrates that nitrate alleviates the bacteriostatic effect of chlorate. The effect of nitrate is apparently specific, for no such alleviation is accomplished by phosphate, borate, chloride, sulphate, arsenate or *p*-aminobenzoate.

This phenomenon is possibly related to that described by Crafts<sup>2</sup> and by Hurd-Karrer<sup>3</sup> in which nitrate reduces the toxicity of chlorate to plants.

Experiments are now being carried out to discover how nitrate exercises its neutralizing effects on chlorate inhibition.

### Summary

Potassium chlorate at low concentrations ( $c. M \times 10^{-5}$  to  $M \times 10^{-6}$ ) exercises a bacteriostatic action on soil organisms oxidizing nitrite to nitrate. The effect is specific, as chlorate at these concentrations has little or no effect on the conversion in soil of ammonia into nitrite. Chlorate administration to a nitrifying soil thus results in nitrite accumulation. Chlorate has little or no effect on nitrite oxidation in a soil which is rich in nitrite-oxidizing organisms. Its effect at low concentrations seems almost wholly concerned with the inhibition of the proliferation of these micro-organisms.

The bacteriostatic action of chlorate is specifically neutralized by the presence of nitrate, the alleviating action of which increases with its concentration.

<sup>1</sup> Lees and Quastel, *Chem. and Ind.*, 238 (1944).

<sup>2</sup> Crafts, *J. Agric. Res.*, 58, 637 (1939).

<sup>3</sup> Hurd-Karrer, *Amer. J. Bot.*, 28, 197 (1941).

## WAR-TIME MEDICAL PROGRESS IN AMERICA

“ONE of the memorable experiences of this war,” writes Prof. D. W. Bronk, in his contribution to the symposium on war-time advances in medicine held by the American Philosophical Society (*Proc. Amer. Phil. Soc.*, 88, 151; 1944), “is to stand at evening in the Great Court of Trinity College, Cambridge, outside Isaac Newton’s rooms, and watch the Flying Forts return.” More memorable, some Cambridge residents might add, was the unforgettable sight, sudden and wonderful after dark years of trial, of the sky one summer evening full of the aeroplanes and men going out on the first one-thousand bomber attack. Such developments have been made possible by the work, in Great Britain and in the United States, of men like Prof. Bronk, who is professor of biophysics at the University of Pennsylvania and co-ordinator of research, Office of the Air Surgeon, Headquarters Army Air Forces. His contribution to this symposium discusses such human problems of aviation as the effects of rising, as modern fliers do, to heights of six miles in six minutes, the effects of high-speed manoeuvres in machines built to withstand the stresses involved (although the human body is not) and problems of night flying and vision.

Such problems could no doubt be classified under the heading of environmental effects, and Colonel G. F. Doriot, of the Quartermaster Corps, shows in another article how profoundly these affect the soldier and the sailor. He points out, also, that we are all concerned with protection from the environment. Clothing, he thinks, has been largely developed for the purpose of dressing the shop window and not to suit the particular tasks of the wearers. His discussion, illustrated by diagrams, of the problems raised by the clothing and equipment of the soldier and sailor, who have to operate in many different climates and have to be able to withstand rapid changes from one set of external conditions to another, has many applications to civilian life. The fighting man needs flexible clothing which is either warm or cool as the conditions demand. Colonel Doriot pleads for more technical education in the scientific principles of rational clothing than those engaged in the textile and clothing industries get at present; in this respect they compare unfavourably, he suggests, with a number of other industries. Fundamental researches are required. To select only one detail, Colonel Doriot rightly considers the problem of boots of great importance, and this point is also emphasized by Prof. E. A. Strecker, of the University of Pennsylvania, in his article on neuropsychiatry. The foundations of morale, Prof. Strecker says, are simple and obvious things, such as satisfactory living conditions, good, appetizing and well-cooked food, comfortable and nice-looking uniforms and, above all, easy-fitting shoes. Sport and diversion are also important. His discussion of fear, which can, he says, no more be suppressed than the heart-beat can be stilled, is full of common sense. Important for those at home is his statement that morale fell when soldiers heard of strikes in the coal and other industries.

Another problem of the environment is discussed by Prof. J. L. Gamble, of Harvard Medical School, in his article on the water requirements of castaways, a subject which has been much studied in Great Britain as well as in the United States (see, for example, Macdonald Critchley's Bradshaw Lecture on "Shipwreck Survivors" (London: J. and A. Churchill, 1943) and the work sponsored by the Medical Research Council Committee on the Care of Shipwrecked Personnel). Assessing the water requirement during fasting with little or no physical activity at about 700 c.c., Prof. Gamble describes experiments which indicate that at least 100 c.c. of this can be replaced by glucose or other food sugars or starches, with all the physiological advantages of this replacement, without disturbing the water balance. There was an appreciable water gain in subjects who drank 500 c.c. of sea water every day (3-4 litres would be needed to cover the daily water requirement of a castaway and even 500-600 c.c. would cause disturbing effects). In these subjects extracellular fluid volume was conserved by the gain from sea water and by increased withdrawal from intracellular water. Experiments done near Cape Cod in hot weather indicated that periodic immersion or wet clothing completely prevented loss of water above the basal rate. Solar radiation without a breeze caused loss of water at ten times the basal rate (more than 2 litres were thus lost by one subject, who, in six hours, thus wasted enough water to cover his intake need for three days). Shade, periodic immersion and wet clothing completely prevented this. Most impressive of all was the protection from water loss afforded

by a breeze (fortunately rarely absent). The castaway's great risk is therefore hot, wind-less weather.

Dr. E. J. Cohn, of Harvard Medical School, contributes a valuable article on blood, blood derivatives and blood substitutes, with a bibliography of forty-eight references, mostly American. The contents of this paper can only be briefly indicated. It discusses plasma proteins, the dimensions in Angstrom units of these proteins and those of suggested blood substitutes, the equilibrium between the albumins and globulins of plasma and the tissues, the dissociation of the globulin molecules of plasma, the separation and concentration into fractions of the plasma albumins and globulins and their stability when separated. The article also discusses the use of gamma globulin antibodies for the prevention of measles and of iso-haemagglutinins in the typing of blood. The remarkable properties which the long, rod-shaped molecules of fibrin confer on fibrin films, made from fibrinogen and thrombin, are described. These films can be used as substitutes for the dura mater in neurosurgery of the brain. Their mechanical properties recall those of plastics; they can, for example, be stretched to twice or three times their original length or made into seamless tubing. Fibrin foam, made also from thrombin and human fibrinogen, may be, when it is dry, of two types. One type is light, fluffy and highly compressible; it wets easily, losing 90 per cent of its dry volume by shrinkage. The other type is dense, firm and less compressible; it wets slowly and then loses only about 50 per cent of its dry volume. Fibrin foam is used for stopping bleeding from veins or oozing surfaces, but not for stopping arterial haemorrhage; it is useful in neurosurgery. By appropriate control of their preparation, other types of fibrin-clot can be made, some of which are used in surgery or for skin-grafting.

Prof. C. S. Keefer, of Boston University School of Medicine, deals with the use of penicillin in the treatment of various bacterial infections, and Prof. A. O. Whipple, of Columbia University, also discusses this substance, together with others, in his article on recent advances in the treatment of wounds. R. E. Dyer, assistant surgeon-general, United States Public Health Service, writes about immunology. He directs attention to recent improvements in the immunizing potency of typhoid vaccine and the discovery and improvement of vaccines against yellow fever and typhus fever and of tetanus toxoid. Compulsory use of tetanus toxoid has removed the menace of tetanus from the United States military and naval forces; we are informed that tetanus is, for the same reason, no longer a menace to British fighting men. Further improvements in these and other immunizing procedures may be expected before long.

Perhaps the most thought-provoking article in the symposium is that contributed by Prof. R. J. Dubos, the discoverer of gramicidin. Drug therapy, he argues—and many experienced observers will agree with him—constitutes only one facet of the complex problem of infection, and we should not be led away from these other aspects by the spectacular and popular appeal of recent chemotherapeutic achievements. Our difficulty is not to prepare more and more antibacterial substances, but to find out how they act in the body. They do not act as gross protoplasmic poisons, but selectively inhibit some vital process in the parasite's life. We need much more work on the problem of how they act.

There have been, on the other hand, important epidemiological and immunological advances towards

the control of such serious diseases as smallpox, yellow fever, diphtheria and infestations with such animal parasites as the hookworms and the schistosomes. We should study the host-parasite relationship much more, including micro-organisms among the parasites, and get away from the rather narrow channels into which the very rapidity of the success of serological and immunological research has directed investigation. The whole picture should be studied by resuming broad biological and biochemical studies of the host and its bacterial and animal parasites. So far as the bacteria are concerned, the study of the complex property of parasites which we call virulence is important. A given parasite can cause epidemics or disease only when it has been able (1) to reach a susceptible host, (2) to overcome the cellular and humoral defences of that host, (3) to multiply in it, and (4) to damage it. Each of these factors can vary independently of the others. In order to cause an epidemic, the parasite must possess them all at the same time. A highly pathogenic strain of haemolytic streptococci, for example, may have only a low degree of communicability, and the converse may be true of other strains. The study of the resistance of the host is likewise very important, and there are other factors which the epidemiologist must consider. Prof. Dubos believes that we shall eventually be able to predict the course of epidemics and to organize 'listening posts' which will detect qualitative and quantitative changes in the number of infectious agents and in those of their properties which affect their virulence. A beginning in this direction has already been made.

It is a matter for conjecture, Prof. Dubos considers, whether preventive chemotherapy will ever become advisable or effective, but preventive immunological treatment can certainly be effective, as immunization against smallpox, typhoid, diphtheria and other diseases has shown. High degrees of immunity produced by means of killed bacterial cultures are, however, very specific and do not protect against related organisms of another immunological type, so that type-specific immunity protects against only the particular organisms concerned. For this reason, effective immunization of whole populations with type-specific vaccines may be impossible. It is, nevertheless, possible in some instances, for example, the pneumococci, to direct the immune response against a component of the bacterial cell which is common to all types of pneumococci. Possibly bacterial cell components will be found in all bacterial groups which can be attacked in this way, so that we may eventually be able to immunize against all the types of each group. The non-specific immunization of this kind which has so far been achieved is, however, lower than that produced by type-specific vaccines; but more research into it might enable us to raise its potency. We have hitherto studied type-specific immunization almost exclusively. Immunization techniques, moreover, have been up to now primitive in their principle of killing the pathogenic organism with heat or antiseptics. It is certain that a very large percentage of the material injected in anti-typhoid vaccination has no immunological value at all and even causes unfavourable reactions in those to whom it is given. It is very important to isolate the chemical components of the cell which do produce the immunity. If we could do this, we might, in the distant future, prepare artificially the substances required to produce the immunity.

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## ORGANIZATION OF INDUSTRIAL RESEARCH

**F**UTURE historians will no doubt record that the opening decades of the twentieth century were characterized by the beginning of a systematic application of the results of scientific research to everyday life and the consequent foundation of research organizations, both large and small, mainly devoted to the best utilization of new knowledge in the service of commerce and industry. Moreover, these organizations, staffed by professional research workers together with technicians and other assistants in considerable numbers, stood out in striking contrast to the research conditions of the days of Faraday, Joule and Kelvin, when even advanced technological research was an entirely private venture. It is often forgotten to-day how young in years organized industrial research really is, and that while there are certain industries, such as heavy chemicals and electrical engineering, which have expanded on a vast scale with laboratories widely distributed over Great Britain, there are also other industries, deeply rooted in history, having as yet no medium for the exploration of fresh ideas and wholly dependent on traditional techniques.

At a meeting of the London Branch of the Institute of Physics on February 17, Dr. R. E. Slade, speaking from a wide practical experience, dealt with those factors which he regards as essential to the successful organization of research in the laboratories of manufacturing firms where most industrial research is now done.

Dr. Slade began by pointing out that the laboratory must be a well-run unit constituting an integral part of the firm's activities and in full sympathy with the industry which it is trying to serve. Research is admittedly an individualistic operation, and its success is not a mere question of organization, though organization can facilitate the performance of the work; for this reason, the director or research manager should himself be an experienced researcher, able to inspire the workers under him, but suiting his methods to the personalities of the various section leaders. "There is room in every laboratory for a scientifically trained organizer to do the administrative work for the director, so as to relieve him of as much administrative work as possible." The ideal chemical research laboratory would thus consist of a director and an administrator with six section leaders, five having charge of researches and the sixth looking after services including the library, analytical department and workshop. Probably the most efficient size of industrial chemical laboratory would have sixty to a hundred university-trained workers and up to four hundred other workers. There is always a tendency for a laboratory to increase in size, but while it is cheaper to allow this rather than start a second new laboratory, it is not advisable to let the laboratory become so big that the director cannot know all his men and be prevented from exercising his personal influence and encouragement. "Not only do we want laboratories with distinctly different outlooks, but we want in each laboratory men with different kinds of training who will look at problems in different ways and tackle them in different ways, too."

Dr. Slade does not believe that the direction of a laboratory can be carried out effectively by a committee; he admitted the utility of advisory panels, but